

# Nutrition Impact Symptoms in Relation to Head and Neck Cancer Survivor's Vegetable Intake and Use of Seasoning

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**Background:** Most head and neck cancer (HNC) patients undergoing aggressive treatments with chemoradiotherapy and surgical resection of tumors suffer from symptoms long after treatment is completed that hinder adequate oral food intake, collectively known as Nutrition Impact Symptoms (NIS). Our aim was to examine the correlations between NIS and HNC survivors' vegetable intake and use of seasoning.

**Methods:** We conducted a 29-item telephone administrated survey to collect vegetable intake and seasoning habits among HNC survivors ( $n=22$ , age  $61.4 \pm 9.8$  years, mean  $\pm$  standard deviation) who received radiation therapy between 6 months and 10 years before recruitment identified through the cancer registry at Carle Foundation Hospital. Treatment-related side-effects (11 items) including difficulty swallowing, dry mouth, and mouth sores reflected NIS. A mean composite score was created for all the symptoms where higher scores indicated greater NIS. Spearman correlations examined the relationships between NIS, vegetable intake, and seasoning.

**Results:** Half (50%) of the participants reported no change in their vegetable intake since diagnosis of cancer, and on average, ate 1 cup/day of total vegetables. Higher NIS scores associated with higher pumpkin and sweet potatoes intake ( $r(20) = .43$ ,  $p < 0.05$ ), and there was a trend for higher scores of difficulties swallowing to be associated with lower corn and peas intake ( $r(20) = -.37$ ,  $p = 0.08$ ). Participants with higher scores of problems with teeth and gums were less likely to use seasoning ( $r(20) = -.42$ ,  $p < 0.05$ ).

**Conclusion:** The findings support that HNC treatment can affect vegetable intake long after completion of radiotherapy. However, it would be premature for any recommendations to be derived from the present study for health professionals. A larger, observational study with a longer follow-up is therefore needed to examine these correlations.

## Introduction

Cancers arising from the oral cavity, oropharynx, nasopharynx, hypopharynx, and larynx are collectively referred to as head and neck cancers (HNCs) [1, 2]. It is the sixth most common cancer [3], affecting more than half a million patients worldwide [4] and approximately 4% of patients in the US [5], with a five-year survival rate of 60% [6] and a high rate of recurrence [7]. The majority of HNC patients undergoing aggressive treatments with chemo-radiotherapy and surgical resection of the tumors suffer from treatment-induced symptoms including dry mouth or mouth sores, difficulty swallowing, and taste dysfunction [8, 9].

Even when treatment ends, these side effects may persist [10]. HNC survivors often complain of an inability to taste their food and poor appetite, leading to compromised food intake [11], malnutrition [12], susceptibility to infection, and decreased survival [13].

The broad spectrum of impediments to oral nutritional intake can be conceptualized as Nutrition Impact Symptoms (NIS) [14] that can occur as side effects of anticancer treatment [15]. Some prior epidemiological and intervention studies have suggested that increasing intake of vegetables before [16] and following diagnosis with HNC may improve clinical outcomes such as disease recurrence [17] and survival [18, 19]. Despite an increasing focus on the beneficial effects of fruits and vegetables on cancer survival [19-21] we still know very little about how the burden of these post-treatment symptoms may influence HNC patients vegetable intake. To our knowledge, this topic has not been investigated in HNC patients, therefore, we explored it with a structured questionnaire. The purpose of this study was to examine how NIS is related to HNC survivors' vegetable intake and use of seasoning. Our hypothesis was that HNC survivors with a higher score of NIS may have lower intake of vegetables and higher use of seasoning in a response to blunt taste perception due to NIS reflected by statistically significant correlation coefficients. This research has the potential to design future observational studies to further evaluate these relationships and develop interventions aimed at increasing vegetable intake among HNC survivors.

