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Relationships Between Symptom Interference Scores, Reduced Dietary Intake, Weight Loss, and Reduced Functional Capacity

by

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Dedication

This thesis would be incomplete without a mention of the support given to me by the most important people in my life. My husband, Arnie, who afforded me the time to write, and who supports me in every aspect of my life. It is a privilege to be your wife. My children, Jakob and Brooke, for filling my life with profound joy and purpose, you are my reason for living. My parents, who have sacrificed so much for me and always encourage me to reach higher.

Abstract

Using an existing data set comprised of 368 individuals newly diagnosed with cancers of the head and neck, we investigated the predictive validity of the Head and Neck Patient Symptom Checklist (HNSC) by comparing scores on the HNSC to scores on the Patient-Generated Symptom Global Assessment (PG-SGA), and by examining the ability of HNSC scores and four demographic variables to predict dietary intake, weight loss, and functional capacity.

HNSC sensitivity (0.79 – 0.98), specificity (0.99 – 1.00), positive predictive value (92% – 100%), and negative predictive value (94% - 100%) were excellent. Pain, loss of appetite and difficulty swallowing predicted 82% of reduced dietary intake. Advanced tumor stage, loss of appetite and difficulty swallowing predicted 79% of weight loss. Loss of appetite, difficulty swallowing, feeling full and lack of energy predicted 78% of reduced functional capacity.

The HNSC appears to be valid and could aid with early symptom identification, intervention and improved outcomes.

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List of Abbreviations, Nomenclature, and Symbols

HNC	Head and Neck Cancer
HNSC	Head and Neck Patient Symptom Checklist
Larynx	Supraglottis, glottis, subglottis
Lip and Oral Cavity	Tongue (anterior 2/3), buccal mucosa, gingiva, hard palate, floor of mouth, alveolar ridge, retromolar trigone, lip
MNA	Mini Nutritional Assessment
MST	Malnutrition Screening Tool
NPV	Negative Predictive Value
Other	Salivary gland, hypopharynx, nasal/paranasal sinus
PG-SGA	Patient-Generated Subjective Global Assessment
Pharynx	Tongue (posterior 1/3), walls of pharynx (oropharynx, nasopharynx), tonsils/arches, soft palate
PPV	Positive Predictive Value
Stage I/II	Early disease
Stage III/IV	Advanced disease

Chapter 1: Introduction

Statement of the Problem

Weight loss in cancer is a common occurrence and has been identified as a negative predictor of survival since the 1930's (Warren, 1932). Weight loss of only 5% over six months is associated with increased treatment complications, disease recurrence, morbidity and mortality (DeWys et al., 1980). Furthermore, weight loss interferes with physical, cognitive, emotional, and social domains related to quality of life, resulting in a decreased sense of well being and impaired functional capacity (Couch et al., 2007; Grant & Rivera, 1995; Huhmann & Cunningham, 2005).

In general, weight loss in individuals with cancer is attributable to catabolism and to symptoms that interfere with eating. Disease processes associated with cancer appear to suppress appetite and increase energy expenditures resulting in involuntary loss of fat and muscle; the primary clinical attributes of cachexia (Baracos, 2006; Tisdale, 2002). In addition, in individuals with head and neck cancer (HNC), the tumor location and symptoms associated with the location may also reduce dietary intake resulting in increased weight loss. These symptoms, referred to as nutritional impact symptoms (NIS) include but are not limited to: nausea, vomiting, taste changes, anxiety, depression, swallowing difficulty, pain, dry/sore mouth, difficulty chewing, dental problems, thick saliva, and constipation (Grosvenor, Bulcavage & Chelbowski, 1989; Kubrak et al., 2010; Larsson, Hedelin, Johansson & Athlin, 2005). In individuals with

HNC, decreased nutritional intake may be further exacerbated by alcohol and tobacco use (Bertrand, Piquet, Bordier, Monnier & Roulet, 2002; Viswanathan & Wilson, 2004).

Weight Loss in Head and Neck Cancer

In this thesis my focus is on the symptoms that interfere with dietary intake and on the relationships among these symptoms, weight loss and reduced functional capacity in individuals with HNC. In 2008 the Canadian Cancer Society estimated that there would be 166,400 new cases of cancer in Canada and that 4,600 (3%) of those would be cancers of the head and neck (Canadian Cancer Society, 2008). Although individuals diagnosed with HNC represent a small number of the total cancer population, I have chosen to study them because of their vulnerability to reduced dietary intake.

Efforts to explore the role of symptoms in relation to reduced dietary intake, weight loss and functional capacity in individuals with HNC have been limited by the lack of assessment tools that include symptoms of particular relevance to this population. The Oncology Nursing Society (2006) recommends the following nutritional screening tools be used in the clinical oncology setting: the Patient-Generated Symptom Global Assessment (PG-SGA), the Mini Nutritional Assessment (MNA), and the Malnutrition Screening Tool (MST). The most commonly used tool is the PG-SGA (see Appendix A). This tool includes a history of current weight, reported dietary intake, functional capacity, and symptoms that have interfered with eating over the past month. Although the

PG-SGA is a validated tool Kubrak et al. (2010) identified that it does not include a measure of symptom intensity or the interference of each symptom with eating. Thus, limiting the ability to identify the predominant underlying cause of the nutritional deficit.

Further, in a population of HNC patients, Kubrak et al. (2010) noted a significant relationship among reduced dietary intake, weight loss, and a set of symptoms (anxiety, depression, thick saliva, and difficulty chewing) not included in the PG-SGA. This finding serves as a reminder to clinicians about the need to tailor nutritional assessments and not rely on one generic assessment tool when they are working with populations who experience particular sets of symptoms that reduce dietary intake.

Kubrak and colleagues developed the Head and Neck Patient Symptom Checklist (HNSC) to assess the particular symptoms associated with reduced dietary intake in individuals with HNC prior to treatment. The HNSC (see Appendix B) was based on an extensive literature review and includes: pain, anxiety, dry mouth, loss of appetite, constipation, feeling full, depression, thick saliva, diarrhea, sore mouth, lack of energy, nausea, difficulty chewing, altered smell, vomiting, difficulty swallowing, and taste changes. There is also a space where patients can add other symptoms. Based on the recommendations of Kirkova et al. (2006), symptoms in the HNSC are rated for both intensity and interference with eating.

Assessment of symptoms prior to treatment provides the clinician with a means to estimate individuals at risk of reduced dietary intake. This is important as symptoms existing prior to treatment, may be further exacerbated by treatment, thus impacting dietary intake during and post treatment. Early identification of these symptoms can guide the clinician toward implementing prophylactic interventions to meet the needs of individuals with HNC proactively rather than reactively.

Purpose

The purpose of this study was to test the validity of the Head and Neck Patient Symptom Checklist (HNSC), a new instrument for assessing 17 symptoms reported in the literature to interfere with dietary intake, and to examine the ability of a subset of these symptoms, plus age, gender, tumor stage, and location to predict weight loss, reduced dietary intake and functional capacity.

Significance

The findings of this study will generate a greater understanding of the relationships among symptoms that interfere with eating, reduced dietary intake, weight loss and reduced functional capacity prior to treatment. This understanding will provide a solid foundation for the development of nursing interventions for the earlier management of symptoms that reduce dietary intake, resulting in better patient outcomes.

Research Questions

1. Is the Head and Neck Patient Symptom Checklist a valid measure of the symptoms experienced by individuals with head and neck cancer?
2. Prior to treatment for head and neck cancer, do selected demographic variables (age, gender, tumor stage, tumor location), and symptom "interference with eating" scores on the HNSC predict reduced dietary intake, weight loss, and reduced functional capacity?

Definition of Key Terms

The definition of key terms is provided below. The ways in which these terms will be measured are discussed in Chapter 3.

Head and Neck Cancer (HNC)

HNC is defined as cancers arising in the oral cavity, oropharynx, hypopharynx, nasopharynx, larynx, nasal fossa, paranasal sinuses, and salivary glands (National Cancer Institute, 2005). I will describe the sample in terms of age, gender, tumor stage, and tumor location but will not include histology since the majority of head and neck cancers are moderately differentiated squamous cell carcinomas (Carr, 2005; Jin & Jin, 2006).

Symptom Interference

Symptom interference is defined as the degree to which the participant considers that a symptom interferes with his or her dietary intake.

