DEMOGRAPHIC CORRELATES OF PATIENTS WITH HEAD-AND-NECK CANCER RECEIVING RADIOTHERAPY

by

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ABSTRACT

Background: Patients with head-and-neck cancer (HNC) often require some form of enteral feeding during their treatment due either to the presence of the tumor or as a result of radiation treatment (RT). Because of the catabolic nature of the disease and severe consequences of the radiation treatment, many patients benefit from enteral nutrition (EN). This improves the nutritional status of the patient and allows the patient to continue with their treatments. Studies have identified clinical predictors associated with the decision to initiate EN, but there is a dearth of information regarding demographic correlates.

Objective: The purpose of this study was to identify whether demographic variables, such as age, gender, religious affiliation, marital status, and ethnicity of patients with HNC are predictors of the decision to initiate EN feedings.

Methods: A retrospective chart review of 123 patients with HNC was conducted. Patients were excluded if there was no information of RT, EN initiation prior to the start of RT, or no primary diagnosis of HNC. Demographic information, anthropometrics, and enteral feeding initiation date were recorded from the Registered Dietitian and oncologist's notes. Percent body weight loss was calculated from the recorded weights at four points throughout the treatment. Results were analyzed with Spearman's correlation, chi square tests, Mann-U Whitney Tests, and linear regression models.

Results: Religious affiliation, weight change from diagnosis to RT completion, and weight change from the start to completion of RT were the only significant predictors of EN initiation

(p=0.008; p=0.01; p=0.001). Age, ethnicity, and marital status were not related to EN initiation or the timing of EN initiation.

Conclusions: Religious affiliation and weight loss were significant predictors of EN initiation. Because of an informal guideline internal to the cancer treatment center monitoring and recommending EN to patients with >5% weight loss, bias was reduced. Therefore, policies that are based on percent body weight loss may be helpful in reducing EN placement bias.

DEDICATION

This thesis is dedicated to all those who supported and guided me through the process of writing this manuscript. In particular, my family, who have been a constant source of comfort and encouragement throughout this arduous process.

LIST OF ABBREVIATIONS AND SYMBOLS

AJCC	American Joint Committee on Cancer
BMI	Body Mass Index
EN	Enteral Nutrition
HNC	Head-and-Neck Cancer
HNSCC	Head-and-Neck Squamous Cell Carcinoma
HPV	Human Papillomavirus
IMRT	Intensity-Modulated Radiation Therapy
MCC	Manderson Cancer Center
NG	Nasogastric
PEG	Percutaneous Endoscopic Gastrostomy
QoL	Quality of Life
RT	Radiation Therapy or Radiotherapy
SEER	Surveillance, Epidemiology, and End Results Program
P	Probability associated with the occurrence under the null hypothesis of a value as extreme as or more extreme than the observed value
R	Spearman product-moment correlation
<	Less than
=	Equal to
>	Greater than
±	Plus or minus
%	Percent

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CHAPTER 1

INTRODUCTION

Head-and-neck cancer (HNC), or head and neck squamous cell carcinoma (HNSCC), are terms used to describe several cancer locations, including: oral cavity, pharynx, paranasal sinuses and nasal cavity, and salivary glands.[1] Patients with HNC constitute about 3.7% of all cancer patients,[2] and over 61,000 new cases were diagnosed in 2016.[3] About 75% of all HNC cases can be attributed to cigarette smoking and/or alcohol consumption.[4] Certain types of human papillomavirus (HPV) can lead to oropharyngeal cancers.[5] Cancer in the head-and-neck region is diagnosed by a medical doctor by an initial physical examination and then by inspecting a sample of the suspected carcinoma under a microscope.[1]

After a positive diagnosis of HNC is made, treatments include surgery, radiation, chemotherapy, or a combination of treatments. These treatments have side effects that can severely impact a patient's ability to maintain nutrition status. Surgery will cause swelling for only a few weeks, unless lymph nodes are also removed, in which case the swelling will remain for longer, which can negatively affect patients' ability to chew and/or swallow.[1] Patients with more advanced stages of cancer will often be treated with a combination of radiation and chemotherapy. Radiation treatment (RT) has many side effects including: redness and irritation of the treatment site, sores in mouth, dry mouth, thickened saliva, difficulty swallowing, changes in taste (including loss of taste in some cases), stiff jaw, and nausea.[6] Side effects of RT inhibit a patient's ability to eat due to a combination of pain, lack of interest in food (related to nausea or changes in taste), and difficulty eating (due to dry mouth, thickened saliva, or difficulty in

opening the mouth).[6] These difficulties from treatments, in addition to the catabolic nature of the disease, lead to malnutrition in many patients with HNC.

Malnutrition is more prevalent in patients with HNC compared to other cancers. In fact, patients who suffer from HNC have a malnutrition rate of 24% prior to RT and 88% after RT.[7] In other cancers, the prevalence of malnutrition is much lower: 30% before and 37% after RT.[7] This difference in the prevalence of malnutrition before and after RT demonstrates how devastating the treatment of HNC is due to the location of the disease. As such, many patients begin to use enteral nutrition (EN) to meet some or all of their nutrition requirements to address the issue of malnutrition.[7]

EN, also referred to as "tube feeding", is a way to deliver nutrients to a patient through a tube inserted directly to the stomach or small intestine, thus bypassing the structures affected by HNC. Two main types of tube feedings are a nasogastric (NG) tube and a percutaneous endoscopic gastrostomy (PEG) tube. A NG tube is placed through a patient's nose to deliver nutrients to the stomach and is indicated for short term use, typically <2 weeks, but no longer than 3-4 weeks. A PEG tube is surgically placed in the stomach and is used for patients requiring EN for >2 weeks.[8]

Many benefits of EN have been reported, including decreased weight loss, improved quality of life (QoL), and reduced number of days spent in the hospital.[9-17] Previous studies have identified several clinical risk factors for EN initiation, but few studies have considered demographic predictors. If groups of patients with specific demographic characteristics are found to initiate EN significantly less often than other groups, future research should identify barriers or bias related to not initiating EN in patients with these specific demographic characteristics. Further, if barriers to initiating enteral nutrition are identified within patients with certain

demographic characteristics, targeted interventions can be developed to address these barriers for these patient populations.

The specific aims of this study were to identify the relationships between demographic variables (age, ethnicity, and marital status) and enteral nutrition initiation as well as the relationships between demographic variables (age, ethnicity, and marital status) and the timing of enteral nutrition initiation. The investigation applied the following hypotheses:

> Hyp 1: Demographic variables (age, ethnicity, and marital status) are significantly related to enteral nutrition initiation in HNC patients receiving RT.
>
> Hyp 2: Demographic variables (age, ethnicity, and marital status) are significantly associated to the timing of enteral nutrition initiation in HNC patients receiving RT.

Additionally, a secondary aim of this study was to explore relationships of gender and religious affiliation with initiation and timing of enteral nutrition. As there is a dearth of literature to support a preliminary hypothesis for the secondary aims, this aim was only be exploratory in nature.

