A comparison of psychosocial outcomes in head and neck cancer patients receiving a coping strategies intervention and control subjects receiving no intervention.

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ABSTRACT

Objective: To compare psychosocial outcomes in head and neck (H&N) cancer patients receiving the Nucare program with a group of matched control subjects who received no intervention.

Methods: A prospective, non-randomized study design was used. Subjects were H&N cancer patients. The Nucare program, a psycho-educational coping strategies intervention, was the test intervention. Control subjects were matched to test subjects by disease stage and time since cancer therapy. Outcomes were quality of life (QL) and depressive symptoms (DS) evaluated at baseline and 3-4 months later.

Results: 138 subjects were recruited and outcome data was available on 101. At outcome evaluation, compared to their baseline scores, the test group had improved physical and social functioning, global QL, fatigue, sleep disturbance and DS, while the control group showed no changes in QL or DS.

Conclusion: The results suggest the Nucare may improve QL and reduce DS in H&N cancer patients.
RÉSUMÉ

Objectif: Comparer les résultats à des mesures d’adaptation psychosociale chez des patients atteints d’un cancer de la bouche ou de la gorge (B/G) et ayant reçu une intervention psychoéducative à ceux obtenus par des sujets d’un groupe contrôle apparié n’ayant pas reçu d’intervention.

Méthodologie: Un devis de recherche prospectif non randomisé a été appliqué. Les sujets du groupe contrôle ont été appariés aux sujets du groupe expérimental au niveau du stade de développement de leur cancer et du temps écoulé depuis leur traitement médical oncologique. La qualité de vie (QV) et les symptômes dépressifs (SD) ont servi à évaluer l’adaptation psychosociale.

Résultats: A l’évaluation post-test, les sujets du groupe expérimental ont démontré une amélioration de leur QV et de leurs SD, tandis que ces indicateurs n’ont pas changé pour le groupe contrôle.

Conclusion: Une intervention psychoéducative pourrait améliorer la QV et réduire les SD de patients atteints d’un cancer B/G.
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1. REVIEW OF THE LITERATURE

1.1 HEAD AND NECK CANCER

Today, cancer is the second most common cause of death in developed countries, exceeded only by heart disease. In 2000, there were over 389,000 new cases of head and neck cancer worldwide, making of it the 11th most common type of cancer in the world. In this study, head and neck cancer, which is also known as upper aerodigestive tract cancer, will comprise malignant neoplasm in the oral cavity, which includes cancer of the lip [International Classification of Disease, 9th Revision (ICD-9) 140.9], tongue (ICD-9 141.4), gum (ICD-9 143), floor of the mouth (ICD-9 144); other parts of the mouth, including cheek mucosa, vestibule of mouth, palate, retromolar area, and uvula (ICD-9 145); oropharynx (ICD-9 146.9); nasopharynx (ICD-9 147.9); hypopharynx (ICD-9 148.9); other sites within the lip, oral cavity, and pharynx (ICD-9 169); upper jaw bone (ICD-9 170.0); mandibular bone (ICD-9 170.1); and cancer of the larynx (ICD-9 161.9). Cancer of the salivary glands, which includes parotid, submandibular, sublingual, and other minor salivary glands (ICD-9 142); nose (ICD-9 160.0); ethmoid (ICD-9 160.3); sphenoid carcinoma (ICD-9 160.5) and neck unknown primary (ICD-9 196.0) will be considered as “other cancer”.

Squamous cell carcinoma is the most common histological tumour type in the head and neck region, accounting for over 95% of tumours in this region (Adenis et al., 1988; Barzan et al., 1998). Head and neck cancer accounts for approximately 6.2% of worldwide cancer incidence (Parkin et al., 2001b), but it may vary from 1-2% in Western Europe to over 45% in some parts of Asia (Pinholt et al., 1997). In Canada the percentage
of incident cases of head and neck cancer is approximately 3.5% (NCIC, 2000), while in the USA it is approximately 2.8% (Ries et al., 2003). In addition, the five-year survival rate for this group of cancers has remained unchanged for the past 30 years, stabilized at approximately 60% (Jemal et al., 2003).