Reduced Dietary Intake

Reduced dietary intake is defined as an oral intake of food that is judged by the participant to be less than normal for him or her.

Weight Loss

Weight loss is defined as unintentionally weight loss greater than or equal to 5% during the past six months, based on patient report.

Reduced Functional Capacity

Functional capacity is defined as an activity level that is judged by the participant to be less than normal for them.

Chapter 2: Literature Review

In this chapter I discuss weight loss in individuals with cancer. First I outline the causes of weight loss in cancer, with special focus on symptoms experienced by individuals with HNC. Next I present the consequences associated with weight loss, and last I discuss the gaps in knowledge that framed this study.

Causes of Weight Loss in Cancer

Several researchers have explored the causes of weight loss in cancer and attribute it to increased energy expenditure and reduced dietary intake (Baracos, 2006; DeWys et al., 1981; Kubrak et al., 2010; Shils, 1979).

Catabolism, Reduced Dietary Intake, and Weight Loss in Cancer

Appetite regulation is centrally controlled by the arcuate nucleus in the hypothalamus. Hormones in the blood stream serve as messengers promoting the hypothalamus to release molecules that stimulate or inhibit dietary intake (Tisdale, 2002). Researchers theorize that dysregulation of hormone secretion disrupts the normal food intake model resulting in metabolic changes including increased resting energy expenditure (Couch et al., 2007; Grant & Rivera, 1995; Huhmann & Cunningham, 2007). This dysregulation in individuals with cancer is associated with cytokines secreted in response to cancer and its treatment, which act on the brain causing appetite suppression and a reduction in dietary intake (Couch et al.). Reduced dietary intake further increases metabolic rate due to catabolism of stored glycogen and protein in the muscle. An increased

metabolic rate by 12% can result in body weight reduction of 1 kg to 2 kg per month (Lindmark, 1984). The combined result of increased energy expenditure and the related reduction in dietary intake is generally defined as cachexia. The primary clinical feature of cachexia is loss of fat-free muscle, particularly skeletal muscle and involuntary weight loss (Baracos, 2006; Tisdale). This loss of skeletal mass results in reduced functional capacity. It also negatively affects the individual's natural ability to eat (masticate and swallow food).

Symptoms Associated with Weight Loss in Individuals with HNC

In individuals with HNC, appetite and dietary intake are further compromised by a number of symptoms that interfere with eating. Campbell, Marbella and Layde (2000) reported that pain was commonly experienced by individuals with HNC. Not only does pain effect the patients desire to eat, but it also stimulates the stress response, thus increasing catabolic activity and further contributing to weight loss. Feuz and Rapin (1994) and Paillaud et al. (2003) both reported that control of pain in individuals with advanced cancer was associated with increased receptivity to food, despite anorexia. This finding suggests that assessment and treatment of pain could improve dietary intake, weight, and functional capacity.

Mouth sores prior to treatment are also associated with reduced dietary intake. Clinical experience has shown that causes of mouth sores prior to treatment may include the tumor itself, xerostomia, and dental problems (ill fitting dentures, dental cavities, and poor dental hygiene). Mucosal breakdown

may lead to increased bacterial growth and production of proinflammatory cytokines. In turn, these cytokines may contribute to increased catabolism and weight loss (Mantovani et al., 2000; Sonis et al., 2004).

Seigel and Longo (1981) reported that oropharyngeal and gastrointestinal symptoms normally present late in the trajectory of care as a result of antineoplastic treatment rather than the disease itself. Kubrak et al. (2010), however, recently reported that in individuals with head and neck cancers, symptoms such as mouth sores, pain and dysphagia often present prior to antineoplastic treatment. As chemotherapy and radiation doses accumulate, symptoms intensify (Cady, 2007), further increasing the risk of weight loss.

The location of the tumor and tumor-related symptoms (thick saliva, feeling full, constipation, nausea, diarrhea, and vomiting) may also interfere with the ability required to eat, drink, taste, smell, and swallow (Larsson, Gedelin & Athlin, 2003; Lees, 1999). The synergistic relationship between symptoms and problems with eating such as difficulty chewing and dysphagia may result in reduced dietary intake and weight loss earlier in the disease trajectory than might otherwise be expected.

In individuals with HNC, alcohol and tobacco use may also contribute to decreased dietary intake (Brookes, 1985; Grosvenor, Bulcavage & Chelbowski, 1988; Larsson et al., 2003; Lees, 1999). The financial, social and physical dependency related to substance abuse contributes to poor dietary habits resulting in poor dietary intake (Brookes; Kubrak et al., 2010; Lees). Alcohol, like

sugar and fat, is high in calories but contains few nutrients. Chronic use of alcohol provides a large number of calories, suppressing appetite and replacing nutrient rich foods. Inadequate protein and nutrient-void calories are the most common contributing factors to weight loss in individuals who consume large amounts of alcohol (Langer, Hoffman & Ottery, 2001; Yavuzsen, Davis, Walsh, LeGrand & Lagman, 2005).

The Consequences of Weight Loss

Reduced dietary intake resulting in weight loss greater than or equal to 5% in the past six months at the time of diagnosis is present in approximately 30-55% of individuals with HNC, and of these patients, 95% report their weight loss is unintentional (Lees, 1999). This is not surprising, given the functional consequences of the disease location (Brookes, 1985; Kubrak et al., 2010; Larsson et al., 2003).

Weight loss is associated with many adverse outcomes including reductions in immune function, functional capacity, quality of life, resistance to disease, increased morbidity, mortality, fatigue, antineoplastic treatment toxicities, and overall medical complications (Larsson et al., 2005; Nixon et al., 1980; Olson et al., 2007). Increased treatment-related toxicities lead to decreased opportunity to treat with optimal dosing and result in decreased treatment response and disease progression (Cady, 2007; DeWys et al., 1980; Huhmann & Cunningham, 2005; Jager-Wittenaar et al., 2007; Mekhail et al., 2001; Tisdale, 2002; Wood, 2005). Increased toxicities may also lead to

increased complications such as dehydration, myelosuppression, dysphagia, mucositis, and nausea, resulting in poor tolerance to antineoplastic treatment and further weight loss.

Tisdale (2002) reported that the increased mortality associated with weight loss may be partly due to the decline in mobility and decreased respiratory function. Thoracic muscle weakness could increase the risk of aspiration due to decreased capacity to expel adequate air from the lungs and clear the breathing passages of secretions and or foreign articles such as food, leading to aspiration pneumonitis (Swaminathan & Naderi, 2008).

Weight loss among individuals with HNC often results in altered body appearance and negative self-image (Larsson et al., 2003). Appearance is important for defining one's identity and changes in appearance may lead to feelings of embarrassment and social isolation (Dropkin, 2001; Larsson et al.). Everyone desires and needs interpersonal contact to feel connected (Halldorsdottir & Hamrin, 1996). Avoidance of such interactions consequently has a negative effect on the individual's purpose and quality of life (Dropkin, 2001; Salter, 1997).

Reduced dietary intake and weight loss are strongly associated with other dimensions of quality of life including functional status. Ravasco, Monteiro-Grillo and Camilo (2003) identified that at any stage (prior, during or end) of treatment individuals with cancer commonly report impaired usual activity with associated pain/discomfort, anxiety and depression. Individuals with HNC have the highest

prevalence of reduced dietary intake, weight loss, and reported quality of life in comparison to other oncologic populations (Donaldson, 1984; Ravasco et al.). Thus, one can assume reduced dietary intake is a significant variable impacting the psychological and physical dimensions of quality of life among this population.

Together with pain and emotional stress, weight loss has a profound effect on fatigue among this population (Tookman, Jones, DeWitte & Lodge, 2008). Fatigue is a common symptom reported among cancer patients and is unrelieved by rest. Tired, weak patients may experience reduced appetite and motivation to prepare nutritious meals (Grant & Kravits, 2000), further decreasing dietary intake, weight loss, and quality of life (Ravasco et al., 2007). Olson and colleagues (2007) have proposed that loss of lean muscle, a key component of weight loss, is central to the development of fatigue in individuals with advanced cancer.

Gaps in the Literature on Symptom Assessment Associated with Weight Loss That Framed This Study

The consequences of decreased dietary intake and weight loss in cancer patients is well documented, and there is a growing body of literature in which contributing symptoms are discussed. None of the assessment tools used, including the Patient Generated Subjective Global Assessment (PG-SGA), which is currently the standard assessment tool, collect the data that would make it possible to explore the relationships among symptom intensity, interference

with eating, and weight loss. The lack of such a tool is a serious gap in the symptom assessment literature, given the adverse outcomes associated with weight loss. Identification of the symptoms that contribute to the inability to eat could aid in earlier intervention and potentially to the improvement in dietary intake and weight. This gap in knowledge was the focus of this study.