CHAPTER 2

LITERATURE REVIEW

About Head-and-Neck Cancer

During oral feedings, food first passes through the oral cavity. This is the area behind the teeth, including the palate (roof of the mouth), tongue, cheeks, lips, and gums. When people swallow, the soft palate and uvula move to prevent food from entering up into the nasal cavity. Food then moves towards the pharynx, more commonly known as the throat. The pharynx is made of three sections: nasopharynx (upper part of pharynx by the nasal cavity), oropharynx (middle section of pharynx at the back of the mouth), and the laryngopharynx (lowest section of pharynx that connects the throat to the esophagus). The upper two sections of the pharynx are heavily involved in the swallowing mechanism; this is the primary function of the pharynx.[18]

Both the oral cavity and the pharynx are lined with stratified squamous epithelium. Epithelial tissue is one of the four primary types of tissue that typically act as barriers. This tissue is made of layers of tightly packed cells, called squamous cells, which have a flattened shape.[19] Their flattened shape allows them to form sheets, and contribute to their ability to act as a barrier. Ninety percent of HNC is cancer of the squamous epithelium, referred to as HNSCC[20] The other 10% of cases generally occur in salivary glands due to their mucus-secreting function, and include: adenoid cystic carcinoma, mucoepidermoid carcinomas, and adenocarcinomas.[21] These are common in salivary glands as these cancer types involve mucus-secreting cells. Some of the symptoms of HNC include a non-healing lump or sore, difficulty in swallowing, and a hoarseness in the voice.[1] The two main risk factors for HNC are cigarette smoking and heavy

alcohol consumption.[1,4] HPV is also a risk factor for HNC, specifically oropharyngeal cancer.[5] Patients with HPV-positive cancers typically have a better prognosis than HPV-negative cancers due to an increased sensitivity of HPV-positive cancers to chemoradiotherapy.[22]

Cancer Staging

The American Joint Committee on Cancer (AJCC) has developed a process to determine the amount of cancer in the body and where that cancer is located. The stage designation ensures clear communication between healthcare professionals.[23]

There are four main steps of staging: clinical, pathological, post-therapy, and restaging. Clinical staging is the initial step that involves physical exams, imaging, and biopsies. Pathological staging involves surgery to remove the tumor and combines the clinical results with the surgical results. Post-therapy staging describes the amount of cancer remaining after systemic treatment (chemotherapy or hormone therapy). Finally, restaging is conducted to evaluate the extent of the disease if cancer comes back after treatment.[23]

The most common staging system used is the TNM system. After determining the primary location of the tumor, the three main factors evaluated are represented by the letters of TNM. The T stands for tumor size and extent of tumor, N represents whether or not the cancer has spread to the lymph nodes, and M indicates the presence of metastasis (if the cancer has spread to distant parts of the body). A numeric designation for each of the letters is given, the higher the number, the more severe the disease.[23]

Treatments

After a diagnosis of HNC, the physician will decide which treatment options are best based on the specific carcinoma. If the carcinoma is accessible, surgery is used to remove the

carcinoma and some of the surrounding healthy tissue. If the physician suspects the tumor has spread, the surrounding lymph nodes will be removed as well. One surgery may not be sufficient to remove all of the tumor, in which case additional surgeries, radiation, or chemotherapy may be completed.[24]

The side effects associated with surgery are dependent on the location of the surgery. However, typical side effects include temporary loss of speech, swelling, difficulty chewing and swallowing, and possible disfigurement.[24] Because of the location of HNC, surgeries may cause a patient to require EN to meet their nutritional needs.

Radiation, also referred to as radiotherapy, is another common treatment for HNC that can be used to remove traces of cancer post-surgery, or as the primary treatment modality. RT involves the use of high amount of x-rays to kill cancer cells and shrink tumors. The most common form of RT is external beam radiation, and more specifically, intensity-modulated radiation therapy (IMRT). IMRT allows the physician to send several beams of radiation of varying intensity to target the tumor and preserve the healthy tissue as much as possible. The physician will develop a treatment plan for the patient that is typically described as the number of radiation sessions over a certain period of time. The typical treatment plan is a once daily dose of radiation, five days a week (typically Monday through Friday), for 6-7 weeks.[6]

The side effects of RT are not insignificant. Fatigue, hair loss, mouth changes (including sores, dry mouth, thick saliva), skin changes (redness, irritation), taste changes (metallic taste, loss of taste), and swallowing issues can all negatively impact a patient's QoL as well as nutrition status.[6] With the litany of side effects that have nutrition implications, it is a wonder that only 42.8% of patients receiving radiotherapy receive a feeding tube.[25] Many of these side effects can linger past completion of treatments.

Chemotherapy uses drugs to inhibit or slow the growth of cancer cells to treat cancer or ease cancer symptoms. In HNC, the most relevant form of chemotherapy is adjuvant chemotherapy, which refers to treatment concurrent with surgery or radiation therapy. The mechanism of action for chemotherapy drugs lies in the ability to inhibit growth of cells. As cancer cells are rapidly dividing cells, the effect from chemotherapy drugs are apparent first in the cancer cells before becoming noticeable in normal, healthy tissues. However, there are some normal cells in the body that are also affected due to their rapid rate of cell division. Epithelial cells, such as skin cells and the lining of the digestive tract, are an example of these normally healthy tissues that are impacted. This damage to normal, rapidly dividing cells causes the common side effects of hair loss, nausea and vomiting, and mouth sores. Additional side effects include fatigue and risk of infection.[26] This combination of side effects affect patients' ability to maintain nutrition status unless they are properly managed through adequate nutrition support.

Targeted therapy is treatment that targets the genes of the cancer itself that are essential to growth and survival. Not all cancers respond to the same targeted genes, so tests should be run to determine the most effective target. Most HNC do respond to the specific tumor protein called epidermal growth factor receptor (EGFR). There are currently three FDA approved drugs for HNC. The most common side effects for these medications are diarrhea and liver complications (such as hepatitis and elevated liver enzymes).[27] Even with these recent advances in targeted therapies, many patients with HNC still receive RT as a first-line of treatment.

Enteral Nutrition

EN is a feeding modality in which the patient's energy needs are partially or completely met by depositing nutrients directly into the gastrointestinal tract through a tube or catheter. There are several options for nutrient delivery in EN, and the type of EN selected is based on

several variables. A few of these variables include: the amount of time that the patient is estimated to require EN, the risk of a patient aspirating (food moving into the lungs), and the clinical status of the patient. The three options for EN entry are: through the nasal passage, or percutaneous insertion into the stomach or small intestine. Because the nares are delicate, EN entry through the nose is only indicated for short-term use (3-4 weeks). If a patient requires EN for a longer period of time, entry into the stomach or small intestine would be more appropriate.[8]

If the stomach is functioning well, gastric entries are typically preferred as more of the gastrointestinal tract is utilized. Additionally, unlike the small intestine, the stomach can expand. Therefore, the patient would be able to receive a feeding with a high volume (bolus feeding). If gastric feedings are not tolerated or are contraindicated, then the patient will be fed jejunally. As the small intestine does not expand, a continuous feeding modality would be selected for jejunal feedings as opposed to a bolus feeding modality for gastric feedings therefore resulting in longer feeding times and limitations on mobility.[8]

If a feeding tube is placed, clinicians still encourage patients to continue eating an oral diet as tolerated and use the feeding tube to supplement. If the patient is not able to tolerate an oral diet, swallowing exercises are an essential part of maintaining the swallowing function to decrease what is called "prolonged feeding tube dependence".[28,29] Prolonged feeding tube dependence is the term used to describe patients who have finished RT and are still reliant on the feeding tube for either the majority or entirety of their energy intake. Prolonged feeding tube dependence can be problematic as feeding tubes are expensive, can interrupt a patient's normal activities, and minor complications can occur.[28] The possibility of becoming feeding tube dependent may partially address the question of why people might resist/avoid PEG placement.