## **Materials and Methods**

### **Ethical approval, survey administration, and data collection**

The study was approved by the Institutional Review Boards of Carle Foundation Hospital. Informed verbal consent was obtained from all participants before data collection. The 29-items telephone administrated survey developed by the research team consisted of data on participants' background information; vegetable intake; seasoning behaviors; and NIS. The scale to collect information on NIS was adapted from the M. D. Anderson Symptom Inventory HNC module (MDASI-HN) [22]. We only used 11 of the 22 MDASI-HN items because we were only interested in those symptoms that were considered NIS and ones that would impact the ability or desire to eat. The 11 items (problems with fatigue, lack of appetite, dry mouth, swallowing difficulty, tasting foods, numbness/tingling, mouth sores, teeth or gums, voice/ speech, choking or coughing, and mucus in the mouth and throat) included a scale between 0 and 10, where "0" represents "not present at all" and "10" represents "as bad as you can imagine". These items were generated from a comprehensive literature review and focus groups with HNC patients, symptom researchers, and a multidisciplinary group of HNC health care workers [22]. Participants who rated the symptom as greater than 0 (no symptom at all) on a scale of 0-10 points were classified as having experienced the symptom at some levels. A mean composite score of NIS was created by summing of 11 individual symptoms scores where higher scores indicated higher NIS (a range of 0 to 10). We further classified the symptoms into two categories: low to moderate (persons who rated the symptom as 5 or less than 5) and moderate to worst (persons who rated the symptom as 5 or greater). Potential study participants (n=40) were enrolled into the SYNQ - "Symptoms, Nutrition, and Quality of Life study with a history of stage I-IV primary cancer of the oral cavity, oropharynx, hypopharynx, or larynx within 6 months to 10 years post-treatment with chemoradiotherapy. Details of the SYNQ study are described elsewhere [23]. HNC survivors who completed the first two SYNQ study visits between March 2018 and May 2019 were re- contacted via telephone and requested to participate in the survey for the current study. If the participant expressed interest, they were interviewed at that time or given the option of scheduling a preferred time in the future. Twelve participants declined to participate for various reasons (i.e., health issues, on feeding tubes, not interested in general) and six potential participants were not reachable at the time called. The final sample consisted of 22 HNC survivors who were interviewed between February and April 2020. Participants' self-reported demographics data were obtained from the SYNQ study and linked to the survey.

### **Statistical analysis**

We conducted descriptive statistics to examine the distribution and frequency of vegetable intake, use of seasoning, and vegetable preparation methods. In some cases, nominal data were condensed

from 4 to 2 categories to clarify results. Vegetable intake was calculated as cup equivalent per week (multiplying vegetable frequency with the portion size in a week), whereas 1 cup equals 1 cup cooked or 2 cups raw vegetables. We conducted chi-square tests to examine if there were any differences between total vegetable intake and participants' demographics, cancer duration, and whether they had changed their vegetable intake since the diagnosis of their cancer or not. Based on the distribution of the data that were not normally distributed, we conducted Spearman correlations to examine the correlations between NIS, vegetable intake, and seasoning. All statistical analyses were performed with SPSS version 25 [24]. Two-tailed P values less than 0.05 were considered statistically significant for all analyses.

## Results

### Descriptive statistics

Table 1 displays descriptive statistics of study variables.