The HNSC was constructed by Kubrak and colleagues following an extensive review of the literature. The HNSC is comprised of 17 symptoms (pain, anxiety, dry mouth, loss of appetite, constipation, feeling full, depressed, thick saliva, diarrhea, sore mouth, lack of energy, nausea, difficulty chewing, altered smell, vomiting, difficulty swallowing, taste changes) that have been reported to interfere with eating in individuals with HNC. The tool is designed to be completed by the patient. Each symptom is rated for severity and interference with eating. All individuals seen in the HNC new patient clinic at the Cross Cancer Institute complete the HNSC; to date, the HNSC database includes data from 368 individuals newly diagnosed with HNC.

Summary

There is considerable evidence to suggest that weight loss in individuals with HNC is a function of cachexia, symptoms that interfere with eating, and extensive use of tobacco and alcohol. The focus of this study was on the symptoms reported to cause weight loss by interfering with eating. In patients with HNC, many of these symptoms are frequently present before treatment begins, and they generally occur earlier in the treatment trajectory than would

otherwise be expected. Although some assessment tools for assessing these symptoms exist, they do not rate both the severity of each symptom and the degree to which it interferes with eating (Kirkova et al., 2006). Following an extensive review of the literature, Kubrak and colleagues constructed an instrument, the Head and Neck Patient Symptom Checklist (HNSC), to address this gap. The study presented in this thesis was designed to begin testing the validity of the HNSC by addressing whether selected demographic variables and the symptom interference scores included in the HNSC could predict reduced dietary intake, weight loss, and reduced functional capacity.

Chapter 3: Methods

In this chapter I outline the methods I used to answer my research question. I will also discuss the limitations of this study, with particular emphasis on the challenges associated with measurement of symptoms that contribute to weight loss.

Design

The data used in this study was originally collected as part of a study that used a prospective observational design.

Sample

My sample was derived from an existing database of 368 individuals who were newly diagnosed with HNC between March 2007 and January 2010 and who lived in northern Alberta or who were referred to the Edmonton region for treatment. The cohort included 259 males and 109 females between the age of 18-94 (mean=62) referred for consideration of surgery, radiation and/or chemotherapy. Sample size calculations were not undertaken since I used an existing dataset.

Data Collection

Following approval by the Health Research Ethics Board at the University of Alberta and the Research Ethics Committee at the Cross Cancer Institute, all patients attending the clinic for individuals with newly diagnosed cancer of the head or neck were given a written invitation to consider participation in the original study. Those indicating an interest in hearing more about the study

were contacted by a member of the study team and given an opportunity to ask questions. Those indicating an interest in taking part in the study provided a written consent. Participants completed the PG-SGA, and the HNSC prior to treatment, mid treatment, and at the end of treatment. The portion of the data set collected prior to treatment was used in this study.

Study Measures

Patient-Generated Subjective Global Assessment (PG-SGA)

The PG-SGA was used to obtain data for weight loss, dietary intake, and functional capacity (see Appendix A). Based on it's high sensitivity (98%) and specificity (82%) (Bauer, Capra, Ferguson, 2002), it is considered a valid nutritional screening tool for detecting the presence of malnutrition among individuals with cancer (Kubrak & Jensen, 2007). The scored section of the PG-SGA is completed by the patient and elicits data on weight history (Box 1), dietary intake (Box 2), symptoms (Box 3), and functional capacity (Box 4). A numerical score is assigned according to the recorded response and used to categorize nutritional status and triage individuals requiring nutritional intervention.

Weight Loss

The amount of weight lost in six months was calculated for each study participant based on the self-reported weights provided in Box 1 of the PG-SGA. Weight loss greater than or equal to 5% in six months was coded as present and weight loss of less than 5% in six months was coded as absent. Adverse patient

outcomes are associated with unintentional weight loss of 5% body weight in 6 months (Ottery, 1996; Dewys et al., 1980).

Dietary Intake

Dietary intake was obtained from Box 2 of the PG-SGA and rated on a scale from 0 (normal or more than usual) to 4 (very little of anything). Score of 0 was coded as absent, score of 1-4 was coded as present.

Functional Capacity

Functional capacity was obtained from Box 4 of the PG-SGA and rated on a scale of 0 (no limitations) to 3 (little activity/bedridden). Score of 0 was coded as absent, score of 1-3 was coded as present.

Head and Neck Patient Symptom Checklist (HNSC)

Symptom interference with eating scores were obtained from the HNSC developed by Kubrak and colleagues (see Appendix B). As this is a new instrument, no reliability and validity data are available. Symptom interference scores for all 17 symptoms included in the HNSC (pain, anxious, dry mouth, loss of appetite, constipation, feeling full, depressed, thick saliva, diarrhea, sore mouth, lack of energy, nausea, difficulty chewing, altered smell, vomiting, difficulty swallowing, and taste changes) were rated on a 5-point scale (1=not at all and 5=a lot).

Analysis

Statistical analysis was conducted using SPSS (SPSS Inc, Chicago, U.S.A.). Descriptive statistics (frequency, mean, mode, and median) were calculated for all variables. The analytic strategies for each research question are described below. In studies of screening tools inter-observer variability is sometimes assessed. In the case of the HNSC, however, each patient completed the tool and hence inter-observer variability is not applicable.

Research Question 1: Validity of the HNSC

The validity of the HNSC was assessed in two ways. First, we calculated sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) using chi-square contingency tables (Harkness, 1995). Referring to Table 1, sensitivity is the number of people for whom a symptom was present on the HNSC divided by the number of people for whom a symptom was present on some "gold standard", in this case the PGSGA (a/(a+b)). Specificity is the number of people for whom a symptom was absent on the HNSC divided by the number of people for whom the symptom was absent on the "gold standard" (d/(c+d)). Positive predictive value is the number of people for whom a symptom was present using the "gold standard" divided by the number of people for whom the symptom was present on the new screening tool, in this case the HNSC (a/(a+c)). Negative predictive value is the number of people for whom a symptom is absent using the "gold standard" divided by the number of

people for whom the symptom was absent using the new screening tool (d/b+d)) (Valanis, 1986).

Table 1

Calculation of Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value

	Symptom present on PGSGA	Symptom absent on PGSGA	Total
Symptom present on HNSC	a	c	a+c
Symptom absent on HNSC	b	d	b+d
Total	a+b	c+d	a+b+c+d

Note. Adapted from "Epidemiology in Nursing and Health Care" by Valanis, B., 1986. East Norwalk, CT: Appleton-Century-Crofts.

Validity was also assessed using correlation. We calculated the correlations between HNSC scores and the scores on the PG-SGA. The study variables were dichotomized and for this reason we used Spearman's rho to report the correlations. We interpreted the strength of the correlations based on the recommendations of Salkind (2008) as follows: "weak or no relationship" 0-0.20, "weak" 0.21-0.40, "moderate" 0.41-0.60, "strong" 0.61-0.80, and "very strong"0.81-1.00.

Research Question 2: Predicting Reduced Dietary Intake, Weight Loss, and Reduced Functional Capacity

Three regression equations were constructed, one for each outcome of interest (reduced dietary intake, weight loss, and reduced functional capacity). In each case, the independent variables were entered first and include demographics (age, gender, tumor stage, tumor location) and the symptoms included in the HNSC. Reduced dietary intake, weight loss and reduced functional capacity were used as the dependent variables in the regression equations. We decided to dichotomize the dependent variables to facilitate comparison to other published studies and because all data were based on self report. As a result we thought there was likely considerable variability across participants in terms of how they evaluated their dietary intake, weight loss, and functional capacity. By dichotomizing the variables, we hoped to minimize this variability.

Chapter 4: Study Results

Sample Description

This study included 368 individuals (109 female, 259 male), mean age 62 years (range 18-94 years), newly diagnosed with HNC between March 09, 2007 and January 15, 2010 and who lived in northern Alberta or who were referred to the Edmonton region for treatment. The locations and stages of cancer for this cohort are outlined in Table 2.

