Prevalence of side-effects and change in nutritional status during radical radiotherapy for head and neck malignancies at Tygerberg Academic Hospital, Western Cape, South Africa

by

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Declaration

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Date: 22 December 2008

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ABSTRACT

Background

This study aimed to define the prevalence of side-effects and the change in weight and BMI during radical radiotherapy for head and neck malignancies (HNM) at Tygerberg Academic Hospital (TBH), Western Cape, South Africa. Acute side-effects may delay or prevent the delivery of a complete curative radiotherapy dose. Weight loss has been shown to significantly worsen prognosis and increase prevalence of treatment complications. However, weight maintenance may lead to beneficial outcomes. Assessing the impact of radical radiotherapy on patients with HNM is therefore critical and can promote development and implementation of medical and nutritional interventions.

Methods

Patients were weighed before and weekly during radiotherapy. Blood was drawn before, during and at the end of radiotherapy so that the Prognostic Inflammatory and Nutritional Index (PINI) could be calculated. Selected clinical data, clinical grades of mucositis and the diagnosis of a fungal infection of the oral cavity were extracted from clinical records. The McMaster Head and Neck Radiotherapy Questionnaire and a Lifestyle and Dietary Questionnaire were administered weekly. Descriptive statistics and the following were used: ANOVA, Repeated Measures ANOVA and McNemar Chi-square tests.

Results

Thirty-eight patients were recruited and 21 completed the study. Follow-up occurred over a maximum of nine weeks. A decrease in the weight ($p = 0.01$) and BMI ($p = 0.01$) and increase in the PINI ($p = 0.04$) occurred during radiotherapy. The mean absolute weight loss was 3.2kg (4.8), the mean percentage weight loss was 4.5% (6.7) and the mean decrease in BMI was 1.2kg/m^2 (1.8). There was an increase in the prevalence of malnutrition ($p = 0.02$), as defined in this study. Oral mucositis occurred in all participants from Week 4; the majority developing Grade II or III Mucositis. Fungal infection of the oral cavity was prevalent throughout radiotherapy, with the highest prevalence (30%) in Week 4. Increases in severity of symptoms related to the mouth ($p = 0.0000$), throat ($p = 0.05$) and skin domains ($p = 0.0000$)

occurred. Fifty-nine percent of inpatients and 45% of outpatients were prescribed supplementation drinks and most participants reported that a dietitian had not consulted them, in each week of radiotherapy.

Discussion

Severe side-effects in the mouth, throat and skin were experienced and a decline in nutritional status was observed. The poor nutritional status prior to commencing and weight loss during radiotherapy could have increased the severity of side-effects. The induction of the acute phase response indicated that this could have contributed to the decline in nutritional status observed. In addition, the infrequent nutritional support is likely to have further contributed to the lack of weight maintenance.

Conclusion

This first study conducted in South Africa has demonstrated the prevalence of significant side-effects and change in weight and BMI in this patient population. It is recommended that more effective analgesic medication is prescribed and that measures are taken to improve oral hygiene of participants to prevent fungal infection of the oral cavity. Improved nutritional support in terms of regular dietetic follow-up of all patients and more frequent prescription of supplementation drinks during radiotherapy is also recommended.

ABSTRAK

Agtergrond

Die doel van hierdie studie was om die voorkoms van newe effekte te omskryf en veranderinge in gewig en LMI tydens radikale radioterapie vir kop en nek maligniteite (KNM) by Tygerberg Akakdemiese Hospitaal (TBH), Wes Kaap, Suid Afrika, te bepaal. Akute newe effekte mag die afhandeling van ‘n volledige kuratiewe radioterapie kursus vertraag of voorkom. Daar word aangedui dat gewigsverlies ‘n beduidende bydrae lewer tot swak prognose en die voorkoms van behandelingskomplikasies verhoog. Instandhouding van gewig mag egter bydra tot positiewe behandelingsuitkoms. Assessering van die impak van radikale radioterapie op pasiënte met KNM is daarom krities en kan bydra tot die ontwikkeling en implementering van mediese en voedingstussenkomste.

Metodes

Pasiënte is voor en weekliks tydens radioterapie geweeg. Bloed is voor, tydens en aan die einde van radioterapie getrek om die Prognostiese Inflammatoriese- en Voedingsindeks (PINI) te kon bereken. Geselekteerde kliniese data, kliniese grade van mukositis en die diagnose van fungus infeksies van die mondholte is van kliniese rekords verkry. Die McMaster Kop en Nek Radioterapie vraelys en ‘n Leefstyl en Dieet vraelys is weekliks ingevul. Beskrywende statistiek en die volgende statistiese metodes is gebruik: ANOVA, Herhaalde Metings ANOVA en McNemar Chi-vierkant toetse.

Resultate

Agt en dertig pasiënte is gewerf en 21 het die studie voltooi. Opvolg het oor ‘n maksimum van nege weke plaasgevind. ‘n Afname in gewig ($p = 0.01$) en LMI ($p = 0.01$) en toename in die PINI ($p = 0.04$) het tydens radioterapie plaasgevind. Die mediaan absolute gewigsverlies was 3.2kg (4.8), die mediaan persentiele gewigsverlies was 4.5% (6.7) en die mediaan afname in LMI was 1.2kg/m^2 (1.8). Daar was ‘n toename in die voorkoms van wanvoeding ($p = 0.02$), soos in hierdie studie gedefineer is. Orale mukositis het vanaf Week 4 by alle deelnemers voorgekom. Die meerderheid het Graade II or III Mucositis ontwikkel. Fungus infeksies van die mondholte was regdeur radioterapie aanwesig, met die hoogste

voorkoms (30%) in Week 4. Toename in die graad van aantasting in die mond (p = 0.0000), keel (p = 0.05) en vel areas (p = 0.0000) is waargeneem. Aanvullingsdrankies is aan 59% van binne pasiënte en 45% van buite pasiënte voorgeskryf en meeste deelnemers het rapporteer dat hulle nie elke week van radioterapie, deur ‘n dieetkundige gekonsulteer is nie.

Bespreking

Erge newe effekte is in die mond, keel en velareas ondervind en ‘n afname in die voedingstatus is waargeneem. Die swak voedingstatus voor aanvang en en gewigsverlies tydens radioterapie kon bydraend gewees het tot die toename in die graad van newe effekte. Die induksie van akute fase respons dui daarop dat dat dit kon bydra tot die afname in die voedingstatus wat waargeneem is. Dit is waarskynlik dat ongereëlde voedingsondersteuning bydraend kon wees tot die onvermoë om gewig in stand te hou.

Gevolgtrekking en aanbevelings

Hierdie eerste studie wat in Suid Afrika uitgevoer is, het die voorkoms van betekenisvolle newe effekte en verandering in gewig en LMI in hierdie pasiënt populasie gedemonstreer. Daar word aanbeveel dat meer effektiewe analgetiese middels voorgeskryf word en dat daar prosedures ingestel word om mondhigiëne van pasiente te verbeter om fungus infeksie van die mondholte te voorkom. Verbeterde voedingondersteuning in die vorm van gereelde dieetkundige opvolg van alle pasiënte en die meer gereëlde voorskryf van dieet-aanvullingsdrankies tydens radioterapie word ook voorgestel.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

LIST OF ABBREVIATIONS

AGP:	Alpha-1-Acid-Glycoprotein
ALB:	Albumin
ANOVA:	Analysis of variance
APP:	Acute-Phase Protein
"BB":	"Best Blend"
BMI:	Body Mass Index
Chemoradiation:	Concomitant chemotherapy and radiotherapy
CRP:	C-reactive protein
ECOG:	Eastern Cooperative Oncology Group
EDTA:	Ethelenediaminetetra acetic acid
HNM:	Head and Neck Malignancies
HNRQ:	The McMaster University Head and Neck Radiotherapy Questionnaire
IV:	Intravenous
KPS:	Karnofsky Performance Score
NSP:	Nutritional Supplementation Programme
PA:	Prealbumin
PEM:	Protein-Energy Malnutrition
PINI:	Prognostic Inflammatory and Nutritional Index
Psychosocial:	Psychological and social
RDA:	Recommended Dietary Allowance
RM:	Repeated Measures
SGA:	Subjective Global Assessment
TBH:	Tygerberg Academic Hospital
USA:	United States of America
WHO:	World Health Organization

DEFINITION OF TERMS

Absolute weight	Weight in kilograms
"BB" tobacco	A pipe tobacco, manufactured in South Africa
Digestive system domain:	Group of symptoms caused by disorders of the digestive system, including nausea, stomach upsets, difficulty with appetite and difficulty in keeping down food or liquids[1]
Energy domain:	Group of symptoms regarding energy level, including lack of energy, difficulty in sleeping and fatigue which interferes with ability to do work or recreational activities[1]
KPS:	A score on a scale from 10 - 100 which describes the level of physical ability of a patient in terms of doing normal daily activities[2]
Lhermitte's phenomenon:	Neurological side-effect of radiotherapy manifest by tingling in the arms and legs, especially when the neck is flexed[3]
Mouth domain:	Group of symptoms caused by disorders in the oral cavity, including pain, dryness, sticky saliva, difficulty in tasting food and difficulty in chewing food[1]
Psychosocial domain:	Group of symptoms / variables affecting psychosocial functioning, including anger, depression, self esteem and relationships with family or friends[1]

Skin domain:	Group of symptoms caused by disorders of the skin in the radiated area, including dryness, itching and pain[1]
SGA:	A validated tool that assesses nutritional status based on the features of medical history and physical examination[4]
PINI:	A formula devised to evaluate nutritional status and prognosis in critically ill patients[5]
Throat domain:	Group of symptoms caused by disorders in the throat, including difficulty swallowing, pain and a hoarse voice[1]

CHAPTER 1: LITERATURE REVIEW AND DESCRIPTION OF THE RESEARCH QUESTION

1.1 Nutritional Implications of Head and Neck Malignancies (HNM)

The majority of cancer patients will experience eating difficulties and weight loss during their disease process or its treatment; however, it is those patients with HNM that are at the greatest risk of developing malnutrition. In addition, a significant number of these patients have a history of heavy smoking and excessive alcohol intake. Many of these patients; therefore, present at diagnosis in poor nutritional status due to poor dietary habits resulting from the social, physical and financial effects of their dependency[6].

It has been reported in a prospective study that 57% of patients had lost 10% of their body weight on commencing radical or palliative radiotherapy. A significant number of patients experienced the side-effects of a dry and / or sore throat, had difficulty masticating and swallowing food and had altered taste perception. These patients also tended to miss meals or have symptoms of uncontrollable nausea and constipation on commencing radiotherapy[6].

Patients with HNM frequently are elderly and as the majority of HNM arise in the upper aerodigestive tract, problems with swallowing are common. Local pain and discomfort, oedema, ulceration and bleeding can all lead to inadequate nutritional intake[7].

Reduced food intake can also result from the systemic effects of malignancy, psychological effects or adverse effects of treatment. Systemic effects of a tumour that alter food intake include anorexia, cachexia, nausea / vomiting, pain, taste / smell changes and fatigue. Cancer cachexia is a specific form of cancer-associated malnutrition, which often occurs in patients with advanced disease[8].

Alterations in nutrient metabolism and resting energy expenditure may also contribute to nutritional status. An acute-phase protein (APP) response has been reported in patients with advanced cancer. The APP response is associated with hypermetabolism, accelerated weight loss as well as poor survival in patients with advanced disease[8].

Side-effects of all forms of treatment for HNM, including surgery, radiotherapy and chemotherapy, can further contribute to the development of malnutrition in these patients. Clinical studies have demonstrated that malnutrition is associated with increased morbidity and mortality after major oncologic surgery and that it decreases patient tolerance to both radiotherapy and chemotherapy[9].

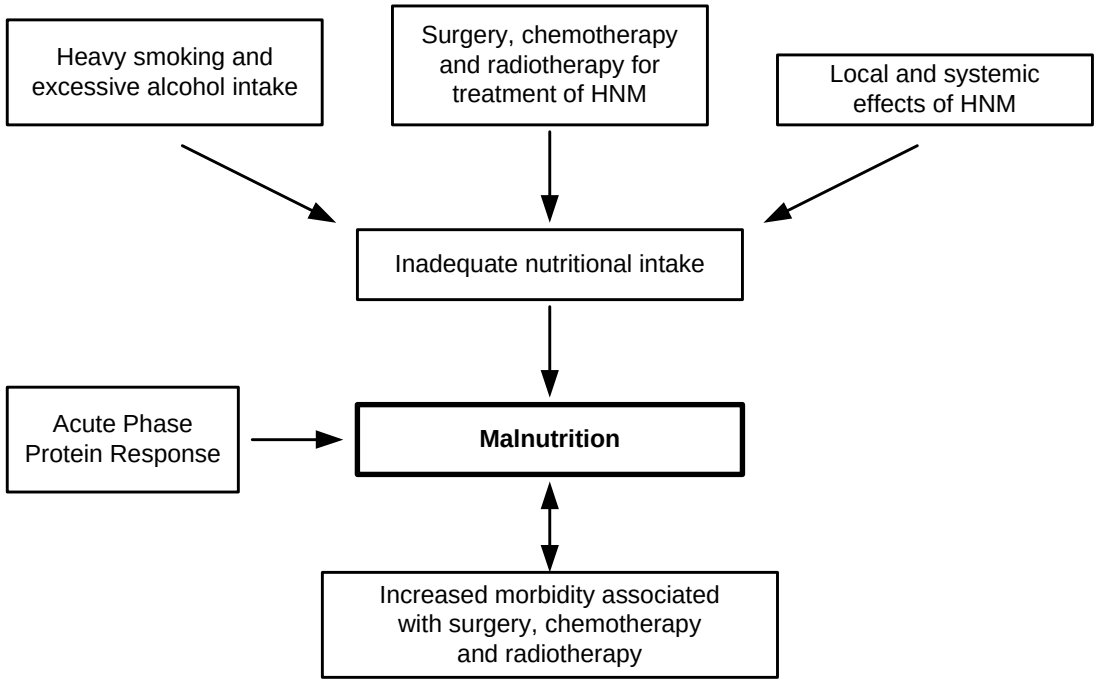

Figure 1.1 Nutritional Implications of HNM*

* Head and neck malignancies

1.2 Nutritional Implications of Treatment Modalities for HNM

1.2.1 Surgery

Surgical resection of HNM can severely restrict or prevent oral intake for a considerable time. Postoperative complications, such as infection, fistulas and wound dehiscence can increase metabolic needs while further restricting oral intake[10].

Surgical interventions to the tongue, salivary glands or olfactory nerve can reduce taste acuity leading to reduced food intake and thus nutritional decline. A temporary loss of taste and smell has been reported to occur in nearly half of patients undergoing upper gastrointestinal surgery. However, this generally resolves within a 6-12 month time-frame[8].

1.2.2 Chemotherapy

The most common adverse effects of chemotherapy that worsen nutritional status include anorexia, nausea and vomiting, mucositis, xerostomia, constipation, diarrhoea and early satiety. Altered perceptions of taste and smell as well as food aversions also impact on nutritional status. Some chemotherapy agents have a more predictable effect on nutritional status than others, as the incidence of each adverse effect varies with the type of chemotherapy used[8].

Oral mucositis can be caused by the direct cytotoxic effects of chemotherapy as well as by the indirect invasion of Gram-negative bacteria and fungal species. Patients are at increased risk for oral infections when they are neutropaenic. The onset of mucositis, secondary to myelosuppression, typically develops 10-21 days after chemotherapy administration. It has been estimated that approximately 40% of patients treated with standard chemotherapy develop mucositis[11].

Chemoradiation has been shown to reduce the rate of tumour recurrence and; therefore, improve survival rate in patients with locally advanced HNM. However, the radio sensitisation effect of chemotherapy may also lead to increased acute toxicity experienced by patients with HNM[22]. It has been reported that more than 90% of patients receiving concomitant chemotherapy and radiotherapy for HNM will develop oral mucositis[11]. A median weight loss of 8 kg (range 0-21 kg) during chemoradiation has been reported. Other studies have reported the mean weight loss during chemoradiation to be 10-12% of the initial body weight[12].

1.2.3 Radiotherapy

1.2.3.1 Side-effects and nutritional status during radical radiotherapy for HNM

Curative radiotherapy for HNM causes very significant side-effects. These radiotherapy reactions may be classified as early and late. Early reactions occur during and/or shortly after treatment ends and may continue for up to 3 months. Late reactions occur months to years after treatment has been completed. This classification is not clear-cut as certain reactions (e.g. xerostomia) occur acutely and persist as a permanent late effect. Alternatively, an exaggerated acute reaction may fail to improve and persist as a chronic effect[3].

Table 1.1 Common early and late side-effects of radiotherapy for HNM*[3]

Early	Late
Mucositis	Xerostomia
Desquamation	Osteoradionecrosis
Xerostomia	Fibrosis
Alopecia	Soft tissue necrosis
Loss of taste	Neurological damage
Lhermitte's phenomenon	Second malignancy

* Head and neck malignancies

Between 30% and 60% of patients receiving radiotherapy for HNM may develop oral mucositis. The degree and duration of mucositis are related to the radiation source, cumulative dose, dose intensity, volume of radiated mucosa, smoking, alcohol consumption and oral hygiene. Symptoms of mucositis vary from pain and discomfort to an inability to tolerate food or liquids. Mucositis may also limit the patient's ability to tolerate chemotherapy or radiotherapy, resulting in dose-limiting toxicity and therefore drastically affecting cancer treatment and outcome[11].

The salivary glands are often included in the volume of treatment during curative radiotherapy to the head and neck. This usually results in varying degrees of xerostomia, which alters taste, increases morbidity during radiotherapy and contributes to deterioration of oral hygiene. Tooth decay, soft tissue ulceration and osteoradionecrosis of the mandible may also result. Oral side-effects of head and neck radiotherapy prior to and once a week during radiotherapy for each patient were investigated in a prospective study. Complaints of soreness, a rise of viscosity of the saliva, dryness of the mouth, taste impairment and dysphagia were recorded and objective oral-mucosa changes were assessed. After 1-2 weeks of radiotherapy 90% of the patients developed a variety of oral symptoms, with each patient experiencing at least one symptom. In this study, dryness of the mouth was reported by 81% of the patients during radiotherapy. It was reported that 22% of the patients were experiencing dryness of the mouth even prior to commencing radiotherapy. Taste

impairment was experienced by 62%, dysphagia by 59%, soreness by 37% and a rise in the viscosity of the saliva by 16% of patients during radiotherapy. Manifestations of mucositis appeared within 1-3 weeks from commencement of radiotherapy. Salivary function was also demonstrated to be extremely sensitive to radiotherapy, with most of the loss of function occurring after 1-2 weeks. The decrease in salivary secretion was demonstrated to be accompanied by a rise in salivary sodium concentration and in oral yeast flora[13]. Patients with HNM undergoing radical radiotherapy are therefore at high risk for developing fungal infection of the oral cavity. The severity of symptoms experienced and the effect of radiotherapy on nutritional status, however, were not investigated. The study also reported that most of the parotids have to be outside of the treated volume while the rest of the major salivary glands are irradiated in order to prevent severe xerostomia[13]. In another prospective study, it was reported that irradiation of the tongue, rather than the parotid gland, is responsible for significant objective and subjective taste loss during radical radiotherapy. It was documented that irradiation of the parotid glands and tongue are both of importance in the development of xerostomia[14].

Two-thirds of the patients undergoing radical radiotherapy to the head and neck had subjective complaints of taste impairment after commencement of radiotherapy. In this prospective study complaints of taste loss and measured decreased taste acuity occurred at approximately the same time during radiotherapy, indicating that rapid changes in taste acuity are commonly perceived by the patient[15]. Another study reported that alterations in taste acuity are associated with weight loss during radiotherapy[16]. This prospective study; however, did not include patients with HNM only and therefore cannot be generalized to this patient population.

In a Canadian study, 68% of patients lost a mean of 10% of their pre-radiotherapy weight within one month after completing radical radiotherapy to the head and neck. Patients who received radiotherapy to the oral cavity or oropharynx experienced the most weight loss. Weight loss at one month following radiotherapy correlated with radiotherapy-induced dysphagia, xerostomia, mouth pain and dysgeusia[17]. The radiotherapy source in the study was Cobalt 60 and radiotherapy duration was only four weeks, which could have contributed to less severe side-effects of radiotherapy. Nutritional support was given in the form of basic dietary counseling regarding

conventional supplements, when required. Two patients received enteral tube feeding during the last week of radiotherapy. The lack of regular nutritional counseling could have contributed to the large weight loss experienced by most of the patients. The 10-cm visual analogue line that was used by patients to record their treatment morbidity was not a validated tool and therefore cannot be used as a sensitive indicator of change of symptoms during radiotherapy. Data analysis was also done without using inferential statistics and the results can therefore not be generalized to similar patient populations.

In a retrospective study conducted in India, 74% of patients lost more than 10% of body weight by the end of radical radiotherapy for HNM. Seventy-five percent of the patients received radiotherapy over more than six weeks, 25% of patients received chemoradiation and 30% of the patients required nasogastric tube feeding during radiotherapy[18]. The BMI of the patients was not measured. A low weight prior to radiotherapy could have contributed to the large percentage weight loss experienced by most of the patients. No dietetic input / nutritional counseling during radiotherapy was reported, which could also have contributed to the weight loss experienced. More than five kilograms of weight loss during radical head and neck radiotherapy was affected by a low initial Karnofsky performance score (KPS), use of chemoradiation and a total radiotherapy dose of > 60 Gray. Many patients with HNM have many years of tobacco and /or alcohol abuse, malnutrition and debilitating physical state, all of which are reflected by a lower KPS[18].

A lower (32%) incidence of severe weight loss during radical radiotherapy for HNM has been found in a retrospective study conducted in the United States of America (USA). There was a 10% rate of admission to hospital for dehydration and emergency room visits for dehydration. Twenty-five percent of the patients had feeding tubes placed before or during radiotherapy. The patients most likely to suffer severe weight loss included patients with tumour sites of nasopharynx and base of tongue, patients treated with chemoradiation and those with severe pretreatment weight loss. A prophylactic feeding gastrostomy tube significantly reduced the incidence of severe weight loss and hospitalization for dehydration during radiotherapy when placed before onset of radiotherapy[19]. Additionally, all patients included in the study were evaluated by the nutrition service before radiotherapy and

received counseling on weight loss and oral supplementation. This, together with the rate of feeding tube placement prior to and during radiotherapy, could have contributed to the lower incidence of severe weight loss reported in this study, compared to the previously mentioned studies. However, regular dietetic / nutritional counseling of patients during radiotherapy, was not reported which could have contributed to the still incidence of severe weight loss documented in this study.

In a prospective study, conducted in Turkey, malnutrition ratios in patients with HNM at the onset and after radical radiotherapy were 24% and 88% respectively. Nutritional status was assessed by means of Subjective Global Assessment (SGA) one day prior to commencing radiotherapy and at the end of the fifth week of radiotherapy[4]. Patients with a stage 4 disease were not included in this study. If they had been included, the prevalence of malnutrition could have been higher at the start of radiotherapy. Nutritional support in the form of an additional portion of a meal was given to all the patients in the moderately (or suspected of being) malnourished group. All the patients in the severely malnourished group were supported with standard enteral feeding formula during radiotherapy. Routine nutritional counseling of all patients did not occur in this study and only those patients presenting with malnutrition on commencing radiotherapy were given nutritional support during radiotherapy. This could have contributed to the lack of impact of nutritional support during this study and the large proportion of patients with malnutrition at the end of the fifth week of radiotherapy. Weight change was not measured in this study, which would have been a more sensitive marker of change in nutritional status during radiotherapy. The SGA is a validated tool that assesses nutritional status; however it has not been proven to be sensitive to changes in nutritional status.

In a retrospective, cross-sectional study in the USA, complications of radiotherapy for HNM were assessed from the patient's perspective. Lethargy and weakness, dry mouth, mouth sores and pain, taste changes and sore throat were the side-effects mentioned most frequently that were troublesome or debilitating during treatment. On being asked to identify the one side-effect that was most debilitating, sore throat was mentioned most frequently (20%), followed by mouth sores and pain (18%) and dry mouth (14%). Reasons for mentioning sore throat and mouth sores included the accompanying pain and burning that caused significant discomfort and also led to an

inability to eat, drink or swallow. Ninety percent of patients reported experiencing changes in their taste sensation during treatment. Fifty-four percent of patients experienced ageusia, 33% of patients had dysgeusia and 13% had hypogeusia. It was reported by patients that oropharyngeal mucositis developed within approximately 2.5 weeks (range 1 - 8 weeks) after the start of radiotherapy. The overall effect of oropharyngeal mucositis was explored. Eighty-eight percent of patients could not eat or drink, or did so with extreme difficulty. Eighty-three percent of patients reported significant weight loss, ranging from 5 – 36 kg (mean of 13 kg). Weight loss led to tube feeding for 29% of patients. Other side-effects experienced that patients also attributed to the changes in their oral cavity, included depression (38%), difficulty talking (29%), sleep disturbance (25%) and hospitalization (13%) [20]. Recall bias could have occurred in this study, which could have resulted in certain side-effects having been forgotten. The exact weight loss and time frame of weight loss of patients could also have been inaccurate. Seventy-five percent of the patients received conventional radiotherapy (radical radiotherapy consisting of one fraction per day for five days each week), lasting an average of 6.4 weeks (range 3-16 weeks). Patients were therefore included in the study that may have received palliative or more intensive radiotherapy (accelerated fractionation radiotherapy). This would have affected the severity of side-effects experienced as well as the nutritional status of patients during radiotherapy. Forty percent of patients received concomitant chemotherapy and 27% of patients were hospitalized due to treatment complications such as dehydration, inability to eat or drink, mouth pain, extreme weakness and fatigue. More severe side-effects would be expected during chemoradiation and this is reflected in the large percentage of patients who were hospitalized during radiotherapy. Data was only collected via questionnaire; therefore, the source of radiation used for radiotherapy was not reported. This could have affected the severity of side-effects experienced.

In a study, which was conducted in the USA, nutrition-related complications of curative radiotherapy for HNM were evaluated prospectively. Subjective changes of mouth dryness, taste, dysphagia, appetite and food preferences were determined by questionnaire before and weekly during radiotherapy. Twenty-five percent of the patients were subjectively aware of dry mouth prior to radiotherapy and by the fourth week of radiotherapy 80% of the patients complained of this problem. Fourteen

percent of the patients reported changes in taste prior to radiotherapy and by the fifth week of radiotherapy this percentage had increased to 84% of patients. Patients tended to sweeten food and fluids more frequently as radiotherapy progressed, but salt intake remained constant. Forty percent of the patients had swallowing difficulties prior to radiotherapy and this problem increased gradually in frequency during treatment. Twenty percent of the patients complained of appetite loss prior to radiotherapy and by the fourth week 60% were aware of this problem. Weight measurements were made before and weekly during radiotherapy. Patients had an average weight loss of five kilograms, compared to their normal weight, prior to radiotherapy. During radiotherapy this weight loss remained constant. It was documented that the reason for the lack of further weight loss during radiotherapy could be due to the continued nutritional support for the patients during treatment; which occurred during the study. Each time the patients participated in the study, nutritional counseling was provided, including the use of nutritional supplements[21]. Inferential statistics were not used for this study; therefore, the lack of weight change during radiotherapy cannot be generalized to similar patient populations. Another shortcoming is that the prevalence and not the severity of side-effects was investigated. All patients received radiotherapy from Cobalt 60 radiation source. More superficial tissue effects would have been experienced than if a higher energy radiation source had been used[22]. Reduced severity of side-effects in the mouth and throat could therefore have resulted in this study. Another factor which could have resulted in reduced severity of side-effects is that none of the patients received concomitant chemotherapy. The stage of malignancy of the patients was not reported. This would have been useful to know as less advanced disease could have resulted in less severe side-effects and weight loss during radiotherapy.

In a prospective study, conducted in Turkey, erythrocyte sedimentation rates and C-reactive protein levels were studied before, during and at the end of radical radiotherapy. It was deduced from this study that the acute phase response is present during radiotherapy. The acute phase response may be the result of many immunologic reactions and inflammatory processes and is characterized by fever, malaise, anorexia, leucocytosis and negative nitrogen balance[23]. The study did not include patients with HNM; therefore, the results cannot be generalized to this patient population. Changes in acute phase proteins occurring during the acute phase

response have been shown to be individually regulated; therefore changes could differ between patients with the same illness and in different pathophysiologic states[24]. Patients with HNM undergoing radical radiotherapy may; however, be at risk for the induction of the acute phase response. No studies have been found that investigated the acute phase response during head and neck radiotherapy. The levels of a variety of acute-phase proteins are affected during the acute phase response, which contribute to a variety of metabolic effects[24]. The study did not measure the combined effect of a variety of positive and negative acute-phase proteins during radiotherapy, e.g. by using the Prognostic Inflammatory and Nutritional Index. This would have given a better indication of the severity of the acute phase response induced, which could have affected the severity of side-effects as well as the change in nutritional status during radiotherapy.

In conclusion, it can be seen that few studies are available in the literature that assess the severity of symptoms / side-effects experienced during radical head and neck radiotherapy. These studies have not used a validated tool for the assessment of severity of symptoms, which is sensitive to change during radical radiotherapy of the head and neck.

A study was conducted in Canada to validate a questionnaire, which measures radiotherapy-related acute morbidity and quality of life from the perspective of patients with HNM treated with radical radiotherapy. In the context of a randomized, controlled clinical trial, the change in severity of symptoms related to six domains was assessed during head and neck radiotherapy. These domains included those related to the oral cavity, throat, skin, digestive system, energy level as well as psychosocial functioning. The percentage change during radiotherapy was assessed for each domain. The skin domain was affected the most (42%), followed by those related to the oral cavity (33%), throat (27%), digestive system, energy level and psychosocial functioning (all 14%)[1]. Due to the study having been a controlled clinical trial, 50% of the patients received concomitant chemotherapy. The change in the symptoms related to the six domains, could therefore have been more severe due to the large proportion of patients who had received chemoradiation. The patients included in the study had a localized stage 3 or 4 squamous cell HNM; therefore, the results are only representative of this patient population. The source of radiation was

not reported, which could have contributed to the severity of side-effects experienced. This instrument was the only one that could be found in the literature, which was specifically designed for use during radical head and neck radiotherapy and has been well validated. No studies could however be found that investigated morbidity, using this instrument, as well as nutritional status during radical head and neck radiotherapy.

1.3 Description of the problem

Head and neck cancer and the treatment thereof may cause pain and regional dysfunction and affect some basic functions of life. These include: speech, chewing, swallowing, social interaction and respiration[25].

Treatment of head and neck cancer may specifically result in acute and chronic complications including: acute and chronic pain, mucositis, mucosal sensitivity, dry mouth, altered or reduced taste, mucosal and bony necrosis, increased risk of dental caries, difficulty with denture function, altered esthetics, reduced mobility of tongue, lips and jaw and limitation of mastication and swallowing[25].

Radiotherapy is widely used either alone or in conjunction with surgery for the management of HNM. A consequence of radiotherapy is the damage to normal tissues included in the treatment field. Damage to these tissues occurs to varying degrees in the treatment of HNM and depends greatly on the dose of radiation delivered and volume of tissue irradiated[26].

The most common oral complications of head and neck radiotherapy that have been reported are oral mucositis, xerostomia, dental caries and taste dysfunction. These complications can cause considerable discomfort, compromise nutritional status and reduce the quality of life of the patient[26]. The importance of acute reactions is that they may delay or even prevent delivery of a full curative radiotherapy dose. Such changes to the usual time-course of radiotherapy dose delivery can result in significant reductions in the likelihood of cure[3].

The degree of radiation reaction can be influenced by conditions that affect tissue repair, including poor nutritional status, high alcohol intake and smoking[3]. A

significant number of patients with HNM have a history of heavy smoking and excessive alcohol intake. It has been found that the majority of these patients may present with dietary disorders and be nutritionally compromised on commencing radiotherapy to the head and neck[6]. These patients are therefore at high risk for increased severity of radiotherapy side-effects.

The single most debilitating side effect of radiotherapy for HNM has been reported to be oropharyngeal mucositis, which was characterized by patients as sore throat, and mouth sores and pain. This has been documented to negatively affect the patient's ability to eat and drink, causing many patients to experience significant weight loss[20]. Appropriate oral care has been documented to significantly reduce the morbidity of radiotherapy-induced mucositis as well as to prevent oral infection, which can cause further damage and pain[27].

The acute phase response, which is characterized by a variety of deleterious metabolic effects including catabolism, has been reported to be induced during radiotherapy[23]. The acute phase response could therefore contribute to weight loss and symptoms experienced during head and neck radiotherapy.

During cancer treatment, maintaining energy balance is the most important nutritional goal. Cancer survivors who receive adequate nutrition maintain body weight and complete treatment with fewer complications[8]. Protein-energy malnutrition (PEM) adversely affects wound healing, reduces immunocompetence and increases risk of infection[9]. Weight loss has also been reported to contribute to fatigue, delay and lengthen recovery and adversely affect quality of life[28].

It has been documented that nutritional status is linked closely to quality of life in terms of appetite, the ability to carry out daily activities, self-image, sense of control and overall aspects of satisfaction. Another aspect of quality of life adversely affected by progressive wasting is the loss of social interaction with family and friends[29].

The degree of malnutrition has been significantly correlated with survival[30]. It has been reported that even small amounts of weight loss (less than 5% of body weight)

may significantly worsen prognosis[31]. In addition, malnutrition can provide an increased economic burden due to increased hospital stays and costs of treatment[8].