| Variables   | N (%)     | Mean (Standard deviation, SD) |
|---|-----------|-------------------------------|
| Demographics  |           |                               |
| Age   | 22        | 61.4 (9.8)                    |
| Sex   | 22        |                               |
| Male  | 10 (45.4) |                               |
| Female  | 12 (54.5) |                               |
| Educational level   | 22        |                               |
| Less than high school   | 1 (4.5)   |                               |
| GED   | 7 (31.8)  |                               |
| Some college  | 7 (31.8)  |                               |
| 4-year college  | 4 (18.2)  |                               |
| More than 4-year college  | 3 (13.6)  |                               |
| Race  | 22        |                               |
| White   | 20 (90.9) |                               |
| Black   | 0 (0)     |                               |
| Asian   | 1 (4.5)   |                               |
| Native Hawaiian   | 0 (0)     |                               |
| American Indian   | 0 (0)     |                               |
| Others  | 1 (4.5)   |                               |
| Household income  | 22        |                               |
| Less than 15,000  | 0 (0)     |                               |
| 15,000-24,999   | 2 (9.1)   |                               |
| 25,000-34,999   | 5 (22.7)  |                               |
| 35,000-44,999   | 0 (0)     |                               |
| 45,000-54,999   | 4 (18.2)  |                               |
| More than 55,000  | 11 (50)   |                               |
| Time frame since HNC diagnosis  | 22        |                               |
| Less than 5 years   | 13 (59.1) |                               |
| More than 5 years   | 9 (40.9)  |                               |
| Vegetable intake and seasoning  |           |                               |
| Changes in vegetable intake since diagnosis                               | 22        |                               |
| Eat the same amount   | 11 (50.0) |                               |
| Eat more vegetable  | 9 (40.9)  |                               |
| Eat fewer vegetable   | 2 (9.1)   |                               |
| Mean vegetable intake; cup/per week (1 cup equivalence= 1 cup cooked or 2 |           |                               |



|   |           |           |
|---|-----------|-----------|
| cups raw vegetable)   |           |           |
| Green leafy vegetables  | 1.5 (1.4) |           |
| Cruciferous   | 0.8 (0.9) |           |
| Carrots and tomatoes  | 2.0 (1.6) |           |
| Sweet potatoes and pumpkin  | 0.3 (0.2) |           |
| Corn and peas   | 0.8 (0.7) |           |
| Potatoes (white)  | 1.0 (0.9) |           |
| Other vegetable   | 0.6 (0.5) |           |
| Total vegetable   | 7.1 (3.9) |           |
| Seasoning vegetables  | 22        |           |
| Yes (if used always and/or half the time)                                 | 3 (13.6)  |           |
| No (if used rarely or not at all)   | 19 (86.4) |           |
| Why do season vegetables  | 3         |           |
| To make them taste better   | 3 (100)   |           |
| Covering up some flavors  | 0 (0)     |           |
| Added health benefits   | 0 (0)     |           |
| Seasoned vegetable taste better   | 22        |           |
| Yes   | 1 (4.5)   |           |
| Some of them  | 7 (31.8)  |           |
| No  | 14 (63.6) |           |
| Buying frozen seasoned vegetables   | 22        |           |
| Yes, half the time  | 5 (22.7)  |           |
| Rarely  | 1 (4.5)   |           |
| No  | 16 (72.7) |           |
| How like vegetables prepared in general                                   | 22        |           |
| Steamed/microwaved  | 4 (18.2)  |           |
| Boiled  | 14 (63.6) |           |
| Roasted/grilled   | 2 (9.1)   |           |
| Stir-fry  | 2 (9.1)   |           |
| How like vegetables prepared at home                                      | 22        |           |
| Steamed/microwaved  | 4 (19.0)  |           |
| Boiled  | 10 (47.6) |           |
| Roasted/grilled   | 2 (9.7)   |           |
| Stir-fry  | 0 (0)     |           |
| Simmered  | 6 (23.8)  |           |
| NIS scores  |           |           |
| Composite (NIS) score (mean)  | 22        | 3.9 (1.6) |
| Individual NIS score  |           |           |
| Fatigue   |           | 3.1 (3.2) |
| Lack of appetite  |           | 2.5 (2.5) |
| Dry mouth   |           | 6.0 (2.7) |
| Numbness  |           | 3.3 (3.4) |
| Mucus in mouth and throat   |           | 3.7 (3.1) |
| Difficulties swallowing   |           | 5.1 (2.9) |
| Choking/ coughing   |           | 4.0 (2.7) |
| Difficulties tasting foods  |           | 5.6 (3.2) |
| Problem with teeth/gums   |           | 3.2 (3.3) |
| Mouth sores   |           | 2.7 (2.9) |
| Problem with voice  |           | 3.8 (2.7) |
| Overall NIS burden  |           |           |
| Low to moderate (participants who rated the symptoms as 5 or less than 5) | 59        |           |
| Moderate to worst (participants who                                       | 41        |           |

rated the symptom as 5 or greater)