Table 2

Demographic Characteristics of Head and Neck Cancer Patients at Presentation

Characteristic (n=368)	Frequency	Percentage
Gender		
Female	109	29.6
Male	259	70.4
Age (years)		
Mean	62	
Median	61	
Range	18 – 94	
< 65	219	59.5
≥ 65	149	40.5
Tumor Location[a]		
Pharynx	133	36.1
Larynx	74	20.1
Lip & Oral Cavity	85	23.7
Other[b]	76	20.7
Stage[c]		
I	57	15.5
II	53	14.4
III	74	20.1
IV	184	49.9
Total	368	100.0

Note.[a] ICD-O codes. [b]Other refers to: salivary gland, hypopharynx, nasal, Paranasal. [c] Greene et al. (2002). AJCC Cancer Staging Manual (6th ed.).

Research Question 1: Validity of HNSC

The objective of question one was to examine the ability of the HNSC to accurately assess a set of 12 symptoms experienced by individuals with HNC. The remaining five HNSC symptoms were not evaluated as we did not have "gold standard" indicators among our other measures for them. We addressed this question by calculating the specificity, sensitivity, PPV and NPV for each symptom on the HNSC. As the PGSGA scores were only rated "present" or "absent" we dichotomized the HNSC scores with a score of 1, defined as "absent" and 2-5 defined as "present".

Specificity, Sensitivity, Positive Predictive Value, and Negative Predictive Value

The specificity, sensitivity, PPV and NPV for pain, smell, dry mouth, loss of appetite, constipation, feeling full, diarrhea, sore mouth, nausea, vomiting, difficulty swallowing, and taste changes, shown in Table 3, are all excellent.

Table 3

Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value of the Best Level of Screening Performance of the HNSC for Nutritional Impact Symptoms

HNSC	Diagnosed by PG-SGA (%)	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Pain	161 (44.4)	0.93	0.99	0.98	0.94
Smell	26 (7.3)	0.88	0.99	0.92	0.99
Dry mouth	82 (22.9)	0.80	0.99	0.96	0.94
Loss of appetite	127 (35.7)	0.94	1.00	0.99	0.97
Constipation	41 (11.6)	0.93	0.99	0.95	0.99
Feeling full	78 (22.0)	0.90	1.00	1.00	0.97
Diarrhea	14 (3.9)	0.79	1.00	1.00	0.99
Sore mouth	120 (33.5)	0.98	0.99	0.98	0.99
Nausea	40 (11.3)	0.98	1.00	0.98	1.00
Vomiting	10 (2.8)	0.90	1.00	1.00	1.00
Difficulty swallow	129 (35.9)	0.91	0.99	0.98	0.95
Taste changes	53 (15.0)	0.89	1.00	0.98	0.98

Note. HNSC = Head and Neck Symptom Checklist; PG-SGA = Patient-Generated Symptom Global Assessment.

The values obtained show that the items for these 12 symptoms on the HNSC correctly identify both those who have and those who do not have each symptom.

Correlations Between Nutritional Impact Symptoms

To further assess the validity of the HNSC, we examined correlations between the symptoms present on both the HNSC and on the PG-SGA (See Table 4 and Table 5).

Table 4

Correlations Among Nutritional Impact Symptoms on the HNSC and the PG-SGA

			PG-SGA Pain	PG-SGA Smell	PG-SGA Dry mouth	PG-SGA Appetite	PG-SGA Constipation	PG-SGA Feeling full	PG-SGA Diarrhea	PG-SGA Sore mouth	PG-SGA Nausea	PG-SGA Vomit	PG-SGA Swallow	PG-SGA Taste
Spearman's rho	HNSC Pain	Correlation Coefficient	.917**VS	.219**W	.323**W	.495**M	.332**W	.352**W	.178**NR	.621**S	.265**W	.164**NR	0.601**M	.370**W
		Sig. (2-tailed)	0	0	0	0	0	0	0.001	0	0	0.002	0	0
		N	363	363	363	363	363	363	363	363	363	363	363	363
	HNSC Smell	Correlation Coefficient		.895**VS	.247**W	.325**W	.279**W	.336**W	.284**W	.231**W	.320**W	.352**W	.279**W	.472**M
		Sig. (2-tailed)		0	0	0	0	0	0	0	0	0	0	0
		N		355	355	355	355	355	355	355	355	355	355	355
	HNSC Dry mouth	Correlation Coefficient			.846**VS	.422**M	.380**W	.313**W	.230**W	.414**M	.164**NR	.132**NR	.411**M	.381**W
		Sig. (2-tailed)			0	0	0	0	0	0	0.002	0.012	0	0
		N			358	358	358	358	358	358	358	358	358	358
	HNSC Appetite	Correlation Coefficient				.945**VS	.376**W	.506**M	.192**NR	.341**W	.348**W	.202**W	.499**M	.470M
		Sig. (2-tailed)				0	0	0	0	0	0	0	0	0
		N				356	356	356	356	356	356	356	356	356
	HNSC Constipation	Correlation Coefficient					.930**VS	.353**W	.156**NR	.283**W	.273**W	.262**W	.312**W	.381**W
		Sig. (2-tailed)					0	0	0.003	0	0	0	0	0
		N					354	353	354	354	354	354	354	354
	HNSC Feeling full	Correlation Coefficient						.934**VS	.205**W	.247**W	.338**W	.215**W	.317**W	.448**M
		Sig. (2-tailed)						0	0	0	0	0	0	0
		N						355	355	355	355	355	355	355
	HNSC Diarrhea	Correlation Coefficient							.883**VS	.118*NR	.193**NR	.264**W	.207**W	.199NR
		Sig. (2-tailed)							0	0.026	0	0	0	0
		N							355	355	355	355	355	355
	HNSC Sore mouth	Correlation Coefficient								.975**VS	.191**NR	.095NR	.463**M	.354**W
		Sig. (2-tailed)								0	0	0.072	0	0
		N								358	358	358	358	358
	HNSC Nausea	Correlation Coefficient									.972**VS	.424**M	.294**W	.375**W
		Sig. (2-tailed)									0	0	0	0
		N									354	354	354	354
	HNSC Vomit	Correlation Coefficient										.947**VS	.180**NR	.234**W
		Sig. (2-tailed)										0	0.001	0
		N										354	354	354
	HNSC Swallow	Correlation Coefficient											.915**VS	.351**W
		Sig. (2-tailed)											0	0
		N											359	359
	HNSC Taste	Correlation Coefficient												.921**VS
		Sig. (2-tailed)												0
		N												354

Note. *p <.05, two-tailed. **<.01, two-tailed. Correlations: VS =Very Strong, S =Strong, M =Moderate, W =Weak, NR = No relation.