This study will specifically examine the use of NG and PEG tubes, as these are the most commonly used tube feeding modalities in patients with HNC. As the names indicate, NG tubes enter through the nose and end in the stomach, whereas PEG tubes enter and deposit nutrients directly to the stomach. There is not a consensus in the literature as to which, NG or PEG placement, predicts better patient outcomes. Corry et al[30] found that patients with a PEG tube had significantly less weight loss than patients with a NG tube (gain of 0.8 kg; loss of 3.7 kg respectively; $p<0.001$), but placement and maintenance of a PEG tube was found to be about ten times more costly. QoL scores, however, were equivalent between the patient groups. A review of eight studies found no difference in weight maintenance or survival, but improved QoL in patients with a PEG tube.[31] However, this may be counter-intuitive as patients with a PEG tube had a delayed return to an oral diet and prolonged duration of radiotherapy as compared with patients with a NG tube.

Outcomes

The literature has shown positive outcomes in patients with HNC after PEG placement, including reduced weight loss, improved body mass index (BMI), and increased QoL. In a retrospective chart review including 565 patients with HNC, an average weight loss before PEG insertion was 23 +/- 17 lbs. After PEG insertion, average weight loss was 2.3 lbs. A total of 44% of these patients gained or maintained weight after PEG removal.[10]

A small study including 20 patients with HNC compared weight loss in patients with a prophylactic PEG with patients without a PEG. The PEG group lost an average of 1.1% of initial body weight by weeks 3-4 of radiation treatment, compared to a 3.0% loss of body weight in the non-PEG group. At the end of radiation treatment (weeks 6-7), the PEG group had lost an

average of 1.8% of body weight compared with 4.9% loss of initial body weight in the non-PEG group ($p=0.04$).[9]

Assenat et al[11] found that patients with a prophylactic PEG had a greater weight loss at the beginning of treatment compared with the patient group without a PEG placement (-5 kg vs -2 kg, respectively; $p<0.0001$). However, at the end of treatment, the prophylactic PEG group had lost less weight than the non-PEG group (-1 kg vs -5 kg; $p<0.05$). Results from a study by Bahl et al[12] report the greatest degree of recovery at one year in patients with a prophylactic PEG placement compared with no PEG placement (92%, 93.6% of baseline weight, respectively). In a study by Rutter et al[13], patients who received a PEG had significantly less weight loss at six weeks after the conclusion of chemoradiotherapy (CRT) compared with patients who did not receive a PEG (9.2% vs. 11.8% of baseline weight, respectively; $p=0.064$). Three months after the conclusion of CRT, the difference between these two groups becomes significant, with the PEG group losing less weight than the non-PEG group (19.5 lbs vs 30.1 lbs, respectively; $p=0.02$).

Much of the literature discusses the benefits of prophylactic PEG placement versus no PEG placement. However, it has been shown that the timing of EN is also important in affecting the amount of weight lost. Specifically, early initiation of EN (before week 3 of treatment) compared with late initiation of EN (after week 3 of treatment) has been shown to reduce weight loss.[13,32,33] In a study of 50 patients with advanced HNC, an average weight loss of 2.8% of baseline was found.[34] The authors attributed this low weight loss to the early EN initiation, as 86% of the patients initiated feeding before 3 weeks of treatment.[34] Beer et al[35] found that patients with a PEG before 2 weeks of RT lost less weight than patients with a PEG placed between 2 weeks and 3 months after the start of RT (-1.03 kg vs -4.0 kg, respectively; $p=0.004$).

One of the most significant benefits of PEG insertion is the improvement of QoL for the patient. Morton et al[14] found that change in BMI was inversely associated with QoL (R= -0.47, p=0.026). Results from a study including 533 patients with HNC further quantify this finding, stating that individuals with a >10% weight loss during treatment had lower QoL scores.[15] In an article reviewing quality of life and nutrition status, all 6 studies of HNC indicated a relationship between increased nutrition status and increased QoL ($p < 0.05$).[16] Because PEG tube placement has been found to improve BMI and nutrition status, it follows that PEG tube placement would improve QoL. In fact, 84% of patients with HNC who had a PEG tube stated that the PEG had a positive or neutral effect on their QoL.[17]

Although PEG tube placement has been shown to improve QoL for patients with HNC, there are negative perceptions to having a PEG tube. Social implications are the top reason patients with a PEG tube dislike the use of a PEG tube.[36-38] Eating food is considered a socially charged event. It is very common to gather with friends and family to share and create memories. The inability to join their loved one and ingest food orally in the same way may feel limiting. Additionally, patients may feel bound to their tube as an inescapable, constant reminder of their illness.[37,38] Therefore, a thorough understanding of the clinical and demographic factors affecting the decision to initiate tube feeding are important to guide culturally-relevant discussions with patients and families.

Clinical Predictors of EN/Rationale for Choosing Demographic Variables

There are several clinical predictors of EN already identified in the literature. These include BMI,[39,40] advanced tumor stage,[39-43] age,[39,42,44] and presence of chemotherapy.[42,43] However, these studies did not assess demographic variables beyond age and gender.

Demographic variables may be related to patient mortality as well as medical decisions, such as EN placement.

Three studies explored the relationship between demographic variables and survival rate in patients with HNC. Both Massa et al[45] and Choi et al[46] identified a relationship between demographic variables (increased age, male sex, black race, and being unmarried) and a decreased survival rate in patients with HNC. Kronski et al[47] specifically investigated the relationship between marital status in males with HNC and survival rate. This study found a negative relationship between unmarried status and survival rate (Hazard Ratio: 1.30; 95% Confidence Interval 1.12-1.51; p=0.0006).

Magnuson et al[48] investigated long-term feeding tube dependence in HNC patients (defined as having a feeding tube in place >12 months after completion of RT). Unmarried patients were 3.33 times more likely to have a feeding tube at 12 months than married patients (p=0.004). Additionally, African American ethnicity was significantly associated with feeding tube dependence in the bivariate analysis, but this association was not present in the multivariate logistic regression model after adjustment for partner status, radiation therapy, or tracheostomy dependence. Locher et al[49] considered demographic variables in prophylactic PEG placement. Unmarried (divorced, separated, widowed, single) patients were more likely to have a PEG tube placed than married patients (Odds Ratio: 1.47-3.55).

There are not currently any published works investigating the relationship between religious affiliation and EN initiation in HNC. In fact, the few published works that include religious affiliation and EN initiation all investigate end-of-life situations. To understand the implications of religion and EN initiation, one must understand the stance of the religion on artificial nutrition, or EN.

One of the main principles of Judaism is the sanctity of life. According to Jewish Law, although illness is a natural part of living, a person's duty is to strive to save a life. However, if a patient is suffering from a terminal disease, then the process of death should not be interrupted. Catholicism, like Judaism, posits that life is to be respected because it is a gift from God. Also like Judaism, the dying process should be respected if a patient is suffering. Islam stipulates that Muslims have a duty to receive the medical care required to heal them. As is the case for Judaism and Catholicism, patients who are terminally ill are not required to prolong death.[50] These views of the main three monotheistic religions could impact the decision-making involved in using EN if it is medically necessary to heal the patient.