In a prospective study, malnutrition ratios in patients with HNM at the onset and after radiotherapy have been documented to be 24% and 88% respectively[4]. Weight loss during radical radiotherapy for HNM has been reported in a variety of studies[20, 17, 18, and 19]. Retrospective studies have; however, demonstrated that intensive nutritional support can decrease the weight loss experienced during radiotherapy to the head and neck and improve quality of life. Methods of enteral nutritional support have included additional oral intake with analgesics and liquid supplements. Frequently; however, a nasogastric or gastrostomy tube has needed to be placed[32].

Intensive nutritional intervention, in terms of individualized nutrition counseling by a dietitian and use of oral supplements weekly during radiotherapy, has been reported to provide beneficial outcomes in terms of minimizing weight loss, deterioration in nutritional status, global quality of life and physical function in patients receiving radiotherapy to the head and neck. Weight maintenance in this population was documented to lead to beneficial outcomes. It was suggested that this, rather than weight gain, might be a more appropriate aim of nutritional support during radiotherapy[33]. In addition, patients undergoing percutaneous gastrostomy tube placement before head and neck radiotherapy have been documented to lose less weight during treatment and enjoy a better quality of life[34].

It can therefore be seen that radical radiotherapy of the head and neck has potentially significant deleterious effects on quality of life of these patients, in terms of side-effects experienced, as well as on nutritional status during radiotherapy. The prevalence and severity of these effects, however, can be improved with appropriate interventions during radiotherapy.

Assessing the impact of radical radiotherapy on patients with HNM is therefore critical and can promote the development and implementation of effective medical and nutritional interventions during radiotherapy.

1.4 Motivation for this study

There are no studies in the literature assessing the prevalence and severity of side-effects / symptoms and change in nutritional status during radical radiotherapy for HNM in South Africa. South Africa consists of diverse ethnic groups; which are culturally unique. This study could be useful in promoting the development and implementation of effective nutrition management programs prior to and during radical radiotherapy of HNM at Tygerberg Hospital, Western Cape, South Africa.

CHAPTER 2: METHODOLOGY

2.1 Aim

The aim of this study was to define the prevalence of side-effects and the change in weight and BMI during radical radiotherapy for head and neck malignancies (HNM) at Tygerberg Academic Hospital (TBH), Western Cape, South Africa.

2.2 Objectives

The primary objectives of this study were:

- To determine the prevalence of mucositis and fungal infection of the oral cavity during radical radiotherapy for HNM.
- To determine the prevalence and severity of symptoms related to the oral cavity, throat, skin, digestive system, energy and psychosocial domains, and evaluate any changes therein during radical radiotherapy for HNM.
- To determine weight and BMI, and evaluate any changes therein during radical radiotherapy for HNM.
- To determine the Prognostic Inflammatory and Nutritional Index (PINI) and evaluate any changes therein during radical radiotherapy for HNM.

The secondary objective of this study was:

- To determine relationships between the above variables.

2.3 Study design

This study was of a longitudinal, analytical, observational design. Quantitative and qualitative data were collected using the following techniques: a socio-demographic questionnaire, a questionnaire assessing severity of symptoms related to the oral cavity, throat, skin, digestive system, energy and psychosocial domains, clinical inspection of the oral cavity, a lifestyle and dietary questionnaire, anthropometrical measurements as well as biochemical measurements. Data was also collected from the clinical records of patients.

2.4 Study population

The study population was all patients with HNM who attended the TBH for the planning of radical radiotherapy between 28th of March and 19th September 2006. Recruitment of subjects took place when patients attended TBH for planning of their

radiotherapy, which occurred approximately 1-2 weeks before commencement of their radiotherapy treatment.

The following inclusion criteria were used:

- All HNM patients who were to receive radical radiotherapy at TBH as an inpatient or an outpatient
- > 18 years of age
- Male or female
- All ethnic groups
- Willing to participate in the study and providing written informed consent

The following exclusion criteria were used:

- Home language not English or Afrikaans, to prevent the need for an interpreter and thus preventing inter-observer bias
- Receiving tube feeding, as the questions ascertaining the severity of symptoms related to the mouth, throat and digestive system domains would not have been relevant for these patients
- Amputees

2.5 Methods

The investigator followed the following sequence of data collection:

Prior to commencing radiotherapy

- Written informed consent
- Socio-demographic questionnaire
- Anthropometrical measurements
- Blood drawn for biochemical measurements

Weekly during radiotherapy

- McMaster University Head and Neck Radiotherapy Questionnaire (HNRQ)
- Lifestyle and Dietary Questionnaire
- Anthropometrical measurements

Week 3 or 4 as well as last week of radiotherapy

- Blood drawn for biochemical measurements

During study

- Relevant clinical details obtained from clinical records

Participants dropped out of the study when any one of the following conditions applied:

- Discontinuation of radiotherapy
- Commencement of tube feeding during radiotherapy
- Unwillingness to continue in the study

Participants dropped out of the study when data could not be collected on two occasions, due to the following reasons:

- Unable to stand without assistance at the time of data collection
- Failure to meet with investigator
- Not attending radiotherapy

The reason/s for dropping out of the study and the week in which the participant dropped out was recorded.

2.5.1 Socio-demographic questionnaire

The socio-demographic data was obtained via a self-administered questionnaire under the supervision of the investigator. If the participant was unable to read, the investigator administered the questionnaire. The questionnaire was developed by the investigator and consisted of 10 questions. The following socio-demographic information was obtained (Appendix 1):

- Date of birth
- Gender
- Race
- Level of education
- Household income and circumstances
- Tobacco use
- Alcohol consumption
- Physical activity

2.5.2 Anthropometrical measurements

The investigator obtained weight and height measurements using standard equipment and standardized techniques[35].

Weight

Weight was determined by using a portable electronic scale. Weekly calibration of the scale during the study revealed that there was consistently a 0.1kg difference between the imperial weight used as a reference (Imperial weight 20kg; Clover Scales; South Africa) and the weight registered by the scale.

The scale was placed on a flat, hard surface. Participants stood still in the middle of the scale's platform without touching anything and with the body weight equally distributed on both feet. The weight was read to the nearest 0,1kg and recorded. Two measurements taken on immediate succession agreed to within 0,1kg.

Participants were requested to empty their bladder before being weighed and to dress in an examination gown, which had previously been weighed, to ensure the accuracy of measurements. In addition, the time of day that participants were weighed was recorded.

A weight loss at the end of radiotherapy of ≥ 5% of pre-radiotherapy weight was considered to be clinically significant[36].

Height

Height was measured with a portable stadiometer.

Participants were barefoot, dressed in an examination gown and stood with heels together, arms to the side, legs straight, shoulders relaxed and head in the Frankfort horizontal plane. Heels, buttocks, scapulae and back of the head were, if possible, against the vertical surface of the stadiometer. Just before the measurement was taken, the participants inhaled deeply, held their breath and maintained an erect posture while the headboard was lowered on the highest point of their head with enough pressure to compress their hair. The measurements were read to the nearest 0,1cm and with the eye level with the headboard to avoid errors caused by parallax. Hair ornamentation was removed if this interfered with the measurement.

Height measurement was used to calculate the BMI pre-radiotherapy and in the last week of radiotherapy for each participant. A BMI < 18,5 indicated underweight[37].

2.5.3 Biochemical measurements

A nurse obtained a blood sample (3ml in an EDTA tube) pre-radiotherapy, in Week 3 or 4 and in the last week of radiotherapy of participants; therefore, a maximum of 9ml of blood was drawn from each participant. All inpatients and selected outpatients had blood drawn routinely each week during radiotherapy. For the purpose of this study, blood was therefore only drawn from those outpatients who did not have blood tests requested by medical doctors in a given week during radiotherapy.

Measurement of plasma albumin (ALB), plasma C-reactive protein (CRP), plasma alpha-1-acid-glycoprotein (AGP) and plasma prealbumin (PA) was done pre-radiotherapy, in Week 3 or 4 and in the last week of radiotherapy. These measurements were used to calculate the Prognostic Inflammatory and Nutritional Index (PINI) pre-radiotherapy, in Week 3 or 4 and in the last week of radiotherapy according to the following formula[38]:

$$\text{PINI} = \frac{\text{AGP (mg/l) X CRP (mg/l)}}{\text{ALB (g/l) X PA (mg/l)}}$$

The PINI takes into account both inflammatory and nutritional parameters, which are two closely interrelated parts of the stress reaction. A PINI of ≥ 1 was regarded as an elevated level and indicated catabolism / inflammation[5]. An increase in the PINI during radiotherapy indicated induction of the acute phase response that could influence the severity of symptoms and weight change during radiotherapy.

Blood was analyzed using nephelometry through the Department of Human Nutrition at TBH. All reagents and standards for quality control were obtained from Dade-Behring, Germany. The coefficient of variation (CV) for the measurement of ALB was 0.8%, for that of PA was 0.6% and for that of CRP was 2.7%. The CV for the measurement of AAG could not be determined as the blood was analyzed in one batch.

2.5.4 McMaster University Head and Neck Radiotherapy Questionnaire (HNRQ)

The HNRQ developed and validated by Browman *et al* was used to measure the severity of symptoms related to the oral cavity, throat, skin, digestive system, energy and psychosocial domains (Appendix 2). The HNRQ is an interviewer-administered questionnaire designed to measure radiation-related acute morbidity and quality of life from the perspective of patients with HNM treated with radiotherapy.

The questionnaire consisted of 22 questions that covered symptoms related to six domains: oral cavity (mouth), throat, skin, digestive system, energy and psychosocial. Each domain was interrogated using at least three questions. Each question was accompanied by seven possible response options using a Likert scale. An additional question ascertained the consistency of foods taken in each week of radiotherapy. For this question, there were three possible response options.

The investigator administered the HNRQ each week after the radiotherapy session of each of the participants so that the study would not interfere with the timing of their radiotherapy sessions. Additionally, the psychological status of participants could have differed before and after their radiotherapy sessions, which could have affected the subjective responses of participants to the questions in the HNRQ. All interviews were standardized and questions were asked in consecutive order beginning with the first question in the questionnaire. After each question, participants were read the response options (if unable to read) or shown a card on which the response options were written, from which they were requested to select a response.

Participants who were inpatients or who had been hospitalized for one or more days during a week were not asked the questions that covered symptoms related to the energy and psychosocial domains that week, as these questions were not applicable to them. Participants who had undergone a total laryngectomy were not asked the questions that covered symptoms related to the throat domain, as one of these questions was not applicable to them.

A score for each domain was obtained; however, a single summary score across all of the domains of the HNRQ was not obtained for this study. The severity of symptoms related to the six domains were investigated separately in order for comparisons to be

made between them and the summary score reflecting the severity of symptoms over all of the domains was not required for the purpose of this study. In the scoring system used, the worst toxicity was associated with the lowest score. The score for each domain was the mean of the questions relevant to that domain.

The questionnaire had the following advantages for this study[1]:

- It is simple and quick to complete.
- It has a simple scoring system for the calculation of a score for each domain separately, to assess individual toxicities.
- It is disease- and treatment-specific and confined to acute morbidity experienced over a limited time frame.
- It is intended as an evaluative instrument to assess changes in morbidity / quality of life over time within individual subjects. These scores are then aggregated to derive group effects.

2.5.4.1 Questionnaire validity

The HNRQ was validated prospectively in the context of a clinical trial. As there is no gold standard for morbidity / quality of life, the concept of construct validity was adopted for validation of the HNRQ. This determines the extent to which the questionnaire results are consistent with other established instruments and with theoretical predictions about how the instrument should behave under certain conditions[1].

The HNRQ was found to have construct validity as the following hypotheses were proven to be correct[1]:

- That the pattern of severity of morbidity through the pretreatment, treatment and post-treatment phases, as measured by weekly scores over 10 weeks, would conform to a shallow U-shape to reflect observed clinical effects of radiation therapy; and
- That the HNRQ and its domains should correlate with other indices currently used to measure radiation toxicity in head and neck cancer [namely World Health Organization (WHO) and Byfield stomatitis indices[39], WHO skin toxicity index[39], Eastern Cooperative Oncology Group (ECOG) and Karnofsky performance status[2]] and the HNRQ domains would show higher

correlations with other indices designed to interrogate the same clinical symptom complex.

A significant change in scores over time was detected for the HNRQ, for each of its domains and for other toxicity indices, namely WHO skin, Byfield stomatitis, WHO stomatitis and ECOG performance status indices ($p < 0{,}00001$ for all indices). The HNRQ correlated well with all other toxicity indices ($r > 0{,}60$) [1].

2.5.4.2 Questionnaire reliability

Evaluation of between-assessment reliability over time was not done due to the following reasons[1]:

- The clinical status of the subjects to whom the questionnaire applies was not stable because they were receiving treatment that is expected to produce changes in the clinical state under interrogation,
- The condition itself may produce different scores over time as the disease progresses and
- Different scores over time may also occur as symptom control measures are administered.

Between-observer reliability was also not assessed so as not to increase respondent burden at a time of distress during subjects' visits to the treatment center. A strictly standardized interviewer approach was therefore used that would minimize any between-observer differences in eliciting responses[1].

It is unlikely that the validity established for the HNRQ would occur, if reliability were suspect[1].

2.5.5 Lifestyle and Dietary Questionnaire

A lifestyle and dietary questionnaire was developed and administered by the investigator (Appendix 3). The following information was obtained by the questionnaire:

- Tobacco use
- Alcohol consumption
- Physical activity
- Supplementation use
- Consultation with a dietitian

Tobacco use, alcohol consumption and the use of vitamin, mineral and herbal supplements during radiotherapy could have influenced the side-effects and symptoms experienced during radiotherapy. The level of physical activity, the use of supplementation drinks and consultation with a dietitian during radiotherapy could have influenced weight during radiotherapy.

2.5.6 Clinical data

All clinical details during radiotherapy were recorded up to and including the last week of follow-up of participants. The investigator extracted the following data from the clinical records of the participants on a pre-prepared data sheet (Appendix 4):

- Tumour histology, site and stage, according to the TNM system for stage grouping of the International Union against Cancer and the American Joint Committee on Cancer[40]
- Total radiotherapy dose and type planned per treatment field
- Treatment field sizes
- Duration of radiotherapy planned
- Prior head and neck surgery
- Prior total laryngectomy
- Prior chemotherapy / radiotherapy for head and neck cancer
- Concomitant chemotherapy and type of chemotherapy received
- Presence of HIV infection or AIDS, Diabetes Mellitus and tuberculosis
- Hospitalized or staying at home in Week 1 and whether accommodation changed during this week

- Referral to the Nutrition Supplementation Program (NSP) of the Integrated Nutrition Program of the Western Cape and when referred (Nutrimil supplementation drink and fortified porridge were provided to these participants during radiotherapy in quantities sufficient for one month. If the participants required further supplies of these supplements during radiotherapy, these were provided to them.)
- Prescription of supplementation drinks each week of radiotherapy in terms of the name and daily quantity prescribed
- Weekly clinical grading of mucositis was assessed by medical doctors from Week 2 of radiotherapy. Increasing mucositis severity was reflected partly by increasing grades of mucositis and provided an indication of the toxic effect of radiotherapy in the mouth and throat. This is generally experienced as increasing pain in these areas. Inspection of the oral cavity occurred, according to the following recognized grades for mucositis[3]:

  Grade 0: No change over baseline

  Grade 1: Hyperaemia

  Grade 2: Patchy mucositis

  Grade 3: Confluent mucositis

  Grade 4: Ulceration, haemorrhage, necrosis
- Presence of a fungal infection during radiotherapy, which was assessed by medical doctors from Week 2 of radiotherapy by inspection of the oral cavity. This was determined by the prescription of anti-fungal medication during radiotherapy. Fungal infection of the oral cavity can contribute to the severity of symptoms experienced in the mouth and throat during radiotherapy.
- Prescription of medication each week of radiotherapy in terms of name, dosage and frequency prescribed
- Prescription of vitamins, minerals and alternative remedies each week of radiotherapy in terms of type and dosage prescribed
- Interruptions in radiotherapy treatments in terms of number of days during radiotherapy and the reason / s for the interruption / s
- Administration of double fractions during the course of radiotherapy and the number of days on which these occurred

- Hospitalization of outpatients after Week 1, in which week / s of radiotherapy this occurred and the reason / s for hospitalization
- Administration of intravenous fluids and in which week / s they were administered
- Whether inpatients went home over one or more weekend and the number of weekends that this occurred
- Presence of a skin infection or sepsis during radiotherapy, as this could influence the severity of symptoms experienced as well as nutritional requirements during radiotherapy
- Occurrence of any other medical disorders.

2.5.7 Pilot study

A pilot study was conducted on five English- and five Afrikaans-speaking patients with HNM who attended TBH for planning of radical radiotherapy. The purpose of the pilot study was to face validate the questionnaires and to test the feasibility of these as research instruments for this study's population.

Socio-demographic questionnaire

Changes that were made to the questionnaire, following the pilot study:

- Question 5: Monthly household income was divided into patient's income, spouse's income and other household income. Type of income was specified as employment, pension, disability grant, state grant, other income or no income.
- Question 6: The number of people living with the patient at home was clarified to include adults and children.
- Question 8: Whether the patient currently smoked was divided into smoking cigarettes, cigars, a pipe or chewing tobacco at present and the quantity being smoked / chewed per day. An additional question was included to ascertain whether the patient smoked in the past and if so, the quantity smoked per day and when the patient stopped smoking, in terms of weeks/months/years ago.
- Question 9: Whether the patient drank alcohol was divided into drinking wine, beer and / or spirits at present and the quantity consumed per day or per week. An additional question was included to ascertain whether the patient drank

alcohol in the past and if so, the quantity consumed per day or per week and when the patient stopped drinking alcohol, in terms of weeks / months / years ago.

- Question 10: To describe the current level of physical activity, response options were altered from ”mostly lying down”, “mostly sitting or walking around” and “doing daily exercise” to the descriptors as follows: “sedendary”, “mild / moderate exercise” and “vigorous exercise”, with examples of each level of activity given in brackets.

McMaster Head and Neck Radiotherapy Questionnaire (HNRQ)

Changes that were made to the questionnaire included the following:

- An additional question for the purposes of screening was inserted before question 1 to establish whether the participant had undergone a total laryngectomy. If so, questions 3, 11 and 19 were not asked in that participant, as one of these questions was not relevant to these participants. These questions were related to the throat domain and one of the questions ascertained whether the participant had a hoarse voice during radiotherapy.
- Question 12: “any upset of stomach” was changed to “any problems with your stomach” as this was better understood. Constipation or diarrhoea was given as examples of possible problems participants could have had with their stomach in the previous week.

Lifestyle and Dietary Questionnaire

The following changes were made to the questionnaire:

- Question 4 and question 6.5: “in the past week” was changed to “in the past 7 days” as this was more specific.
- Question 5.1 and question 6.1: For describing the patient’s level of physical activity, instead of giving ”mostly lying down”, “mostly sitting or walking around” and “doing daily exercise” as response options, the words “sedentary”, “mild / moderate exercise” and “vigorous exercise” were used, with examples of each level of activity given in brackets.
- Question 5.2 and question 6.2: The wording “supplementation drinks” was changed to ”special energy drinks”.

- Question 5.3 and question 6.3: The wording "vitamin supplements" was changed to "vitamin pills".
- Question 5.4 and question 6.4: The wording "herbal supplements" was changed to "herbal pills / herbal medicine".

2.5.8 Ethical considerations

Prior to the study

The study protocol was submitted to and approved by (reference N05/10/175) the Committee for Human Research, Faculty of Health Science, University of Stellenbosch (Appendix 5). The investigator met with the potential participants in a private room at the radiotherapy outpatient department to explain the nature of the study and obtain a written informed consent. The standard informed consent form used by the Faculty of Health Sciences of the University of Stellenbosch was adapted for this particular research study (Appendix 6). Participation in the study was voluntary and participants were informed that they could withdraw at any time without penalty. After the participant had signed the informed consent form, the investigator initiated the collection of data. A copy of the informed consent form was provided to the participant.

During the study

On commencement of the study the investigator informed the oncology dietitian at TBH of the days on which participants would meet with the investigator. The participant was informed that the investigator would meet with them every Friday from their first week of radiotherapy and weekly thereafter until their last week of radiotherapy (Week 6 or 7). It was also explained that these meetings would take place after their radiotherapy sessions each week. If the Friday was a public holiday, another day that week was used for data collection. English interview schedules had been translated for Afrikaans-speaking participants who were interviewed in their own language. All of the questionnaires were administered in a private room at the radiotherapy outpatient department unless the participant was unwell or had been hospitalized during radiotherapy, in which case the questionnaires were administered on the radiation oncology ward. Anthropometrical measurements and blood samples were obtained at the radiation oncology ward, by the investigator and a nurse

respectively prior to commencing radiotherapy, and in a private room at the radiotherapy outpatient department during radiotherapy. If the participant was unwell or had been hospitalized during radiotherapy, the anthropometrical measurements were obtained at the radiation oncology ward. All data were managed in strict confidence. Participant identification information was omitted from study-related material and documentation to ensure confidentiality of study participants. All usual clinic practices were carried out during the study and no advice or care was withheld at any stage.

2.5.9 Data analysis

An "intention to treat" analysis was made. Descriptive statistics (mean, standard deviation, median and range) were used to summarize all the appropriate socio-demographic, clinical, anthropometrical and biochemical data. The absolute weight change was calculated for each participant as the weight (in kilograms) in the last week of radiotherapy subtracted from that pre-radiotherapy. The percentage change in weight was the absolute weight change as a percentage of the pre-radiotherapy weight of each participant. T-tests were used to describe the changes in the HNRQ scores related to the six domains (mouth, throat, skin, digestive system, energy and psychosocial domains) from Week 1 to the last week of radiotherapy. Analysis of Variance (ANOVA) or the Mann-Whitney test was used to analyze whether the means of the following differed between the presence or the absence of Grade III Mucositis and that of fungal infection during radiotherapy: absolute weight change, change in the BMI and change in the PINI from pre-radiotherapy to the last week of radiotherapy as well as the change in the HNRQ scores related to the six domains from Week 1 to the last week of radiotherapy.

Repeated Measures (RM) ANOVA was used to analyze the change from pre-radiotherapy to the last week of radiotherapy in the means of weight, BMI and the PINI of study participants. RM ANOVA was also used to analyze the change in mean weight and the mean PINI over the weeks of radiotherapy. The same statistical test was used to analyze the change in the mean HNRQ scores related to the 6 domains from Week 1 to the last week of radiotherapy and over the weeks of radiotherapy. Statistical significance of these analyses was confirmed with either the Wilcoxon test for two repetitions or the Friedman non-parametric test for more than two repetitions.

Spearman correlation analysis was used to determine relationships between the PINI in the last week of radiotherapy, as well as the change in the PINI from pre-radiotherapy to the last week of radiotherapy with the following variables: percentage weight change, absolute weight change and the change in the BMI from pre-radiotherapy to the last week of radiotherapy. This analysis was also used to determine relationships between the change in the HNRQ scores related to the six domains from Week 1 to the last week of radiotherapy and the following: percentage weight change, absolute weight change, change in the BMI and change in the PINI from pre-radiotherapy to the last week of radiotherapy as well as the PINI in the last week of radiotherapy. Regression and correlation analysis was used to determine relationships between the maximum daily energy intake of study participants from supplementation drinks during radiotherapy and the following variables: percentage weight change, absolute weight change, change in the BMI and change in the PINI from pre-radiotherapy to the last week of radiotherapy as well as the change in the HNRQ scores related to the 6 domains from Week 1 to the last week of radiotherapy.

The McNemar Chi-square test was used to analyze the change in prevalence from pre-radiotherapy to the last week of radiotherapy in the following: BMI < 18.5, PINI ≥ 1 and malnutrition, as defined in this study (BMI < 18.5 or PINI ≥ 1 pre-radiotherapy; and BMI < 18.5 or PINI ≥ 1 or $\geq 5\%$ of pre-radiotherapy weight lost at the end of radiotherapy). The same statistical test was used to analyze the change in prevalence from Week 2 to the last week of radiotherapy in the clinical grades of mucositis obtained from the medical records of study participants. The McNemar Chi-square test was also used to analyze the change in frequency from Week 1 to the last week of radiotherapy in the levels of consistency of foods consumed. In addition this statistical test was used for the analysis of the change in frequency from Week 1 to the last week of radiotherapy in the prescription of the following medications: analgesics, anti-emetics, laxatives, sedatives and antibiotics.

CHAPTER 3: RESULTS

3.1 Study population

A total of 40 patients with HNM who attended TBH for planning of radical radiotherapy were screened with a view to being included in the study. Of these, 38 patients met the inclusion criteria and were included in this study. The other two patients were Xhosa speaking (N = 1) and unwilling to participate in the study (N = 1). Recruitment of subjects took place from March to September 2006. Of the 38 patients who agreed initially to participate, 16 (42%) dropped out of the study during radiotherapy (Table 3.1). Dropouts occurred throughout the duration of the study (Figure 3.1). One patient had missing values in Week 7 of radiotherapy, due to failure to meet with the investigator on the day of data collection. A total of 21 patients therefore completed the study.

Table 3.1 Reasons for participants dropping out of the study

Reasons for dropping out of study	***N* (%)**
Discontinuation of radiotherapy	2 (5)
Commencement of nasogastric feeding	2 (5)
Unwilling to continue in study	7 (18)
Failure to meet with investigator on day of data collection	4 (11)
Not attending radiotherapy on day of data collection	1 (3)
Unable to stand without assistance at time of data collection	1 (3)

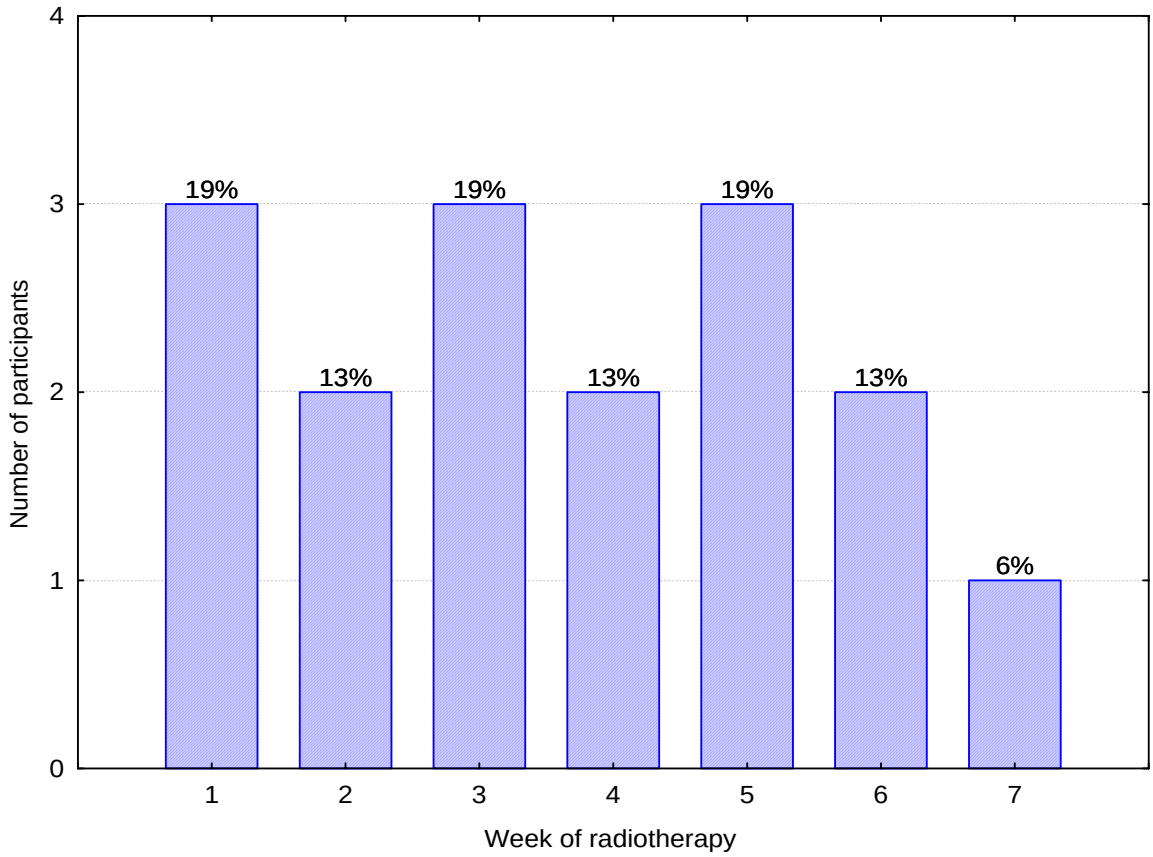

Figure 3.1 Weeks during radiotherapy in which participants dropped out of study

3.2 Socio-demographic characteristics of study participants

The mean age of participants was 60.8 [Standard Deviation (SD) 11.0] and the median age was 60.0 (range 41.2 – 87.5 years). Participants were primarily of the male gender [male 29 (76%) and female 9 (24%) participants], with 33 (87%) of the participants being of the Coloured, 4 (10%) of the White and 1 (3%) of the Black ethnic group.

Twenty-one percent of the participants had no education and 46% of them had a level of Primary School education ranging from Grade 2 – Grade 7. A further 34% of participants had a level of High School education, ranging from Grade 8 – Grade 12. No participants had tertiary education.

A total of 71% of participants were receiving a monthly income, of which only 16% were receiving it from employment. Spouses contributed to the household income of

27% of participants. Income from other members of the household or from other sources was received by 53% of the participants. Employment of other household members contributed the largest mean monthly income to households of participants. Total household income ranged greatly from no income to R8280 per month (Table 3.2).

Table 3.2 Monthly household income of participants

Type of household income	*N* (%)	Mean (range)
Participant		
Employment	6 (16)	R1392 (R590 – R2500)
Pension	13 (34)	R812 (R740 – R840)
Disability grant	8 (21)	R759 (R520 – R820)
Spouse		
Employment	2 (5)	R1650 (R300 – R3000)
Pension	4 (11)	R820 (R820 – R820)
Disability grant	3 (8)	R783 (R708 – R820)
State grant	1 (3)	R380
Other household members		
Employment	11 (29)	R2119 (R300 – R5000)
Pension	2 (5)	R660 (R520 – R800)
Disability grant	4 (11)	R1020 (R800 – R4640)
Other	3 (8)	R330 (R190 – R400)
Total household income	38 (100)	R1684 (R0 – R8280)

All participants lived in their own homes except one participant who lived in an old age home at the commencement of the study. The member density of households varied considerably, with 11% of the participants living alone and 9% living with 8 - 12 people. The majority (79%) of the participants had a fridge at home (Table 3.3).

Approximately one-third of the participants were smoking cigarettes at commencement of the study, with the majority smoking 1-4 cigarettes per day. Only one participant reported smoking up to one packet of cigarettes per day, however did

not know the exact daily quantity. The majority (61%) of the participants had stopped smoking prior to the study. The largest proportion of these participants (55% of the participants), had smoked 1 - 20 cigarettes per day; however, 5% had smoked more heavily prior to the study (Table 3.3).

None of the participants were smoking cigars, a pipe or tobacco at commencement of the study; however, prior to the study, 11% had smoked cigars and 24% had smoked a pipe or tobacco. Of the cigar smokers, 50% had smoked 1 – 2 per day and the rest had not smoked daily. The tobacco smokers did not know the weight of tobacco smoked per week, but most could describe the size of the packet or type of tobacco smoked. The largest proportion of the participants who smoked a pipe or tobacco prior to the study (11%), reported smoking "small packets of tobacco". "BB" tobacco was smoked in the largest quantity. None of the participants had ever chewed tobacco. Cigar smoking had been stopped the longest time prior to the study and cigarette smoking had been stopped the shortest time (Table 3.3).

At the commencement of the study a minority of participants were consuming wine (11%), beer (16%) and spirits (3%), although prior to the study 79% and 63% of the participants, consumed wine and beer respectively and 5% consumed spirits. The largest quantity of alcohol consumed per week on commencement of the study and prior to the study, was that of wine (Table 3.3).

The consumption of spirits had been stopped the longest time prior to the study and that of beer the shortest time prior to the study. There was missing data for one participant regarding the number of years prior to the study that the consumption of wine and beer had been stopped (Table 3.3).

The majority (55%) of participants were doing mild / moderate exercise such as leisurely walking and leisurely cycling before commencing radiotherapy treatment. Thirty-four percent of participants were sedentary including lying down, sitting and doing household activities and 11% of participants were doing vigorous exercise such as swimming, jogging, brisk walking and moderate cycling before commencement of radiotherapy treatment (Table 3.3).