Table 5

Correlations Among Nutritional Impact Symptoms on the HNSC

			HNSC Pain	HNSC Smell	HNSC Dry mouth	HNSC Appetite	HNSC Constipation	HNSC Feeling full	HNSC Diarrhea	HNSC Sore mouth	HNSC Nausea	HNSC Vomit	HNSC Swallow	HNSC Taste	HNSC Anxious	HNSC Depression	HNSC Thick Saliva	HNSC Lack Energy	HNSC Diff. Chew
Spearman's rho	HNSC Pain	Correlation Coefficient	1	.284**W	.393**W	.541**M	.355**W	.358**W	.147**NR	.640**S	.291**W	.156**NR	.652**S	.367**W	.378**W	.379**W	.464**M	.421**M	.595**M
		Sig. (2-tailed)	.	0	0	0	0	0	0.006	0	0	0.003	0	0	0	0	0	0	0
		N	363	353	355	354	352	353	353	354	352	352	356	351	355	353	352	354	352
	HNSC Smell	Correlation Coefficient		1	.300**W	.341**W	.285**W	.310**W	.268**W	.230**W	.320**W	.306**W	.275**W	.503**M	.252**W	.337**W	.201**W	.278**W	.229**W
		Sig. (2-tailed)		.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		N		355	354	355	353	354	354	354	354	354	354	353	354	354	353	354	353
	HNSC Dry mouth	Correlation Coefficient			1	.435**M	.392**W	.327**W	.202**W	.404**W	.175**NR	.105**NR	.427**M	.427**M	.293**W	.316**W	.368**W	.406**M	.369**W
		Sig. (2-tailed)			.	0	0	0	0	0	0.001	0.049	0	0	0	0	0	0	0
		N			358	355	353	354	354	354	353	353	354	352	356	354	353	355	353
	HNSC Appetite	Correlation Coefficient				1	.394**W	.495**M	.183**NR	.344**W	.369**W	.189**NR	.507*M*	.472M	.502**M	.499**M	.385**W	.413**M	.398**W
		Sig. (2-tailed)				.	0	0	0.001	0	0	0	0	0	0	0	0	0	0
		N				356	353	354	354	354	354	354	355	353	355	354	353	354	354
	HNSC Constipation	Correlation Coefficient					1	.342**W	.193**NR	.301**W	.301**W	.282**W	.317**W	.438**M	.284**W	.399**W	.437**M	.424**M	.318**W
		Sig. (2-tailed)					.	0	0	0	0	0	0	0	0	0	0	0	0
		N					354	353	353	352	352	352	352	351	352	]353	352	353	351
	HNSC Feeling full	Correlation Coefficient						1	.217**NR	.243**W	.347**W	.194**NR	.331**W	.482**M	.458**M	.397**W	.405**M	.367**W	.322**W
		Sig. (2-tailed)						.	0	0	0	0	0	0	0	0	0	0	0
		N						355	354	353	353	353	353	352	353	354	353	354	352
	HNSC Diarrhea	Correlation Coefficient							1	.118*NR	.193**NR	.281**W	.220**W	.231**W	.206**W	.191**NR	.202**NR	.222**NR	.159*NR
		Sig. (2-tailed)							.	0.027	0	0	0	0	0	0	0	0	0.003
		N							355	354	354	354	354	353	353	354	354	354	353
	HNSC Sore mouth	Correlation Coefficient								1	.207**W	.078NR	.498**M	.339**W	.276**W	.354**W	.331**W	.432**M	.701**S
		Sig. (2-tailed)								.	0	0.141	0	0	0	0	0	0	0
		N								358	354	354	355	354	355	353	353	355	353
	HNSC Nausea	Correlation Coefficient									1	.424**M	.294**W	.375**W	.377**W	.399**W	.332**W	.367**W	.278**W
		Sig. (2-tailed)									.	0	0	0	0	0	0	0	0
		N									354	354	354	354	353	353	353	353	353
	HNSC Vomit	Correlation Coefficient										1	.192**NR	.198**NR	.053NR	.109**NR	.194**NR	.104*NR	.161**NR
		Sig. (2-tailed)										.	0	0	0.319	0.041	0	0.050	0.002
		N										354	354	353	353	353	353	353	353
	HNSC Swallow	Correlation Coefficient											1	.356**W	.285**W	.350**W	.511**M	.441**M	.511**M
		Sig. (2-tailed)											.	0	0	0	0	0	0
		N											359	353	355	353	353	353	354
	HNSC Taste	Correlation Coefficient												1	.396**W	.427**M	.419**M	.452**M	.357**
		Sig. (2-tailed)												.	0	0	0	0	0
		N												354	352	352	352	352	352
	HNSC Anxious	Correlation Coefficient													1	.629**S	.350**W	.461**M	.315**W
		Sig. (2-tailed)													.	0	0	0	0
		N													358	353	352	354	353
	HNSC Depression	Correlation Coefficient														1	.435**M	.574**M	.292**W
		Sig. (2-tailed)														.	0	0	0
		N														355	353	354	353
	HNSC Thick Saliva	Correlation Coefficient															1	.513**M	.396**W
		Sig. (2-tailed)															.	0	0
		N															354	353	352
	HNSC Lack Energy	Correlation Coefficient																1	.428**M
		Sig. (2-tailed)																.	0
		N																357	352
	HNSC Diff. Chew	Correlation Coefficient																	1
		Sig. (2-tailed)																	.
		N																	354

Note. *p<.05, two-tailed. **p<.01, two-tailed. Correlations: ^{VS}= Very Strong, ^{S}=Strong , ^{M}=Moderate, ^{W}=Weak, ^{NR}=No relation.

The correlations between each symptom on the HNSC (pain, smell, dry mouth, appetite, constipation, feeling full, diarrhea, sore mouth, nausea, vomit, difficulty swallowing, and taste changes) and it's corresponding symptom as measured on the PG-SGA were very strong, with Spearman's rho ranging from 0.85 – 0.98, positive and highly significant ($p<0.01$), further supporting the validity of the items on the HNSC for these 12 symptoms. We also found significant correlations among the 17 symptoms scores on the HNSC .The majority of these relationships were weak in strength.

Relationships Among Reduced Dietary Intake, Weight Loss, and Reduced Functional Capacity

Moderate correlations among reduced dietary intake, and both weight loss, and reduced functional capacity were found. The correlation between weight loss and reduced functional capacity was significant but weak (See Table 6).

Table 6

Correlation Among Reduced Dietary Intake, Weight Loss of ≥ 5% or More in Six Months, and Reduced Functional Capacity

Spearman's rho			5% weight loss in past six months	Reduced dietary intake	Reduced functional capacity
	≥5% weight loss in past six months	Correlation Coefficient	1	.449**M	.321**W
		Sig. (2-tailed)	.	0	0
		N	360	360	360
	Reduced dietary intake	Correlation Coefficient		1	.427**M
		Sig. (2-tailed)		.	0
		N		368	368
	Reduced functional capacity	Correlation Coefficient			1
		Sig. (2-tailed)			.
		N			368

Note. *p<.05, two-tailed. **p<.01, two-tailed. Correlations:,^{M} =Moderate, ^{W}=Weak.

Research Question 2: Predicting Reduced Dietary Intake, Weight Loss, and Reduced Functional Capacity

We used logistic multivariate regression analysis to examine the ability of the HNSC symptoms (pain, anxious, dry mouth, loss of appetite, constipation, feeling full, depressed, thick saliva, diarrhea, sore mouth, lack of energy, nausea, difficulty chewing, altered smell, vomiting, difficulty swallowing, and taste changes) together with age, gender, tumor stage, and tumor location to predict weight loss, reduced dietary intake, and reduced functional capacity. Although we only had validity evidence for 12 of the symptoms, we included all 17 of the HNSC symptoms in our analysis because Kubrak and colleagues (2010) had

included each of the symptoms based on evidence from the published literature indicating that they were associated with dietary intake.

Using a standard model building strategy to build our model, we performed a univariate analysis examining the ability of each independent variable to predict our three outcomes (Mickey & Greenland, 1989). At the univariate level, all variables were significant at $p < 0.1$. We then examined the ability of all 17 HNSC symptoms together with age, gender, tumor stage, and tumor location to predict reduced dietary intake, weight loss, and reduced functional capacity. In this model pain, loss of appetite, and difficulty swallowing were predictors of reduced dietary intake. Stage, difficulty swallowing, and loss of appetite were predictors of weight loss greater than or equal to 5% in six months. Loss of appetite, feeling full, difficulty swallowing, and lack of energy were predictors of reduced functional capacity. The remaining variables were not significant predictors of our dependent variables at $p < 0.05$ and not included in the final model. To finalize the three outcome models we ran the models again with the demographic variables and the significant independent variables (see Table 7).

Advanced tumor stage, loss of appetite, and difficulty swallowing were able to predict 79% of the probability of weight loss. Pain, loss of appetite and difficulty swallowing were able to predict 82% of the probability of reduced dietary intake. Loss of appetite, feeling full, difficulty swallowing, and lack of

energy were able to predict 78% of the probability of reduced functional capacity. Detailed results are shown in Table 8.