Taken collectively, the existing literature suggests that early EN is beneficial for patients with HNC in terms of QoL and nutrition status (weight loss). However, there are demographic discrepancies in survival rates and PEG placements. Additionally, no previous studies have examined the relationship between religious affiliation and PEG placement. This current study can be helpful in identifying predictors and barriers in certain populations which could, in turn potentially have implications on patient health outcomes. If barriers to initiating enteral nutrition are identified, research can be done on interventions to alleviate these barriers for these patient populations.

CHAPTER 3

METHODOLOGY

Introduction

This pilot study was a retrospective chart review of patients treated for cancer of the head-and-neck region at the Manderson Cancer Center (MCC) in Tuscaloosa, AL. All data were obtained through the two medical record systems in use at MCC: ARIA and MediTech. The Institutional Review Boards at DCH Regional Medical Center and The University of Alabama have reviewed and approved this study.

Subjects

Charts were initially screened by the dietitian currently employed at the MCC for the diagnosis of cancer in the head-and-neck region. Two hundred and three patients were initially identified in this convenience sample and further screened by the principle investigator to meet inclusion/exclusion criteria until 123 charts were finally included. Patients that were 18 years of age and older with a diagnosis of cancer of the head-and-neck region treated with radiation were included. Patients were excluded from the study if the carcinoma was not in the head-and-neck region, had not completed RT, or had a PEG or NG tube placement prior to commencement of RT.

Variables collected included: specific cancer location, TNM stage, date of birth, gender, ethnicity, marital status, religious affiliation, smoking status, weight (at diagnosis, beginning and end of RT, and EN initiation), height, RT modality, RT initiation date, RT plan (total number of

sessions/period of time), presence of concurrent chemotherapy, type of chemotherapy used, weight change, EN initiation (yes/no), type of EN, date of EN initiation, and number of radiation treatment sessions completed at the point of EN initiation.

Weight change data were assessed from 5 different points, between: 1) diagnosis and start of RT, 2) diagnosis and completion of RT, 3) start of RT and completion of RT, 4) start of RT and EN initiation, and 5) EN initiation and completion of RT.

Statistical Analysis

Descriptive statistics for this study include age at the time of diagnosis, gender, ethnicity, marital status, religious affiliation, BMI, AJCC stage, smoking status, chemotherapy treatment, and type of EN used After assessing the data for distribution normality, the appropriate parametric or non-parametric tests were used. All tests were two-tailed and a significance level of $p<0.05$ was used. Chi square test for independence and Mann-Whitney U Tests were used to analyze the relationship between EN vs no EN (NEN) groups and age, gender, ethnicity, marital status, and religious affiliation. Spearman's correlation, independent sample t-tests, and ANOVA were used to assess the relationship between the timing of enteral nutrition initiation and age, gender, ethnicity, marital status, and religious affiliation. Weight change data were analyzed via Mann-Whitney U tests and Wilcoxon Signed Rank tests. Linear and logistic regression models were used to further analyze the data to determine predictors of EN initiation.

CHAPTER 4

RESULTS

A total of 203 patients with head-and-neck cancer were initially identified; however 82 patients were excluded from the study due to: a lack of a primary diagnosis of HNC (n=3), RT not being completed (n=8), EN that was initiated prior to the first RT session (n=48), or lack of treatment information available (n=20). A total of 123 patients met the inclusion criteria, with a mean age at diagnosis 64.1 years (SD ±12.3 years), and a mean BMI of 26.5 kg/m^2 (SD ±5.3 kg/m^2). A majority of this population was male (78%) and about half were unmarried (42.3%). Additional demographic information for patients included in the study (n=123) are presented in Table 1.

The results of Mann-Whitney U tests showed no significant difference in percent weight change between diagnosis and initiation of RT between the EN and NEN groups. It did show a significant difference in percent weight change between diagnosis and completion of RT between EN and NEN groups (p=0.01) as well as between the beginning and end of RT (p=0.001). Additionally, results of related-samples Wilcoxon Signed Rank testing showed a significant difference between percent weight change before and after EN initiation (-9% before, -1% after; p=0.004). Results for percent weight change at five different analysis intervals are presented in Table 2.

Spearman's correlational analysis was performed with all demographic and weight change variables to investigate relationships with EN initiation (Hypothesis 1). After this univariate analysis, three variables were significantly correlated to EN initiation: percent weight

change between diagnosis and completion of RT (p=0.007), percent weight change between start and completion of RT (p=0.001), and religious affiliation (p=0.008). However, religious affiliation had 9 categories, which were then condensed down to three for analysis purposes: Christian (n=63), none specified (n=57), and other (n=3). Due to the small sample size, "other" was not included in analysis. After condensing the religious affiliation variable, Spearman's correlation was performed again, with religious affiliation remaining significant, indicating that patients that self-identified as Christians were more likely to initiate EN than those who did not specify a religion (R= -0.202; p=0.011). Therefore patients that identified as Christian were more likely to initiate EN than patients who did not specify a religion. Other demographic variables (age, gender, marital status, race) were not found to be significantly related to EN initiation.

The three significant variables from the univariate analysis were entered into a linear regression model to identify predictors of EN initiation. As the variables 'percent weight change between diagnosis and completion of RT' and 'percent weight change between start and completion of RT' exhibit multicollinearity, percent weight change between start and completion of RT was used in linear regression analysis along with religious affiliation. In the regression model, religious affiliation and percent weight change between RT start and completion remained significant (p=0.012, p=0.004, respectively). To investigate the relationship of demographic variables with timing of EN, measured as days from start of RT date to date of EN initiation (Hypothesis 2), Spearman's correlation analyses were performed. No variables collected were found to be associated with the number of days from RT initiation to EN initiation.