Table 3.3 Socio-demographic characteristics of participants

Socio-demographic characteristic	*N* (%)	Mean (range)
Lived alone	4 (11)	
Lived with 1-4 people	23 (62)	
Lived with 5-7 people	7 (19)	
Lived with 8-12 people	3 (9)	
Had a fridge at home	30 (79)	
Smoked cigarettes at commencement of study	13 (34)	
Cigarettes per day: 1-4	10 (26)	
5-10	2 (5)	
< 1 packet	1 (3)	
Smoked cigarettes prior to study	23 (61)	
Cigarettes per day: 1-15	15 (39)	
16-20	6 (16)	
35-40	2 (5)	
Years prior to study, cigarette smoking stopped	23 (61)	2.7 (0.1-20.0)
Smoked cigars prior to study	4 (11)	
Cigars per month: 3	1 (3)	
16	1 (3)	
30-60	2 (5)	
Years prior to study, cigar smoking stopped	4 (11)	11.5 (1.0-20.0)
Smoked a pipe / tobacco prior to study	9 (24)	
Packets of tobacco per week: "BB" tobacco	3 (8)	7.3 (0.5-14.0)
"Tobacco"	1 (3)	1.0
"Small packets"	4 (11)	2.8 (0.3-7.0)
"Large packet"	1 (3)	1.0
Years prior to study, pipe / tobacco smoking stopped	9 (24)	6.5 (0.1-25.0)

Table 3.3 Socio-demographic characteristics of participants (Cont'd)

Consumed wine at commencement of study	4 (11)	
Glasses of wine per week	3 (8)	10.2 (10.1-10.5)
	1 (3)	<1.0
Consumed wine prior to study	30 (79)	
Glasses of wine per week	29 (76)	31.9 (3.0-125.0)
	1 (3)	<1.0
Years prior to study, wine consumption stopped	29 (76)	4.4 (0.1-24.0)
Consumed beer at commencement of study	6 (16)	
Cans / bottles of beer per week	6 (16)	5.6 (1.0-14.0)
Consumed beer prior to study	24 (63)	
Cans / bottles of beer per week	22 (58)	9.8 (1.0-42.0)
	2 (5)	<1.0
Years prior to study, beer consumption stopped	23 (61)	4.0 (0.1-20.0)
Consumed spirits at commencement of study	1 (3)	
Tots of spirits per week	1 (3)	<1.0
Consumed spirits prior to study	2 (5)	
Years prior to study, spirit consumption stopped	2 (5)	12.5 (5.0-20.0)
Physical activity level at commencement of study		
Sedentary	13 (34)	
Mild / moderate exercise	21 (55)	
Vigorous exercise	4 (11)	

3.3 Clinical characteristics of study participants

The clinical records of one of the participants could not be traced, and therefore, the clinical characteristics obtainable from the medical records prior to and during radiotherapy relate to 37 of the participants, unless otherwise reported.

Forty-one percent of the participants had received head and neck surgery prior to commencement of radiotherapy of which 73% had undergone a total laryngectomy. The presence of HIV infection was not reported in any of the clinical records. Two

(5%) of the participants were reported to be diabetic and one was receiving medication for the treatment of tuberculosis (Table 3.4).

Four (11%) of the participants received concomitant Cisplatin during the study, 3 of whom received a dosage of 20mg/m^2 and the fourth participant received a dosage of 40mg/m^2.

Table 3.4 Clinical characteristics of participants included in this study

Characteristic	*N*	%
Received head and neck surgery prior to radiotherapy	15	41
Had a total laryngectomy	11	29
Received chemotherapy prior to radiotherapy	2	5
Received radiotherapy before commencement of the study	1	3
Presence of HIV infection	0	0
Presence of Diabetes Mellitus	2	5
Presence of tuberculosis	1	3
Received concomitant chemotherapy during the study	4	11
Received 20mg/m^2 Cisplatin	3	8
Received 40mg/m^2 Cisplatin	1	3

Thirty-six of the participants (97%) had a diagnosis of squamous cell carcinoma with one participant (3%) having been diagnosed with a fibrous histiocytoma. Glottis tumour was the most prevalent (19% of participants). The tumour sites of 14 (38%) of the participants were in the oral cavity and those of 20 (54%) of the participants were in the throat (Table 3.5). The majority (57%) of the participants were diagnosed with a stage 4 malignancy; the corresponding percentages for stage 3, 2 and 1 malignancy were 24, 11 and 8% respectively.

Table 3.5 Tumour sites among the participants diagnosed with a malignancy

Tumour site	*N* (%)
In the oral cavity	
Tongue	1 (3)
Tonsil	3 (8)
Soft palate	2 (5)
Floor of mouth	1 (3)
Uvula	2 (5)
Tonsil pillar	1 (3)
Retro molar	1 (3)
In the throat	3 (8)
Sub glottis	1 (3)
Vocal cord	1 (3)
Tran glottis	3 (8)
Supraglottis	4 (11)
Oropharynx	1 (3)
Hypo pharynx	3 (8)
Glottis	7 (19)
Other	
Mandible	1 (3)
Maxillary sinus	1 (3)
Unknown	1 (3)

The majority (92%) of the participants were planned to receive ≥ six weeks of radiotherapy. More than one-third (35%) of the participants were planned to receive 35 days (7 weeks) of radiotherapy (Table 3.6). One daily radiotherapy fraction of two

Gray (radiotherapy source Cobalt 60; Linear accelerator) per treatment field was administered to all of the participants.

Table 3.6 The number of days of radiotherapy planned for the study participants

Days of radiotherapy planned	*N* (%)
27	2 (5)
28	1 (3)
30	8 (22)
33	4 (11)
34	9 (24)
35	13 (35)

In terms of radiotherapy fields, clinical details were only available for 36 (95%) of the participants (Table 3.7 and Table 3.8). The anterior neck and glottis were the most prevalent radiotherapy fields, which were used for 72% and 28% of participants respectively. The anterior neck was often used (N = 26) together with other fields during radiotherapy, to target lymph nodes situated in the neck. Eighty-one percent of the participants received a dosage of 60 Gray to a treatment field. Sixty-one percent of the fields used were predominantly delivered radiotherapy from the Cobalt 60 unit (Table 3.7).

Table 3.7 Types and total dosages of radiotherapy treatment per field planned to be administered to the study participants

Field	Dose (Gray)	*N* *(%)	Radiotherapy source	*N** (%)
Glottis	60	10 (28)	Co60** LA[#]	9 (25) 1 (3)
Anterior neck	50	26 (72)	Co60 LA	23 (64) 3 (8)
Soft palate	60	3 (8)	Co60 LA	2 (6) 1 (3)
Tongue	60	2 (6)	Co60	2 (6)
Maxilla	54	1 (3)	LA	1 (3)
Larynx	60	1 (3)	LA	1 (3)
Tongue base	40 60	1 (3) 1 (3)	Co60 LA	1 (3) 1 (3)
Vallekula	20	1 (3)	LA	1 (3)
Uvula	50 60	1 (3) 1 (3)	Co60 LA	1 (3) 1 (3)
Subglottis	60	1 (3)	Co60	1 (3)
Hypopharynx	60	3 (8)	Co60	3 (8)
Supraglottis	54 56 60	1 (3) 1 (3) 1 (3)	Co60 LA	2 (6) 1 (3)
Retromolar	60	1 (3)	Co60	1 (3)
Tonsil / tonsil pillar	60 68	2 (6) 1 (3)	Co60 LA	2 (6) 1 (3)
Floor of mouth	60	1 (3)	Co60	1 (3)
Glottis & tongue base	60	1 (3)	LA	1 (3)

Table 3.7 Types and total dosages of radiotherapy treatment per field planned to be administered to the study participants (Cont'd)

Mandible	56	1 (3)	LA	1 (3)
Nasopharynx	60	1 (3)	Co60	1 (3)

* The treatment field details of one of the participants cannot be reported due to the incomplete clinical records that were available for this participant.

** Cobalt 60

Linear accelerator

The largest field sizes were used for the nasopharynx and uvula fields. These fields were each used for 1 participant and the field sizes were 182 and 168cm^2 respectively. The smallest field size was that of the glottis, which had a mean of 81 (33.7) and a median of 94.8 (30.0 – 123.5cm^2) (Table 3.8). Twenty-seven (73%) of the participants received a localized boost to the primary tumour site during their radiotherapy course (64% Cobalt and 36% linear accelerator). The most frequently delivered boost dose was 10 Gray, but the boost dose ranged from 6 – 16 Gray during the radiotherapy courses of the different participants (Figure 3.1). Boosts were all delivered at the end of the radiotherapy courses of participants; except for 1 of the boosts that was delivered concomitantly. The daily dosage of all boosts was 2 Gray; except for the concomitant boost which was delivered at a dosage of 1.4 Gray over 10 days. The mean field size of the boosts was 34 (10.9) and the median field size was 34 (16 – 54cm^2) ($N = 24$).

Table 3.8 Field sizes (cm^2) used for radiotherapy treatments of participants included in the study

Field	Mean (SD) (cm^2)	Median (range) (cm^2)	*N**
Glottis	81.1 (33.7)	94.8 (30.0 – 123.5)	10
Anterior neck	122.4 (24.6)	119.0 (90.0 – 190.0)	22
Soft palate	131.6 (0.5)	131.6 (131.3 – 132.0)	2
Tongue	107.0 (43.1)	107.0 (76.5 – 137.5)	2
Tongue base	118.0 (4.2)	118.0 (115.0 – 121.0)	2
Vallekula	105.0	105.0 (105.0 – 105.0)	1
Uvula	168.0	168.0 (168.0 – 168.0)	1
Subglottis	126.0	126.0 (126.0 – 126.0)	1
Hypopharynx	114.0 (8.5)	114.0 (108.0 – 120.0)	2
Supraglottis	90.4 (13.6)	90.4 (80.8 – 100.0)	2
Retromolar	132.0	132.0 (132.0 – 132.0)	1
Tonsil / tonsil pillar	138.0 (25.5)	138.0 (120.0 – 156.0)	2
Floor of mouth	121.5	121.5 (121.5 – 121.5)	1
Glottis & tongue base	120.0	120.0 (120.0 – 120.0)	1
Nasopharynx	182.3	182.3 (182.3 – 182.3)	1

* The treatment field details of one of the participants cannot be reported due to the incomplete clinical records that were available for this participant.

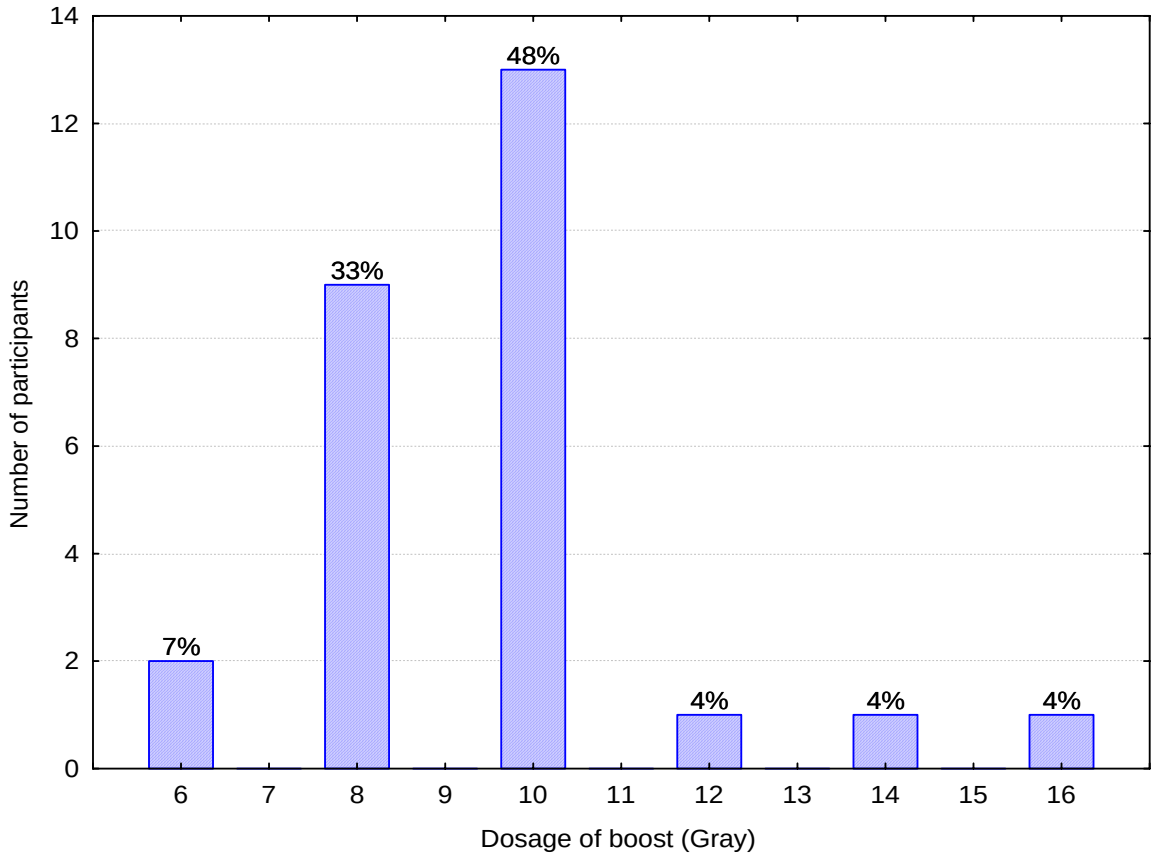

Figure 3.2 Frequency of boost dosages received at the end of the radiotherapy course of the study participants

Clinical data, obtained from the medical records, during the radiotherapy courses relates to 33 participants, as four participants did not meet with the investigator for the purpose of this study during this time.

The interruptions in radiotherapy treatment and the delivery of double fractions of radiotherapy relates to 32 of the participants, due to incomplete clinical records having been available for one of the participants. The majority (84%) of the participants had interruptions in their radiotherapy treatments. Radiotherapy treatments were interrupted for four (13%) of the participants by the radiotherapy unit/s having been out of order. For two (6%) of the participants this interruption occurred for four days and for the other two (6%) of the participants this occurred for two or three days during radiotherapy. Twenty-five (78%) of the participants had treatments interrupted by public holidays, of which the majority (88% of these participants) were interrupted for one day. Seven (22%) of the participants had

interruptions caused by non-attendance of radiotherapy treatments. The majority (71%) of these participants had an interruption for this reason for one day during radiotherapy. Two (6%) of the participants did not attend radiotherapy on four or five days during their radiotherapy course (Figure 3.3). Interruptions in radiotherapy treatments were therefore most commonly caused by public holidays, although the radiotherapy unit/s having been out of order caused interruptions most frequently over a larger number of days during radiotherapy of the participants.

Less than one-third (28%) of the participants received double fractions during radiotherapy, due to treatment interruptions. The majority (78%) of these participants received double fractions on one day during radiotherapy. The remaining percentage of participants was delivered double fractions on two days.

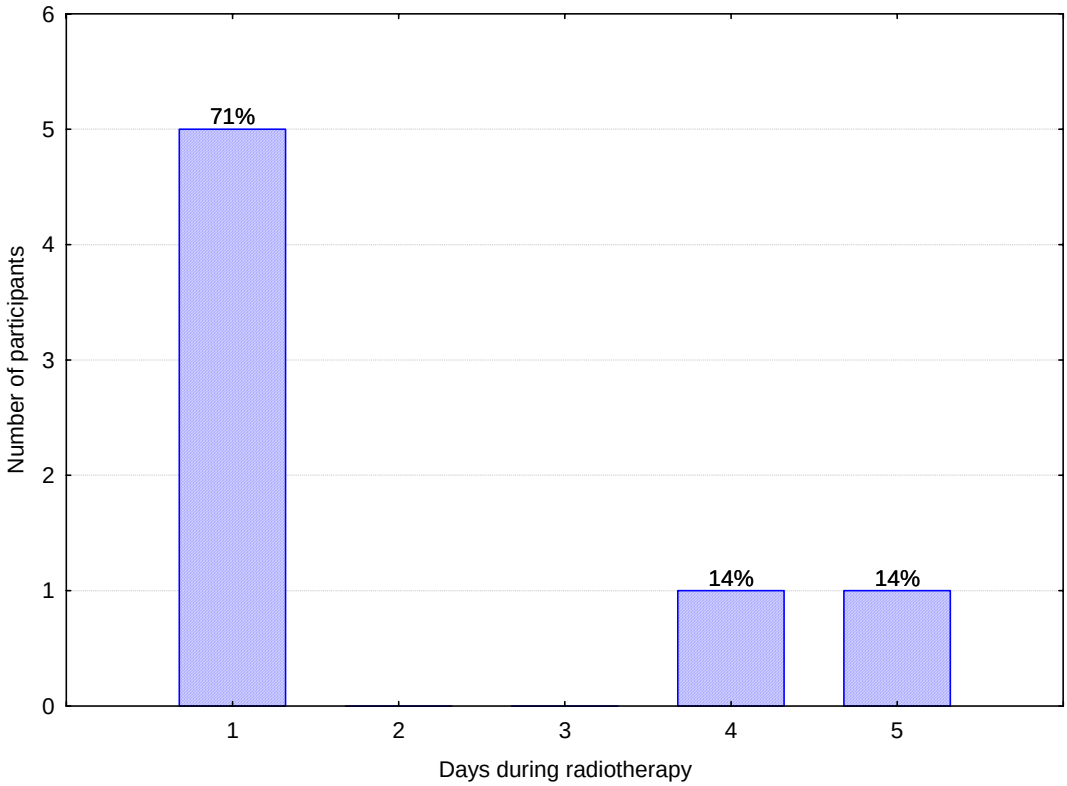

Figure 3.3 Number of days on which participants did not attend radiotherapy

Most (68%) of the participants stayed in hospital for the duration of their radiotherapy course because they lived too far from the hospital to commute daily (Table 3.9). It could be only determined for 22 of the participants whether they went home over weekends as the clinical records were incomplete for one participant. Fifty-five

percent of these participants went home over one or more weekends. The majority of the participants (59%) who went home over one or more weekends, did so for 1 - 2 weekends. The remainder of these participants went home for 3 - 5 weekends during radiotherapy.

Table 3.9 Place of residence of participants on commencement of radiotherapy

Place of residence	*N*	%
Home	11	32
Hospital	23	68

Six (55%) of the outpatients were hospitalized during radiotherapy. Two of the participants were hospitalized for dehydration towards the end of their radiotherapy course. Two of the participants were hospitalized before Week 3 of radiotherapy, due to requiring a blood transfusion (N = 1) and temporary accommodation (N = 1). Nasogastric feeding was required by one participant, from Week 3 of radiotherapy, and one participant was admitted to hospital in Week 4 of radiotherapy due to poor food intake. Four (36%) of the participants who were living at home during radiotherapy were therefore admitted to hospital during their radiotherapy course due to inadequate food and / or fluid intake as a result of treatment complications (Table 3.10).

Table 3.10 Reasons and timing of hospitalization during radiotherapy

Reason for hospitalization	When hospitalized	*N*
Dehydration	From Week 5 From Week 6	1 1
Nasogastric feeding required	From Week 3	1
Poor food intake	In Week 4	1
Blood transfusion	In Week 1	1
Temporary accommodation	In Week 1	1

3.4 Nutritional status of study participants

3.4.1 *Nutritional status pre-radiotherapy*

The mean BMI pre-radiotherapy [20.6 (5.0)] did not indicate underweight; however, the median BMI [19.2 (14.5 – 38.6kg/m^2)] indicated that half of the participants had a BMI below 19.2 pre-radiotherapy. More than one-third (42%) of the participants were underweight (BMI < 18.5) prior to the commencement of radiotherapy (Table 3.11).

More than half (53%) of the participants had an elevated PINI (PINI ≥ 1) prior to commencement of radiotherapy, indicating catabolism or the induction of the acute phase response in the majority of the participants pre-radiotherapy (Table 3.11). The prevalence of malnutrition pre-radiotherapy, as defined in this study (a BMI < 18.5 or a PINI ≥ 1), was 45%.

Table 3.11 Nutritional status of study participants pre-radiotherapy

Indicator of nutritional status	*N* (%)	Mean (SD)	Median (range)
Weight	38 (100)	56.4 (14.9)	54.0 (37.6 - 97.7)
BMI	38 (100)	20.6 (5.0)	19.2 (14.5 – 38.6)
BMI < 18.5	16 (42)		
The PINI*	38 (100)	5.5 (16.8)	1.1 (0.0 – 101.3)
A PINI ≥ 1	20 (53)		

*: Prognostic Inflammatory and Nutritional Index

3.4.2 *Nutritional status at the end of radiotherapy*

Fifteen (44%) of the 34 participants who were followed up during radiotherapy by the investigator were not weighed at the same time of day each week. This was usually due to the times of radiotherapy treatments changing between weeks of radiotherapy or inpatients being in a hurry to get back to the ward after radiotherapy treatments. One of the participants refused to be weighed in the last week of radiotherapy; therefore, anthropometrical data in this week relates to 20 of the study participants who did not drop out of the study.

The mean weight of participants decreased significantly (RM ANOVA; p = 0.01) from pre-radiotherapy to the last week of radiotherapy (Figure 3.4). The mean weight of the participants (*N* = 20) in the last week of radiotherapy was 59.5 (15.1) and the median weight was 54.8 (42.5 – 93.9kg). The mean absolute weight loss was 3.2 (4.8) and the absolute weight change of participants ranged from 4.8kg weight gain to 14kg weight loss during radiotherapy. The mean percentage weight loss [4.5 (6.7)] is not regarded as clinically significant in this study (Table 3.12). More than one-third (40%) of the participants; however, experienced clinically significant weight loss (≥ 5%) from pre-radiotherapy to the last week of radiotherapy and 30% of the participants experienced a weight loss of ≥ 10% of their pre-radiotherapy weight by the end of radiotherapy.

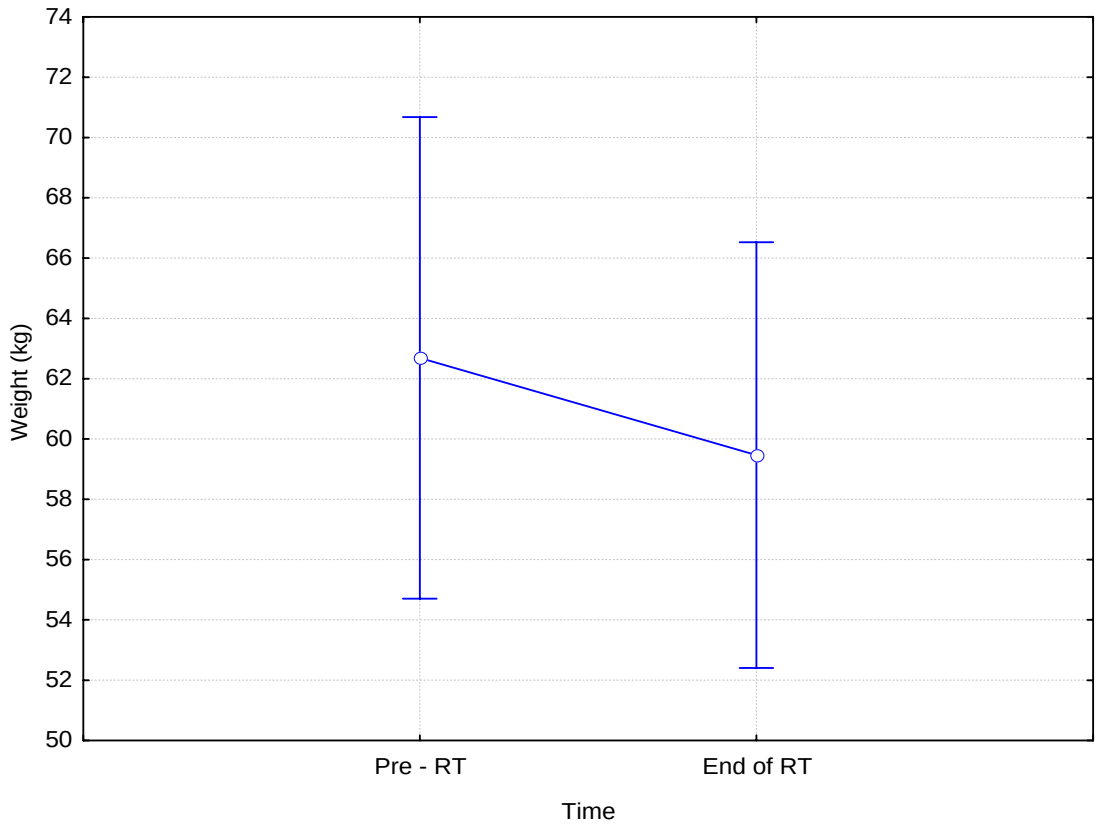

Figure 3.4 Mean weight and 95% confidence interval prior to and at the end of radiotherapy (RT) (*N* = 20; p = 0.01*)

* RM ANOVA (p ≤ 0.05)

Five (38%) of the 13 participants, who were planned to receive seven weeks of radiotherapy, completed the study and were weighed every week during radiotherapy. In these participants, the mean weight increased from pre-radiotherapy to Week 2, then decreased to Week 5, remained stable to Week 6 and decreased again to Week 7 of radiotherapy. The change in weight during radiotherapy in these participants was, however, not statistically significant (RM ANOVA; p = 0.40) (Figure 3.5).

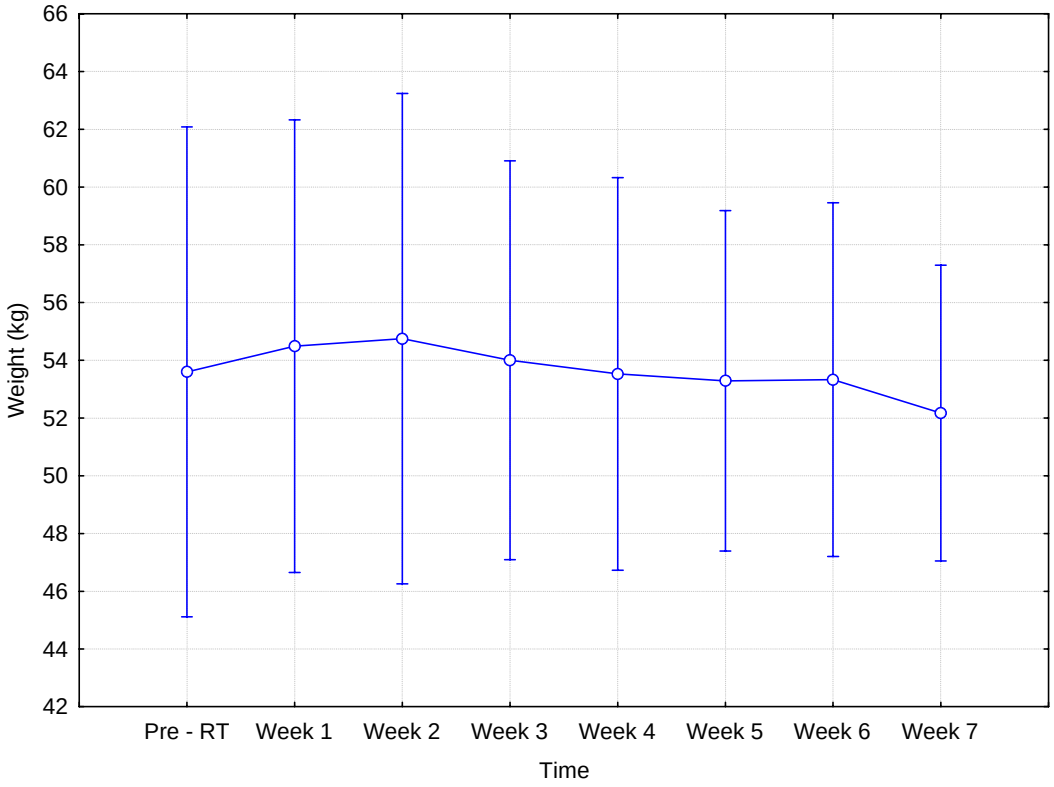

Figure 3.5 Pattern of weight change from pre - radiotherapy (RT) to the last week of RT (*N* = 5; p = 0.40)

A significant decrease in the BMI (RM ANOVA; p = 0.01) of participants from pre-radiotherapy to the last week of radiotherapy was observed (Figure 3.6). The mean BMI of the participants (*N* = 20) in the last week of radiotherapy was 21.5 (5.1) and the median BMI was 20.4 (16.0 – 33.0kg/m^2). The mean decrease in BMI of participants during radiotherapy was 1.2 (1.8) and the change in BMI of participants ranged from an increase of 1.8kg/m^2 to a decrease of 5.5kg/m^2 (Table 3.12). The prevalence of underweight (BMI < 18.5) in the last week of radiotherapy was 40%; however, the change in the prevalence of underweight from pre-radiotherapy to the last week of radiotherapy was not statistically significant (Table 3A.1).

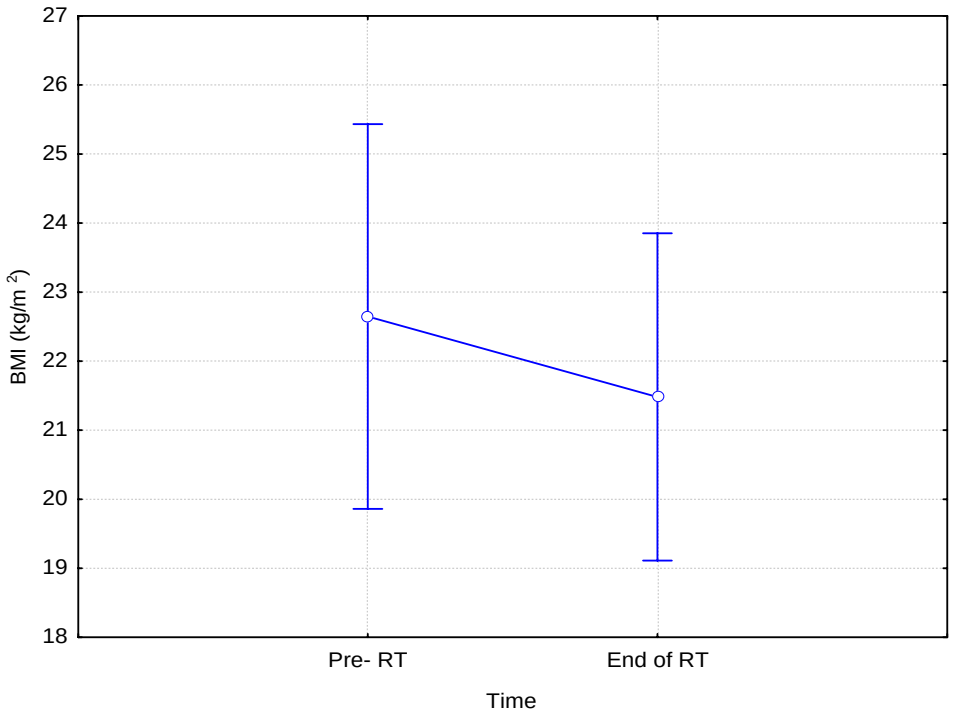

Figure 3.6 Mean BMI and 95% confidence interval prior to and at the end of radiotherapy (RT) (*N* = 20; p = 0.01*)

* RM ANOVA ($p \leq 0.05$)

Blood was drawn routinely from hospital inpatients the day before the investigator met with the participants. Two of these inpatients from whom blood had been drawn in their last week of radiotherapy, dropped out of the study at this stage. The PINI of 23 of the participants could therefore be calculated in the last week of radiotherapy.

There was a statistically significant increase in the PINI from pre-radiotherapy to the last week of radiotherapy (RM ANOVA; p = 0.04) when severe outliers were removed from the analysis (Figure 3.7). The mean PINI in the last week of radiotherapy (*N* = 23) was 35.8 (107.3) and the median PINI was 2.3 (0.1 – 509.2). Insufficient blood was obtained from one of the participants in Week 3 or 4 of radiotherapy; therefore, the PINI was calculated for 22 of the participants prior to, during and at the end of radiotherapy. The PINI was observed to increase greatly between Week 3 or 4 and the last week of radiotherapy. The acute phase response; therefore, appeared to be induced between Week 3 or 4 and the last week of radiotherapy in this study. This change in the PINI during radiotherapy was statistically significant (Friedman ANOVA Chi-square test; p = 0.00002) (Figure 3.8).

The PINI increased by a mean of 30.2 (104.9) during radiotherapy in this study. The median increase in the PINI [1.5 (-0.3 – 506.2)] was much smaller than the mean increase in the PINI (Table 3.12). More than three-quarters (83%) (*N* = 19) of the participants had an elevated PINI (≥ 1) in the last week of radiotherapy and the change in the prevalence of a PINI ≥ 1 from pre-radiotherapy to the last week of radiotherapy was statistically significant (McNemar Chi-square test; p = 0.01) (Table 3A.2).

The prevalence of malnutrition in the last week of radiotherapy of participants, as defined in this study (a BMI < 18.5 or a PINI ≥ 1 or ≥ 5% of pre-radiotherapy weight lost), was 90%. The change in the prevalence of malnutrition from pre-radiotherapy to the last week of radiotherapy was statistically significant (McNemar Chi-square test; p = 0.02) (Table 3A.3).