Table 7

Univariate and Multivariate Logistic Regression Analysis of Nutritional Impact Symptoms, Reduced Dietary Intake, Weight Loss, and Reduced Functional Capacity for Head and Neck Cancer Patients at Presentation

	Univariate Analysis			Multivariate Analysis		
	Reduced Dietary Intake	≥5% Weight Loss in Past Six Months	Reduced Functional Capacity	Reduced Dietary Intake	≥5% Weight Loss in Past Six Months	Reduced Functional Capacity
	Odds ratio (CI – 95%)	Odds ratio (CI – 95%)	Odds ratio (CI – 95%)	Odds ratio (CI – 95%)	Odds ratio (CI – 95%)	Odds ratio (CI – 95%)
Gender (Male)						
Female	1.6-- (1.0 - 2.6)	1.0-- (0.6 – 1.6)	1.4-- (0.9 – 2.2)	1.5-- (0.8 – 3.0)	0.8-- (0.4 – 1.5)	1.2-- (0.7 – 2.2)
Age (≥65)						
<65	0.9-- (0.6 - 1.4)	1.1-- (0.7 – 1.7)	0.7-- (0.5 – 1.1)	0.7-- (0.4 – 1.4)	0.9-- (0.5 – 1.6)	0.6-- (0.4 – 1.1)
Tumor Location (Pharynx)						
Larynx	0.5-- (0.3 - 1.0)	0.8-- (0.4 – 1.5)	0.8-- (0.5 – 1.5)	0.5-- (0.2 – 1.4)	1.2-- (0.5 – 2.7)	0.9-- (0.4 – 1.9)
Lip & Oral Cavity	1.2-- (0.7 - 2.1)	0.7-- (0.4 – 1.4)	0.9-- (0.5 – 1.5)	0.9-- (0.4 – 2.2)	1.0-- (0.4 – 2.1)	0.6-- (0.3 – 1.3)
Other	0.8-- (0.5 - 1.5)	1.0-- (0.6 – 2.0-	1.3-- (0.8 – 2.4)	1.0-- (0.4 – 2.2)	1.4-- (0.7 – 3.1)	1.3-- (0.6 – 2.5)
Tumor Stage (I/II)						
III/IV	3.4-- (2.1 - 5.7)	3.7*** (2.0 - 6.8)	2.2*** (1.4 – 3.4)	2.0-- (1.0 – 4.3)	2.1*(1.0-4.5)	1.3-- (0.7 – 2.4)
Nutrition Impact Symptom						
Pain	11.5*** (7.0 - 19.0)	3.9*** (2.4 – 6.4)	5.2*** (3.3 – 8.1)	2.5* (1.2-5.3)	--	--
Smell	8.8***(3.0 - 26.3)	4.3*** (1.9 – 2.0)	6.7*** (2.3 – 20.0)	--	--	--
Dry mouth	5.5***(3.1 - 9.8)	2.8*** (1.6 – 4.9)	4.9*** (2.7 – 9.1)	--	--	--
Loss of Appetite	19.5***(11.0 -34.5)	7.2*** (4.3 – 12.0)	7.5*** (4.5 – 12.6)	8.0***(4.2-15.4)	4.3***(2.4-7.9)	2.5**(1.3-4.9)
Constipation	7.3**(3.3 - 16.4)	3.3*** (1.7 – 6.6)	7.7***(3.2 – 18.9)	--	--	--
Feeling full	8.2*** (4.4 - 15.3)	3.3*** (1.9 – 5.7)	8.8*** (4.4 – 17.5)	--	--	2.6* (1.1-6.2)
Diarrhea	15.7** (2.0 - 123.8)	3.2-- (0.9 – 10.7)	3.1-- (0.8 – 12.0)	--	--	--
Sore mouth	4.5** (2.8 - 7.2)	2.1** (1.3 – 3.4)	2.8***(1.8-4.4)	--	--	--
Nausea	7.2*** (3.2 - 16.2)	4.8*** (2.4 – 9.5)	12.9***(4.5-37.2)	--	--	--
Vomiting	5.3* (1.1 - 26.0)	5.4* (1.3 – 22.1)	9.6* (1.2 – 77.4)	--	--	--
Difficulty Swallowing	13.1*** (7.7 - 22.2)	6.1*** (3.7 – 10.2)	7.2***(4.4 – 12.0)	4.0***(1.9-8.6)	2.9***(1.6-5.4)	3.4***(1.8-6.4)
Taste Changes	9.9*** (4.5 – 21.8)	5.9** (3.1 – 11.5)	6.3***(3.0 – 13.4)	--	--	--
Difficulty Chewing	7.8*** (4.7 – 12.9)	3.5*** (2.1 – 5.7)	4.5***(2.8-7.4)	--	--	--
Anxious	5.2*** (3.2 – 8.5)	2.6*** (1.6 – 4.2)	5.8***(3.5 – 9.6)	--	--	--
Depressed	4.8*** (2.9 – 7.9)	2.7*** (1.6 – 4.5)	6.1***(3.5-10.6)	--	--	--
Thick Saliva	8.4*** (4.4 – 15.9)	4.9*** (2.8 – 8.6)	8.5***(4.3-17.0)	--	--	--
Lack of Energy	6.6*** (4.0 – 11.2)	3.4*** (2.0 – 5.6)	9.9***(5.5-17.9)	--	--	4.0***(2.0-8.0)

Note. *(p ≤ .05), two-tailed. **(p ≤ .01), two-tailed. ***(p ≤ .001). (--) not significant.

Table 8

Predictive Probability of Significant Nutritional Impact Symptoms and Reduced Dietary Intake, Weight Loss, and Reduced Functional Capacity

Multivariate Analysis			
Outcome Variable	Nutritional Impact Symptoms	Odds ratio (CI – 95%)	Predictive Probability
Reduced Dietary Intake	Pain	2.5*(1.2-5.3)	
	Loss of Appetite	8.0***(4.2-15.4)	
	Difficulty Swallowing	4.0***(1.9-8.6)	0.82
≥ 5% Weight Loss in Past Six Months	Tumor Stage	2.1*(1.0-4.5)	
	Loss of Appetite	4.3***(2.4-7.9)	
	Difficulty Swallowing	2.9***(1.6-5.4)	0.79
Reduced Functional Capacity	Loss of Appetite	2.5*(1.3-4.9)	
	Feeling Full	2.6*(1.1-6.2)	
	Difficulty Swallowing	3.4***(1.8-6.4)	
	Lack of Energy	4.0***(2.0-8.0)	0.78

Note. *(p≤ .05), two-tailed. **(p ≤ .01), two-tailed. ***(p ≤ .001).

Chapter 5: Discussion

The aim of this study was to evaluate the validity of the HNSC as a nutritional screening tool for individuals with HNC prior to initiating treatment and to examine relationships among the symptoms on the HNSC and three important clinical outcomes: reduced dietary intake, weight loss greater than or equal to 5% or more in 6 months, and reduced functional capacity.

Validity of the HNSC

Our study findings confirm the validity of the HNSC for use in the HNC population. The 12 symptoms on the HNSC that we assessed, accurately identified HNC patients who had those symptoms as indicated on the PG-SGA; sensitivity ranged from 79% - 98% and specificity ranged from 99% - 100%. Both the positive predictive value and the negative predictive value were excellent, ranging from 0.92 – 1.00.

Sensitivity and specificity are generally inversely related. In this study, the specificity was very high, indicating that individuals who did not have the symptom were correctly identified. The sensitivity is very good, but was a little lower, indicating that some individuals who had the symptom according to the PGSGA may have been missed by the HNSC. Clinically, it is always worrisome to miss a symptom. We do not yet know whether the PG-SGA was over-reporting or whether the HNSC was missing important symptoms, but we will evaluate this issue in our further studies. The positive and negative predictive value results show that one may have confidence in assessment conducted using the HNSC;

nearly all participants who scored negative for any given symptom on the PG-SGA also scored negative on the HNSC and similarly, nearly all participants who scored positive for any given symptom on the PG-SGA also scored positive on the HNSC.

Correlations Among Symptoms on the HNSC and PG-SGA

When we compared the HNSC to the PG-SGA, all 12 symptoms evaluated showed strong correlation with the corresponding PG-SGA symptoms. Based on the work of Salkind (2008), the strength of these correlations was an important component of the validity assessment. If the correlations had been smaller, we would have been less convinced of the validity of the HNSC.

Symptom Clusters

Given recent interest in symptoms clusters, we also examined correlations among the HNSC symptoms. Symptoms cluster are defined as three or more related symptoms occurring concurrently with each other (Dodd et al., 2001). Robust correlation among concurrent symptoms supports the existence of symptom clusters that may have an adverse effect on patient outcomes (Dodd et al.; Olson et al., 2008; Walsh & Rybicki, 2006). The identification of symptom clusters is difficult because the relationships among symptoms change over time (Olson et al., Hayduk et al., 2010), but the accurate identification of clusters is important because these interrelationships need to be considered when planning and evaluating symptom interventions (Yarbro, Frogge, & Goodman, 2004).

There appear to be several interesting symptom clusters among the HNSC symptoms in our study. The first cluster is comprised of pain, difficulty swallowing, sore mouth, and loss of appetite, with Spearman's rho ranging from 0.541 to 0.652. Research among the HNC population has identified pain and difficulty swallowing as common causes of eating problems (Toporcov & Antunes, 2006; Larrson et al., 2005). Recently, Kubrak et al. (2010) identified sore mouth in addition to pain and difficulty swallowing as a cause of reduced dietary intake. This finding is consistent with our study findings and was expected as sore mouth is painful and clinically we have seen that pain often impedes difficulty swallowing in the HNC population.