Table 1. Demographic Data of Patients with HNC Previously Treated with RT

Variable	Overall N (%) n=123	EN N (%) n=30	No EN N (%) n=93	Significance
Gender				
Male	96 (78%)	22 (73.3%)	74 (79.6%)	p=0.477
Female	27 (22%)	8 (26.7%)	19 (20.4%)	
Race				
White	92 (74.8%)	25 (83.3%)	67 (72.0%)	p=0.260
African American/Black	30 (24.4%)	4 (13.3%)	26 (28.0%)	
Asian	1 (0.8%)	1 (3.3%)	0 (0.0%)	
Marital Status				
Married	71 (57.7%)	20 (66.7%)	51 (54.8%)	p=0.267
Single	23 (18.7%)	5 (16.7%)	18 (19.4%)	
Divorced	16 (13.0%)	2 (6.7%)	14 (15.0%)	
Widowed	13 (10.6%)	3 (10.0%)	10 (10.8%)	
Religious Affiliation				
Christian	63 (51.2%)	22 (73.3%)	42 (45.2%)	**p=0.011**
None Specified	57 (46.3%)	8 (26.6%)	48 (51.6%)	
Other	3 (2.4%)	0 (0.0%)	3 (3.2%)	
BMI				
Underweight (<18.5)	7 (5.7%)	1 (3.3%)	6 (6.5%)	p=0.647
Normal (18.5-24.9)	42 (34.1%)	12 (40.0%)	30 (32.6%)	
Overweight (25-29.9)	46 (37.4%)	11 (36.6%)	35 (38.0%)	
Obese I (30-34.4)	17 (13.8%)	3 (10.0%)	14 (15.2%)	
Obese II (35-39.9)	8 (6.5%)	3 (10.0%)	5 (5.4%)	
Obese III (>40)	2 (1.6%)	0 (0.0%)	2 (2.2%)	
AJCC Stage (n=117)				
I	12 (9.8%)	1 (3.4%)	11 (12.5%)	p=0.254
II	22 (17.9%)	3 (10.3%)	19 (21.6%)	
III	30 (24.4%)	10 (34.5%)	20 (22.7%)	
IVA-C	53 (43.1%)	15 (51.7%)	38 (43.2%)	
Tobacco Use				
Never	27 (22%)	7 (23.3%)	20 (21.5%)	p=0.858
Former	54 (43.9%)	13 (43.3%)	41 (44.1%)	
Current	42 (34.1%)	10 (33.3%)	32 (34.4%)	
Primary Cancer Location				
Oral Cavity	6 (4.9%)	2 (6.6%)	4 (4.3%)	**p=0.002**
Nasopharynx	5 (4.1%)	0 (0.0%)	5 (5.4%)	
Oropharynx	49 (39.8%)	20 (66.7%)	29 (31.2%)	
Hypopharynx	4 (3.3%)	2 (6.6%)	2 (2.2%)	
Larynx	36 (29.3%)	5 (16.6%)	31 (33.3%)	
Salivary Glands	14 (11.4%)	1 (3.3%)	13 (14.0%)	
Paranasal Sinus/Nasal Cavity	1 (0.8%)	0 (0.0%)	1 (1.1%)	
Not Specified	5 (4.1%)	0 (0.0%)	5 (5.4%)	

Unknown	3 (2.4%)	0 (0.0%)	3 (3.2%)	
Chemotherapy				
Yes	82 (66.7%)	27 (90.0%)	55 (40.8%)	**p=0.002**
No	41 (33.3%)	3 (10.0%)	38 (59.1%)	
Chemotherapy Types (n=82)				
CISplatin	57 (69.5%)	22 (81.5%)	35 (63.6%)	p=0.069
Erubix	15 (18.3%)	4 (14.8%)	11 (20.0%)	
Carboplatin	1 (1.2%)	0 (0.0%)	1 (1.8%)	
Combination (2 or more)	9 (10.9%)	1 (3.7%)	8 (14.5%)	

Table 2. Percent Weight Change

% Weight Change for All Patients (n=123)	**Mean (+/- SD)**	**Range**	**Significance**
(1) Diagnosis to Radiation Start	0.02% (3.6)	-15% - +21%	
EN	0.39% (4.7)		p=0.759
No EN	-0.09% (3.2)		
(2) Diagnosis to Radiation End	-8.13 (6.0)	-24% - +11.46%	
EN	-13.2% (17.7)		**p=0.01***
No EN	-9.9% (18.3)		
(3) Radiation Start to Radiation End*	-8.08% (5.3)	-22.6% - +6.43%	
EN	-15.0%(30.9)		**p=0.001***
No EN	-10.2% (14.5)		
% Weight Change for EN Patients (n=30)			
Before and After EN initiation			
(4) Diagnosis to EN initiation	-9.02% (6.78)	-26% – +6.84%	**p=0.004****
(5) EN initiation to RT end	-1.03% (8.1)	-11% – +23.3%	

*Mann-Whitney test for statistically significant differences between patients with EN versus patients without EN

** Wilcoxon test for statistically significant differences before and after EN initiation

CHAPTER 5

DISCUSSION

The primary aim of this study was to investigate the relationship between demographic variables (age, ethnicity, and marital status) and the initiation of EN. Additionally, the relationship between demographic variables (age, ethnicity, and marital status) and the timing of EN was examined. The results of this investigation did not support the study hypotheses which were:

> Hyp 1: Demographic variables (age, ethnicity, and marital status) are significantly related to EN initiation in HNC patients receiving radiotherapy.
>
> Hyp 2: Demographic variables (age, ethnicity, and marital status) are significantly associated to the timing of EN initiation in HNC patients receiving radiotherapy.

Contrary to our original hypotheses, these demographic variables were not found to be significant predictors of EN initiation or timing of EN initiation.

The secondary aim was to investigate the relationship between religious affiliation and gender and initiation of enteral initiation. Although gender was not associated with feeding tube placement, religious affiliation was a significant independent predictor. In particular, patients who identified with the Christian faith were more likely to initiate EN.

The primary hypotheses were established based on results from previous studies. Sachdev et al[44] found that age was the single independent predictor of EN initiation after multivariate

analysis (p=0.003) and patients >60 years of age were 4.18 times more likely to initiate EN compared with patients <60 years of age (p=0.0019)[44]. Cheng et al[42] also found increased age to be related to EN initiation (Odds Ratio 1.3, p=0.02)[42]. Although this study had similar median, mean, and range of ages, the current study did not find the same relationship between increased age and increased EN initiation. Cheng et al[42] did not include protocols for recommending NG/PEG tube placement, which could explain the difference in the results of the study, as PEG tubes in the current study were recommended specifically based on percent body weight loss.

Results from a SEER-Medicare survey (n=8,306) showed that unmarried patients with HNC (including separated, divorced, widowed) were more likely to initiate prophylactic EN.[49] This current study did not show this result, possibly due to a much smaller sample size (n=123).

Magnuson et al[48] found a relationship between ethnicity and feeding tube dependence in univariate analysis, but this association was not present in multivariate analysis considering other factors. This lack of result in the multivariate analysis is consistent with the results of our study. Magnuson's study was conducted in Birmingham, AL; therefore both of these studies were conducted in a similar geographical area. This lends strength to the result of this study that ethnicity is not related to EN initiation. However, in studies looking at nursing home patients with severe cognitive impairment, African American patients were more likely to initiate EN than white patients.[51,52] This ethnic preference to initiate EN has not been found in studies in patients with HNC. A potential reason for this difference could be the lower number of African Americans in the present study.

However, this study used a convenience sample of the patients available at the MCC. The ethnicities of the study population (74.8% white and 24.4% African American) do not accurately reflect that of Tuscaloosa and the surrounding counties, which average 57.1% white and 41.0%

Black/African American according to the 2015 US Census Bureau.[53] This discrepancy can potentially explain the null result related to ethnicity. More significantly, this discrepancy points to a larger issue of access to care. This disparity in results points to a possible barrier to accessing proper medical care for African American patients. Further research should fully identify and address this issue.

Another reason could be the difference in purpose for utilizing EN in HNC compared with end-of-life scenarios. In HNC, patients generally can resume oral intake, and EN is a temporary measure. However, at the end-of-life, patients and their caregivers ponder ethical questions such as whether EN is prolonging life or prolonging death.[54] This ethnic disparity based on end-of-life situations is also seen in the Coping with Cancer study which included 606 patients with advanced cancer from across 5 states.[55] This study showed that black and Latino patients were more likely than non-Latino white patients to prefer life-prolonging care, such as a feeding tube, if it would extend life for 1 day (46% black patients, 41% Latino patients, 26% non-Latino white patients; $p<0.001$).[55] These results show that future studies should stratify the decision to initiate EN by prognosis.