**Table 1. Descriptive Statistics of Study Variables: Demographics, Vegetable Intake, Seasoning, and NIS.**

The mean age of study participants (n=22) was  $61.4 \pm 9.8$ . Most participants (31.8%) either completed high school or GED or some college degree, 54.5% were female, 90% were White, and most (50%) had annual household incomes of \$55,000 or more. More than half (59.1%) of the participants were diagnosed with HNC for less than 5 years. Half (50%) of the participants reported that they had not changed their vegetable intake since their cancer diagnosis. Most participants (86.4%) did not use or rarely used seasonings, and among those who used seasonings regularly (n=3), all reported that they used seasonings to make vegetables taste better. Almost half of the participants (40.9%) preferred boiled as their vegetable preparation method. On average, participants ate green leafy vegetables as 1.5 cups eq/week, cruciferous as 0.8 cups/week, carrots, and tomatoes as 2 cups/week, sweet potatoes and pumpkin as 0.3 cups/week, corn/peas as 0.8 cup/week, others as 0.6 cup/week, and total vegetables as 7.1 cups/week. Only one participant (Female, aged 65 years old) met the recommended weekly value of total vegetable intake which is 2 cups/day (USDA and HHS, n.d.). We did not find any statistically significant difference between participants' vegetable intake and whether they had changed their vegetable intake since HNC diagnosis. We were also interested to see if there were differences in demographics by total vegetable intake, however, we did not find any significant differences observed between high vs. low vegetable intake and demographics such as sex, race, education, and income. The mean composite score of NIS was 3.9 (SD = 1.6, Range: 6.2, minimum 1.8, maximum 8.0), indicating that on average, most participants had suffered from some forms of NIS and experienced symptoms burden. More than 50% of the participants reported experiencing at least one symptom. Over half of the participants (59.0%) had experienced symptoms at the low to moderate level.

## Correlation between NIS, vegetable, and seasoning

Table 2 presents the correlation matrix among NIS, vegetable intake, and seasoning. The NIS composite score had positive, moderate correlations with sweet potatoes and pumpkin intake,  $r(20) = .43$ ,  $p < 0.05$ .

| Variables            | Composite score of NIS                |
|----------------------|---------------------------------------|
| Vegetable intake     |                                       |
| Green leafy          | 0.14                                  |
| Cruciferous          | 0.17                                  |
| Carrots and tomatoes | 0.1                                   |
| Sweet potato/pumpkin | .43*                                  |
| Corn/peas            | -0.16                                 |
| Potatoes             | -0.06                                 |
| Others               | -0.06                                 |
| Total                | 0.18                                  |
| Use of seasonings    | -0.02                                 |
|                      | Individual NIS: Difficulty swallowing |
| Vegetable intake     |                                       |
| Green leafy          | -0.25                                 |
| Cruciferous          | -0.33                                 |
| Carrots and tomatoes | -0.01                                 |
| Sweet potato/pumpkin | 0.17                                  |
| Corn/peas            | -0.37                                 |
| Potatoes             | -0.36                                 |
| Others               | -0.38                                 |
| Total                | -0.3                                  |
| Use of seasonings    | 0.01                                  |

|                      | Individual NIS: Problems with teeth and gums |
|----------------------|--|
| Vegetable intake     |  |
| Green leafy          | -0.01  |
| Cruciferous          | 0.27   |
| Carrots and tomatoes | -0.16  |
| Sweet potato/pumpkin | 0.24   |
| Corn/peas            | -0.11  |
| Potatoes             | 0.01   |
| Others               | -0.18  |
| Total                | -0.08  |
| Use of seasonings    | -.42*  |

**Table 2. Bivariate Correlations among NIS, Vegetable Intake, and Use of Seasoning.**

\*Correlation is significant at the 0.05 level (2-tailed)

None of the correlations were significant ( $p < .05$ ) (results not shown) for individual NIS score and seasoning, except for the problems with teeth and gums (Table 2). Problems with teeth and gums had a negative, moderate correlation with seasonings,  $r(20) = -.42$ ,  $p=0.04$ . Difficulty swallowing was negatively correlated with corn and pea intake; however, the relationship was not significant,  $r(20) = -.37$ ,  $p=0.08$ .