We also identified a second possible cluster comprised of loss of appetite, feeling full, difficulty swallowing, taste changes, anxiety, and depression with Spearman's rho ranging from 0.472 to 0.507. This finding is consistent with the work of Larsson et al. (2003) who found that physical symptoms such as feeling full, difficulty swallowing, and taste changes were associated with loss of appetite, decreased will, and desire to eat. As physical symptoms intensify individuals experience increased levels of anxiety and depression further compromising one's appetite.

In our study we also found a significant correlation between pain and loss of appetite. Several physiological and psychological dimensions play a role in regulating appetite. Physiological causes including unrelieved pain can activate the stress response, increasing hormone production, followed by decreased

gastrointestinal activity and loss of appetite (Grant & Rivera, 1995; Grant & Kravits, 2000; Lees, 1999).

This study identified a correlation between dry mouth and sore mouth, swallowing difficulties, and loss of appetite. The function of saliva is to protect and cleanse the oral mucosa and aid with swallowing by lubricating food. Decreased saliva production among HNC patients prior to treatment may be caused by compression of the nerves that innervate the saliva gland. Reduced saliva production can lead to mucosa breakdown and increased risk of infection caused by bacteria. Dry mucous membranes and infections with organisms such as oral candida can cause sore mouth and hinder one's desire to consume food orally, resulting in loss of appetite. Thick saliva and lack of saliva makes swallowing food difficult and negatively affects the will to eat (Yeung, Escalante & Gagel, 2009; Lees, 1999).

As expected loss of appetite was correlated with taste changes and feeling full. Taste changes are often associated with cancer prior to treatment as a result of chemicals released by the tumor (Grant & Kravitz, 2000). When food does not taste as it should, food aversions develop, followed by decreased desire to eat and avoidance of oral dietary intake (Tisdale, 2009; Lees, 1999).

Fuez and Rapin (1994) report management of pain and other symptoms associated with nutrition enhanced opportunity for spontaneous dietary intake among elderly, terminal cancer patients despite having little or no appetite. This finding suggests that effective symptom management prior to treatment may

promote dietary intake, thus reducing the risk of involuntary weight loss and reduced functional capacity. Additionally, identification of symptom clusters and knowledge of the synergistic relationships among symptoms can aid the clinician in providing appropriate, timely interventions.

Correlations Among Outcome Variables

A moderate correlation was identified between involuntary weight loss, reduced dietary intake and reduced functional capacity. This relationship was expected as reduced dietary intake equates with absent calories and leads to weight loss. Furthermore, reduced dietary intake together with increased metabolic body requirements due to cancer contributes to the cancer cachexia syndrome, which results in profound loss of body muscle mass and decreased functional capacity (Grant & Rivera, 1995). Muscle mass and dietary intake are important factors in providing the required fuel to promote adequate functional capacity. Weight loss drawn from muscle mass compromises the ability to store energy and results in reduced functional capacity and quality of life (Dewys et al., 1980; Grant & Rivera).

Weight Loss

Weight loss is a key issue among individuals with HNC; weight loss prior to treatment ensues from the disease course itself and symptoms that interfere with eating (Baracos, 2006; Tisdale, 2002; Kubrak et al., 2010). The clinical manifestations and treatment-related causes of weight loss among the oncology population have been well explored, however, limited research has been

conducted on the relationships among weight loss symptoms specific to the HNC population.

Reduced Dietary Intake

Recent work completed by Kubrak et al. (2010) found that several symptoms specific to individuals with HNC played a role in reduced dietary intake. The authors suggested further study of these symptoms before, during, and after treatment could aid in understanding the underlying cause. Subsequent to the above study Kubrak and colleagues developed the HNSC to assess particular symptoms associated with reduced dietary intake in individuals with HNC prior to treatment.

Strengths and Limitations of the HNSC

In comparison to the PG-SGA the HNSC has several advantages. First, the HNSC identifies the presence and severity of each symptom rather than presence alone; providing opportunity to triage patients according to urgency and in turn, utilize resources more efficiently. Secondly, the HNSC can be self administered in a short amount of time, thus, minimal effort is required to implement its' use repeatedly during the disease trajectory. Repeated use of the tool provides documentation of variations in symptom presence and severity and thus can aid in evaluating the effects of interventions. Lastly, the HNSC includes symptoms specific to the HNC population (including difficulty chewing, thick saliva, anxiety, and depression) giving opportunity to report disease specific symptoms that may

benefit from intervention. Unless symptoms relevant to the population are identified opportunity to intervene may be neglected.

Although all of the symptoms included in the HNSC were drawn from published studies indicating that they adversely influenced nutrition, only some of them predicted reduced dietary intake in this study. This suggests that it may be possible to shorten the instrument. Before doing this, however, we want to use the instrument in clinic to follow patients over time, as symptoms not present prior to treatment may develop secondary to treatment, and become predictive of dietary intake later in the treatment trajectory.

At present, the HNSC does not include any information about interpretation. Further research is needed but if results are similar to ours, information to guide interpretation could be placed in a note at the bottom of the tool. Such information could flag symptoms indicative of primary patient outcomes (reduced dietary intake, weight loss, and reduced functional capacity).

Predicting Reduced Dietary Intake, Weight Loss, and Reduced Functional Capacity

To prepare for regression analysis we conducted univariate analyses with each independent variable. Age, gender, tumor location, and tumor stage were not significant predictors of reduced dietary intake in our study; these findings are consistent with those of Larsson et al. (2005). We were somewhat surprised by these results as tumor location seems to be associated with reduced dietary intake in our clinical practice. It is important to remember that the participants

in our study had not yet started treatment. The relationship we see in clinic between tumor location and reduced dietary intake is likely due to the location of the treatment and the treatment-related symptoms such as sore mouth and difficulty swallowing.

As expected, tumor stage was a predictor of weight loss and reduced functional capacity, while age, gender and tumor location had no significant relation to either outcome. This finding is consistent with previous studies completed in the HNC population which report weight loss occurs more frequent in individuals with tumor stage classification III and IV (Jager-Wittenaar et al., 2007). In the absence of reduced dietary intake, the relationship between tumor stage classification and weight loss may be the result of increased caloric utilization by tumor tissues. As disease advances and tumor cells multiply the caloric demands of the tumor tissue increase and subsequently muscle is broken down (cachexia syndrome) to provide energy to the tumor (Dewys et al., 1980; Tisdale, 2002). As expected, loss of muscle mass results in weakness, immobility and overall reduced functional capacity.

To predict reduced dietary intake, weight loss and reduced functional capacity we constructed three final regression models. Of the 17 NIS included on the HNSC only pain, loss of appetite and difficulty swallowing significantly predicted reduced dietary intake. Tumor stage, loss of appetite and difficulty swallowing significantly predicted weight loss. Loss of appetite, feeling full,

difficulty swallowing and lack of energy significant predicted reduced functional capacity.

Reduced Dietary Intake

The relationship between reduced dietary intake with pain and loss of appetite suggest that the two symptoms have a common basis. We know that unrelieved pain stimulates the stress response, increasing the production of catecholamines leading to delayed gastric emptying (Grant & Kravits, 2000). Impaired gastric peristalsis causes feelings of fullness and loss of appetite followed by reduced dietary intake. Additionally, medications such as narcotics administered to treat pain also contribute to delay gastric emptying resulting in reduced dietary intake (Payne & Foley, 1985).

Loss of appetite in relation to reduced dietary intake may also be caused by functional changes related to difficulty swallowing. Individuals who experience difficulty swallowing have reported decreased oral intake of food due to fear of aspiration. Diminished will and desire to eat as a result of fear may contribute to loss of appetite and in turn reduced dietary intake (Larsson et al., 2003).

Weight Loss

This study identified loss of appetite and difficulty swallowing as predictive of weight loss. Previous qualitative research done among HNC patients suggest physical problems such as swallowing difficulties contribute to loss of appetite (Larrson et al., 2003). When it is difficult to eat the will and

desire to consume food is diminished further compromising the ability to overcome the physical problem (Larrson).