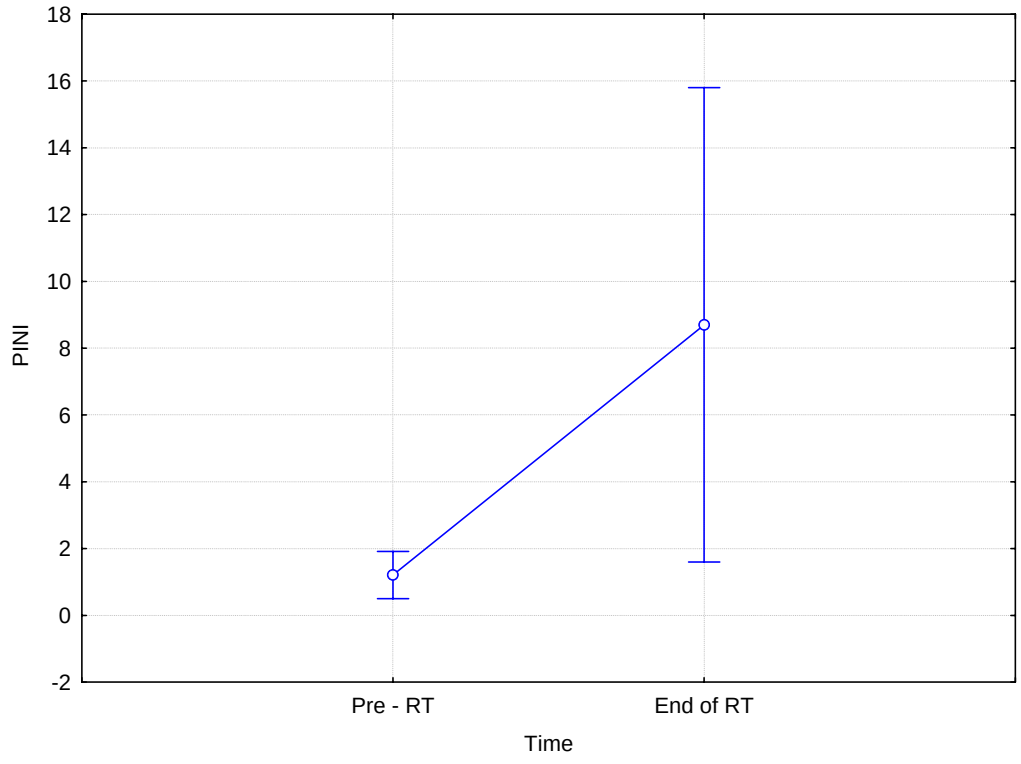

Figure 3.7 Mean PINI* and 95% confidence interval prior to and at the end of radiotherapy (RT) (*N* = 21; p = 0.04)**

* Prognostic Inflammatory and Nutritional Index

** RM ANOVA (p ≤ 0.05)

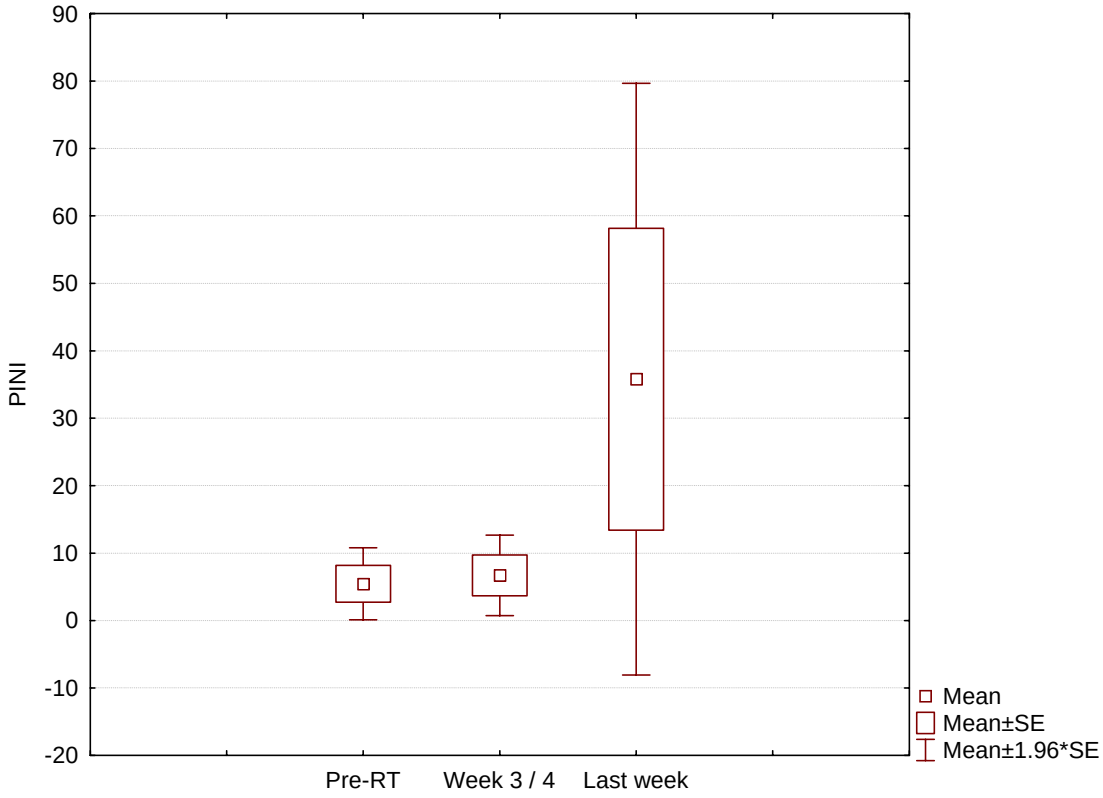

Figure 3.8 Box and Whisker Plot of the pattern of PINI* change during radiotherapy (RT) (*N* = 22; p = 0.00002)**

* Prognostic Inflammatory and Nutritional Index

** Friedman ANOVA Chi-square test ($p \leq 0.05$)

Table 3.12 Change in nutritional status of study participants during radiotherapy (from pre-radiotherapy to the last week of radiotherapy)

Indicator of nutritional status	*N*	Mean (SD)	Median (range)
Absolute weight loss (kg)	20	3.2 (4.8)	2.7 (-4.8 – 14.0)
% Weight loss	20	4.5 (6.7)	4.6 (-10.0 – 14.3)
Decrease in BMI (kg/m^2)	20	1.2 (1.8)	0.9 (-1.8 – 5.5)
Increase in the PINI*	23	30.2 (104.9)	1.5 (-0.3 – 506.2)

* Prognostic Inflammatory and Nutritional Index

3.4.3 Relationships between the anthropometrical and biochemical parameters

There was a trend towards statistical significance in the correlation between the percentage weight change from pre-radiotherapy to the last week of radiotherapy and the PINI in the last week of radiotherapy (Spearman correlation analysis; $p = 0.06$). There was also a trend towards statistical significance in the correlation between the absolute weight change from pre-radiotherapy to the last week of radiotherapy and the PINI in the last week of radiotherapy (Spearman correlation analysis; $p = 0.07$) (Table 3A.4).

The correlation between the PINI in the last week of radiotherapy and the change in BMI from pre-radiotherapy to the last week of radiotherapy was not statistically significant. The correlations between the change in the PINI (from pre-radiotherapy to the last week of radiotherapy) and the following were also not found to be statistically significant: the percentage change in weight, the absolute change in weight and the change in BMI from pre-radiotherapy to the last week of radiotherapy (Table 3A.4).

3.5 Side-effects and symptoms experienced by study participants during radiotherapy

3.5.1 Mucositis

The grades of mucositis recorded during radiotherapy relates to a maximum of 31 of the participants. The reasons for this are that five of the participants dropped out of the study in Week 1 or 2 of radiotherapy, the medical records of one of the participants could not be traced and one of the participants had incomplete medical records available. Clinical grading of oral mucositis was not obtained every week from Week 2 of radiotherapy for all participants. This was due to some participants not attending the clinic every week as well as doctors not recording clinical grades of mucositis every week for all participants. Participants were not always consulted by the same doctor every week of radiotherapy, which could have affected the reliability of the clinical grades of mucositis reported.

Mucositis was observed in all of the participants from Week 4 of radiotherapy. The prevalence of Grade I Mucositis decreased from 50% in Week 2 to 11% in Week 7. The change in the prevalence of Grade I Mucositis from Week 2 to the last week of

radiotherapy was not statistically significant (Table 3A.5). The change in the prevalence of Grade II Mucositis from Week 2 to the last week of radiotherapy was statistically significant (McNemar Chi-square test; p = 0.02) (Table 3A.6). Grade III Mucositis became prevalent from Week 3 of radiotherapy; however, the change in prevalence to the last week of radiotherapy was not statistically significant (Table 3A.7). More than 50% of participants each week had Grade II or III Mucositis from Week 4 of radiotherapy onwards (Figure 3.9).

No statistically significant differences were found between participants who were reported to have had and those reported not to have had Grade III Mucositis in the absolute change in weight, the change in BMI or the change in the PINI from pre-radiotherapy to the last week of radiotherapy (Table 3A.8 – Table 3A.10).

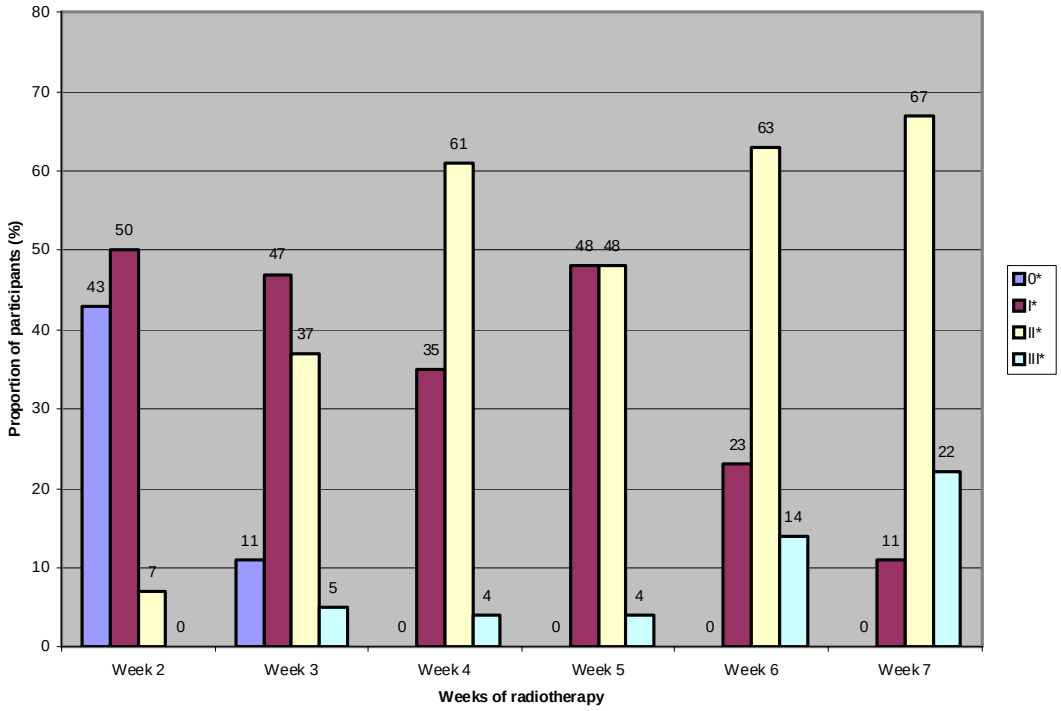

Figure 3.9 Prevalence and severity of mucositis during radiotherapy

* Grades of mucositis

3.5.2 Fungal infection of the oral cavity

The presence of fungal infection of the oral cavity was determined by the prescription of anti-fungal medication. The prevalence of fungal infection relates to a maximum of 33 of the participants in any week of radiotherapy, as the clinical records of one of the participants were incomplete.

Fungal infection of the oral cavity became prevalent from Week 2 of radiotherapy. The prevalence of fungal infection increased each week from 0% in Week 1– to 30% in Week 4. The highest prevalence of fungal infection occurred in Weeks 4 and 7 of radiotherapy, with a prevalence of 30% and 29% respectively (Figure 3.10).

There was a trend towards statistical significance in the difference in the mean absolute weight change from pre-radiotherapy to the last week of radiotherapy, between participants who had and those who did not have a fungal infection of the oral cavity (ANOVA; p = 0.09) (Table 3A.11). No statistically significant differences were found in the change in BMI or the change in the PINI from pre-radiotherapy to the last week of radiotherapy between these two groups of participants (Table 3A.12; Table 3A.13).

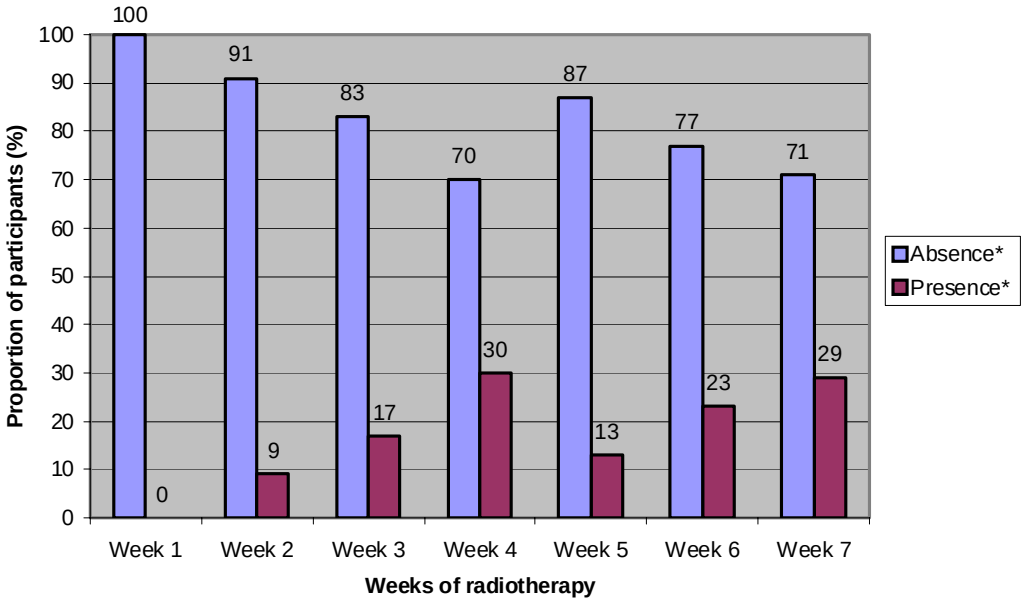

Figure 3.10 Prevalence of fungal infection of the oral cavity during radiotherapy

* Absence or presence of fungal infection

3.5.3 Other side-effects

One of the participants had a skin infection during radiotherapy. This was a fungal infection of the axilla. Four of the participants had other medical disorders occurring as a result of radiotherapy or chemotherapy (Table 3.13).

Table 3.13 Other medical disorders during radiotherapy

Disorder	*N*
Gynecomastia	1
Otitis Media	1
Otitis Externa	1
Dermatitis under eye lid	1

3.5.4 Symptoms reported in the HNRQ by study participants

Two of the participants were not administered the HNRQ in their last week of radiotherapy ($N = 1$ was confused in their last week of radiotherapy; $N = 1$ refused to be administered the HNRQ in their last week of radiotherapy), thus leaving 19 participants with completed questionnaires. Thirteen of the participants could not be administered the HNRQ in one of the weeks of radiotherapy; therefore, six participants were administered this questionnaire every week during their radiotherapy course.

Mouth domain

There was a statistically significant increase (RM ANOVA; $p = 0.0000$) in severity of symptoms related to this domain between Week 1 and the last week of radiotherapy (Figure 3.11). The change in the mean weekly mouth domain scores during radiotherapy showed a downward pattern; therefore, indicating an increasing severity of symptoms between the weeks of radiotherapy (Figure 3.12). This change was also statistically significant (RM ANOVA; $p = 0.0000$).

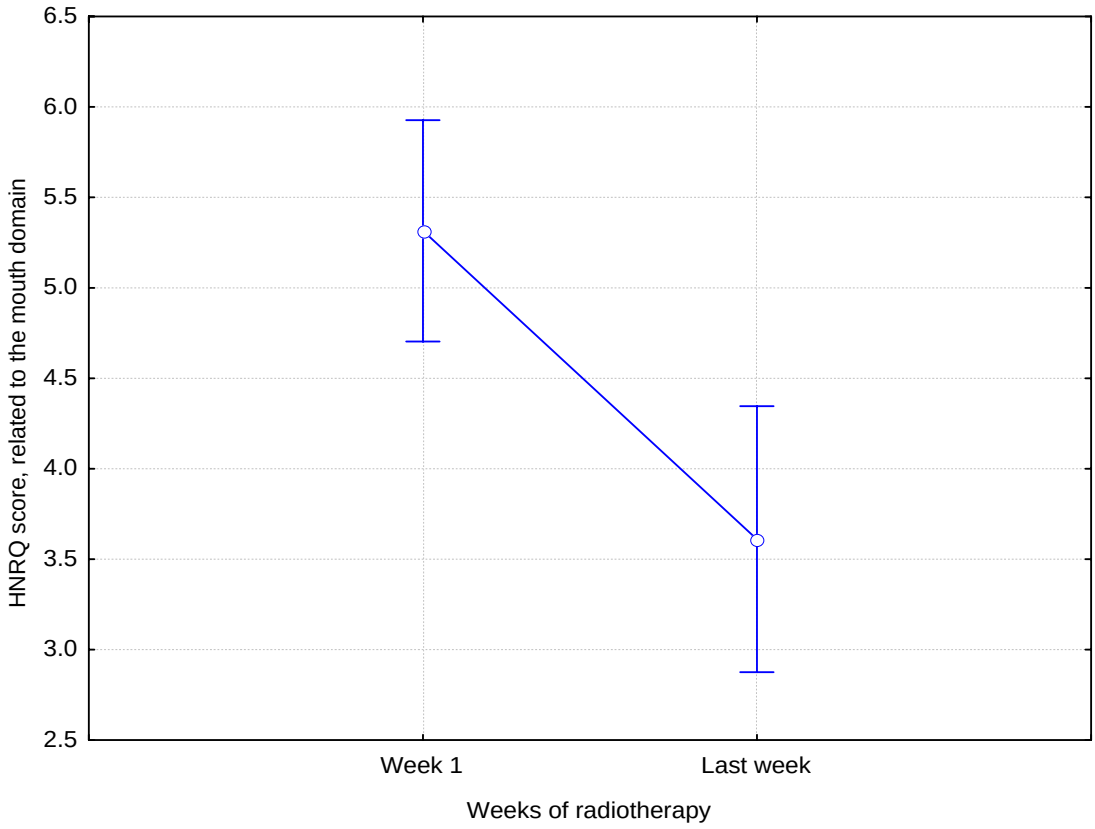

Figure 3.11 Mean HNRQ* score, related to the mouth domain, and 95% confidence interval in Week 1 and the last week of radiotherapy (*N* = 19; p = 0.0000)**

* Head and Neck Radiotherapy Questionnaire

** RM ANOVA ($p \leq 0.05$)

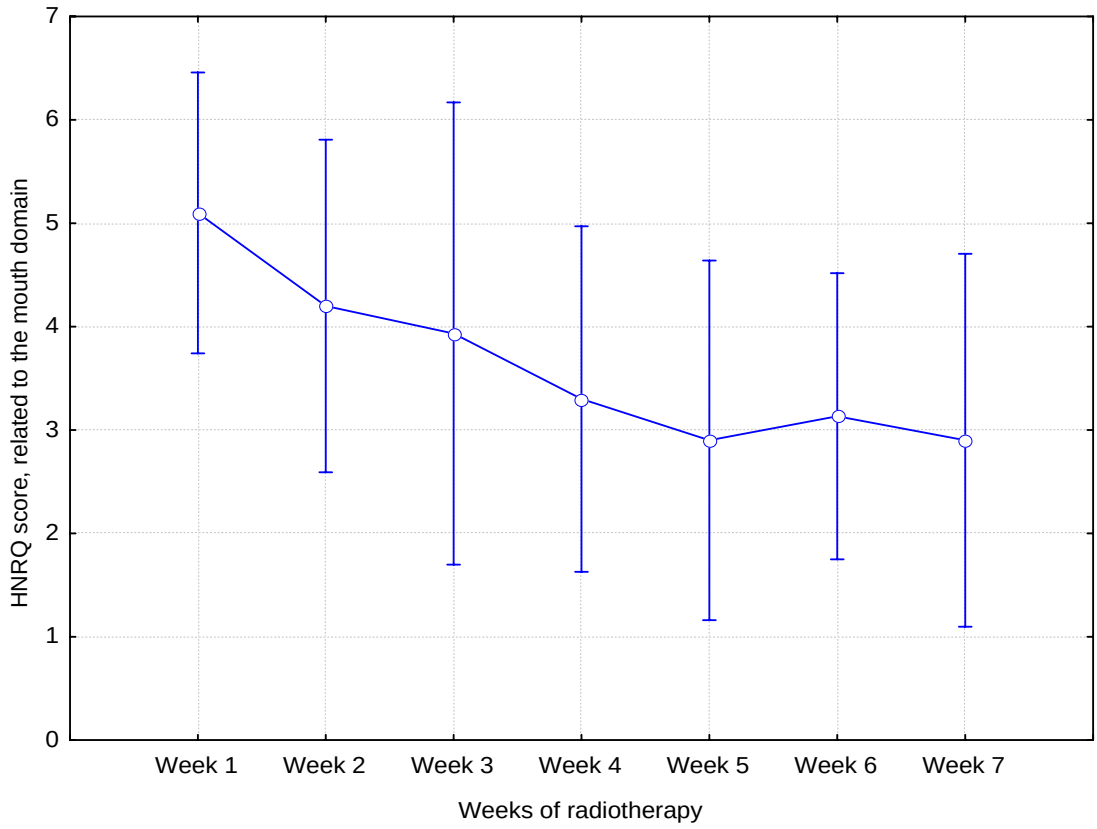

Figure 3.12 Pattern of change in the HNRQ* scores, related to the mouth domain during radiotherapy (*N* = 6; p = 0.0000)**

*: Head and Neck Radiotherapy Questionnaire

** RM ANOVA ($p \leq 0.05$)

Throat domain

Of the 19 participants who completed the HNRQ, 13 participants were eligible to be asked the questions related to the throat domain as they had not undergone a total laryngectomy. There was a statistically significant increase (RM ANOVA; p = 0.05) in severity of symptoms related to this domain (Figure 3.13). The pattern of change in severity of symptoms could not be obtained, due to an insufficient number of participants having been eligible to be asked the questions in the HNRQ related to this domain in every week of radiotherapy.

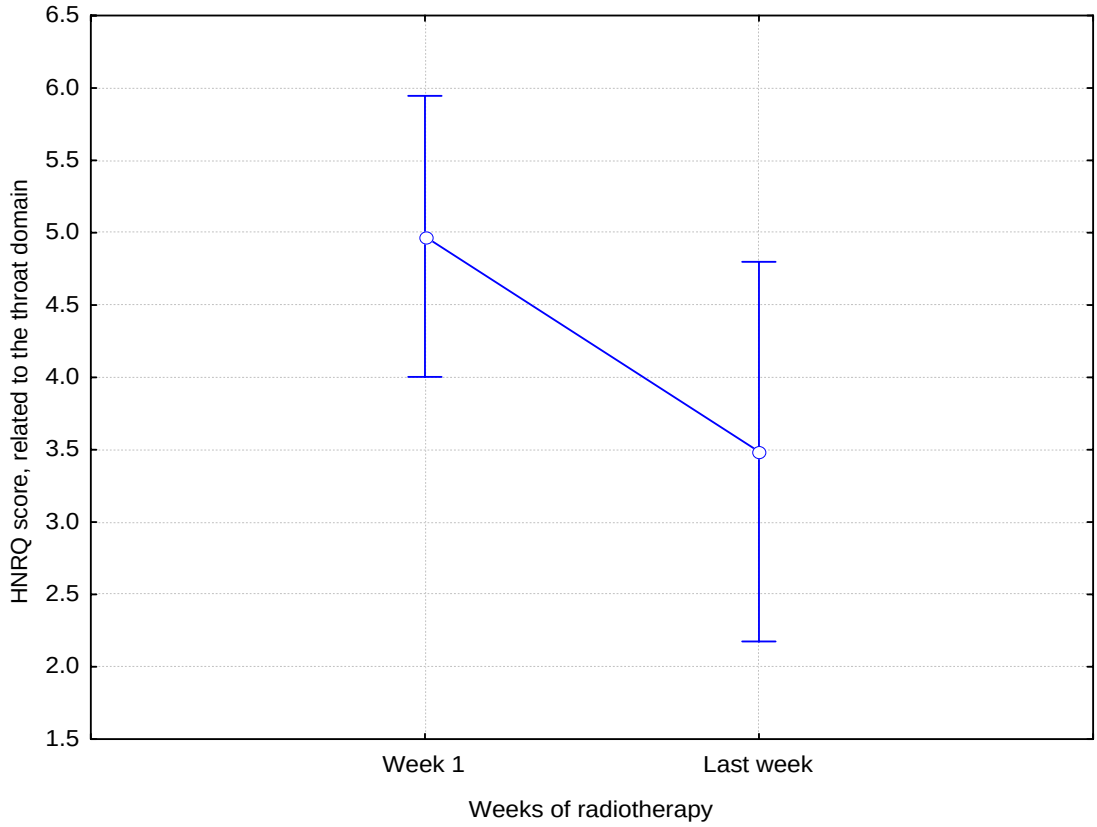

Figure 3.13 Mean HNRQ* score, related to the throat domain, and 95% confidence interval in Week 1 and the last week of radiotherapy (*N* = 13; p = 0.05)**

*: Head and Neck Radiotherapy Questionnaire

** RM ANOVA ($p \leq 0.05$)

Digestive system domain

There was a trend towards statistical significance in the increase in severity of symptoms related to the digestive system domain from Week 1 to Week 7 of radiotherapy (RM ANOVA; p = 0.06) (Figure 3.14). Severity of symptoms related to this domain increased from Week 1 to Week 6 and decreased from Week 6 to Week 7 of radiotherapy in this study. These changes; however, were not statistically significant (RM ANOVA; p = 0.16) (Figure 3.15).

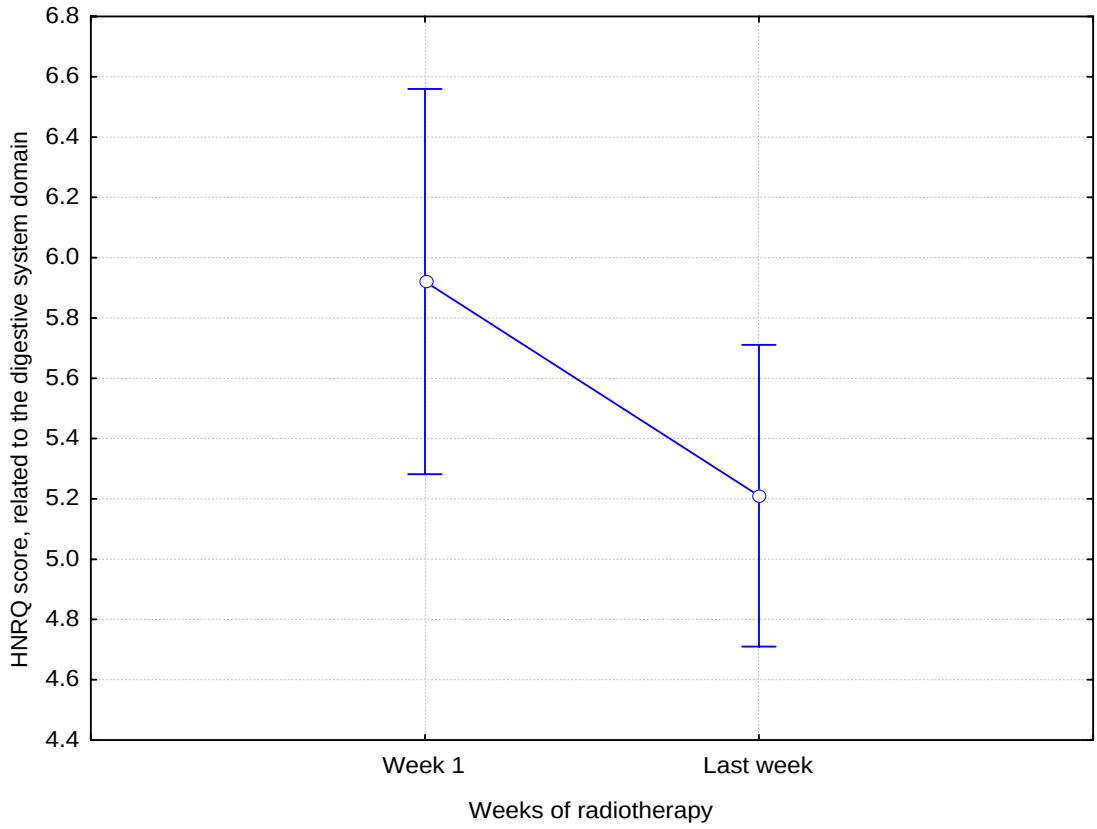

Figure 3.14 Mean HNRQ* score, related to the digestive system domain, and 95% confidence interval in Week 1 and the last week of radiotherapy (N = 19; p = 0.06)**

*: Head and Neck Radiotherapy Questionnaire

** Trend towards statistical significance

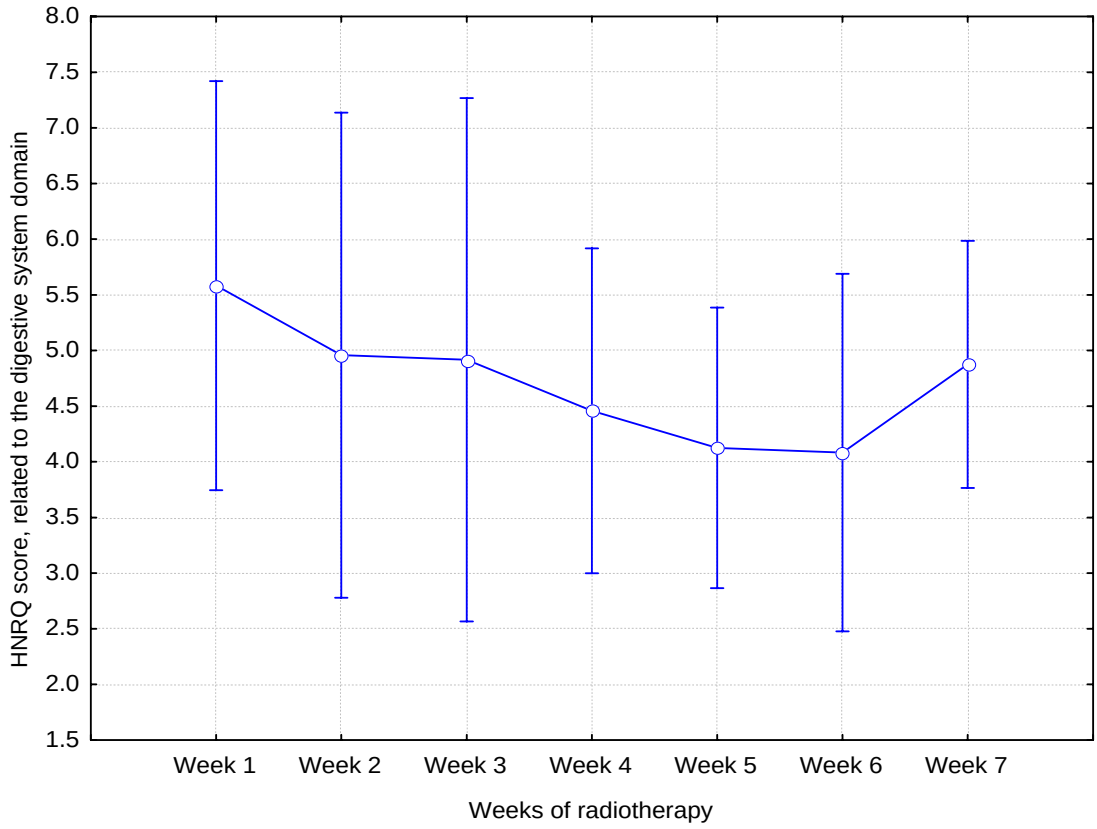

Figure 3.15 Pattern of change in the HNRQ* scores, related to the digestive system domain during radiotherapy (*N* = 6; p = 0.16)

*: Head and Neck Radiotherapy Questionnaire

Psychosocial domain

Of the 19 participants who completed the HNRQ, five participants were eligible to be asked the questions related to the psychosocial and energy domains as they were living at home during radiotherapy. An increase in severity of symptoms related to the psychosocial domain was observed in this study (Figure 3.16). This change was not statistically significant (RM ANOVA; p = 0.62). The pattern of change in severity of symptoms related to the psychosocial domain could not be obtained, due to an insufficient number of participants having been eligible to be asked the questions related to this domain in every week of radiotherapy.