## Discussion

NIS has been reported to negatively affect the HNC patient's eating behavior and quality of life throughout the period of treatment as well as a period of time after treatment [14, 25]. We found that over half of the participants (59.0%) had experienced NIS at the low-to- moderate level and more than 50% reported experiencing at least one symptom. A study [25] describing the prevalence of symptoms in HNC survivors ( $n=54$ ) reported that nearly all participants (95%) reported experiencing at least one symptom from the original version of MDASI-HN. However, that study only recruited 5-year HNC survivors, whereas most (59.1%) of our participants were 5 or less than 5-year HNC survivors. They also used the original version of MDASI-HN with more than 22 items while we used the adapted version of MDASI-HN with 11 items. In a qualitative study involving in-depth interviews with 15 HNC patients undergoing treatments, researchers found patient's decreased quality of life with intense symptoms that included the mucosa in the oral cavity and the salivary gland, leading to chewing and swallowing difficulty and poor nutrition status [26]. Another study [27] that evaluated changes in NIS using a different tool (HNC symptom checklist) found that about 80% HNC patients had NIS before the start of treatment, followed by all patients experiencing taste changes and a dry mouth. Similarly, we found that more than 95% of participants experienced dry mouth or difficulty swallowing. In contrast, a study [14] that developed and piloted a NIS checklist among advanced nutrition- fatigue clinic patients ( $n=52$ ) found that only 27% of HNC patients had taste and smell alterations, followed by difficulty swallowing (11.5 %). Similarly, in a cross- sectional study comparing the taste and smell intensities among HNC survivors and healthy control, researchers found no significant differences between groups in the whole mouth. However, HNC survivors were less likely to identify low concentrations of bitter, sweet, or salty stimuli in the tongue tip relative to healthy controls [28]. Although a few reported studies involving HNC survivors have shown the negative effects of NIS on patient's nutritional status [27] and the overall quality of life [29], to the best of our knowledge, there are no studies that have evaluated the relationship between NIS, vegetables, and seasonings. This study is therefore timely as interest grows in interventions for HNC survivors and ones that may increase vegetable intake. About half of the participants reported that they had not changed their vegetable intake since the diagnosis of their cancer. On average, our participants ate 7.1 cups equivalent of total vegetables per week (1.01 cup/day), which is far below the federal vegetable intake

recommendation(USDA and HHS, n.d.). However, our findings did not deviate from the national daily consumption of vegetables [30, 31]. Using data from the National Health and Nutrition Examination Survey (NHANES), Hoy et al. [30] examined adults' dietary intake and reported that among the low, moderate, and high levels, total daily vegetable intakes were 0.3, 0.6, and 1.4 cups of vegetables (excluding potatoes), respectively, which is similar to our participant's daily vegetable intake. A report published from NHANES 2007-2010 data also confirmed that the vegetable intakes among US adults are still below recommendations (USDA and HHS, n.d.). Only one study participant (female, aged 65 years old) met the recommended weekly value of total vegetable intake.

Most (>50%) of the participants did not use or rarely used seasonings (herbs and spices used other than salt, oil or butter, and pepper), and among those who used seasonings regularly, most users reported that using seasonings made their vegetables taste better. Isbill et al [32] conducted an exploratory study to understand the spice use behavior among the US adult population and found that the majority of participants (n = 380, 54%) were currently using one or more spices on a daily basis (black pepper and garlic were the 2 most commonly used spices daily). However, we asked our participants to list any seasonings other than plain salt, butter or oil, or black pepper. That might affect our findings that most of the participants did not use or rarely used seasonings since most people use salt, butter, or black pepper as their seasonings. Although a few studies reported that, given a choice, consumers were more likely to select a seasoned vegetable [33], or consumers purchased seasoned more often than steamed for most vegetables [34], we still know very little about the seasoning behavior among cancer survivors, especially when they cook at home rather than purchasing at the restaurant or takeout. Future studies could further explore the seasoning behavior among cancer survivors and compare these behaviors between home-cooked meals and takeout or dine-out.