With regards to the secondary aim, religious affiliation was found to be significantly related to EN initiation after univariate analysis ($p=0.008$). After condensing the nine categories into Christian, none-given, and other, religious affiliation was still found to be significantly associated with EN initiation ($R= -0.202$, $p=0.027$). There was a negative correlation, showing that patients who identified as Christians were more likely to initiate EN compared with patients who did not specify a religion.

Religion, faith, and spirituality are well documented to affect medical decisions.[56-58] In fact, in a study with 100 patients with advanced lung cancer and 257 medical oncologists,

Silvestri et al[59] found that, after the oncologist, the patient's faith in God was the most important factor affecting their treatment decisions. However, no previous studies have examined this in relation to EN. There are a few possible explanations for the correlation between self-identified Christians and EN initiation. One reason is that patients who specified Christian religion may have more social support through their church. One of the barriers to receiving EN is fear and anxiety surrounding the procedure and management of the feeding tube.[60] Religion can provide a social support for a patient that may ease the anxiety of initiating EN.[56,57]

A final possibility is that a pillar of Christianity is the sanctity of life.[50] Therefore, a patient who identifies as Christian may be more willing to begin EN to improve their life because their life is sacred according to their beliefs. A study examining spiritual coping mechanisms at the end of life found that patients who used spiritual coping were more likely to choose life-sustaining measures.[61]

After bivariate analysis, weight change between the start and completion of radiation treatment was also found to be significantly related to EN initiation ($p=0.004$). An informal interview with the radiation oncologists at MCC revealed that the oncologists recommended reactive EN on a case-by-case basis. Specifically, if a patient lost 5% of his/her body weight, special attention would be given, and by a 10% loss in body weight, EN would be placed. This is not a written hospital policy, but rather a general guideline that the radiation oncologists follow. The results of this study suggest that physicians were following this guideline. Additionally, based on the lack of significant differences between age, gender, ethnicity, and marital status and EN initiation, this informal guideline seems to have reduced potential bias in EN placement.

The results of this study have also shown that EN initiation reduced weight loss from 9% before EN initiation to 1% after EN initiation ($p=0.004$). This confirms similar results from

Burney et al[9] that showed a reduction in weight loss after EN placement (23 lbs before, 2.3 lbs after). Previous studies have shown that weight loss in patients with HNC is associated with a reduced QoL.[13,14] Specifically, Languis et al[14] showed a 10% weight loss was associated with a reduced QoL.

Because EN is shown to reduce weight loss, which can improve outcomes and QoL, there is an argument to implement a standard policy in which EN is recommended before a patient has a 10% weight loss. The informal guidelines that the oncologists at MCC follow (monitoring a patient at 5% weight loss, if there is no improvement, then recommend EN initiation) demonstrate the ability to reduce a patient's weight loss and reduce bias in EN placement.

This study was limited by the small amount of patients who received EN. This limits the ability to draw conclusions about the population that did receive EN. However, no other variables tested were close to being significant, and the authors are confident that the religious affiliation and weight change were the only significant predictors of EN initiation in this population.

Another limitation was the retrospective design. This limited the variables available to be collected. Religious affiliation was a question on an initial admittance questionnaire, and if a patient did not fill out a religious affiliation, it is unclear as to the reason. Thus, the meaning of the association between religious affiliation and EN initiation cannot be fully explained. As there was such a small sample size of patients with EN (n=30), future studies should include a larger amount to further investigate demographic correlates of the timing of enteral initiation (days from RT start to EN initiation).

As demonstrated above, a policy based on weight loss appears beneficial in reducing bias related to EN initiation. In particular, a policy in which patients with a 5% weight loss are closely monitored, and if weight does not stabilize EN is initiated, was helpful. Therefore, a larger, prospective study is warranted using this policy. Patient attitudes towards the recommendations should be collected, as this will add to the literature.

In conclusion, while age, ethnicity, and marital status were not associated with EN initiation or timing of EN initiation, patients who identify as Christian tend to start EN more than patients who do not specify a religion, and percent weight loss is a predictor of EN initiation. Because of an informal guideline monitoring and recommending EN to patients with >5% weight loss, bias was reduced. Hospitals would benefit from implementing a formal policy to initiate EN in patients with this weight loss.

REFERENCES

1. Head and Neck Cancers. National Cancer Institute website. https://www.cancer.gov/types/head-and-neck/head-neck-fact-sheet#r29. Reviewed February 1, 2013. Accessed February 18, 2017.
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. *CA Cancer J Clin*. 2017;67:7-30.
3. American Cancer Society. *Cancer Facts and Figures 2016*. Atlanta, GA: American Cancer Society; 2016. https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2016.html. Accessed February 18, 2017.
4. Hashibe M, Brennan P, Benhamou S, et al. Alcohol drinking in never users of tobacco, cigarette smoking, in never drinkers, and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. *J Natl Cancer Inst.* 2007;99(10):777-89.
5. Chaturvedi AK, Engels EA, Pfeiffer RM, et al. Human papillomavirus and rising oropharyngeal cancer incidence in the United States. *J Clin Oncol*. 2011;29(32):4294-301.
6. Radiation Therapy. National Cancer Institute website. https://www.cancer.gov/about-cancer/treatment/types/radiation-therapy#WRRT. Updated February 2, 2017. Accessed February 20, 2017.
7. Unsal D, Mentes B, Akmansu M, et al. Evaluation of nutrition status in cancer patients receiving radiotherpy: A prospective study. *Am J Clin Oncol*. 2006;29:183-188.
8. Mahan LK, Escott-Stump S, Raymond JL. Food and Nutrient Delivery: Nutrition Support Methods. *Krause's Food and the Nutrition Care Process*. 13th ed. St. Louis, MS: Elsevier Saunders; 2012:309-14.
9. Mercuri A, Lim Joon D, Wada M, et al. The effect of an intensive nutritional program on daily set-up variations and radiotherapy planning margins of head and neck cancer patients. *J Med Imaging Radiat Oncol*. 2009;53:500-505.
10. Burney RE, Bryner BS. Safety and long-term outcomes of percutaneous endoscopic gastrostomy in patients with head and neck cancer. *Surg Endosc*. 2015;29:3689-3689.
11. Assenat E, Thezenas S, Flori N, et al. Prophylactic percutaneous endoscopic gastrosotmy in patients with advanced head and neck tumors treated by combined chemoradiotherapy. *J Pain Symptom Manage*. 2011;42(4):548-556.

12. Bahl M, Siu LL, Pond GR, et al. Tolerability of the Intergroup 0099 (INT 0099) Regimen in locally advanced nasopharyngeal cancer with a focus on patients' nutritional status. *Int J Radiation Oncology Biol Phys*. 2004;60(4):1127-1136.

13. Rutter CE, Yovino S, Taylor R, et al. Impact of early percutaneous endoscopic gastrostomy tube placement on nutritional status and hospitalization in patients with head and neck cancer receiving definitive chemoradiation therapy. *Head and Neck*. 2011;10.

14. Morton RP, Crowder VL, Mawdsley R, et al. Elective gastrostomy, nutritional status and quality of life in advanced head and neck cancer patients receiving chemoradiotherapy. *ANZ J Surg*. 2009;79:713-718.