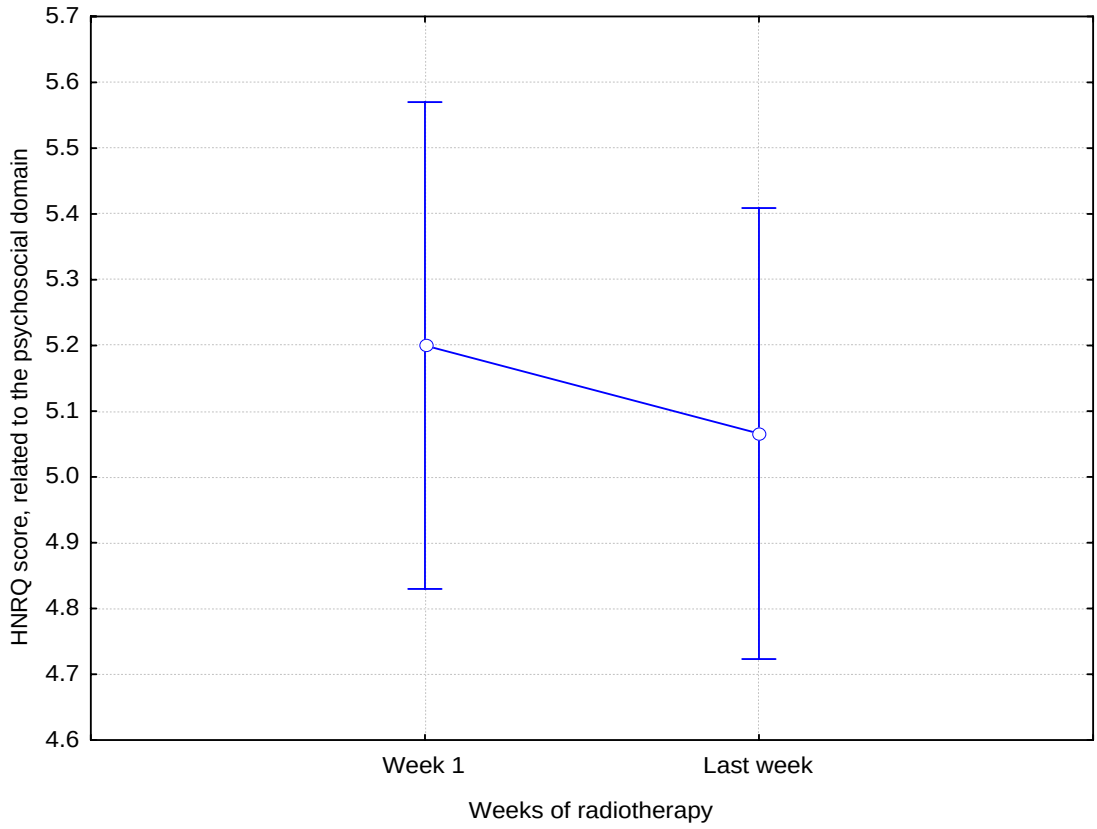

Figure 3.16 Mean HNRQ* score, related to the psychosocial domain, and 95% confidence interval in Week 1 and the last week of radiotherapy (*N* = 5; p = 0.62)

*: Head and Neck Radiotherapy Questionnaire

Energy domain

There was an increase in severity of symptoms related to the energy domain during radiotherapy in this study (Figure 3.17). This change was; however, not statistically significant (RM ANOVA; p = 0.21). The pattern of change in severity of symptoms related to this domain could not be obtained, due to an insufficient number of participants having been eligible to be asked the questions related to this domain in every week of radiotherapy.

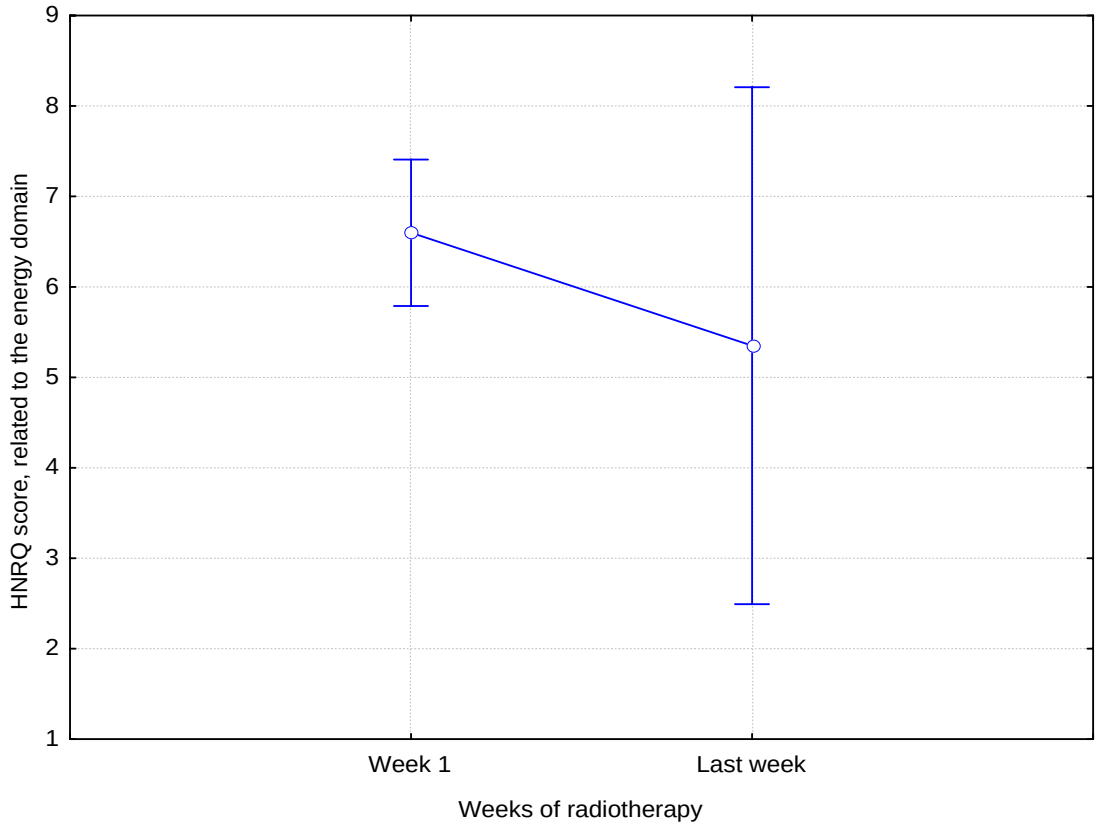

Figure 3.17 Mean HNRQ* score, related to the energy domain, and 95% confidence interval in Week 1 and the last week of radiotherapy (*N* = 5; p = 0.21)

*: Head and Neck Radiotherapy Questionnaire

Skin domain

A statistically significant increase (RM ANOVA; p = 0.0000) in severity of symptoms related to the skin domain was observed from Week 1 to Week 7 of radiotherapy (Figure 3.18). From Week 1 to Week 5 the severity of these symptoms increased and then remained unchanged until Week 7 (Figure 3.19). This change was also statistically significant (RM ANOVA; p = 0.0000).

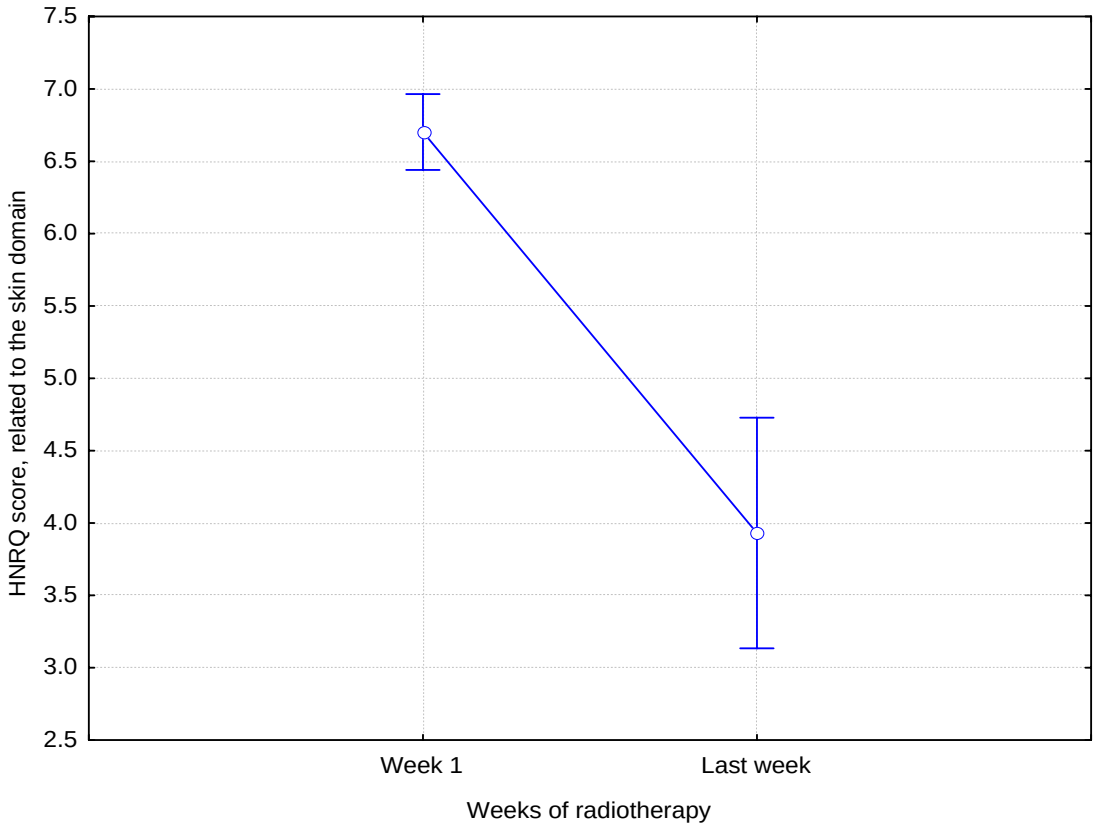

Figure 3.18 Mean HNRQ* score, related to the skin domain, and 95% Confidence Interval in Week 1 and the last week of radiotherapy (*N* = 19; p = 0.0000)**

*: Head and Neck Radiotherapy Questionnaire

** RM ANOVA ($p \leq 0.05$)

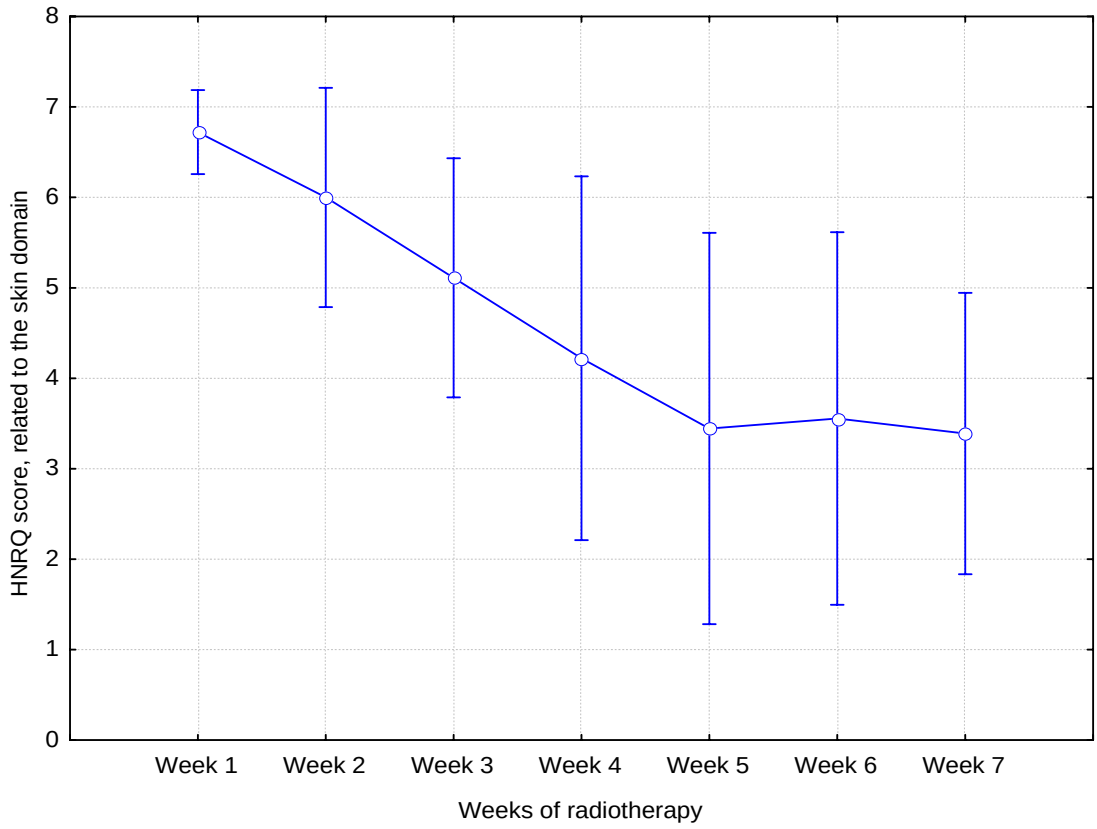

Figure 3.19 Pattern of change in the HNRQ* scores, related to the skin domain during radiotherapy (*N* = 6; p = 0.0000)**

*: Head and Neck Radiotherapy Questionnaire

** RM ANOVA ($p \leq 0.05$)

The largest mean change in severity of symptoms from Week 1 to the last week of radiotherapy, was that related to the skin domain [mean change in the HNRQ score, related to this domain was 2.8 (1.8)], followed by that related to the mouth domain [2.0 (1.2)] and the throat domain [1.5 (2.5)]. All of these mean changes were statistically significant (T–test; p = 0.0000 for the skin and the mouth domains; p = 0.05 for the throat domain). The mean changes in the severity of symptoms related to the rest of the domains were not statistically significant; except for that of the digestive system domain which had a trend towards statistical significance (T-test; p = 0.06) (Table 3.14).

Table 3.14 Change in the HNRQ* scores related to the six domains from Week 1 to the last week of radiotherapy

Domain	*N*	Mean (SD)	P - value
Mouth	19	2.0 (1.2)	0.00**
Throat	13	1.5 (2.5)	0.05**
Digestive system	19	0.7 (1.6)	0.06#
Psychosocial	5	0.2 (0.7)	0.56
Skin	19	2.8 (1.8)	0.00**
Energy	5	1.3 (1.9)	0.21

* Head and Neck Radiotherapy Questionnaire

** T-test ($p \leq 0.05$)

Trend towards statistical significance

Symptoms reflected in the consistency of foods consumed

During radiotherapy there was a decrease in the proportion of participants who consumed solid foods and an increase in the proportion of those who consumed liquids only and soft foods only. Forty-two percent of participants were consuming solid foods in Week 1 and 14% were consuming these foods in Week 7 (Figure 3.20). The change in the frequency of consumption of solid foods from Week 1 to the last week of radiotherapy was statistically significant (McNemar Chi-square test; $p = 0.01$) (Table 3A.14).

In each week of radiotherapy, the majority of participants were consuming liquids and soft foods only. More than half (58%) of the participants were consuming liquids and soft foods only in Week 1. Seventy-two percent of the participants were consuming this consistency of foods by Week 7. From Week 3 of radiotherapy, 4% of participants began tolerating liquids only and this proportion increased to 18% in Week 6 (Figure 3.20). The change in the frequency of consumption of liquids and soft foods only from Week 1 to the last week of radiotherapy was not statistically significant (Table 3A.15).

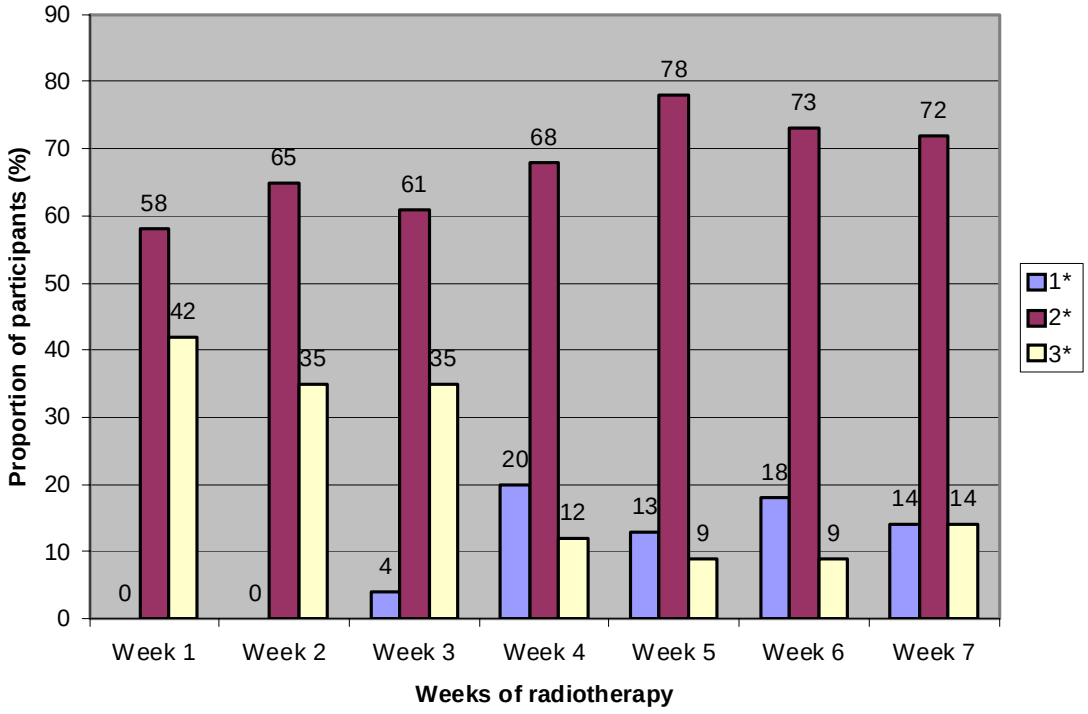

Figure 3.20 Frequency of consumption of the different levels of consistency of foods during radiotherapy

* Levels of consistency of foods: level 1 = liquids only; level 2 = liquids and soft foods only; level 3 = liquids, soft foods and solid foods

Relationships between the severity of symptoms and the nutritional status during radiotherapy

A statistically significant positive correlation was found between the change in the HNRQ score related to the throat domain from Week 1 to the last week of radiotherapy and the absolute weight change from pre-radiotherapy to the last week of radiotherapy (Spearman correlation analysis; $p = 0.04$). There was a statistically significant negative correlation between the change in the HNRQ score related to the skin domain from Week 1 to the last week of radiotherapy and the change in the PINI from pre-radiotherapy to the last week of radiotherapy (Spearman correlation analysis; $p = 0.04$). All of the other correlations between the severity of symptoms and the nutritional status during radiotherapy were not statistically significant (Table 3A.16).

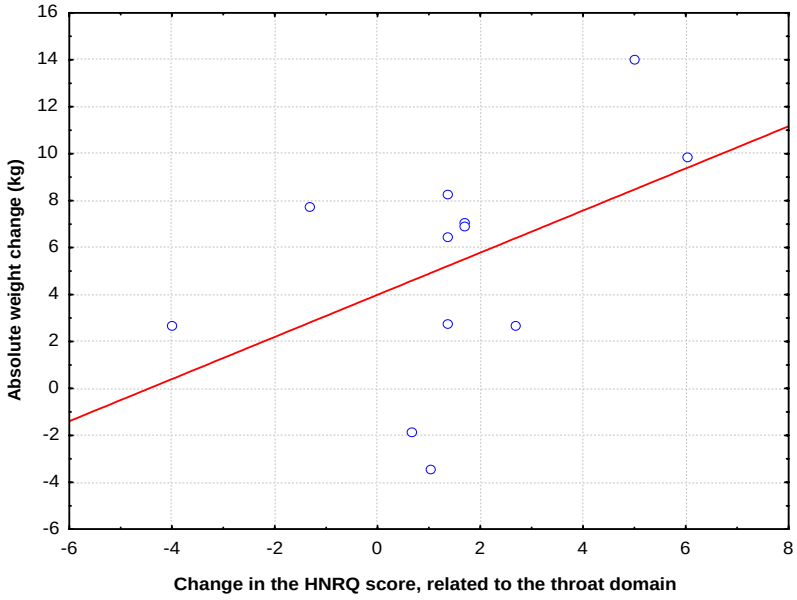

Figure 3.21 Relationship between the change in the absolute* weight and the change in the HNRQ score related to the throat domain (p = 0.04[#])**

* Weight in kg

** Head and Neck Radiotherapy Questionnaire

[#] Spearman correlation analysis ($p \leq 0.05$)

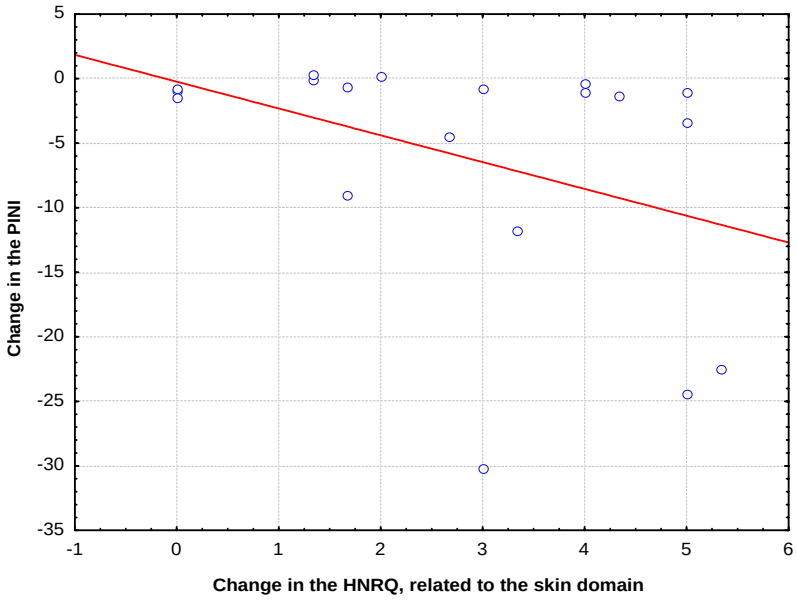

Figure 3.22 Relationship between the change in the PINI* and the change in the HNRQ score related to the skin domain (p = 0.04[#])**

* Prognostic Inflammatory and Nutritional Index

** Head and Neck Radiotherapy Questionnaire

[#] Spearman correlation analysis ($p \leq 0.05$)

Differences in the severity of symptoms experienced between participants with and without Grade III Mucositis and a fungal infection of the oral cavity

No statistically significant differences were found in the mean changes in the HNRQ scores, related to the mouth, throat, digestive system and skin domains from Week 1 to the last week of radiotherapy, between participants who had and those who did not have Grade III Mucositis or a fungal infection of the oral cavity during radiotherapy (Table 3A.17 – Table 3A.26). Insufficient observations were available to determine the differences in the mean changes in the HNRQ scores related to the energy and psychosocial domains between the groups of participants with and without Grade III Mucositis.

3.6 Medical treatment prescribed for study participants during radiotherapy

The prescription of medical treatment relates to a maximum of 33 of the participants during radiotherapy, as the clinical records of one of the participants were incomplete. Medical treatments were recorded if they were prescribed on at least one day.

Analgesic, sedative and anti-inflammatory medication

The analgesic medications were prescribed most frequently throughout radiotherapy. There was a trend towards statistical significance in the change in the frequency of prescription of analgesics from Week 1 to the last week of radiotherapy (McNemar Chi-square test; $p = 0.07$) (Table 3A.27). The analgesics that were prescribed for the most participants in a week were Andolex mouthwash and Dolorol forte (for 82% and 70% of participants respectively). One to 2 tablets of Dolorol forte were prescribed 3-6 times per day. Morphine was prescribed in a tablet form (i.e. MST) and in a syrup form (i.e. Mist morphine), for a maximum of 3 (9%) and 5 (15%) of the participants respectively during radiotherapy. More than half (55%) of the participants were prescribed mucaine for use before meals as local pain relief. Codis and Brufen also have anti-inflammatory properties. These medications were prescribed for a maximum of 15 (45%) and 11 (33%) of the participants respectively in a week during radiotherapy (Table 3.15).

Table 3.15 Prescription of analgesics during radiotherapy

Analgesic prescribed	*N* (%)* Maximum / week	Dosage	Frequency
MST (mg)	3 (9)	10 –20	3-4
Dolorol forte (tablets)	23 (70)	1 – 2	3-6
Codis (tablets)	15 (45)	1 – 2	3-4
Mucaine (mls)	18 (55)	5-10	2-3
Panado (tablets)	2 (6)	1-2	4
Cepacaine (lozenges)	1 (3)	1	4
Brufen (mg)	11 (33)	400	1-3
Mist morphine (mls) (concentration 20mg/5ml)	5 (15)	2.5-5	4-6
Andolex mouthwash	27 (82)	Prn	Prn
Bonjela ointment	1 (3)	Prn	Prn
Kenalog-in-orabase (paste)	2 (6)	Prn	Prn

* Percentage of the 33 participants from whose medical records this data was collected

Prn = as required

The frequency of prescription of sedatives increased from 18% in Week 1 to 43% in Week 7 (Table 3.23). The change in the frequency of prescription of sedatives from Week 1 to the last week of radiotherapy was not statistically significant (Table 3A.28). Serepax was prescribed for a maximum of 18% of participants and Tryptanol was prescribed for a maximum of 3% of participants in a week of radiotherapy. A range of 5-15mg per day of Serepax was prescribed. Ten milligrams of Tryptanol per day was prescribed during radiotherapy (Table 3.16). Anti-inflammatory medication was prescribed for 1-2 participants in a week from Week 2 to 7 (Table 3.23). The only anti-inflammatory medications prescribed were Indocid and Decadron which were each prescribed for one participant in any week.

Table 3.16 Prescription of sedatives during radiotherapy

Sedatives prescribed	*N* (%)* Maximum / week	Dosage	Frequency
Serepax (mg)	6 (18)	5-15	1
Tryptanol (mg)	1 (3)	10	1

* Percentage of the 33 participants from whose medical records this data was collected

Medication for treatment of symptoms related to the digestive system

The prescription of anti-emetics increased in frequency from 6% in week 1 to 26% in Week 4 of radiotherapy. Anti-emetics were prescribed the most frequently over all the weeks of radiotherapy, in Weeks 4 and 7 (Table 3.23). The change in the frequency of prescription of anti-emetics from Week 1 to the last week of radiotherapy was not statistically significant (Table 3A.29). Maxalon was prescribed the most frequently (for 15% of participants) out of all the anti-emetics, in a week during radiotherapy. The prescription of Maxalon was 10mg 3 times per day during radiotherapy. A maximum of 1-2 participants per week were prescribed each of the other anti-emetics (Table 3.17).

Table 3.17 Prescription of anti-emetics during radiotherapy

Anti-emetic prescribed	*N* (%)* Maximum / week	Dosage	Frequency
Maxalon (mg)	5 (15)	10	3
Zofran (mg)	1 (3)	8	As required
Clopamon (mg)	2 (6)	10	3
Stemetil (suppository)	1 (3)	1	4
Valoid (suppository)	2 (6)	1	2-3

* Percentage of the 33 participants from whose medical records this data was collected

Forty-five to 100% of participants were prescribed laxatives each week during radiotherapy. The frequency of laxative prescription increased each week, from Week 1 to Week 7 (Table 3.23). The change in the frequency of prescription of laxatives from Week 1 to the last week of radiotherapy was statistically significant (McNemar Chi-square test; p = 0.01) (Table 3A.30). Sorbitol was prescribed for the most participants [17 (52%)] in a week during radiotherapy. Ten to 20mls of Sorbitol 1-3 times per day was prescribed during radiotherapy (Table 3.18).

Table 3.18 Prescription of laxatives during radiotherapy

Laxatives prescribed	*N* (%)* Maximum / week	Dosage	Frequency
Senekot (tablet)	5 (15)	2-3	1-2
Normacol (mls)	4 (12)	5-10	1-2
Sorbitol (mls)	17 (52)	10-20	1-3
Dulcolax suppository	4 (12)	1	1-2
Dulcolax (tablet)	1 (3)	1	As required

* Percentage of the 33 participants from whose medical records this data was collected

The highest frequency of the prescription of antacids was during Weeks 6 and 7 (Table 3.23). Of all the antacids Losec was prescribed for the most participants [(2 (6% of participants)] in a week and the prescribed dosage was 20mg 1-2 times per day (Table 3.19).

Antispasmodic medication was prescribed for one participant in Weeks 5 and 6 (Table 23). Buscopan was prescribed for this participant at a dosage of 1 tablet 3 times per day.

Table 3.19 Prescription of antacids during radiotherapy

Antacids prescribed	*N* (%)* Maximum / week	Dosage	Frequency
Tagamet	1 (3)	800	1
AlOH	1 (3)	10	3
Losec	2 (6)	20	1-2

*: Percentage of the 33 participants from whose medical records this data was collected

Antibiotic and anti-fungal medication

The highest frequencies of prescription of antibiotics over all the weeks of radiotherapy were in Weeks 3 and 7. Less than 10% of participants were prescribed antibiotics in the other weeks of radiotherapy (Table 3.23). Augmentin was prescribed for the most participants [2 (6%)] in a week of radiotherapy, at a dosage of 375mg 3 times per day. The other antibiotics were each prescribed for a maximum of 1 participant in a week of radiotherapy. Streptamycin was prescribed as treatment for tuberculosis together with Rifater for 1 of the participants from Week 1 to Week 7 of radiotherapy (Table 3.20).

Table 3.20 Prescription of antibiotics during radiotherapy

Antibiotics prescribed	*N* (%)* Maximum / week	Dosage	Frequency
Streptamycin (mg)	1 (3)	750	1
Amoxil (mg)	1 (3)	500	3
Augmentin (mg)	2 (6)	375	3
Zinnat (mg)	1 (3)	500	2

* Percentage of the 33 participants from whose medical records this data was collected

The frequency of prescription of anti-fungal medication increased each week from 0% in Week 1 to the highest frequencies of 30% in Week 4 and 29% in Week 7 (Table

3.23). Nystatin and Mycostatin were each prescribed for the most participants (12% of participants) in a week of radiotherapy, at dosages of 2ml and 1-2ml respectively, 4 times per day (Table 3.21).

Table 3.21 Prescription of anti-fungal medication during radiotherapy

Anti-fungal medication prescribed	***N* (%)* Maximum / week**	**Dosage**	**Frequency**
Nystatin (ml)	4 (12)	2	4
Diflucan (mg)	2 (6)	200-400	1
Mycostatin (ml)	4 (12)	1-2	4
Flaggyl (mg)	1 (3)	400	3
Fungizone (lozenges)	2 (6)	1	3-4

* Percentage of the 33 participants from whose medical records this data was collected

Other medical treatment

Glycothymol mouthwash was prescribed each week and was also the most frequently prescribed in a week, out of all the other medical treatment prescribed. Bactigras antiseptic dressing and Scheriproct ointment were also more frequently prescribed than the "other" medical treatment. Three (9%) of the participants received intravenous fluids during radiotherapy (Table 3.22).

Table 3.22 Other medical treatment prescribed during radiotherapy

Medication prescribed	Weeks of radiotherapy prescribed	*N* (%)* Maximum / week
Rifater	1-7	1 (3)
Natreale tear drops	4-7	2 (6)
Mistablon nasal spray	1-7	1 (3)
Chloromex eye ointment	2-4	1 (3)
Bactigras antiseptic dressing	4-7	8 (24)
Scheriproct ointment	3-7	7 (21)
Glycothymol mouthwash	1-7	28 (85)
Salt / bicarbinate mouthwash	7	1 (3)
Duratears eye ointment	6	1 (3)
Canesten (cream)	6	1 (3)
Nebulizers	1; 5; 6	1 (3)
Intravenous (IV) fluids	5; 6	3 (9)

* Percentage of the 33 participants from whose medical records this data was collected

Table 3.23 The number and percentage* of study participants who were prescribed each type of medication during radiotherapy

Type of medication	Wk 1 *N* (%)	Wk 2 *N* (%)	Wk 3 *N* (%)	Wk 4 *N* (%)	Wk 5 *N* (%)	Wk 6 *N* (%)	Wk 7 *N* (%)
Analgesic	26 (79)	28 (88)	28 (97)	26 (96)	23 (96)	21 (95)	7 (100)
Anti-emetic	2 (6)	4 (13)	4 (14)	7 (26)	5 (21)	5 (23)	4 (57)
Laxative	15 (45)	20 (63)	22 (76)	22 (81)	20 (83)	20 (91)	7 (100)
Sedative	6 (18)	5 (16)	4 (14)	4 (15)	5 (21)	7 (32)	3 (43)
Antibiotic	1 (3)	2 (6)	3 (10)	1 (4)	2 (8)	1 (5)	1 (14)
Anti-fungal	0 (0)	3 (9)	5 (17)	8 (30)	3 (13)	5 (23)	2 (29)
Antacid	0 (0)	1 (3)	1 (3)	1 (4)	2 (8)	3 (14)	1 (14)
Anti-spasmodic	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	1 (5)	0 (0)
Anti-inflammatory	0 (0)	1 (3)	1 (3)	2 (7)	2 (8)	2 (9)	1 (14)

* Percentage of participants who were being followed-up, in each week of radiotherapy

3.7 Nutritional intake / support of study participants during radiotherapy

Twenty-three participants remained in hospital from commencement of radiotherapy and four were admitted to hospital after Week 1. Prescription of supplementation drinks relates to these inpatients; however, prescription of vitamins and minerals relates to the 33 participants who had complete clinical records.

Data obtained from the Dietary and Lifestyle Questionnaire, including the intake of vitamin, mineral and herbal / alternative supplements and supplementation drinks as well as the number of participants who reported to have been consulted by a dietitian during radiotherapy, relates to a maximum of 34 participants. These participants included both in- and outpatients. This data could not be obtained for 18 (53%) of these participants in one of the weeks of radiotherapy (N = 16 did not meet with the investigator; N = 1 was unable to stand / too weak; N = 1 did not attend radiotherapy).

Supplementation drinks prescribed

Fifty-nine percent of the total inpatients were prescribed supplementation drinks. Build-Up and Ensure were each prescribed alone with the former being prescribed most frequently. Ensure alternating with Build-Up or Nutren Diabetes alternating with Build-Up was also prescribed. One participant was prescribed Ensure and Build-Up simultaneously (Table 3.24).

Table 3.24 Number of inpatients who were prescribed the various types of supplementation drinks during radiotherapy

Types of supplementation drinks	*N* / Total *N* (%)
Build-Up	6 / 27 (22)
Ensure	3 / 27 (11)
Ensure and Build-Up	1 / 27 (4)
Ensure or Build-Up	5 / 27 (19)
Nutren Diabetes or Build-Up	1 / 27 (4)

The mean daily quantity (ml) of supplementation drinks prescribed for the inpatients ranged from 570 (50.0) to 680 (199.2) per day, and the median quantity was 600 over all the weeks of radiotherapy. Prescription of supplementation drinks increased in frequency over the weeks of radiotherapy from 3% of participants in Week 1 to 50% in Week 7 (Table 3.25).