Tumor stage was predictive of weight loss but not reduced dietary intake or functional capacity. The cause of weight loss in relation to tumor classification can be explained as a result of the cancer cachexia syndrome.

Reduced Functional Capacity

Loss of appetite, feeling full, difficulty swallowing, and lack of energy were predictive of reduced functional capacity. We know that multiple factors related to loss of appetite, feeling full, and difficulty swallowing result in reduced dietary intake. Under normal circumstance carbohydrates that you eat are stored in muscle and converted into energy for use during physical activity. Reduced dietary intake together with reduced muscle mass limits the amount and storage of fuel required for adequate muscle function resulting in reduced functional capacity.

Limitations of the Study

There were several noteworthy sources of bias in this study including: self report, recall, and confounding associated with co-morbidities. Reliance on self-report for the measurement of both dependent and independent variables may limit the validity of the conclusions. Individuals diagnosed with HNC will have thought about their state of health and may be more attentive to factors (such as weight loss), which have a negative effect on health. For this reason individuals may over-report or under-report such variables (Frese & Zapf, 1988).

Recall bias may also limit the findings of this study. Several factors including time period, personal demographics (age, education, socioeconomic status), social acceptance, and significance of events (Coughlin, 1990) may have influenced participants' abilities to recall the information required to complete the assessment tools in this study. Cognitive factors related to age and education may affect memory and misinterpretation of the question and in turn threaten the validity of the causal conclusions among variables. McClement (2005) suggests people differ with respect to their perceived experience and social acceptance of disease indicators such as weight loss and reduced dietary intake and as a result recall related to weight loss, functional capacity, dietary intake and symptoms may be inconsistently reported by individuals with HNC.

Co-morbidities and acute changes in symptoms may have further threatened the validity of this study. Co-morbidities experienced by study participants may be associated with symptoms that were similar to those experienced by individuals with HNC and thus may have an effect on outcome measure.

Chapter 6: Implication for Clinical Practice, Education, Research, and Policy

The prevalence of nutritional impact symptoms and their relationships to reduced dietary intake, involuntary weight loss and reduced functional capacity in individuals with HNC population have been identified by many research groups. The development of the HNSC has resulted in an instrument that brings all of the most relevant symptoms together in one instrument. It is clear from this study and the work completed by Kubrak and colleagues (2010) that the majority of individuals with HNC experience symptoms that adversely affect their nutritional intake prior to treatment. Since cancer therapy may further exacerbate these symptoms it is important to implement early nutritional assessments and interventions in the clinical setting (Larsson et al., 2005, Kubrak et al., 2010).

Implications for Clinical Practice

Nurses who work with individuals who have HNC are in an ideal position to conduct early nutritional assessments. The findings of this study indicate that the HNSC is able to provide valid information about symptoms that influence dietary intake. Given the early stage of its recent development and limited use in clinical settings, the HNSC is best used as a supplemental resource to a complete clinical assessment. Initially it can be used to “screen” individuals at risk for nutritional impact symptoms, to document severity, and as a basis for triaging individuals who may warrant a more costly multi disciplinary assessment. Once interventions have been implemented the HNSC can be used

again to evaluate intervention effectiveness and track symptom changes. The process of screening is important because if symptoms are left untreated they may become exacerbated during treatment and result in nutritional deterioration, treatment delays, toxicities, decreased response to treatment, costly hospitalization, and mortality (Ottery, 1996; Nitenberg & Raynard, 2000).

Implications for Education

Nurses who work with individuals who have HNC are in the ideal position to use the HNSC to screen individuals, to promote discussion of reported symptoms, and to collaborate with other members of the health care team to implement appropriate interventions. The HNSC is very easy to use, but it must be implemented correctly in order to obtain valid results. Professional development programs for nurses working in HNC should include orientation to the HNSC.

The HNSC is a good example of an instrument that is evidence based. As such it could be included as an example of a good screening tool in nursing education programs at the graduate and undergraduate levels.

Implications for Research and Policy

The aim of this study was to validate a nutritional screening tool designed to improve identification of nutritional impact symptoms specific to individuals with HNC prior to commencing treatment. Further research is needed to evaluate its utility in the clinical setting, including any challenges associated with implementing the tool in practice such as clinician commitment, staffing

resources and variation in assessment time. The HNSC is an easy-to-use, quick, and simple screening tool and for this reason we expect that its testing will require minimal effort. The data gathered from this tool could be easily entered into a database and used in future studies to get a better understanding of the usefulness of the HNSC. It is important to keep in mind that a screening tool used to identify NIS is only as valuable as the interventions available to treat the symptoms. For this reason it is important to also include evaluation of interventions in future research studies. Future directions of this study could also include redoing analysis for each tumor site and then comparing the results to see if the predictors of the three outcome variables change.

Conclusion

Individuals with HNC are at a high risk of malnutrition which correlates with poor clinical outcomes including treatment delays, costly hospitalizations, and morbidity. Consequently tailored strategies to identify individuals at risk of malnutrition specific to the HNC population are essential to implementing appropriate interventions in a timely manner. This study has identified the HNSC as a valid, concise, nutritional screening tool specific to the HNC population. We recommend that all individuals newly diagnosed with HNC receive nutritional screening at presentation and again through out the treatment trajectory. If individuals at risk of malnutrition are identified and assessed early then symptoms impacting dietary intake can be treated improving treatment outcome, survival and quality of life.

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Appendix A: Patient-Generated Subjective Global Assessment (PG-SGA)

Box 1.Weight	**Box 2. Food Intake:** As compared to my normal intake. I would rate my food intake during the past month as:
In summary of my current and recent weight: I currently weight about _____kg Six months ago I weighed about _____kg During the past two weeks my weight has: ☐decreased ☐not changed ☐ increased	☐ unchanged ☐ more than usual ☐less than usual I am now taking: ☐*normal food* but less than normal amounts ☐ little solid food ☐ only liquids ☐ only nutritional supplements ☐very little of anything ☐only tube feeding or only nutrition by vein
Box 3. Symptoms: I have had the following problems that have kept me from eating enough during the past two weeks (check all that apply): ☐ no problems eating ☐ no appetite, just did not feel like eating ☐ nausea ☐ constipation ☐ mouth sores ☐ things taste funny or have no taste ☐ problems swallowing ☐ pain; where?_____ ☐ vomiting ☐ diarrhea ☐ dry mouth ☐ smells bother me ☐ feel full quickly ☐ other** **Examples: depression, money, or dental problems	**Box 4. Activities and Function:** Over the past month, I would generally rate my activity as: ☐ normal with no limitations ☐ not my normal self, but able to be up and about with fairly normal activities ☐ not feeling up to most things, but in bed or chair less than half the day ☐ able to do little activity and spend most of the day in bed or chair ☐pretty much bedridden, rarely out of bed

Appendix B: Head and Neck Patient Symptom Checklist (HNSC)

Head & Neck Patient Symptom Checklist

Instructions: Below is a list of 17 symptoms. Please circle the number that best describes how often you experienced the symptom **during the past 3 days,** and if it interferred with your eating.

During the past 3 days:	How often did you have this symptom?					Has this symptom interferred with eating?				
Symptom	Not at all	A little bit	Some what	Quite a bit	A lot	Not at all	A little bit	Some what	Quite a bit	A lot
Pain	1	2	3	4	5	1	2	3	4	5
Anxious	1	2	3	4	5	1	2	3	4	5
Dry mouth	1	2	3	4	5	1	2	3	4	5
Loss of appetite	1	2	3	4	5	1	2	3	4	5
Constipation	1	2	3	4	5	1	2	3	4	5
Feeling full	1	2	3	4	5	1	2	3	4	5
Depressed	1	2	3	4	5	1	2	3	4	5
Thick saliva	1	2	3	4	5	1	2	3	4	5
Diarrhea	1	2	3	4	5	1	2	3	4	5
Sore mouth	1	2	3	4	5	1	2	3	4	5
Lack of energy	1	2	3	4	5	1	2	3	4	5
Nausea	1	2	3	4	5	1	2	3	4	5
Difficulty chewing	1	2	3	4	5	1	2	3	4	5
Smells bother me	1	2	3	4	5	1	2	3	4	5
Vomiting	1	2	3	4	5	1	2	3	4	5
Difficulty swallowing	1	2	3	4	5	1	2	3	4	5
Taste changes	1	2	3	4	5	1	2	3	4	5
Other: Specify	1	2	3	4	5	1	2	3	4	5