15. Languis J, van Dijk A, Doornaert P, et al. More than 10% weight loss in head and neck cancer patients during radiotherapy is independently associated with deterioration in quality of life. *Nutr Cancer*. 2013;65:76-83.

16. Lis CG, Gupta D, Lammersfeld CA. Role of nutritional status in predicting quality of life outcomes in cancer – a systematic review of the epidemiological literature. *Nutr J*. 2012;11:27.

17. Osborne JB, Collin LA, Posluns EC, et al. The Experience of head and neck cancer patients with a percutaneous endoscopic gastrostomy tube at a Canadian cancer center. *Nutr Clin Pract*. 2012;27(5):661-668.

18. Amerman EC. The Digestive System. *Human Anatomy & Physiology*. New York, NY: Pearson Education, Inc; 2016: 852-859.

19. Amerman EC. The Digestive System. *Human Anatomy & Physiology*. New York, NY: Pearson Education, Inc; 2016:124-132.

20. Sanderson R, Ironside AD. Sqamous cell carcinomas of the head and neck. *BMJ*. 2002;325:822-7.

21. Lopez F, Williams MD, Slavova A. How phenotype guides management of the most common malignant salivary neoplasms of the larynx? *Adv Ther*. 2017;34:813-825.

22. Fakhry C, Westra WH, Li S, et al. Improved survival of patients with human papillomavirus-positive head and neck squamous cell carcinoma in a prospective clinical trial. *J Natl Cancer Inst*. 2008;100:261-9.

23. Cancer Staging System. American Joint Committee on Cancer website. https://cancerstaging.org/references-tools/Pages/What-is-Cancer-Staging.aspx. Updated 2017. Accessed February 19, 2017.

24. Surgery. National Cancer Institute website. https://www.cancer.gov/about-cancer/treatment/types/surgery. Updated April 29, 2015. Accessed February 20, 2017.

25. Locher JL, Bonner JA, Carroll WR. Gastrostomy tube placement use in patients with head and neck cancer. *Head & Neck*. 2011.

26. Murphy BA, Gilbert J. Dysphagia in head and neck cancer patients treated with radiation: Assessment, sequelae, and rehabilitation. *Semin Radiat Oncol*. 2009;19:35-42.

27. Schindler A, Denaro N, Russi EG. Dysphagia in head and neck cancer patients treated with radiotherapy and systemic therapies: Literature review and consensus. *Crit Rev Onc*. 2015;96:372-384.

28. Chemotherapy. National Cancer Institute website. https://www.cancer.gov/about-cancer/treatment/types/chemotherapy. Updated April 29, 2015. Accessed February 20, 2017.

29. Targeted Cancer Therapies. National Cancer Institute website. https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies/targeted-therapies-fact-sheet#q7. Reviewed April 25, 2014. Accessed February 20, 2017.

30. Corry J, Poon W, McPhee N. Prospective study of percutaneous endoscopic gastrostomy tubes versus nasogastric tubes for enteral feeding in patients with head and neck cancer undergoing (Chemo)Radiation. *Head & Neck*;2008.

31. Nasogastric Feeding Tube versus Percuataneous Endoscopic gastrostomy for patients with head or neck cancer: A review of clinical effectiveness and guidelines. *Rapid Response Report: Summary with Critical Appraisal*. Ottawa(ON): Canadian Agency for Drugs and Technologies in Health;2014.

32. Lewis SL, Brody R, Touger-Decker R, et al. Feeding tube use in patients with head and neck cancer. *Head and Neck*. 2014;29.

33. Cady J. Nutrition Support During Radiotherapy for head and neck cancer: the role of prophylactic feeding tube placement. *Clin J Oncol Nurs*. 2006;11(6):875-880.

34. Wiggenraad, RGJ, Flierman, L, Goossens, A. Prophylactic gastrostomy placement and early tube feeding may limit loss of weight during chemoradiotherapy for advanced head and neck cancer, a preliminary study. *Clin Otolaryngol*. 2007;32:384-390.

35. Beer KT, Krause KB, Zuercher T. Early percutaneous endoscopic gastrostomy insertion maintains nutritional state with aerodigestive tract cancer. *Nutr Cancer*. 2005;52(1):29-34.

36. Mayre-Chilton KM, Talwar BP, Goff LM. Different experiences and perspectives between head and neck cancer patients and their care-givers on their daily impact of a gastrostomy tube. *J Hum Nutr Diet*. 2011;24:449-459.

37. Ehrsson YT, Sundberg K, Laurell G, Langius-Eklof A. Head and neck cancer patients' perceptions of quality of life and how it is affected by the disease and enteral tube feeding during treatment. *Ups J Med Sci.* 2015;120:280-289.

38. Roger SN, Thomson R, O'Toole P, Lowe D. Patients experience with long-term percutaneous endosopic gastrostomy feeding following primary surgery for oral and oropharyngeal cancer. *Oral Oncol*. 2007;43:499-507.

39. Mangar S, Slevin N, Mais K, Sykes A. Evaluating predictive factors for determining enteral nutrition in patients receiving radical radiotherapy for head and neck cancer: A retrospective review. *Rad Onc*. 2006;78:152-158.

40. Strom T, Trotti AM, Kish J, et al. Risk factors for percutaneous endoscopic gastrostomy tube placement during chemoradiotherapy for oropharyneal cancer. *Otolaryngol Head Neck Surg*. 2013;139(11):1242-1246.

41. Gokhale AS, McLaughlin BT, Flickinger JC, et al. Clinical and dosimetric factors associated with a prolonged feeding tube requirement in patients treated with chemoradiotherapy (CRT) for head and neck cancers. *Annals of OncologyI*. 2010;21:145-151.

42. Cheng SS, Terrell JE, Bradford CR, et al. Variables associated with feeding tube placement in head and neck cancer. *Arch Otolarngol Head Neck Surg*. 2006;132(6):655-661.

43. Bhayani MK, Hutchenson KA, Barringer DA, et al. Gastrostomy tube placement in patients with oropharyngeal carcinoma treated with radiotherapy or chemotherapy: Factors affecting placement and dependence. *Head Neck*. 2013;35:1634-1640.

44. Sachdev S, Refaat T, Bacchus ID, Sathiaseelan V, Mittal BB. Age most significant predictor of requiring enteral feeding in head-and-neck cancer patients. *Rad Onco*. 2015;10:93.

45. Massa ST, Osazuwa-Peters N, Christopher KM, et al. Competing causes of death in the head and neck cancer population. *Oral Oncol*. 2017;65:8-15.

46. Choi SH, Terrell JE, Fowler KE, et al. Socioeconomic and other demographic disparities predicting survival among head and neck cancer patients. *PLoS ONE*. 2016;11(3):e0149886.

47. Konski AA, Pajak TF, Movsas B. Disadvantage of men living alone participating in radiation therapy oncology group head and neck trials. *J Clin Oncol*. 2006;24:4177-4183.

48. Magnuson JS, Durst J, Rosenthal EL. Long-term gastrostomy tube dependence more likely in head and neck cancer survivors without partners. *Head Neck.* 2013;35(3):420-425.

49. Locher JL, Bonner JA, Carroll WR, et al. Patterns of prophylactic gastrostomy tube placement in head and neck cancer patients: A consideration of the significance of social support and practice variation. *Laryngoscope*. 2013;123(8):1918-25.