Table 3.25 Quantity of supplementation drinks (ml/24 hours) prescribed for inpatients during radiotherapy

Week of radiotherapy	*N* (%)*	Mean (SD) (ml/24 hours)	Median (range) (ml/24 hours)
1	1 (3)	600	600 (600 – 600)
2	4 (6)	600 (0.0)	600 (600 – 600)
3	9 (30)	570 (50.0)	600 (500 – 600)
4	11 (39)	670 (219.5)	600 (500 – 1200)
5	12 (48)	680 (199.2)	600 (600 – 1200)
6	10 (43)	580 (42.2)	600 (500 – 600)
7	4 (50)	580 (50.0)	600 (500 – 600)

* Percentage of the participants (in- and outpatients) who were being followed-up, in each week of radiotherapy

Five (45%) of the 11 participants, who were living at home on commencement of radiotherapy, were referred to the Nutrition Supplementation Programme (NSP) of the Integrated Nutrition Program of the Western Cape. The majority (60%) of these participants were referred in Week 3 (Table 3.26).

Table 3.26 Weeks in which outpatients were referred to the NSP*

Week of radiotherapy	*N* / Total *N* (%)
1	1 / 11 (9)
3	3 / 11 (27)
4	1 / 11 (9)

* Nutrition Supplementation Program of the Integrated Nutrition Program of the Western Cape

Intake of supplementation drinks

Fifty percent of the participants reported taking supplementation drinks daily, with the largest proportion taking Build-Up alone (Table 3.27).

Table 3.27 Types of supplementation drinks consumed during radiotherapy

Supplementation drink/s	*N* (%)*
Nutrimil alone	3 (18)
Build-Up alone	7 (41)
Ensure alone	2 (12)
Ensure and Build-Up simultaneously	1 (6)
Ensure and Build-Up alternating	2 (12)
Nutren Diabetes	1 (6)
Nutrimil and Ensure simultaneously	1 (6)

* Percentage of the participants (*N* = 17) who reported consuming supplementation drinks daily

The mean quantity (ml) of supplementation drinks reported to have been taken per day ranged from 350 – 670. In Week 6 the largest mean quantity of supplementation drinks was consumed 670 (264.6). The energy (kcal) content of all the supplementation drinks consumed during radiotherapy was 1kcal / ml; therefore, the volume of supplementation drinks consumed by participants is equivalent to the energy (kcal) intake from these drinks. (Table 3.28)

Table 3.28 Quantity (ml) of / energy intake (kcal) from supplementation drinks consumed per day* during radiotherapy

Week of radiotherapy	*N*	Mean (SD) (ml/24hours)	Median (range) (ml/24hours)
2	2	400 (0.0)	400 (400 – 400)
3	4	350 (191.5)	300 (200 – 600)
4	9	530 (438.7)	400 (100 – 1600)
5	11	620 (256.2)	600 (200 – 1100)
6	9	670 (264.6)	600 (400 – 1200)
7	4	500 (115.5)	500 (400 – 600)

* As determined by the administration of the Lifestyle and Dietary Questionnaire

A statistically significant correlation was found between the maximum energy intake from supplementation drinks taken and the change in the HNRQ scores related to the skin domain from Week 1 to the last week of radiotherapy (Spearman correlation analysis; $p = 0.02$) (Figure 3.23). No statistically significant correlations were found between the maximum energy intake from supplementation drinks consumed by participants and the following: the percentage change in weight, the absolute change in weight, the change in BMI and the change in the PINI from pre-radiotherapy to the last week of radiotherapy as well as the change in the HNRQ scores related to the mouth, throat and digestive system domains from week 1 of radiotherapy to the last week of radiotherapy (Table 3A.31). Insufficient observations were available to determine the correlations between the maximum energy intake from supplementation drinks consumed and the change in the HNRQ scores related to the energy and psychosocial domains during radiotherapy.

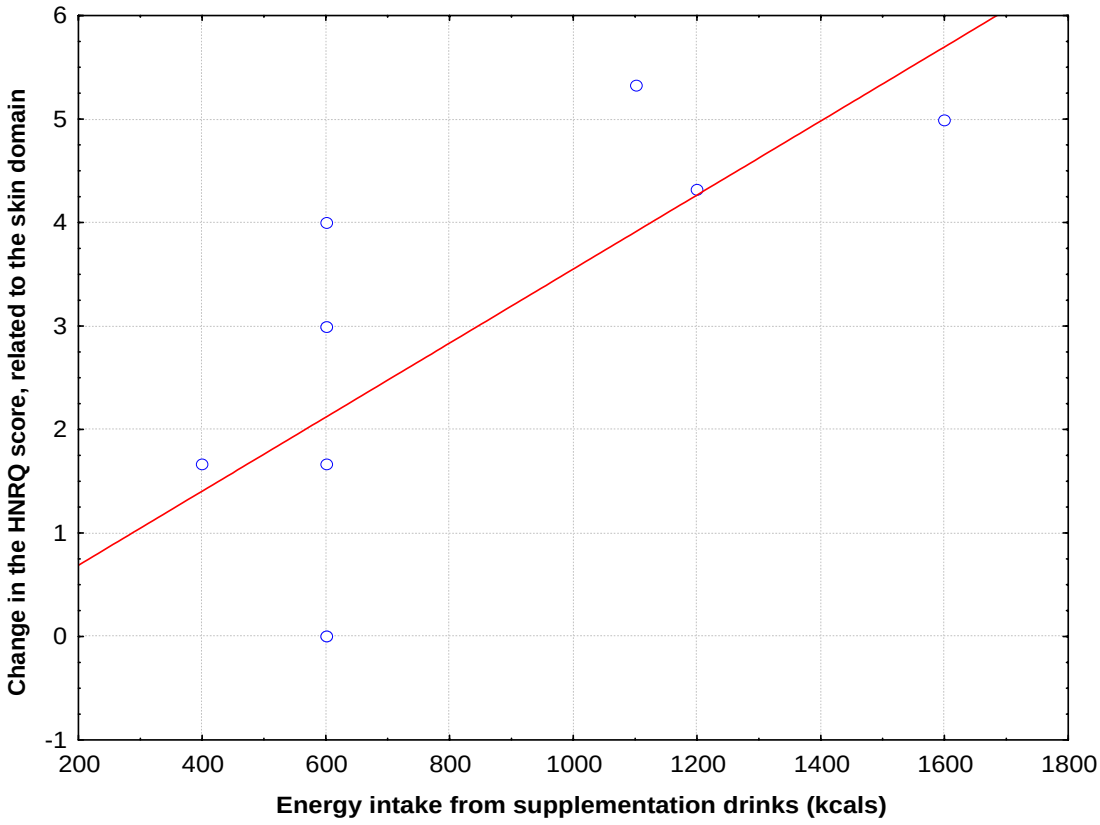

Figure 3.23 Relationship between the change in the HNRQ* score related to the skin domain and the maximum daily energy intake from supplementation drinks during radiotherapy (p = 0.02)**

* Head and Neck Radiotherapy Questionnaire

** Spearman correlation analysis ($p \leq 0.05$)

Vitamin and mineral supplements prescribed

Eight (24%) of the participants were prescribed vitamin or mineral supplements during radiotherapy. A megadose (10 or more times the RDA) of vitamin B6 was prescribed for one of the participants from Week 1 to Week 7, due to having received medication for tuberculosis (Rifater) during radiotherapy. One or more of the B-vitamins were prescribed for six (18%) participants and one participant was prescribed vitamin C. No herbal supplements were prescribed during radiotherapy (Table 3.28).

Table 3.28 Daily dosages and timing of prescription of vitamin and mineral supplements during radiotherapy

Type of supplement (dosage)	X RDA*	Weeks of radiotherapy	*N* (%)
Vitamin B complex (4 tablets):		1 – 6	1 (3)
Vitamin B1 (20mg)	20		
Vitamin B2 (28mg)	8		
Vitamin B3 (80mg)	4		
Vitamin B6 (8mg)	4		
Vitamin B complex (2 tablets):		3; 5; 6	2 (6)
Vitamin B1 (10mg)	10		
Vitamin B2 (4mg)	4		
Vitamin B3 (40mg)	2		
Vitamin B6 (4mg)	2		
Slow-Mag (2 tablets):		1; 5	2 (6)
Magnesium (1070mg)	3		
Vitamin C (300mg)	3	4–6	1 (3)
Vitamin B6 (25mg)	15	1-7	1 (3)
Vitamin B1 (20mg)	17	5	1 (3)
Vitamin B1 (100mg)	83	6	1 (3)

* Recommended Dietary Allowance (for males aged 51 – 70 years)

Intake of vitamin, mineral and herbal / alternative supplements

Six participants (18%) took a B-vitamin supplement and four (12%) took vitamin C. Supplementation of B-vitamins occurred in four of the weeks and vitamin C in three of the weeks of radiotherapy. One (3%) of the participants took a zinc supplement at a dosage of 2 – 3 times the RDA in two of the weeks of radiotherapy. The herbal / alternative supplements milk thistle and melatonin were taken over 3 weeks and 4 weeks respectively (Table 3.29).

One (3%) of the participants applied vitamin E-enriched oil to their skin in two of the weeks of radiotherapy. Ciplaton multivitamin was taken by one (3%) of the participants in four of the weeks of radiotherapy; which provided up to 5 times the RDA of a variety of vitamins and minerals. This supplement also included Panax Ginseng (200mg). Stressvite multivitamin was also taken by one (3%) of the participants, during three of the weeks of radiotherapy. The intake of this multivitamin provided megadoses of vitamins B1 (thiamine), B2 (riboflavin), B12, C and folic acid as well as 5 – 10 times the RDA of vitamin B3 (niacin) and zinc.

Table 3.29 Daily dosages and timing of intake of vitamin, mineral and herbal / alternative supplements during radiotherapy

Type of supplement (dosage)	X RDA*	Weeks of radiotherapy	*N* (%)**
Vitamin B complex (2 tablets):		1; 2; 3; 5	5 (15)
Vitamin B1 (10mg)	10		
Vitamin B2 (4mg)	4		
Vitamin B3 (40mg)	2		
Vitamin B6 (4mg)	2		
Folavite B12 (1 tablet):		3; 4	1 (3)
Vitamin B12 (25micrograms)	10		
Folic acid (800micrograms)	2		
Vitamin C (200mg)	2	1	1 (3)
(300mg)	3	4; 6	3 (9)
Zinc (30mg)	3	3; 4	1 (3)
Milk thistle (2 tablets/day)	N/A[#]	2-4	1 (3)
Melatonin (2 capsules/day)	N/A	3-6	1 (3)

* Recommended Dietary Allowance (for males aged 51 – 70 years)

** Percentage of the 34 participants who were followed-up during radiotherapy

[#] Not applicable

Consultation by a dietitian

The minority of participants reported to have been consulted by a dietitian in every week of radiotherapy, with the largest proportion (36%) of participants having reported to be consulted in Week 4 (Table 3.30). Three (9%) of the participants, who were administered The Lifestyle and Dietary Questionnaire, did not know whether they had been consulted by a dietitian. one of the weeks of radiotherapy, and therefore were excluded from the analysis of this data in these weeks of radiotherapy.

Table 3.30 Proportion of study participants who reported to have been consulted by a dietitian during radiotherapy

Week of radiotherapy	*N* (%)*
1	5 (16%)
2	2 (7%)
3	3 (12%)
4	9 (36%)
5	7 (32%)
6	6 (27%)
7	2 (33%)

* Percentage of participants who were administered the Lifestyle and Dietary Questionnaire each week of radiotherapy

3.8 Lifestyle of study participants during radiotherapy

Data obtained from the Dietary and Lifestyle Questionnaire, including the smoking of cigarettes, consumption of alcohol and the level of physical activity, related to a maximum of 34 participants. This data could not be obtained for 18 (53%) of these participants in one of the weeks of radiotherapy (N = 16 did not meet with the investigator; N = 1 was unable to stand / too weak; N = 1 did not attend radiotherapy).

The number of participants who reported to have smoked cigarettes decreased over the weeks of radiotherapy from 8 (24%) in Week 1 to none in Week 7. The number of cigarettes reported to have been smoked per day also decreased during radiotherapy (Table 3.31).

Table 3.31 Proportion of study participants who smoked cigarettes during radiotherapy

Week of radiotherapy	Cigarettes / day	*N* (%)*
1	3 – 4	7 (21)
	10	1 (3)
2	2 – 4	4 (12)
	10	1 (3)
3	1 – 2	3 (9)
4	1 – 2	4 (12)
5	2	1 (3)
6	2	1 (3)
7	0	0 (0)

* Percentage of the 34 participants who were followed-up during radiotherapy

Alcohol was reported to only have been consumed in Week 3 of radiotherapy. One participant reported to have consumed three cans of beer and one to consume seven glasses of dessert wine in that week of radiotherapy.

The level of physical activity reported by the participants decreased from Week 1 to Week 7 of radiotherapy. By Week 7 the proportions increased to 50% of participants who were sedentary and decreased to 50% of participants who were doing mild / moderate exercise (Table 3.32).

Table 3.32 The level of physical activity of study participants during radiotherapy

Week of radiotherapy	%* of participants who were sedentary	%* of participants who were doing mild / moderate exercise	%* of participants who were doing vigorous exercise
1	39	61	0
2	42	55	3
3	38	54	8
4	44	52	4
5	43	57	0
6	50	50	0
7	50	50	0

* Percentage of the participants who were followed-up, in each week of radiotherapy

CHAPTER 4: DISCUSSION

This study has demonstrated that severe side-effects occur during radical radiotherapy to the head and neck at TBH and that nutritional status is compromised by the end of radiotherapy. As this study was performed on a small number of subjects the results should be interpreted with caution. A decrease in the weight ($p = 0.01$) and BMI ($p = 0.01$) and increase in the PINI ($p = 0.04$) occurred. An increase in the prevalence of malnutrition ($p = 0.02$) was also observed. Oral mucositis occurred in all participants from Week 4; the majority of these developing severe mucositis. Fungal infection of the oral cavity was prevalent throughout radiotherapy, with the highest prevalence (30%) in Week 4. Increases in severity of symptoms related to the mouth ($p = 0.0000$), throat ($p = 0.05$) and skin domains ($p = 0.0000$) were observed.

This study is the first to have been conducted in South Africa on this patient population. In addition, no other study could be found that investigated the change in the PINI during radical head and neck radiotherapy. This study has addressed critical issues facing a vulnerable patient population. Only fifty-nine percent of inpatients and 45% of outpatients were prescribed supplementation drinks and most participants reported that a dietitian had not consulted them, in each week of radiotherapy.

4.1 Change in nutritional status

For the purpose of this study measures of nutritional status were weight, BMI and the PINI. No studies could be found that used a combination of a low BMI (< 18.5), an elevated PINI (≥ 1) and weight loss ($\geq 5\%$ by the end of radiotherapy) for defining malnutrition before and at the end of radiotherapy. Using this combination of measures of nutritional status was more sensitive to identifying malnutrition in this study than if only one measure was used. The proportion of participants who had malnutrition in this study pre-radiotherapy (45%) is higher than that reported in a study conducted in Turkey by Unsal *et al* (24%)[4]. Patients with Stage 4 malignancies were however, excluded from the latter study which could have reduced the prevalence of malnutrition in that study. Malnutrition on completion of radiotherapy in the present study (90%) was similar to that found in the study by Unsal *et al* (88%). The duration of radiotherapy was shorter in the latter study, which could have reduced the prevalence of malnutrition; however, nutritional support was only provided to patients who had malnutrition (as determined by subjective global assessment) on

commencement of radiotherapy in that study, which could have contributed to the higher prevalence of malnutrition than would have been expected.

Change in weight

Statistically significant weight loss was demonstrated in this study, which is a reason for concern as it has been reported that even small amounts of weight loss may significantly worsen prognosis in cancer patients[12]. The purpose of radical radiotherapy is to provide patients with a chance of cure; therefore, any weight loss of patients during radical radiotherapy should be avoided. Weight loss of patients with HNM during radical radiotherapy has previously been reported in the literature[17, 18, 19, and 20].

The mean percentage weight loss of the participants was not clinically significant according to the criteria set (≥ 5%); however, 40% of the participants demonstrated clinically significant weight loss and 30% of the participants demonstrated severe weight loss, of ≥ 10% of their pre-radiotherapy weight by the last week of radiotherapy. This is comparable to a study by Beaver *et al*, which was conducted in the USA, in which there was a 33% incidence of severe weight loss during radical radiotherapy of patients with HNM[19]. The definition of severe weight loss, which was used in that study, was, however, not provided. Feeding tube placement was provided for 25% of these patients before or during radiotherapy, compared to only a 5% rate of feeding tube placement during radiotherapy in the present study. The higher rate of feeding tube placement in the study of Beaver *et al*, could have prevented more severe weight loss from having been experienced in that study. The fractionation schedules of the radiotherapy administered was not reported; therefore, accelerated fractionation (more than one fraction of radiotherapy per day) could have been received by a proportion of those patients and led to more severe side-effects experienced than that in the present study. In addition, the radiation source, which was also not reported, could have resulted in worse side-effects being experienced. A similar rate of administration of IV fluids (10%) occurred in both studies; which suggests similar severity of side-effects experienced in the mouth and throat.

The proportion of participants who experienced severe weight loss in the present study is less than that experienced in a study by Munshi *et al*, which was conducted in

India, in which 74% of the patients lost > 10% of their pre-radiotherapy weight by the end of their treatment. However, 25% of those patients received concurrent chemoradiation, compared to 11% of participants in the present study. This could have resulted in worse side-effects experienced. No dietetic input was provided to patients during radiotherapy in that study; which could also have resulted in the larger proportion of patients who experienced severe weight loss[18].

In a study by Chencharick and Mossman, no weight loss during radical radiotherapy of patients with HNM was reported. Reasons for this could have been the continued nutritional support of all the patients during radiotherapy, the radiation source of Cobalt 60 having been used for all the patients and the lack of delivery of concurrent chemoradiation to any of the patients[21].

Change in BMI

No studies were found in the literature that assessed the change in BMI of patients with HNM undergoing radical radiotherapy. The statistically significant decrease in the BMI of participants in the present study indicates that nutritional status is compromised during radiotherapy in TBH.

Change in the Prognostic Inflammatory and Nutritional Index (PINI)

The statistically significant increase in the PINI during radiotherapy in this study indicates that the acute phase response is induced during radical head and neck radiotherapy. The acute phase response is known to have a negative impact on nutritional status[7]; therefore, the increase in the PINI in this study demonstrates the declining nutritional status during radiotherapy.

The trend towards statistical significance in the correlations between the severity of the acute phase response induced and both the absolute weight loss and percentage weight loss of participants from pre-radiotherapy to the last week of radiotherapy suggests that the acute phase response induced during radiotherapy could partly be responsible for the change in weight of patients with HNM undergoing radical radiotherapy. The increase in the PINI occurred between Week 3 / 4 and the last week of radiotherapy, which reflects the high prevalence of severe mucositis from Week 4 as well as that of fungal infection in Week 4. This also suggests that the

weight loss that was observed occurred between Week 3 / 4 and the end of radiotherapy.

4.1.1 Factors that could have affected nutritional status

Socio-demographic factors

The low socio-economic status of the participants could have contributed to the poor nutritional status observed on commencement of this study. The history of heavy smoking and excessive alcohol consumption of some of the participants could also have had a detrimental effect[6]. In addition the high member density of households, the low household income and the proportion of participants who had no refrigerator at home could have compromised nutritional status of those participants who were living at home during radiotherapy.

Clinical factors

Eighty-one percent of participants in the present study had a stage 3 or 4 malignancy, which would have negatively affected the nutritional status of participants[29]. Cachexia as reflected by an elevated PINI in 53% of the participants prior to commencement of radiotherapy, could have contributed to an increased severity of weight loss during radiotherapy[8]. The large proportion of the participants who had undergone head and neck surgery prior to the commencement of radiotherapy, could have adversely affected the ability to chew and / or swallow. This could have resulted in inadequate nutritional intake and, thus malnutrition in these participants on commencement and during the study. The administration of chemotherapy or radiotherapy in 8% of the participants prior to commencement of the present study, could have contributed to the poor nutritional status at the commencement of radiotherapy. The severity of weight loss that was experienced by the participants could have been partly attributed to the concomitant chemotherapy received by 11% of participants[12]. The hospitalization of most of the participants during radiotherapy could have improved the nutritional status of participants during the study, due to the provision of meals in hospital as well as the dedication of a dietitian to the oncology wards at Tygerberg Hospital.

Nutritional support

Only 59% of the inpatients were prescribed supplementation drinks during the study and less than half of participants, who were outpatients during radiotherapy, were referred to the NSP for nutritional support. This is likely to have adversely affected nutritional intake of participants during radiotherapy. The criteria that needed to be met for participants to have been referred to the NSP, were as follows: BMI < 18.5 or > 10% weight loss over the previous 6 months or > 5% weight loss over the previous month. A reason for the limited referral of participants to the NSP could have been the low proportion of those who met these criteria during radiotherapy. The difference between the minimum prescribed and the minimum consumed quantity of supplementation drinks during radiotherapy, indicates that participants did not consume the entire quantity of supplementation drinks prescribed for them. Build-Up supplementation drink, which was prescribed most frequently, is provided with the meals which are supplied by the kitchen at TBH, while the other types of supplementation drinks are delivered to inpatients in the mornings for use at any time during the day. It is possible that providing Build-Up at mealtimes could have discouraged their intake due to the sensation of satiety.

The majority of participants reported that they had not been consulted by a dietitian each week of radiotherapy, which suggests that limited personal contact with participants was made on the hospital wards even though there was a dedicated dietitian to these wards. This could have resulted in a lack of encouragement to participants with oral intake and appropriate nutritional support, which is crucial during radiotherapy for HNM[33]. In Week 4 of radiotherapy, when 61% of participants had Grade II Mucositis only 36% of participants reported having been consulted by a dietitian.

4.2 Prevalence and severity of side-effects

The administration of concomitant chemotherapy in 11% of the participants during this study could have resulted in more severe side-effects of radiotherapy to have been experienced[12]. The majority of the participants in this study were planned to receive at least 6 weeks of radiotherapy; which could have worsened the severity of side-effects experienced during this study[3]. The intake of B-vitamins (up to 10 times the RDA), vitamin C (up to four times the RDA) or zinc (at three times the RDA) by a

maximum of 18% of the participants during radiotherapy could have reduced the severity of side-effects due to their roles in tissue repair. These micronutrients were each; however, only taken over 2 to 4 weeks of radiotherapy.

The severity of side-effects caused by radiotherapy is also known to be influenced by nutritional status[3]. The high proportion (42%) of participants who were underweight or who had an elevated PINI (53%), i.e. cachexia, prior to commencement of radiotherapy and the weight loss experienced by participants during radiotherapy in the present study could have worsened the severity of side-effects experienced and negatively affected the participants' tolerance of these side-effects.

Poor tolerance / severity of radiotherapy side-effects during the present study is reflected in the large proportion (36%) of the participants who were hospitalised during radiotherapy due to dehydration and/or inadequate food intake. It is also reflected in the proportion of participants who discontinued radiotherapy (5%), those who received nasogastric feeding (5%) and those who received IV fluids (9%) during radiotherapy in this study.

Side-effects related to the mouth and throat

All of the participants in this study developed mucositis; however a 30% to 60% prevalence of mucositis has previously been reported in the literature in patients with HNM undergoing radiotherapy[11]. Oropharyngeal mucositis has been documented in the literature to be the single most debilitating side-effect of radiotherapy to the head and neck[20]. In this study the clinical grading of mucositis was only determined by inspection of the oral cavity; therefore, the degree of mucositis severity in the throat is not known in this study. The prevalence of Grade III Mucositis from Week 3 of radiotherapy in this study indicates that severe oral mucositis was experienced during this study. This is reflected in the prevalence of participants who were tolerating liquids only from Week 3 of radiotherapy in this study.

The clinical grading of mucositis is a subjective measure, which could result in intervariability. The grading system used for mucositis assessment can only be applied for clinically visible mucositis[11]. The severity of mucositis recorded by doctors during this study may therefore not be an accurate reflection of the severity of

pain experienced by participants. Assessment of the severity of symptoms related to the mouth and throat domains in the HNRQ includes that of pain. The significant decrease in the scores of these domains suggests that pain was experienced in the mouth and throat. The trend towards statistical significance in the increase from Week 1 to the last week of radiotherapy in the proportion of participants who were prescribed analgesic medication also demonstrates the increase in the level of pain in the mouth and the throat that was experienced. In addition, the mean increases in severity of symptoms related to the mouth and throat domains, indicated that these symptoms were the most severe, second only to those related to the skin domain. The increasing severity of symptoms experienced in the mouth and throat is also demonstrated by the statistically significant increase in the prevalence of Grade II Mucositis as well as the decrease in the proportion of participants who were consuming solid foods.

The low frequency of prescription of morphine during this study suggests that few participants reached the highest level of analgesic prescription during radiotherapy, which implies that pain of participants could have been more effectively controlled. The high prevalence of the prescription of Andolex and Glycothymol mouthwash could have aggravated the pain experienced in the mouth and throat. Standard mouthwashes have been reported to be unsuitable for an irradiated mouth, due to irritation of the damaged mucosa. It has been suggested that frequent, mechanical cleansing of the oral cavity during head and neck radiotherapy is more important in oral care than the antiseptic properties of a mouthwash[27]. Pain experienced from use of the above mouthwashes, could have led to the avoidance of frequent, mechanical cleansing of the mouth and; therefore, increased the risk of oral infection. It has been reported that most of the loss of salivary function occurs after 1-2 weeks of radiotherapy to the head and neck[13]. The prevalence of fungal infection from Week 2 of radiotherapy in this study; could reflect the onset of xerostomia, as a decrease in salivary secretion has been demonstrated to be accompanied by a rise in oral yeast flora during head and neck radiotherapy[13].

The prevalence of bacterial and fungal infection of the oral cavity in this study, could have contributed to the prevalence and severity of mucositis diagnosed. It is possible that the poor oral hygiene contributed to the prevalence of these oral infections.

Protein-energy malnutrition (PEM) has been documented to negatively affect wound healing, reduce immunocompetence and increase risk of infection[9]. PEM of participants could therefore have also played a role in contributing to the prevalence of oral infections during this study. This is illustrated in the trend towards statistical significance in the difference in the mean absolute weight loss between those participants who had and those who did not have a fungal infection of the oral cavity. No statistically significant differences in the mean weight loss of participants or the severity of change in the PINI could be found between the participants who had and those who did not have Grade III Mucositis during radiotherapy. This might have been due to the small number of participants who were assessed by a medical doctor and given a clinical grading of mucositis between Week 3 and the last week of radiotherapy.

The majority of tumour sites of participants were in the throat; which could have increased the prevalence of side-effects / symptoms experienced in the throat during the study. The glottis field, which was used for the largest proportion of the participants, had the smallest mean field size out of all of the fields used in this study. This could have reduced the severity of side-effects, which were experienced in the throat during this study, as the volume of tissue irradiated is known to affect the severity of side-effects experienced[26]. The smoking of cigarettes and the consumption of alcohol by participants during radiotherapy could have contributed to the prevalence of mucositis as well as the symptoms experienced in the mouth and throat[39]. The statistically significant positive correlation between the extent of change in severity of symptoms related to the throat domain and the extent of weight loss during radiotherapy indicates that patients experiencing pain in the throat, hoarse voice and/or difficulty swallowing during radical head and neck radiotherapy are at increased risk for weight loss during radiotherapy.

Side-effects related to the skin

The symptoms related to the skin domain were experienced the worst out of all the domains, during radiotherapy in this study. A reason for this could be that for the majority of fields, radiotherapy was delivered predominantly from the Cobalt 60 unit. This source of radiation is known to produce more superficial radiotherapy reactions; therefore, resulting in more severe skin reactions than if higher-energy radiation was

delivered[22]. This could also; therefore, mean that less severe tissue reactions below the skin could have resulted.

The statistically significant correlation obtained in this study between the severity of the acute phase response induced and the extent of change in severity of symptoms related to the skin domain suggests that the severity of inflammation in the skin during radiotherapy contributes to the severity of the acute phase response induced by radiotherapy. The statistically significant correlation between the extent of change in severity of symptoms related to the skin domain and the maximum energy intake from supplementation drinks consumed during radiotherapy; could reflect the increased energy requirements of participants with more severe skin reactions.

Side-effects related to the digestive system

The statistically significant increase in the proportion of participants that were prescribed laxatives from Week 1 (45%) to the last week of radiotherapy (100%) reflects the increasing severity of symptoms related to the digestive system domain during radiotherapy in this study. Factors that could have contributed to the increase in the prevalence of constipation (as reflected by the prescription of laxatives) include the proportion (70%) of participants who were prescribed codeine-containing analgesic medication as well as that (24%) of participants who were prescribed morphine during radiotherapy. The statistically significant decrease in the frequency of consumption of solid food as well as the decrease in the level of physical activity during radiotherapy could have further contributed to the high prevalence of constipation by the end of radiotherapy.

Side-effects related to the energy and psychosocial domains

The increases in severity of symptoms related to the energy and psychosocial domains during radiotherapy in this study were not statistically significant, but this could be due to the smaller sample size used to assess symptoms in these domains in this study. The increase in severity of symptoms related to the energy domain during radiotherapy correlated with the decrease in the level of physical activity observed during radiotherapy in this study. The psychosocial domain was the least affected in this study. The prescription of sedatives for participants in all the weeks of radiotherapy and the high frequency (more than one third of participants) of

prescription of sedatives in Week 7 of radiotherapy could have decreased the effect of radiotherapy on the symptoms related to the psychosocial domain. The frequency of prescription of sedatives could reflect the pain in the mouth and throat as pain can cause depression. The ethnic and cultural composition of this study population may also have been a factor contributing to less severe changes in the psychosocial domain during radiotherapy.

4.3 Shortcomings of this study

The high dropout rate in this study is a shortcoming, which is predominantly due to the lack of co-operation of participants during this study. This study; however, required regular contact of participants with the investigator during a distressing time and required dedication and patience of participants. The HNRQ used for this study did not distinguish between specific symptoms in the various domains that were assessed during radiotherapy. It is therefore unknown from the results of the HNRQ, which of the specific symptoms were experienced during radiotherapy and the severity to which they were experienced.

Weight loss experienced prior to commencement of radiotherapy was not assessed in this study. Severe weight loss prior to radiotherapy is a known risk factor for severe weight loss during radiotherapy[19]. The type of surgery received prior to commencing radiotherapy, apart from laryngectomy, was not recorded. This would have provided an indication of types of problems with eating that the participants would have been experiencing on commencing radiotherapy; which would have affected the mouth and throat domain scores of the HNRQ in Week 1 of radiotherapy. The proportion of the parotids and tongue included in the radiation field was not recorded during this study. This could have given an indication of the participants' risks of experiencing a dry mouth and problems with taste during radiotherapy[14].

Some participants reported consuming "bottles" of wine and others reported their consumption in terms of "glasses" prior to commencement of the study. One bottle of wine was converted to 6.7 glasses of wine in this study. The quantity of wine per glass could therefore have differed between participants. The amount of tobacco reported to have been smoked prior to commencement of radiotherapy was subjective and non-specific and therefore not comparable between participants. An accurate

reflection of the quantity of wine consumed and of tobacco smoked prior to the study could therefore not be obtained.

The consumption of dessert wine by participants prior to the commencement of radiotherapy was not determined; therefore, the level of intake of this type of alcohol prior to and during the study cannot be reported. One participant; however, did report consuming dessert wine during radiotherapy; their intake of which was reported in terms of "bottles". The measurement was converted into "glasses" for this study, by using one bottle = 14 glasses (of 56mls each). This could have resulted in an inaccurate reflection of intake for this participant.

The participants reported their intake of supplementation drinks in terms of "glasses". This was converted into millilitres, by using 1 glass = 200mls. Build-Up is served in 200ml portions and Nutrimil has a serving size of 200mls; however, Ensure and Nutren Diabetes are served in containers for patients to portion out themselves. The quantity of supplementation drink per glass could therefore have differed between the participants. This could have affected the accuracy of the quantity of intake of supplementation drinks reported. The composition of the IV fluids (i.e. glucose or saline) received by three of the participants was not recorded. If glucose had been received this could have contributed to the energy intake of those participants.

Another shortcoming of this study is that the clinical grading of mucositis was not assessed in all participants every week from Week 2 of radiotherapy. This would have provided a more accurate reflection of the prevalence of mucositis during radiotherapy. This study did not assess the change in the total protein and energy intake of participants during radiotherapy. This would have provided another method in this study for assessing change in nutritional status during radiotherapy. Decrease in the protein and energy intake of participants during radiotherapy could have contributed to the weight loss observed in this study.

CHAPTER 5: CONCLUSIONS AND RECOMMENDATIONS

The purpose of this study was to define the prevalence of side-effects and the change in weight and BMI during radical radiotherapy of patients with HNM at Tygerberg Academic Hospital, Western Cape, South Africa. It has been demonstrated that severe side-effects in the mouth, throat and skin are experienced by these patients. In addition, a decrease in nutritional status is observed, with clinically significant weight loss being experienced by 40% of patients.