We found that participants ate more sweet potatoes and pumpkin if they had a higher score of NIS. One possible explanation of this finding could be that participants could fully cook (i.e., boiled or baked) sweet potatoes or pumpkins, and since these vegetables are naturally sweet and become soft following cooking, that was somewhat easy for them to swallow considering their challenges to eat. This finding is consistent with our finding that almost half of the participants preferred boiling followed by steaming as their vegetable preparation method, and they could either easily boil or steam sweet potatoes or pumpkin. Our findings are supported by the study conducted by Kimmons et al. [31], where they found that potatoes (including sweet potatoes) dominated vegetable consumption among the US adult population. Kimmons' work confirms that for the US population in general, whether they are healthy or have any chronic medical condition and associated complications, prefer starchy vegetables over other vegetable categories. We did not find any other significant correlations between NIS and vegetable intake, except sweet potatoes and pumpkins. Similarly, a study [27] evaluating NIS on nutritional status among HNC survivors did not find any significant change in patients' total energy and total protein intake over time. The effect of NIS on HNC survivors' dietary intake and the overall quality of life is still inconclusive; more studies with a larger sample size and long follow-up are warranted to further explore this association, with particular focus on fruit and vegetable intake.

We further evaluated whether individual NIS score was correlated with vegetable intake and seasonings and only found a statistically significant inverse correlation between problems with teeth and gums and seasoning. One possible explanation for this finding could be that patients who have problems with teeth and gums might have pain in their gums that might be further triggered using seasoning in the food. A review conducted by Miranda-Rius et al [35] reported that people with teeth and gum problems in general experienced burning sensation or pain that is intensified by eating hot, acidic, or spicy foods. In contrast, in a recent meta-analysis of five prophylactic trials including 223 patients, researchers found curcumin's beneficial effect in reducing the severity (RR 0.48, 95% CI=0.23,0.99) and delaying of the onset of treatment- induced oral mucositis, OM (RR 0.38, 95% CI=0.18,0.80), but not preventing the overall incidence (RR 0.99 95%CI=0.95,1.03) [36]. However, this population is different than that of our study population who might not be using the



same seasoning in their vegetable preparation. Therefore, more research is needed among a diverse group of HNC patients to confirm the effect of various herbs and spices in reducing treatment-induced unpleasant side-effects that may hinder their overall oral intake.

To our knowledge, this is the first study to examine the relationship between NIS, vegetable intake, and seasonings. Although previous reviews of the literature show that cancer treatment side effects are associated with decreased nutrition and quality of life, our data suggested that NIS had little to do with the patient's vegetable intake or use of seasonings. However, our study was limited in scope in that the participant's overall oral intake was not evaluated. Other limitations included a small sample size, self-reported data on vegetable intake, seasoning use, and NIS. It is also important to note that, the population for this survey is not reflective of the overall HNC population in terms of sex and race, which might affect some findings including the report of not changing vegetable intake since diagnosis or eating more vegetables now (e.g., potential for social desirability bias, for example, female is more likely to report positive health behaviors such as eating more fruits and vegetables).

Since some studies have shown the effect of NIS on cancer patients' overall oral intake, future interventions that aim to promote fruit and vegetable intake among HNC survivors should be designed to continuously monitor and manage these symptoms throughout the cancer continuum and adapt accordingly. Before developing an effective intervention, future studies to further evaluate the effect of NIS on vegetable intake should focus on rigorous study design (e.g. large sample size, at least 100 -500, to narrow the margin of error to  $\pm 5\%$ , long follow-up (e.g. at least 1 year, with 2-3 times of both NIS and dietary assessments, objective measures (e.g. a well-designed food frequency questionnaire along with a recovery biomarkers such as vitamin C or other nutrients, as of true intake of vegetables [37-39]. Future research could also further identify the symptoms in detail and their effect on vegetable intake using a combination of research methods, possibly focus groups and surveys.

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