50. Clarfield AM, Gordon M, Markwell H, Alibhai SMH. Ethical issues in end-of-life geriatric care: The approach of three monotheistic religions – Judaism, Catholicism, and Islam. *J Am Geriatr Soc.* 2003;51:1149-1154.

51. Gessert CE, Curry NM, Robinson A. Ethnicity and end-of-life care: the use of feeding tubes. *Ethn Dis*. 2001;11(1):97-106.

52. Mitchell S, Teno J, Roy J, et al. Clinical and organizational factors associated with feeding tube use among nursing home residents with advanced cognitive impairment. *JAMA*. 2003;290(1):73-80.

53. QuickFacts. The United States Census Bureau. https://www.census.gov/quickfacts/table/PST045215 /01125. Accessed May 4, 2017.

54. Farrow AM, McCallum TJ, Messinger-Rapport BJ. Preferences of older African-Americans for long-term tube feeding at the end of life. *Aging Ment Health*. 2004;8(6):530-534.

55. Garrido MM, Harrington ST, Prigerson HG. End-of-life treatment preferences: A key to reducing ethnic/racial disparities in advance care planning? *Cancer*. 2014;120(24):3981-3986.

56. Koenig HG. Religion, spirituality, and medicine: Research findings and implications for clinical practice. *South Med J*. 2004;97(12):1194-1200.

57. Puchalski CM. The role of spirituality in health care. *BUMC Proceedings*. 2001;14:352-7.

58. Johnson J, Hayden T, True J, et al. The impact of faith beliefs on perceptions of end-of-life care and decision making among African American church members. *J Palliat Med*. 2016;19(2)143-8.

59. Silvestri GA, Knitting S, Zoller JS, Nietert PJ. Importance of faith on medical decisions regarding cancer care. *J Clin Oncol*. 2003;21:1379-1382.

60. Jaafar MH, Mahadeva S, Morgan K, Tan MP. Systematic review of qualitative and quantitative studies on the attitudes and barriers to percutaneous endoscopic gastrostomy feeding. *Clin Nutr*. 2016;35(6):1226-1235

61. True Gala, Phipps EJ, Braitman LE, et al. Treatment preferences and advance care planning at end of life: The role of ethnicity and spiritual coping in cancer patients. *Ann Behav Med*. 2005;30(2):174-9.

APPENDIX A:

Research Approval Letter from DCH Institutional Review Board

DCH Health System
Caring. For life.

January 24, 2017

Alexis Willman, RD
The University of Alabama
Department of Human Nutrition
431 Russell Hall
Tuscaloosa, AL 35487

RE: "Are Demographic Variables Predictors of Enteral Nutrition Initiation in Head-and-Neck Cancer Patients Receiving Radiotherapy?"

Dear Ms. Willman:

The Application for Review and materials you submitted to the Institutional Review Board (IRB) for the above named study were reviewed and granted approval via expedited review. This approval applies to DCH Regional Medical Center only as requested. In addition, the request to waive the IRB application fee was approved.

It is expected that you and the study staff will work closely with other DCH staff to ensure the safety and welfare of patients who enroll in this study. Once enrollment begins, the medical record of each patient participating in the study is to reflect appropriate information regarding discussions, consent, and treatments/procedures. As principal investigator, you are expected to keep appropriate records concerning the study and your subjects. Furthermore as a condition of this approval, the Institutional Review Board must be notified of any complications or unanticipated circumstances encountered. Study amendments are not to be implemented without prior IRB approval except when necessary to eliminate apparent immediate hazards to human subjects.

Your application will expire on January 24, 2018. If the study continues beyond that date, you must complete a Continuing Review / Status Report. The IRB should be notified upon completion of the study and a copy of the final results provided.

We look forward to working with you and good luck with your research.

Sincerely,

Chris Jones, J.D.
General Counsel
IRB Signatory Designee

: dw

APPENDIX B:

Research Approval Letter from UA Institutional Review Board

THE UNIVERSITY OF ALABAMA | Office of the Vice President for Research & Economic Development
Office for Research Compliance

February 17, 2017

Alexis Willman
Human Nutrition & Hospitality Mgmt.
College of Human Environmental Sciences
The University of Alabama
Box 870158

Re: IRB # 17-OR-066-ME: "Are Demographic Variables Predictors of Enteral Feeding Initiation in Head-and-Neck Cancer Patients Receiving Radiotherapy?"

Dear Ms. Willman,

The University of Alabama Institutional Review Board has granted approval for your proposed research. Your application has been given expedited approval according to 45 CFR part 46. You have been granted a waiver of consent and HIPAA authorization for the retrospective chart review. Approval has been given under expedited review category 5 as outlined below:

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis).

Your approval will expire on February 16, 2018. If the study continues beyond that date, you must complete and submit the Renewal Form within e-Protocol. If you modify the application, please submit the Revision Form. Changes in this study cannot be initiated without IRB approval, except when necessary to eliminate apparent immediate hazards to participants. When the study closes, please complete the Final Report Form.

Should you need to submit any further correspondence regarding this application, please include the assigned IRB approval number. Good luck with your research.

Sincerely,

Carpantato T. Myles, MSM, CIM, CIP
Director & Research Compliance Officer
Office for Research Compliance

cc: Dr. Jeannine Lawrence

APPENDIX C:

Review Outcome for Revisions to Approved Study from DCH Institutional Review Board

DCH Health System
Caring. For life.

April 17, 2017

Institutional Review Board
FWA #00006291
REVIEW OUTCOME FOR REVISIONS TO APPROVED STUDY

Name of Study:	"Are Demographic Variables Predictors of Enteral Nutrition Initiation in Head-and-Neck Cancer Patients Receiving Radiotherapy"
Principal Investigator:	Alexis Willman, RD – Graduate Teaching Assistant
Items(s) for Review:	Revision to protocol
Date Reviewed:	April 17, 2017
Review Outcome:	Approved

General Counsel
IRB Signatory Designee

:dw

APPENDIX D:

Approval of Protocol Revision from UA Institutional Review Board

THE UNIVERSITY OF ALABAMA | Office of the Vice President for Research & Economic Development
Office for Research Compliance

April 17, 2017

Alexis Willman
Department of Human Nutrition & Hospitality Management
College of Human Environmental Sciences
The University of Alabama
Box 870158

Re: IRB # 17-OR-066-ME-A "Are Demographic Variables Predictors of Enteral Feeding Initiation in Head-and-Neck Cancer Patients Receiving Radiotherapy?"

Dear Ms. Willman:

The University of Alabama Institutional Review Board has reviewed the revision to your previously approved expedited protocol. The board has approved the change in your protocol.

Please remember that your protocol will expire on February 16, 2018.

Should you need to submit any further correspondence regarding this proposal, please include the assigned IRB application number. Changes in this study cannot be initiated without IRB approval, except when necessary to eliminate apparent immediate hazards to participants.

Good luck with your research.

Sincerely,

Carpantato T. Myles, MSM, CIM, CIP
Director & Research Compliance Officer
Office for Research Compliance

358 Rose Administration Building | Box 870127 | Tuscaloosa, AL 35487-0127
205-348-8461 | Fax 205-348-7189 | Toll Free 1-877-820-3066