Oral mucositis was observed in all participants from Week 4 of radiotherapy, the majority of whom had developed Grade II or III Mucositis. There was a significant increase in the prevalence of Grade II Mucositis from Week 2 to the last week of radiotherapy. Fungal infection of the oral cavity was prevalent throughout radiotherapy, with the highest prevalence (30%) in Week 4 of radiotherapy.

A statistically significant decrease in the weight and BMI of participants, as well as an increase in the PINI occurred from pre-radiotherapy to the last week of radiotherapy. Severe (≥ 10%) weight loss was experienced by 30% of the participants from pre-radiotherapy to the last week of radiotherapy and there was a statistically significant increase in the prevalence of malnutrition (as defined in this study) from 45% pre-radiotherapy to 90% in the last week of radiotherapy. The increase in the PINI of participants indicated the induction of the acute phase response between Week 3 / 4 and the last week of radiotherapy.

Approximately 20% of the participants experienced significant complications of radiotherapy; which resulted in discontinuation of radiotherapy or the provision of nasogastric feeding or intravenous fluids during radiotherapy. Poor nutritional status on commencement of radiotherapy and weight loss during radiotherapy could have increased the severity of side-effects experienced during this study. The infrequent nutritional support in terms of supplementation drinks prescribed, nasogastric feeding as well as the infrequent consultations with a dietitian during each week of radiotherapy, could have contributed to the lack of maintenance of nutritional status.

Statistically significant correlations were found between the change in severity of symptoms related to the skin domain during radiotherapy and the following: the change in the PINI and the maximum energy intake from supplementation drinks

consumed during radiotherapy. A statistically significant correlation was also found between the change in severity of symptoms related to the throat domain and the absolute weight loss during radiotherapy. There was a trend towards statistical significance in the correlation between the change in the PINI from pre-radiotherapy to the last week of radiotherapy and the following: the absolute weight loss and percentage weight loss from pre-radiotherapy to the last week of radiotherapy. There was a trend towards statistical significance in the difference in the mean absolute weight loss between the participants who had and those who did not have a fungal infection of the oral cavity. It can therefore be concluded that the severe side-effects experienced by the participants in this study contributed to the decrease in the nutritional status observed during radiotherapy.

Recommendations

Prescription of more effective analgesic medication during radiotherapy is recommended, which could improve the symptoms of pain in the mouth and throat. Alternative mouthwashes to Glycothymol mouthwash and Andolex mouthwash should be considered to prevent further irritation of the mouth and throat mucosa during radiotherapy. Sodium chloride rinses have been suggested in the literature to be more effective in oral care than using a more astringent mouthwash during radiotherapy[27]. Frequent mechanical cleansing of teeth or dentures during radiotherapy should be encouraged to prevent oral infections. Use of artificial saliva preparations could be useful for improving symptoms of dry mouth[26]. Advice to avoid alcohol and smoking during radiotherapy should be provided to prevent more severe mouth and throat pain from being experienced. In addition, encouragement of intake of soft foods instead of solid foods during radiotherapy could improve ability of patients to chew and swallow. These recommendations could positively affect both the nutritional and the psychosocial status of patients during radiotherapy.

It is suggested that the management of acute skin reactions to radiotherapy is improved during radical head and neck radiotherapy at Tygerberg Hospital. Advice regarding avoidance of skin irritants and use of moisturizing and anti-inflammatory creams during radiotherapy should be given to patients. It is suggested that specialized nursing care is dedicated to head and neck patients during radiotherapy, to assist in addressing symptoms experienced during radiotherapy.

Improved nutritional support is suggested prior to the commencement of radiotherapy. Dietetic referral is recommended when these patients are admitted to TBH for head and neck surgery as well as at their initial visit to the head and neck outpatient clinic at TBH so as to improve nutritional intake and therefore nutritional status of these patients before commencing radiotherapy.

It is strongly recommended that dietetic assessment be made of all patients with HNM who are planned to receive radical radiotherapy at Tygerberg Hospital. These patients should then be routinely followed-up by a dietitian each week during radiotherapy. Appropriate individualized nutritional support and encouragement with oral intake can then promptly be provided to these patients to prevent or control weight loss. It is suggested that tins of Build-Up are provided to the oncology wards at Tygerberg Hospital so that nurses can prepare this supplementation drink for the patients with HNM undergoing radical radiotherapy, for whom this is prescribed. This can then be provided to the relevant patients on the oncology wards between meals, so as to encourage their intake during the day. It is recommended that the criteria set by the NSP for the provision of supplementation drinks is revised to include all patients undergoing radical radiotherapy for HNM. These patients are at high risk for malnutrition and nutritional support should be made accessible to them. The number of dietitians dedicated to consulting the patients with HNM undergoing radical radiotherapy at TBH, should be increased, so that adequate nutritional support of all of these patients can be provided.

It is strongly recommended that percutaneous endoscopic gastrostomy tube placement prior to commencement of radical head and neck radiotherapy at Tygerberg Hospital should be considered at least in those patients who are at greatest risk for severe weight loss during radiotherapy. These patients would include those with HNM sites of nasopharynx and base of tongue as well as those to receive concomitant chemotherapy and those with severe pre-radiotherapy weight loss (≥ 10% of usual body weight lost in 6 months) [19].

It is suggested that the definition of malnutrition used in this study, is used in future studies for this patient population. This definition provides a sensitive tool for

assessment of malnutrition and is useful for comparing the prevalence prior to and at the end of radiotherapy. It could also be used to determine the effectiveness of nutritional and medical interventions during radical radiotherapy of HNM.

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APPENDIX 1

SOCIO-DEMOGRAPHIC QUESTIONNAIRE

Please provide the following personal details by circling the appropriate answer, where applicable:

1. Date of birth: …….. (day/month/year)

2. Gender: Male Female

3. Race: Black White Coloured
   Asian Oriental Other: …….…….
   (If other, please specify)

4. Highest level of education achieved: …….

5. Own monthly income:

Employment	R…….....
Pension	R……
Disability Grant	R……
State Grant	R……
Other	R……
None	

Husband/wife's monthly income:

Employment	R……
Pension	R……
Disability Grant	R……
State Grant	R……
Other	R……
None	

Monthly income of other members of household:

Employment	R……
Pension	R……
Disability Grant	R……
State Grant	R……
Other	R……
None	

6. Total number of people (adults and children) living with you at home:
……

7. Do you have a fridge at home? Yes No

8.1 Do you smoke cigarettes at present? Yes No

If yes,

8.1.1 How many cigarettes are you smoking per day? ……

If no,

8.1.2 Did you smoke cigarettes in the past? Yes No

If yes,

8.1.2.1 How many cigarettes were you smoking per day? ……

8.1.2.2 When did you stop smoking cigarettes? ..……weeks/
……..months/
……..years ago

8.2 Do you smoke cigars at present? Yes No

If yes,

8.2.1 How many cigars are you smoking per day? ……

If no,

8.2.2 Did you smoke cigars in the past? Yes No

If yes,

8.2.2.1 How many cigars were you smoking per day? …….

8.2.2.2 When did you stop smoking cigars? ..……weeks/

……..months/

……..years ago

8.3 Do you smoke a pipe at present? Yes No

If yes,

8.3.1 How much tobacco are you smoking per day? …….. grams

If no,

8.3.2 Did you smoke a pipe in the past? Yes No

If yes,

8.3.2.1 How much tobacco were you smoking per day?…….grams

8.3.2.2 When did you stop smoking a pipe? ……..…… weeks/

……..... months/

…....…….. years ago

8.4 Do you chew tobacco at present? Yes No

If yes,

8.4.1 How much tobacco are you chewing per day? …… grams

If no,

8.4.2 Did you chew tobacco in the past? Yes No

If yes,

8.4.2.1 How much tobacco were you chewing per day? …… grams

8.4.2.2 When did you stop chewing tobacco? …….weeks/

……..months/

…..……..years ago

9.1 Do you drink wine at present? Yes No

If yes,

9.1.1 How much wine do you drink? …..…….. glasses/day or

…..…..…. glasses/week

If no,

9.1.2 Did you drink wine in the past? Yes No

If yes,

9.1.2.1 How much wine did you drink? …..…….. glasses/day or

…..…..…. glasses/week

9.1.2.2 When did you stop drinking wine? ..…… weeks/

……. months/

…..……..... years ago

9.2 Do you drink beer at present? Yes No

If yes,

9.2.1 How much beer do you drink? ……cans or bottles/day or

…….…cans or bottles/week

If no,

9.2.2 Did you drink beer in the past? Yes No

If yes,

9.2.2.1 How much beer did you drink? ……cans or bottles/day or

……cans or bottles/week

9.2.2.2 When did you stop drinking beer? ...……. weeks/

……. months/

…..……..... years ago

9.3 Do you drink spirits at present? Yes No

If yes,

9.3.1 How much spirits do you drink? …….. tots/day or

…….. tots/week

If no,

9.3.2 Did you drink spirits in the past? Yes No

If yes,

9.3.2.1 How much spirits did you drink? ……..……. tots/day or

……..…… tots/week

9.3.2.2 When did you stop drinking spirits? ……. weeks/

……..… months/

…….…..... years ago

10. At present, are you:

Sedentary (eg: lying down; sitting; doing household activities),

Doing mild/moderate exercise (eg: leisurely walking; leisurely cycling) or

Doing vigorous exercise (eg: swimming; jogging; brisk walking; moderate cycling)?

Sosio-Demografiese Vraelys

Voorsien asseblief die volgende persoonlike besonderhede deur die toepaslike antwoorde te omkring, waar nodig:

1. Geboorte datum: ……..(dag/maand/jaar)

2. Geslag: Manlik Vroulik

3. Ras: Swart Wit Kleurling
   Asieer Oosters Ander:…….....……..
   (Indien ander, spesifiseer asseblief)

4. Hoogste vlak van opvoedkunde behaal: ..…….

5. Eie maandelikse inkomste:

Werksaam	R……...
Pensioen	R……...
Ongeskiktheidstoelaag	R……...
Staatstoelaag	R……...
Ander	R……...
Geen	

U man/vrou se maandelikse inkomste:

Werksaam	R……...
Pensioen	R……...
Ongeskiktheidstoelaag	R……...
Staatstoelaag	R……...
Ander	R……...
Geen	

Enige ander maandelikse huishoudelike inkomste:

Werksaam	R……...
Pensioen	R……...
Ongeskiktheidstoelaag	R……...
Staatstoelaag	R……...
Ander	R……...
Geen	

6. Totale hoeveelheid mense (volwassenes en kinders) wat saam met u in die huis bly:……

7. Het u ‘n yskas by die huis? Ja Nee

8.1 Rook u sigarette tans? Ja Nee

Indien ja, 8.1.1 Hoeveel sigarette rook u per dag? …….....……

Indien nee, 8.1.2 Het u voorheen sigarette gerook? Ja

Nee

Indien ja, 8.1.2.1 Hoeveel sigarette het u per dag gerook? ……..……

8.1.2.2 Wanneer het u opgehou sigarette rook? ……. weke/

..…..... maande/

……. jare gelede

8.2 Rook u sigars tans? Ja Nee

Indien ja, 8.2.1 Hoeveel sigars rook u per dag? ……..

Indien nee, 8.2.2 Het u voorheen sigars gerook? Ja Nee

Indien ja, 8.2.2.1 Hoeveel sigars het u per dag gerook?…….

8.2.2.2 Wanneer het u opgehou sigars rook? ……..weke/

..…..... maande/

……. jare gelede

8.3 Rook u ‘n pyp tans? Ja

Nee

Indien ja, 8.3.1 Hoeveel tabak rook u per dag? …….. gramme

Indien nee, 8.3.2 Het u voorheen ‘n pyp gerook? Ja

Nee

Indien ja, 8.3.2.1 Hoeveel tabak het u per dag gerook? ……. gramme

8.3.2.2 Wanneer het u opgehou pyp rook? .....……..weke/

..…..... maande/

……. jare gelede

8.4 Kou u tabak tans? Ja

Nee

Indien ja, 8.4.1 Hoeveel tabak kou u per dag? ……..……...… gramme

Indien nee, 8.4.2 Het u tabak voorheen gekou? Ja

Nee

Indien ja, 8.4.2.1 Hoeveel tabak het u per dag gekou? …… gramme

8.4.2.2 Wanneer het u opgehou tabak kou? .....……..weke/

..…..... maande/

……. jare gelede

9.1 Drink u wyn tans? Ja

Nee

Indien ja, 9.1.1 Hoeveel wyn drink u? …..……. glase/dag

of ...……..... glase/week

Indien nee, 9.1.2 Het u voorheen wyn gedrink? Ja

Nee

Indien ja, 9.1.2.1 Hoeveel wyn het u gedrink? ……glase/dag of

……glase/week

9.1.2.2 Wanneer het u opgehou wyn drink? .....…… .weke/

..…..... maande/

……. jare gelede

9.2 Drink u bier tans? Ja

Nee

Indien ja, 9.2.1 Hoeveel bier drink u? …….kanne of bottels/dag of

……..…kanne of bottels/week

Indien nee, 9.2.2 Het u voorheen bier gedrink? Ja

Nee

Indien ja, 9.2.2.1 Hoeveel bier het u gedrink?

……kanne of bottels/dag of

……kanne of bottels/week

9.2.2.2 Wanneer het u opgehou bier drink? .....…… .weke/

..…..... maande/

……. jare gelede

9.3 Drink u spiritualie tans? Ja

Nee

Indien ja, 9.3.1 Hoeveel spiritualie drink u? …….sopies/dag of

…….sopies/week

Indien nee, 9.3.2 Het u spiritualie voorheen gedrink? Ja

Nee

Indien ja, 9.3.2.1 Hoeveel spiritualie het u gedrink? …….sopies/dag of

…….. sopies/week

9.3.2.2 Wanneer het u opgehou spiritualie drink? ..... .weke/

..…..... maande/

……. jare gelede

10. Tans, is u:

Fisies onaktief (bv: le; sit; doen huishoudelike aktiwiteite) of

Doen u ligte/matige oefening (bv: ontspanne stap; ontspanne fietsry) of

Doen u strawwe oefening (bv: swem; draf; vinnige stap; matige fietsry)?

APPENDIX 2

McMaster University Head and Neck Radiotherapy Questionnaire

1. Have you had any pain or soreness in your mouth in the past week?

   1. Yes (Continue to Part b)

   7. No

   Part b: How *troublesome* was this for you?

      1. A Great Deal
      2. A Lot
      3. A Fair Bit
      4. Somewhat
      5. A Little
      6. Hardly Any

2. Have you had dryness of your skin, where it was treated, in the past week?

   1. Yes (Continue to Part b)

   7. No

   Part b: How *troublesome* was this for you?

      1. A Great Deal
      2. A Lot
      3. A Fair Bit
      4. Somewhat
      5. A Little
      6. Hardly Any

- Do not ask the following question if the participant has had a total laryngectomy:

3. Have you had any difficulty swallowing in the past week?

   1. Yes (Continue to Part b)

   7. No

   Part b: How *troublesome* was this for you?

      1. A Great Deal
      2. A Lot
      3. A Fair Bit

4. Somewhat
5. A Little
6. Hardly Any

4. Have you felt low in energy, in the past week?

1. Yes (Continue to Part b)
7. No

Part b: How *often* did you feel this way?

1. A Great Deal of the time
2. A Lot of the time
3. A Fair Bit of the time
4. Somewhat of the time
5. A Little of the time
6. Hardly any of the time

5. In general, have you felt angry, depressed or down in the dumps in the past week?

1. Yes (Continue to Part b)

7. No

Part b: How *often* did you feel this way?

1. A Great Deal of the time
2. A Lot of the time
3. A Fair Bit of the time
4. Somewhat of the time
5. A Little of the time
6. Hardly any of the time

6. Have you felt nauseated, in the past week?

1. Yes (Continue to Part b)

7. No

Part b: How *troublesome* was this for you?

1. A Great Deal
2. A Lot
3. A Fair Bit
4. Somewhat
5. A Little
6. Hardly Any

7. Have you had any itching of the skin, in treated area, in the past week?

1. Yes (Continue to Part b)

7. No

Part b: How *troublesome* was this for you?

1. A Great Deal
2. A Lot
3. A Fair Bit
4. Somewhat
5. A Little
6. Hardly Any

8. Have you had any difficulty getting a good night's sleep, in the past week?

1. Yes (Continue to Part b)

7. No

Part b: How *often* did you feel this way?

1. A Great Deal of the time
2. A Lot of the time
3. A Fair Bit of the time
4. Somewhat of the time
5. A Little of the time
6. Hardly any of the time

9. Have you had any dryness of your mouth in the past week?

    1. Yes (Continue to Part b)

    7. No

    Part b: How *troublesome* was this for you?

        1. A Great Deal

        2. A Lot

        3. A Fair Bit

        4. Somewhat

        5. A Little

        6. Hardly Any

10. Have you felt tired or fatigued, in the past week, such that you are prevented from doing social or recreational activities?

    1. Yes (Continue to Part b)

    7. No

    Part b: How *often* did you feel this way?

        1. A Great Deal of the time

        2. A Lot of the time

        3. A Fair Bit of the time

        4. Somewhat of the time

        5. A Little of the time

        6. Hardly any of the time

- Do not ask the following question if the participant has had a total laryngectomy:

11. Have you had a sore or painful throat in the past week?

    1. Yes (Continue to Part b)

    7. No

    Part b: How *troublesome* was this for you?

        1. A Great Deal

        2. A Lot

        3. A Fair Bit

        4. Somewhat

        5. A Little

        6. Hardly Any

12. Have you had any problems with your stomach in the past week?

    1. Yes (Continue to Part b)

    7. No

    Part b: How *troublesome* was this for you?

        1. A Great Deal

        2. A Lot

        3. A Fair Bit

        4. Somewhat

        5. A Little

        6. Hardly Any

13. Have you found your saliva to be very sticky, in the past week?

    1. Yes (Continue to Part b)

    7. No

    Part b: How *troublesome* was this for you?

        1. A Great Deal

        2. A Lot

        3. A Fair Bit

        4. Somewhat

        5. A Little

        6. Hardly Any

14. Have you had any fatigue or tiredness which interfered with your work or routine daily activities, in the past week?

    1. Yes (Continue to Part b)

    7. No

    Part b: How *often* did you feel this way?

        1. A Great Deal of the time

        2. A Lot of the time

        3. A Fair Bit of the time

        4. Somewhat of the time

        5. A Little of the time

        6. Hardly any of the time

15. Have you had difficulty tasting your food in the past week?

1. Yes (Continue to Part b)

7. No

Part b: How *often* did you feel this way?

1. A Great Deal of the time
2. A Lot of the time
3. A Fair Bit of the time
4. Somewhat of the time
5. A Little of the time
6. Hardly any of the time

16. Have you had difficulty with your appetite in the past week?

1. Yes (Continue to Part b)

7. No

Part b: How *often* did you feel this way?

1. A Great Deal of the time
2. A Lot of the time
3. A Fair Bit of the time
4. Somewhat of the time
5. A Little of the time
6. Hardly any of the time

17. Have you felt good about yourself in the past week?

    1. Yes (Continue to Part b)

    7. No

    Part b: How *often* did you feel this way?

        1. A Great Deal of the time

        2. A Lot of the time

        3. A Fair Bit of the time

        4. Somewhat of the time

        5. A Little of the time

        6. Hardly any of the time

18. Have you had difficulty keeping down foods or liquids, in the past week?

    1. Yes (Continue to Part b)

    7. No

    Part b: How *troublesome* was this for you?

        1. A Great Deal

        2. A Lot

        3. A Fair Bit

        4. Somewhat

        5. A Little

        6. Hardly Any

- Do not ask the following question if the participant has had a total laryngectomy:

19. Have you had a hoarse voice, in the past week?

    1. Yes (Continue to Part b)

    7. No

    Part b: How *troublesome* was this for you?

        1. A Great Deal

        2. A Lot

        3. A Fair Bit

        4. Somewhat

        5. A Little

        6. Hardly Any

20. Have you had any pain or soreness of your skin in the treated area, in the past week?

    1. Yes (Continue to Part b)

    7. No

    Part b: How *troublesome* was this for you?

        1. A Great Deal

        2. A Lot

        3. A Fair Bit

        4. Somewhat

        5. A Little

        6. Hardly Any

21. Have you had any difficulty chewing your food, in the past week?

1. Yes (Continue to Part b)

7. No

Part b: How *troublesome* was this for you?

1. A Great Deal
2. A Lot
3. A Fair Bit
4. Somewhat
5. A Little
6. Hardly Any

22. Do you feel your relationships with your family or friends have been affected because of your treatments, in the past week?

1. Yes (Continue to Part b)

7. No

Part b: How *troublesome* was this for you?

1. A Great Deal
2. A Lot
3. A Fair Bit
4. Somewhat
5. A Little
6. Hardly Any

23. Are you now taking

1. liquids only?
2. liquids and soft foods only?
3. liquids, soft foods and solid foods?

McMaster University Head and Neck Radiotherapy Questionnaire

1. Het u enige pyn of teerheid in u mond in die laaste week gehad?

   1. Ja (Gaan na deel b)

   7. Nee

   Deel b: Hoe *moeilik* was dit vir jou?

   1. ‘n groot deel
   2. baie
   3. taamlik baie
   4. taamlik
   5. ‘n bietjie
   6. amper niks

2. Het u enige droogheid van u vel, waar dit behandel was, in die laaste week gehad?

   1. Ja (Gaan na deel b)

   7. Nee

   Deel b: Hoe *moeilik* was dit vir jou?

   1. ‘n groot deel
   2. baie
   3. taamlik baie
   4. taamlik
   5. ‘n bietjie
   6. amper niks

• Do not ask the following question if the participant has had a total laryngectomy:

3. Het u enige moeilikheid om te sluk in die laaste week ondervind?

   1. Ja (Gaan na deel b)

   7. Nee

   Deel b: Hoe *moeilik* was dit vir jou?

   1. ‘n groot deel
   2. baie
   3. taamlik baie

4. taamlik

5. ‘n bietjie

6. amper niks

4. Het u ‘n lae vlak van energie in die laaste week ondervind?

1. Ja (Gaan na deel b)

7. Nee

Deel b: Hoe *moeilik* was dit vir jou?

1. ‘n groot deel van die tyd

2. baie van die tyd

3. taamlik baie van die tyd

4. somtyds

5. ‘n bietjie van die tyd

6. amper glad nie

5. Oor die algemeen, het u kwaad, depressief of ongelukkig in die laaste week gevoel?

1. Ja (Gaan na deel b)

7. Nee

Deel b: Hoe *moeilik* was dit vir jou?

1. ‘n groot deel van die tyd
2. baie van die tyd
3. taamlik baie van die tyd
4. somtyds
5. ‘n bietjie van die tyd
6. amper glad nie

6. Het u naar in die laaste week gevoel?

1. Ja (Gaan na deel b)

7. Nee

Deel b: Hoe *moeilik* was dit vir jou?

1. ‘n groot deel
2. baie
3. taamlik baie
4. taamlik
5. ‘n bietjie
6. amper niks

7. Het u enige jeukgevoel van die vel, in die behandelde area, in die laaste week gehad?

1. Ja (Gaan na deel b)

7. Nee

Deel b: Hoe *moeilik* was dit vir jou?

1. ‘n groot deel
2. baie
3. taamlik baie
4. taamlik
5. ‘n bietjie
6. amper niks

8. Het u enige moeilikheid gehad om ‘n goeie nag slaap te kry, in die laaste week?

1. Ja (Gaan na deel b)

7. Nee

Deel b: Hoe *moeilik* was dit vir jou?

1. ‘n groot deel van die tyd
2. baie van die tyd
3. taamlik baie van die tyd
4. somtyds
5. ‘n bietjie van die tyd
6. amper glad nie

9. Het u enige droogheid van u mond in die laaste week ondervind?

1. Ja (Gaan na deel b)

7. Nee

Deel b: Hoe *moeilik* was dit vir jou?

1. ‘n groot deel
2. baie
3. taamlik baie
4. taamlik
5. ‘n bietjie
6. amper niks

10. Het u so moeg of lam, in die laaste week gevoel, dat dit u verhoed het om deel te neem aan sosiale- of ontspanningsaktiwiteite?

1. Ja (Gaan na deel b)

7. Nee

Deel b: Hoe *dikwels* het u so gevoel?

1. ‘n groot deel van die tyd
2. baie van die tyd
3. taamlik baie van die tyd
4. somtyds
5. ‘n bietjie van die tyd
6. amper glad nie

- Do not ask the following question if the participant has had a total laryngectomy:

11. Het u seer of pynlike keel in die laaste week gehad?

    1. Ja (Gaan na deel b)

    7. Nee

    Deel b: Hoe *moeilik* was dit vir jou?

        1. ‘n groot deel

        2. baie

        3. taamlik baie

        4. taamlik

        5. ‘n bietjie

        6. amper niks

12. Het u enige probleme met u maag in die laaste week gehad?

    1. Ja (Gaan na deel b)

    7. Nee

    Deel b: Hoe *moeilik* was dit vir jou?

        1. ‘n groot deel

        2. baie

        3. taamlik baie

        4. taamlik

        5. ‘n bietjie

        6. amper niks

13. Het u opgelet dat u speeksel baie taai was, in die laaste week?

    1. Ja (Gaan na deel b)

    7. Nee

    Deel b: Hoe *moeilik* was dit vir jou?

        1. ‘n groot deel

        2. baie

        3. taamlik baie

        4. taamlik

        5. ‘n bietjie

        6. amper niks

14. Het u enige moegheid of lamheid ondervind wat u werk of daaglikse roetiene aktiwiteite belemmer, in die laaste week?

    1. Ja (Gaan na deel b)

    7. Nee

    Deel b: Hoe *dikwels* het u so gevoel?

        1. ‘n groot deel van die tyd

        2. baie van die tyd

        3. taamlik baie van die tyd

        4. somtyds

        5. ‘n bietjie van die tyd

        6. amper glad nie

15. Het u enige moeilikheid gehad om u kos te proe, in die laaste week?

1. Ja (Gaan na deel b)

7. Nee

Deel b: Hoe *dikwels* het u so gevoel?

1. ‘n groot deel van die tyd
2. baie van die tyd
3. taamlik baie van die tyd
4. somtyds
5. ‘n bietjie van die tyd
6. amper glad nie

16. Het u enige moeilikheid met u aptyt in die laaste week ondervind?

1. Ja (Gaan na deel b)

7. Nee

Deel b: Hoe *dikwels* het u so gevoel?

1. ‘n groot deel van die tyd
2. baie van die tyd
3. taamlik baie van die tyd
4. somtyds
5. ‘n bietjie van die tyd
6. amper glad nie

17. Het u goed oor uself gevoel in die laaste week?

1. Ja (Gaan na deel b)

7. Nee

Deel b: Hoe *dikwels* het u so gevoel?

1. ‘n groot deel van die tyd
2. baie van die tyd
3. taamlik baie van die tyd
4. somtyds
5. ‘n bietjie van die tyd
6. amper glad nie

18. Het u dit moeilik gevind om kos of vloeistowwe in te hou, in die laaste week?

1. Ja (Gaan na deel b)

7. Nee

Deel b: Hoe *moeilik* was dit vir jou?

1. ‘n groot deel
2. baie
3. taamlik baie
4. taamlik
5. ‘n bietjie
6. amper niks

• Do not ask the following question if the participant has had a total laryngectomy:

19. Het u ‘n hees stem gehad, in die laaste week?

    1. Ja (Gaan na deel b)

    7. Nee

    Deel b: Hoe *moeilik* was dit vir jou?

        1. ‘n groot deel

        2. baie

        3. taamlik baie

        4. taamlik

        5. ‘n bietjie

        6. amper niks

20. Het u enige pyn of seerheid van u vel in die behandelde area ondervind, in die laaste week?

    1. Ja (Gaan na deel b)

    7. Nee

    Deel b: Hoe *moeilik* was dit vir jou?

        1. ‘n groot deel

        2. baie

        3. taamlik baie

        4. taamlik

        5. ‘n bietjie

        6. amper niks

21. Het u enige moeilikheid ondervind om u kos te kou in die laaste week?

1. Ja (Gaan na deel b)

7. Nee

Deel b: Hoe *moeilik* was dit vir jou?

1. ‘n groot deel
2. baie
3. taamlik baie
4. taamlik
5. ‘n bietjie
6. amper niks

22. Voel u dat u verhoudings met u familie of vriende geaffekteer was as gevolg van u behandelinge in die laaste week?

1. Ja (Gaan na deel b)

7. Nee

Deel b: Hoe *moeilik* was dit vir jou?

1. ‘n groot deel
2. baie
3. taamlik baie
4. taamlik
5. ‘n bietjie
6. amper niks

23. Neem u nou

1. vloeistowwe alleen?
2. vloeistowwe en sagte kossoorte alleen?
3. vloeistowwe, sagte kossoorte en soliede kossoorte?

APPENDIX 3

LIFESTYLE AND DIETARY QUESTIONNAIRE

1. If the participant uses tobacco before starting radiotherapy, ask about the relevant form of tobacco use, in week 1 of radiotherapy:

   1.1 Are you smoking cigarettes/cigars/a pipe/chewing tobacco at present?

   Yes No

   1.1 Rook u sigarette/sigars/'n pyp/kou u tabak tans?

   Ja Nee

   If yes, 1.1.1 How many cigarettes/cigars are you smoking per day or how much tobacco are you smoking/chewing per day? ……..

   If yes, 1.1.1 Hoeveel sigarette/sigars rook u per dag of hoeveel tabak rook/kou u per dag?

2. If the participant uses tobacco in week 1 of radiotherapy, ask the following question weekly during radiotherapy from Week 2 (about the relevant form of tobacco use):

   2.1 How many cigarettes/cigars are you smoking per day or how much tobacco are you smoking/chewing per day? ……..

   Hoeveel sigarette/sigars rook u per dag of hoeveel tabak rook/kou u per dag? ……..

3. If the participant drinks alcohol before starting radiotherapy, ask about the relevant type/s of alcohol consumed, in Week 1 of radiotherapy:

   3.1 Have you had any wine since starting radiotherapy? Yes No

   3.1 Het u enige wyn gedrink vandat u met radioterapie begin het? Ja Nee

   If yes, 3.1.1 How much wine have you had?

   …… glasses/day or

   …… glasses since starting radiotherapy

   If yes, 3.1.1 Hoeveel wyn het u gedrink?

   ……glase/dag of

   ..……glase vandat u met radioterapie begin het

   3.2 Have you had any beer since starting radiotherapy? Yes No

3.2 Het u enige bier gedrink vandat u met radioterapie begin het? Ja

Ne

e

If yes, 3.2.1 How much beer have you had?

……. cans or bottles/day or

……. cans or bottles since starting radiotherapy

If yes, 3.2.1 Hoeveel bier het u gedrink?

…….. kanne of bottels/dag of

…….. kanne of bottels vandat u met radioterapie begin het

3.3 Have you had any spirits since starting radiotherapy? Yes No

3.3 Het u enige spiritualie gedrink vandat u met radioterapie begin het? Ja

Nee

If yes, 3.3.1 How much spirits have you had?

……. tots/day or

……. tots since starting radiotherapy

If yes, 3.3.1 Hoeveel spiritualie het u gedrink?

……. sopies/dag of

……. sopies vandat u met radioterapie begin het

4. If the participant drinks alcohol in week 1 of radiotherapy, ask weekly during radiotherapy from Week 2 (about the relevant type/s of alcohol consumed):

4.1 How much wine have you had in the past 7 days?

…… glasses/day or

…… glasses in the past 7 days

4.1 Hoeveel wyn het u in die laaste 7 dae gedrink?

…… glase/dag of

…… glase in die laaste 7 dae

4.2 How much beer have you had in the past 7 days?

…… cans or bottles/day or

…… cans or bottles in the past 7 days

4.2 Hoeveel bier het u in die laaste 7 dae gedrink?

…… kanne of bottles/dag of

…… kanne of bottles in die laaste 7 dae

4.3 How much spirits have you had in the past 7 days?

…… tots/day or

…… tots in the past 7 days

4.3 Hoeveel spiritualie het u in die laaste 7 dae gedrink?

…… sopies/dag of

…… sopies in die laaste 7 dae

5. Ask all participants in Week 1 of radiotherapy:

5.1 Since starting radiotherapy, have you been:

Sedentary (eg: lying down; sitting; doing household activities) or

Doing mild/moderate exercise (eg: leisurely walking; leisurely cycling) or

Doing vigorous exercise (eg: swimming; jogging; brisk walking; moderate cycling)?

5.1 Vandat u met radioterapie begin het, was u:

Fisies onaktief (bv: le; sit; doen huishoudelike aktiwiteite) of

Het u ligte/matige oefening (bv: ontspanne stap; ontspanne fietsry) of

Strawwe oefening (bv: swem; draf; vinnige stap; matige fietsry) gedoen?

5.2 Have you taken any special energy drinks since starting radiotherapy?:

Yes No

5.2 Het u enige spesiale energiedrankies geneem vandat u met radioterapie begin het? Ja Nee

If yes, 5.2.1 Have you taken the special energy drinks every day?

Yes No

If yes, 5.2.1 Het u die spesiale energiedrankies elke dag geneem?

Ja Nee

If yes, 5.2.1.1 Which special energy drinks have you been taking?…….

5.2.1.2 How much have you been taking per day? …..… glasses

If yes, 5.2.1.1 Watter spesiale energiedrankies het u geneem? ……..

5.2.1.2 Hoeveel neem u per dag? …… glase

5.3 Have you taken any vitamin pills since starting radiotherapy?

Yes No

5.3 Het u enige vitamien pille geneem vandat u met radioterapie begin het?

Ja Nee

If yes, 5.3.1 Have you been taking the vitamin pills every day?

Yes No

If yes, 5.3.1 Het u die vitamienpille elke dag geneem?

Ja

Nee

If yes, 5.3.1.1 Which vitamin pills and how much have you been taking per day? ……..

If yes, 5.3.1.1 Watter vitamienpille en hoeveel het u per dag geneem? ……...

5.4 Have you taken any herbal pills/herbal medicine since starting radiotherapy?

Yes No

5.4 Het u enige kruiepille/kruiemedisyne geneem vandat u met radioterapie begin het? Ja Nee

If yes, 5.4.1 Have you been taking the herbal pills/herbal medicine every day

Yes No

If yes, 5.4.1 Het u die kruiepille/kruiemedisyne elke dag geneem?

Ja

Nee

If yes, 5.4.1.1 Which herbal pills/herbal medicine and how much have you been taking per day? …….

If yes, 5.4.1.1 Watter kruiepille/kruiemedisyne en hoeveel het u per dag

geneem?……..

5.5 Have you been consulted by a dietitian since starting radiotherapy?

Yes No

5.5 Is u deur ‘n dieetkundige gekonsulteer vandat u met radioterapie begin het?

Ja Nee

6. Ask all participants weekly during radiotherapy from Week 2:

6.1 In the past week, have you been:

Sedentary (eg: lying down; sitting; doing household activities) or

Doing mild/moderate exercise (eg: leisurely walking; leisurely cycling) or

Doing vigorous exercise (eg: swimming; jogging; brisk walking; moderate cycling)?

6.1 In die laaste week, was u:

Fisies onaktief (bv: le; sit; doen huishoudelike aktiwiteite) of

Het u ligte/matige oefening (bv: ontspanne stap; ontspanne fietsry) of

Strawwe oefening (bv: swem; draf; vinnige stap; matige fietsry) gedoen?

6.2 Have you taken any special energy drinks in the past week?

Yes No

6.2 Het u enige spesiale energiedrankies in die laaste week geneem?

Ja Nee

If yes, 6.2.1 Have you been taking the special energy drinks every day?

Yes No

If yes, 6.2.1 Het u die spesiale energiedrankies elke dag geneem?

Ja

Nee

If yes, 6.2.1.1 Which special energy drinks have you been taking?

……..…

6.2.1.2 How much have you been taking per day? ……...

If yes, 6.2.1.1 Watter spesiale energiedrankies het u geneem? ……

6.2.1.2 Hoeveel neem u per dag? …… glase

6.3 Have you taken any vitamin pills in the past week? Yes No

6.3 Het u enige vitamienpille in die laaste week geneem? Ja Nee

If yes, 6.3.1 Have you taken the vitamin pills every day? Yes No

If yes, 6.3.1 Het u die vitamienpille elke dag geneem? Ja Nee

If yes, 6.3.1.1 Which vitamin pills have you been taking and how much per day? ……

If yes, 6.3.1.1 Watter vitamienpille en hoeveel het u per dag geneem? ……

6.4 Have you taken any herbal pills/herbal medicine in the past week? Yes No

6.4 Het u enige kruiepille/kruiemedisyne in die laaste week geneem? Ja

Nee

If yes, 6.4.1 Have you taken the herbal pills/herbal medicine every day?

Yes No

If yes, 6.4.1 Het u die kruiepille/kruiemedisyne elke dag geneem?

Ja

Nee

If yes, 6.4.1.1 Which herbal pills/herbal medicine and how much have you been taking per day? ……

If yes, 6.4.1.1 Watter kruiepille/kruiemedisyne en hoeveel het u per dag geneem?……...

6.5 Have you been consulted by a dietitian in the past 7 days? Yes No

6.5 Is u deur ‘n dieetkundige in die laaste 7 dae gekonsulteer? Ja

Nee

APPENDIX 4

Participant No.:

CLINICAL DATA

Tumour histology: squamous cell / adeno / other: ……...……

Tumour site: ……..……

Tumour stage: …… TNM classification: …….....……

Radiotherapy dose and type/s planned per treatment field/s:

Name of field	Dose (Gray)	Radiotherapy type

Field size/s:

Name of field	Field size

Received head and neck surgery before commencing current radiotherapy: Yes / No

Had a total laryngectomy: Yes / No

Received chemotherapy before commencing current radiotherapy: Yes / No

Presence of HIV infection / AIDS (if available in notes): Yes / Not available in notes

Presence of Diabetes Mellitus (if available in notes): Yes / Not available in notes

Recorded up to last week of follow-up of participant:

Date of starting radiotherapy: ……..

Received concomitant chemotherapy: Yes / No

If yes, type of chemotherapy received: …….

Place of residence in Week 1: hospital ward / at home

If accommodation changed during Week 1, describe change: ……

Referred to the NSP: Yes / No

If yes, when referred: …… (Week ……)

Vitamins and / or minerals prescribed: Yes / No

If yes,

Date prescribed (Week of radiotherapy)	**Supplement type**	**Dosage & frequency**

Weekly clinical grading of mucositis:

Week 2 Grade:

Week 3 Grade:

Week 4 Grade:

Week 5 Grade:

Week 6 Grade:

Week 7 Grade:

Prescription of medication:

Date prescribed (Week of radiotherapy)	Type of medication	Dosage	Frequency

Interruptions occurred in radiotherapy treatments: Yes / No

If yes,

Number of days	Reason for interruption

Double fractions received: Yes / No

If yes, number of days on which double fractions received: ……..……

IV fluids administered: Yes / No

If yes, administered in which week/s of radiotherapy: ……..……

Presence of a skin infection during radiotherapy: Yes / No

Presence of sepsis during radiotherapy: Yes / No

Any other medical disorders occurring during radiotherapy: Yes / No

If yes, which medical disorder/s: ……

Outpatients only: Admitted to hospital after Week 1: Yes / No

If yes, admitted in which week of radiotherapy: ....……..….

Reason for hospitalization: ...……...

Inpatients only: Went home over one or more weekend: Yes / No

If yes, after which week/s of radiotherapy: ……...…

APPENDIX 5

16 February 2006

Ms J de Pomeroy-Legg
Discipline of Human Nutrition
Dept Interdisciplinary Health Sciences

Dear Ms De Pomeroy-Legg

RESEARCH PROJECT : **"PREVALENCE OF SIDE-EFFECTS AND CHANGE IN NUTRITIONAL STATUS DURING RADICAL RADIOTHERAPY FOR HEAD AND NECK MALIGNANCIES AT THE TYGERBERG ACADEMIC HOSPITAL, WESTERN CAPE, SOUTH AFRICA"**

PROJECT NUMBER : N05/10/175

My letter dated 23 January 2006 refers.

At a meeting that was held on 7 February 2006 the Committee for Human Research ratified the interim approval of the above-mentioned project.

Yours faithfully

CJ VAN TONDER
RESEARCH DEVELOPMENT AND SUPPORT (TYGERBERG)
Tel: +27 21 938 9207 / E-mail: cjvt@sun.ac.za

CJVT/ev

Copy to: Prof D Labadarios

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APPENDIX 6

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF THE RESEARCH PROJECT:

Prevalence of side-effects and change in nutritional status during radical radiotherapy for head and neck malignancies at the Tygerberg Academic Hospital, Western Cape, South Africa.

REFERENCE NUMBER: N05/10/175

PRINICIPAL INVESTIGATOR: Jeanita de Pomeroy-Legg

ADDRESS: 122 Eastlake Island Way
Marina Da Gama
7945

CONTACT NUMBER: 788 8999 / 084 420 5391

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is **entirely voluntary** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by the Committee for Human Research at Stellenbosch University **and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.**

What is this research study all about?

- The research study will be conducted at the Tygerberg Academic Hospital. 60 participants will be recruited for this study.
- The study aims to define the prevalence of side-effects experienced and change in weight during radiotherapy. By determining the severity of side-effects experienced and the amount of weight change during radiotherapy as well as possible causes for these changes, strategies could be implemented to improve the side-effects experienced and weight change of patients during radiotherapy.
- Procedures for the study include: a questionnaire completed by yourself (if possible), under the supervision of the investigator before starting radiotherapy; two questionnaires administered weekly during radiotherapy by the investigator; weight measured before radiotherapy and weekly during radiotherapy; height measured before radiotherapy and a 3ml blood sample drawn before radiotherapy (from all participants) and in week 3/4 and the last week of radiotherapy (from some participants). A total of 9ml of blood could therefore be drawn from you during the study. Various relevant medical details will be obtained from your medical records during the study.

Why have you been invited to participate?

- All patients with head and neck malignancies who will be attending Tygerberg Hospital for daily radiotherapy are being invited to participate in this study.

What will your responsibilities be?

- You will be required to meet with the investigator weekly during your radiotherapy course after attending your radiotherapy sessions. A place to meet and a day of the week on which to meet at the radiotherapy outpatient department will be arranged before starting radiotherapy. Failure to meet with the investigator on the arranged day on more than one occasion, will result in discontinuation of your participation in the study.
- If you are admitted to hospital during radiotherapy, the investigator will meet with you on the hospital ward.

Will you benefit from taking part in this research?

- There are no personal benefits; however your participation in this research could benefit other patients with head and neck malignancies who attend Tygerberg Hospital for daily radiotherapy in the future.

Are there any risks involved in your taking part in this research?

- The drawing of blood can cause discomfort, therefore this is a risk involved in your taking part in this research.

Who will have access to the information/data obtained from you or your medical notes during the study?

- All information/data obtained by the investigator will be regarded as confidential. Your identity will remain anonymous, as your name will not appear on any study-related material or documentation. Information/data obtained by the investigator will only be used for this study and will not be shared for other purposes or studies.

Will you be paid to take part in this study and are there any costs involved?

- You will not be paid to take part in this study and there will be no costs involved for you, if you do take part.

You will receive a copy of this information and consent form for your own records.

By signing below, I…….. agree to take part in a research study entitled:

Prevalence of side-effects and change in nutritional status during radical radiotherapy for head and neck malignancies at the Tygerberg Academic Hospital, Western Cape, South Africa.

I declare that:

- I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is **voluntary** and I have not been pressurized to take part.
- I may choose to leave the study at any time and will not be penalized or prejudiced in any way.
- I may be asked to leave the study before it has finished, if I do not follow the study plan, as agreed to.

Signed at (*place*)……..on (*date*) ……2006

…….. ……

Signature of participant Signature of witness

Declaration by investigator

I (name) ……declare that:-

- I explained the information in this document to ……..
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above.
- I did/did not use a translator.

Signed at (*place*)……..on (*date*) ……2006

…….. ……

Signature of investigator Signature of witness

DEELNEMERINLIGTINGSBLAD EN -TOESTEMMINGSVORM

TITEL VAN DIE NAVORSINGSPROJEK

Prevalensie van newe-effekte en verandering in voedingstatus tydens radikale radioterapie vir kop-en-nek maligniteit by die Tygerberg Akademiese Hospitaal, Weskaap, Suid- Afrika.

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U word genooi om deel te neem aan 'n navorsingsprojek. Lees asseblief hierdie inligtingsblad op u tyd deur aangesien die detail van die navorsingsprojek daarin verduidelik word. Indien daar enige deel van die navorsingsprojek is wat u nie ten volle verstaan nie, is u welkom om die navorsingspersoneel of dokter daaroor uit te vra. Dit is baie belangrik dat u ten volle moet verstaan wat die navorsingsprojek behels en hoe u daarby betrokke kan wees. U deelname is ook **volkome vrywillig** en dit staan u vry om deelname te weier. U sal op geen wyse hoegenaamd negatief beïnvloed word indien u sou weier om deel te neem nie. U mag ook te eniger tyd aan die navorsingsprojek onttrek, selfs al het u ingestem om deel te neem.

Hierdie navorsingsprojek is deur die Komitee vir Mensnavorsing van die Universiteit Stellenbosch goedgekeur en sal uitgevoer word volgens die etiese riglyne en beginsels van die Internasionale Verklaring van Helsinki en die Etiese Riglyne vir Navorsing van die Mediese Navorsingsraad (MNR).

Wat behels hierdie navorsingsprojek?

- Die navorsingsstudie sal by die Tygerberg Akademiese Hospitaal uitgevoer word. 60 deelnemers sal vir hierdie studie gewerf word.
- Die doel van die studie is om die prevalensie van newe-effekte en veranderinge in gewig tydens radioterapie te omskryf. Deur die graad van ernstigheid van newe-effekte wat ondervind word, en die omvang van gewigsverandering tydens radioterapie te bepaal, sowel as die moontlike oorsake van hierdie veranderinge, kan strategie ge-implementeer word om die lewenskwaliteit te verbeter, asook die gewig van pasiente tydens radioterapie.
- Prosedure vir die studie sluit in: ‘n vraelys wat deur u voltooi word (indien moontlik) onder toesig van die navorser voordat u met radioterapie begin; twee vraelyste wat weekliks deur die navorser tydens radioterapie, voltooi sal word; bepaling van gewig voor radioterapie en weekliks tydens radioterapie; lengte gemeet voor radioterapie en ‘n 3ml bloedmonster getrek voor radioterapie (van alle deelnemers) en in week 3/4 asook die laaste week van radioterapie (van sommige deelnemers). ‘n Totaal van 9ml bloed mag; dus, gedurende die studie van u getrek word. ‘n Verskeidenheid nodige mediese details sal tydens die studie uit u mediese notas getrek word.

Waarom is u genooi om deel te neem?

- Alle pasiente met kop-en-nek maligniteite, en wie daaglikse radioterapie by Tygerberg Hospitaal ontvang, word uitgenooi om deel te neem aan hierdie studie.

Wat sal u verantwoordelikhede wees?

- U sal verwag word om weekliks tydens radioterapie nadat u u radioterapiesessies bygewoon het met die navorser te ontmoet. ‘n Vergaderingslokaal in die radioterapie buitepasiente departement en die dag

van die week vir die ontmoeting sal gereel word voor die aanvang van u radioterapie. As u die afspraak met die navorser op die bepaalde dag by meer as een geleentheid nie nakom nie, sal dit veroorsaak dat u deelname in die studie gestaak word.

- Indien u toegelaat word in die hospitaal tydens radioterapie, sal die navorser u in die hospitaal saal kom spreek.

Sal u voordeel trek deur deel te neem aan hierdie navorsingsprojek?

- Daar is geen persoonlike voordele nie, maar u deelname in die navorsing sal moontlik tot voordeel wees vir ander pasiente met kop en nek maligniteite wie in die toekoms daaglikse radioterapie by Tygerberg Hospitaal ontvang.

Is daar enige risiko's verbonde aan u deelname aan hierdie navorsingsprojek?

- Die trek van bloed kan ongemak veroorsaak, dus is daar hierdie moontlike risiko as gevolg van u deelname in hierdie navorsing.

Wie sal toegang hê tot die versamelde inligting?

- Alle inligting/data wat deur die navorser verkry word sal as konfidensieel beskou word. U identiteit sal anoniem bly, aangesien u naam op geen studie-verwante materiaal of dokumentasie sal verskyn nie. Inligting/data versamel deur die navorser sal net vir die doeleindes van hierdie studie gebruik word en sal nie vir ander doeleindes of studies gedeel word nie.

Sal u betaal word vir deelname aan die navorsingsprojek en is daar enige koste verbonde aan deelname?

- U sal nie betaal word om deel te neem aan hierdie studie nie en daar sal geen koste verbonde wees vir u nie, indien u deelneem.

U sal 'n afskrif van hierdie inligtings- en toestemmingsvorm ontvang vir u eie rekords.

Met die ondertekening van hierdie dokument onderneem ek,

……..……, om deel te neem aan 'n navorsingsprojek getiteld:

Prevalensie van newe-effekte en verandering in voedingstatus tydens radikale radioterapie vir kop-en-nek maligniteit by die Tygerberg Akemiese Hospitaal, Weskaap, Suid- Afrika.

Ek verklaar dat:

- Ek hierdie inligtings- en toestemmingsvorm gelees het of aan my laat voorlees het en dat dit in 'n taal geskryf is waarin ek vaardig en gemaklik mee is.
- Ek geleentheid gehad het om vrae te stel en dat al my vrae bevredigend beantwoord is.
- Ek verstaan dat deelname aan hierdie navorsingsprojek **vrywillig** is en dat daar geen druk op my geplaas is om deel te neem nie.
- Ek te eniger tyd aan die navorsingsprojek mag onttrek en dat ek nie op enige wyse daardeur benadeel sal word nie.
- Ek gevra mag word om van die navorsingsprojek te onttrek voordat dit afgehandel is indien ek nie die ooreengekome navorsingsplan volg nie.

Geteken te (*plek*)……..op (*datum*) ……2006

…….. ……

Handtekening van deelnemer Handtekening van getuie

Verklaring deur navorser

Ek (naam) ……verklaar dat:

- Ek die inligting in hierdie dokument verduidelik het aan ……..
- Ek hom/haar aangemoedig het om vrae te vra en voldoende tyd gebruik het om dit te beantwoord.
- Ek tevrede is dat hy/sy al die aspekte van die navorsingsprojek soos hierbo bespreek, voldoende verstaan.
- Ek ’n tolk gebruik het/nie ’n tolk gebruik het nie.

Geteken te (*plek*)……..op (*datum*) …….. 2006

…….. ……

Handtekening van navorser Handtekening van getuie

APPENDIX 7

Table 3A.1 McNemar Chi-Square test of (Y) presence and (N) absence of BMI < 18.5 (p = 0.48)

BMI pre*	BMI last** - N	BMI last - Y	Row - Totals
N	13 (92.86%)	1 (7.14%)	14
Y	1 (16.67%)	5 (83.33)	6
Totals	14	6	20

*: BMI pre-radiotherapy

**: BMI in the last week of radiotherapy

Table 3A.2 McNemar Chi-square test of (Y) presence and (N) absence of PINI ≥ 1 (p = 0.01*)

PINI pre**	PINI last# - N	PINI last – Y	Row - Totals
N	4 (30.77%)	9 (69.23%)	13
Y	0 (0%)	7 (100%)	7
Totals	4	16	20

* $p \leq 0.05$

** The PINI (Prognostic Inflammatory and Nutritional Index) pre-radiotherapy

The PINI in the last week of radiotherapy

Table 3A.3 McNemar Chi-square test of (Y) presence and (N) absence of malnutrition* (p = 0.02)**

Malnutrition pre[#]	Malnutrition last[##] - Y	Malnutrition last - N	Row - Totals
N	10 (90.91%)	1 (9.09%)	11
Y	8 (88.89%)	1 (11.11%)	9
Totals	18	2	20

* BMI < 18.5 or PINI ≥ 1 pre-radiotherapy, and BMI < 18.5 or PINI ≥ 1 or ≥ 5% of pre-radiotherapy weight loss in the last week of radiotherapy

** $p \leq 0.05$

[#] Malnutrition pre-radiotherapy

[##] Malnutrition in the last week of radiotherapy

Table 3A.4 Spearman correlation coefficients and (p-values) of relationships between the biochemical data and the anthropometrical data

Anthropometrical data	The PINI* in the last week of radiotherapy	Change in the PINI
% Weight change	0.42 (0.06)**	-0.34 (0.14)
Absolute weight[#] change	0.41 (0.07)**	-0.29 (0.22)
Change in the BMI	0.38 (0.10)	-0.29 (0.22)

* Prognostic Inflammatory and Nutritional Index

** Trend towards statistical significance

[#] Weight in kg

Table 3A.5 McNemar Chi-square test of (Y) presence and (N) absence of Grade I Mucositis (p = 0.13)

Grade I Mucositis Week 2*	Grade I Mucositis Last** - N	Grade I Mucositis Last - Y	Row - Totals
Y	6 (100%)	0 (0%)	6
N	4 (80%)	1 (20%)	5
Totals	10	1	11

* Grade I Mucositis in Week 2 of radiotherapy

** Grade I Mucositis in the last week of radiotherapy

Table 3A.6 McNemar Chi-square test of (Y) presence and (N) absence of Grade II Mucositis (p = 0.02)*

Grade II Mucositis Week 2**	Grade II Mucositis Last[#] - N	Grade II Mucositis Last - Y	Row - Totals
N	7 (70%)	3 (30%)	10
Y	1 (100%)	0 (0%)	1
Totals	8	3	11

* $p \leq 0.05$

** Grade II Mucositis in Week 2 of radiotherapy

[#] Grade II Mucositis in the last week of radiotherapy

Table 3A.7 McNemar Chi-square test of (Y) presence and (N) absence of Grade III Mucositis (p = 1.00)

Grade III Mucositis Week 2*	Grade III Mucositis Last** - N	Grade III Mucositis Last - Y	Row - Totals
N	9 (90%)	1 (10%)	10
Y	0 (0%)	1 (100%)	1
Totals	9	2	11

* Grade III Mucositis in Week 2 of radiotherapy

** Grade III Mucositis in the last week of radiotherapy

Table 3A.8 ANOVA Mann-Whitney test of difference in absolute* weight change between (Y) presence and (N) absence of Grade III Mucositis (p = 0.20)

Grade III Mucositis Y/N	Weight change Mean	Weight change- Std.Err.	Weight change -95.00%	Weight change +95.00%	*N*
N	2.850000	1.731260	-1.24378	6.94378	6
Y	5.600000	2.448372	-0.18948	11.38948	3

* Change in weight (in kg)

Table 3A.9 ANOVA Mann-Whitney test of difference in BMI change between (Y) presence and (N) absence of Grade III Mucositis (p = 0.44)

Grade III Mucositis Y/N	BMI change Mean	BMI change Std.Err.	BMI change -95.00%	BMI change +95.00%	*N*
N	1.000000	0.579135	-0.369436	2.369436	6
Y	1.833333	0.819020	-0.103341	3.770008	3

Table 3A.10 ANOVA Mann-Whitney test of difference in PINI* change between (Y) presence and (N) absence of Grade III Mucositis (p = 0.44)

Grade III Mucositis Y/N	PINI change Mean	PINI change Std.Err.	PINI change -95.00%	PINI change +95.00%	*N*
N	-1.2938	3.714689	-10.0777	7.490016	6
Y	-10.7524	5.253364	-23.1746	1.669863	3

* Prognostic Inflammatory and Nutritional Index

Table 3A.11 ANOVA Mann-Whitney test of difference in absolute* weight change between (Y) presence and (N) absence of fungal infection (p = 0.09)**

Fungal Infection Y/N	Weight change Mean	Weight change Std.Err.	Weight change -95.00%	Weight change +95.00%	*N*
Y	4.750000	1.295009	2.02929	7.470712	12
N	0.943750	1.586055	-2.38843	4.275928	8

* Change in weight (in kg)

** Trend towards statistical significance

Table 3A.12 ANOVA Mann-Whitney test of difference in BMI change between (Y) presence and (N) absence of fungal infection (p = 0.11)

Fungal Infection Y/N	BMI change Mean	BMI change Std. Err.	BMI change -95.00%	BMI change +95.00%	*N*
Y	1.646729	0.502660	0.590679	2.702780	12
N	0.443922	0.615631	-0.849470	1.737315	8

Table 3A.13 ANOVA Mann-Whitney test of difference in the PINI* change between (Y) presence and (N) absence of fungal infection (p = 0.34)

Fungal Infection Y/N	PINI change Mean	PINI change Std.Err.	PINI change -95.00%	PINI change +95.00%	*N*
Y	-48.1629	28.69953	-108.029	11.70326	14
N	-2.3673	37.96591	-81.563	76.82819	8

* Prognostic Inflammatory and Nutritional Index

Table 3A.14 McNemar Chi-square test of (Y) presence and (N) absence of consumption of Level 3 Consistency foods*(p = 0.01)**

Level 3 Consistency Week 1[#]	Level 3 Consistency Last[##] - N	Level 3 Consistency Last - Y	Row - Totals
N	9 (100%)	0 (0%)	9
Y	8 (80%)	2 (20%)	10
Totals	17	2	19

* Liquids, soft foods and solid foods

** $p \leq 0.05$

[#] Level 3 Consistency foods in Week 1 of radiotherapy

[##] Level 3 Consistency foods in the last week of radiotherapy

Table 3A.15 McNemar Chi-square test of (Y) presence and (N) absence of consumption of Level 2 Consistency foods*(p = 0.13)

Level 2 Consistency Week 1**	Level 2 Consistency Last# - Y	Level 2 Consistency Last - N	Row - Totals
Y	8 (88.89%)	1 (11.11%)	9
N	6 (60%)	4 (40%)	10
Totals	14	5	19

* Liquids and soft foods only

** Level 2 Consistency foods in Week 1 of radiotherapy

Level 2 Consistency foods in the last week of radiotherapy

Table 3A.16 Spearman correlation coefficients and (p-values) of relationships between the change in the HNRQ* scores related to the six domains and the following: the anthropometrical and the biochemical data

	Mouth domain	Throat domain	Skin domain	Energy domain	Psycho-social domain	Digestive system domain
% Weight change	-0.04 (0.87)	0.43 (0.16)	0.35 (0.16)	-0.22 (0.72)	-0.46 (0.43)	-0.28 (0.26)
Absolute weight change	0.00 (1.00)	0.61 (0.04)**	0.33 (0.18)	-0.22 (0.72)	-0.46 (0.43)	-0.35 (0.15)
Change in BMI	-0.08 (0.75)	0.37 (0.23)	0.28 (0.27)	-0.22 (0.72)	-0.46 (0.43)	-0.29 (0.25)
Change in the PINI#	0.18 (0.47)	-0.01 (0.97)	-0.47 (0.04)**	0.34 (0.58)	0.15 (0.80)	0.17 (0.49)
The PINI in last week	-0.25 (0.31)	0.21 (0.48)	0.38 (0.10)	-0.22 (0.72)	0.21 (0.74)	-0.30 (0.21)

* Head and Neck Radiotherapy Questionnaire

** Spearman correlation analysis ($p \leq 0.05$)

Prognostic Inflammatory and Nutritional Index

Table 3A.17 ANOVA Mann-Whitney test of difference in change in HNRQ* score related to the mouth domain between (Y) presence and (N) absence of Grade III Mucositis (p = 0.88)

Grade III Mucositis Y/N	Mouth change Mean	Mouth change Std.Err.	Mouth change -95.00%	Mouth change +95.00%	*N*
N	2.473571	0.340873	1.639485	3.307658	5
Y	2.503571	0.440065	1.426771	3.580372	3

* Head and Neck Radiotherapy Questionnaire

Table 3A.18 ANOVA Mann-Whitney test of difference in change in HNRQ* score related to the throat domain between (Y) presence and (N) absence of Grade III Mucositis (p = 0.38)

Grade III Mucositis Y/N	Throat change Mean	Throat change Std.Err.	Throat change -95.00%	Throat change +95.00%	*N*
N	1.083333	1.583626	-2.98751	5.154174	4
Y	1.555556	1.828614	-3.14505	6.256157	3

* Head and Neck Radiotherapy Questionnaire

Table 3A.19 ANOVA Mann-Whitney test of difference in change in HNRQ* score related to the digestive system domain between (Y) presence and (N) absence of Grade III Mucositis (p = 0.46)

Grade III Mucositis Y/N	Digest change Mean	Digest change Std.Err.	Digest change -95.00%	Digest change +95.00%	*N*
N	0.800000	0.770281	-1.08481	2.684811	5
Y	-0.500000	0.994429	-2.93328	1.933280	3

* Head and Neck Radiotherapy Questionnaire

Table 3A.20 ANOVA Mann-Whitney test of difference in change in HNRQ* score related to the skin domain between (Y) presence and (N) absence of Grade III Mucositis (p = 0.10)

Grade III Mucositis Y/N	Skin change Mean	Skin change Std.Err.	Skin change - 95.00%	Skin change +95.00%	*N*
N	2.000000	0.579571	0.581842	3.418158	5
Y	3.443333	0.748223	1.612499	5.274168	3

* Head and Neck Radiotherapy Questionnaire

Table 3A.21 ANOVA Mann-Whitney test of difference in change in HNRQ* score related to the mouth domain between (Y) presence and (N) absence of fungal infection (p = 0.56)

Fungal Infection Y/N	Mouth change Mean	Mouth change Std.Err.	Mouth change -95.00%	Mouth change +95.00%	*N*
Y	2.103247	0.381990	1.293465	2.913029	11
N	1.751020	0.478849	0.735905	2.766136	7

* Head and Neck Radiotherapy Questionnaire

Table 3A.22 ANOVA Mann-Whitney test of difference in change in HNRQ* score related to the throat domain* between (Y) presence and (N) absence of fungal infection (p = 0.83)

Fungal Infection Y/N	Throat change Mean	Throat change Std.Err.	Throat change -95.00%	Throat change +95.00%	*N*
Y	1.600333	0.846919	-0.28672	3.487386	10
N	0.666667	1.893768	-3.55291	4.886245	2

* Head and Neck Radiotherapy Questionnaire

Table 3A.23 ANOVA Mann-Whitney test of difference in change in HNRQ* score related to the digestive system domain between (Y) presence and (N) absence of fungal infection (p = 0.62)

Fungal Infection Y/N	Digest change Mean	Digest change Std.Err.	Digest change -95.00%	Digest change +95.00%	*N*
Y	0.681818	0.483036	-0.342172	1.705808	11
N	0.535714	0.605517	-0.747925	1.819354	7

* Head and Neck Radiotherapy Questionnaire

Table 3A.24 ANOVA Mann-Whitney test of difference in change in HNRQ* score related to the skin domain between (Y) presence and (N) absence of fungal infection (p = 0.16)

Fungal Infection Y/N	Skin change Mean	Skin change Std.Err.	Skin change -95.00%	Skin change +95.00%	*N*
Y	3.211212	0.525839	2.096483	4.325942	11
N	1.904286	0.659174	0.506898	3.301673	7

* Head and Neck Radiotherapy Questionnaire

Table 3A.25 ANOVA Mann-Whitney test of difference in change in HNRQ* score related to the psychosocial domain* between (Y) presence and (N) absence of fungal infection (p = 1.00)

Fungal Infection Y/N	Psychosocial change Mean	Psychosocial change Std.Err.	Psychosocial change -95.00%	Psychosocial change +95.00%	*N*
Y	0.316667	0.339256	-0.76300	1.396330	4
N	-0.330000	0.678511	-2.48933	1.829326	1

* Head and Neck Radiotherapy Questionnaire

Table 3A.26 ANOVA Mann-Whitney test of difference in change in HNRQ* score related to the energy domain between (Y) presence and (N) absence of fungal infection (p = 1.00)

Fungal Infection Y/N	Energy change Mean	Energy change Std.Err.	Energy change -95.00%	Energy change +95.00%	*N*
Y	1.562500	1.012294	-1.65907	4.784072	4
N	0.000000	2.024588	-6.44314	6.443144	1

* Head and Neck Radiotherapy Questionnaire

Table 3A.27 McNemar Chi-square test of (Y) presence and (N) absence of prescription of analgesic medication (p = 0.07)*

Analgesics Week 1**	Analgesics Last[#] - Y	Analgesics Last - N	Row - Totals
Y	14 (100%)	0 (0%)	14
N	5 (83.33%)	1 (16.67%)	6
Totals	19	1	20

* Trend towards statistical significance

** Analgesic medication in Week 1 of radiotherapy

[#] Analgesic medication in the last week of radiotherapy

Table 3A.28 McNemar Chi-square test of (Y) presence and (N) absence of prescription of sedative medication (p = 0.62)

Sedatives Week 1*	Sedatives Last** - Y	Sedatives Last - N	Row - Totals
N	3 (18.75%)	13 (81.25%)	16
Y	3 (75%)	1 (25%)	4
Totals	6	14	20

* Sedative medication in Week 1 of radiotherapy

** Sedative medication in the last week of radiotherapy

Table 3A.29 McNemar Chi-square test of (Y) presence and (N) absence of prescription of anti-emetic medication (p = 0.37)

Anti-emetics Week 1*	Anti-emetics Last** - N	Anti-emetics Last - Y	Row - Totals
N	14 (77.78%)	4 (22.22%)	18
Y	1 (50%)	1 (50%)	2
Totals	15	5	20

* Anti-emetic medication in Week 1 of radiotherapy

** Anti-emetic medication in the last week of radiotherapy

Table 3A.30 McNemar Chi-square test of (Y) presence and (N) absence of prescription of laxative medication (p = 0.01)*

Laxatives Week 1**	Laxatives Last# - Y	Laxatives Last - N	Row - Totals
N	9 (90%)	1 (10%)	10
Y	10 (100%)	0 (0%)	10
Totals	19	1	20

* $p \leq 0.05$

** Laxative medication in Week 1 of radiotherapy

Laxative medication in the last week of radiotherapy

Table 3A.31 Spearman correlation coefficients and (p-values) of relationships between the maximum energy (kcals) intake from supplementation drinks consumed and the anthropometrical, biochemical and HNRQ* data

	Energy (kcals) intake from supplementation drinks
% Weight change	0.29 (0.41)
Change in the BMI	0.29 (0.41)
Absolute weight change	0.34 (0.33)
Change in the PINI	0.04 (0.90)
Change in the HNRQ score related to the mouth domain	0.25 (0.49)
Change in the HNRQ score related to the throat domain	0.27 (0.60)
Change in the HNRQ score related to the digestive system domain	0.47 (0.17)
Change in the HNRQ score related to the skin domain	0.71 (0.02)*

* Head and Neck Radiotherapy Questionnaire

** Spearman correlation analysis ($p \leq 0.05$)