Head and neck cancer is one of the most traumatic types of cancer, not only because of the emotional trauma of the diagnosis itself, but also because of the impairment caused by the treatment and the potential psychological trauma that accompanies it. Besides the high levels of symptomatic (e.g. pain, voice hoarseness, and dry mouth) (List et al., 1999; Wijers et al., 2002) and functional problems (e.g. speech, eating and swallowing) (Epstein et al., 1999; Gillespie et al., 2004; Rogers et al., 1999) faced by head and neck cancer patients, they are also prone to experience a variety of other problems, such as mood disorder and facial disfigurement (Dropkin, 1999; Rogers et al., 1999; Rumsey et al., 2003). Such situations often lead to the increase of psychosocial distress, anxiety and depression. Also, the fear of death and disease recurrence is quite constant, which leads the disease adjustment towards a long and burdensome process (Bjordal and Kaasa, 1995; Rapoport et al., 1993).

In the literature, there is a vast number of studies documenting the deterioration in quality of life and the physical and psychological impacts faced by head and neck cancer patients as well as by patients with other types of cancer. At the same time, there is an impressive number of psychosocial and educational interventions addressed in the literature to help cancer patients better cope with their emotional and social behavior. Unfortunately, there
are only a few studies of this genre addressing the improvement in the quality of life and
the reduction of psychological problems in the head and neck cancer populations.

Given the lack of intervention programs aiming to improve the quality of life of head and
neck cancer patients and the unchanged survival rates among this population, future
research should address new approaches in order to improve cancer patients’ quality of
life and possibly the survival length in this population.

1.1.1 Epidemiology of head and neck cancer

Head and neck cancer is a major public health problem in most developed countries, and
it is amongst the most frequently occurring cancers in the world. The year of 2000 marks
the world’s most recent age-specific incidence rate for head and neck cancer data. Among
the global male population, there were 17.4 new cases per 100,000 population, whereas
among females there were 5.3 new cases per 100,000 population (Parkin et al., 2001a).
The highest incidence of these cancers tends to be where there is a higher prevalence of
tobacco and alcohol use, except for nasopharyngeal cancer which is highly associated
with the Epstein-Barr virus infection and which is also found mainly in areas where there
is a high consumption of salted fish. In regions like India, for example, where tobacco
(especially chewing tobacco and betel quid) and alcohol habits are very common, cancer
of the head and neck region may account for up to 25% of male and 10% of female
cancers (Jayant and Yeole, 1987; Yeole et al., 2000). Furthermore, some recent studies
conducted by Pisani et al. (1999) and Licintra et al. (2003) confirmed the existence of a
higher prevalence and incidence of head and neck cancer among males compared to
females, with a Male:Female ratio of 4.4:1 for pharyngeal cancer, and 2.0:1 for cancers of
the oral cavity (Pisani et al., 1999); however, some authors suggest a gender ratio variation of 2-15:1 (WHO and IARC, 2004). In addition, the prevalence of head and neck cancer is also higher in those in lower socio-economic classes (Licitra et al., 2003; Muir and Weiland, 1995; Ostman et al., 1995).

In the USA, cancer is the second most common cause of death. It accounts for 23% of all deaths, with the relative survival rates between 1974-1976 and 1992-1998 decreasing only 3% for larynx cancer, and increasing 5% for oral cavity cancer (Jemal et al., 2003). The Globocan 2000 reported an annual age-specific incidence rate of 15.29 for males per 100,000 population, and 5.75 for females per 100,000 population, with oral cavity cancer accounting for most of this incidence rate. The average incidence rate for oral cavity in males was 5 per 100,000 population and in females the incidence was 1.6 per 100,000 population (Parkin et al., 2001a).

In Canada, head and neck cancer is the 7th most common type of cancer among males, and the 13th among females. It was estimated that, during 2003, there were over 4,000 new cases of head and neck cancer, with on average, 75% of those cancers affecting males; and over 1,000 deaths. The 2003 age-standardized incidence rates per 100,000 population in men were 12 for oral cavity and pharyngeal cancer, and 6 for laryngeal cancer; while in women they were 5 for oral cavity and pharyngeal cancer (NCIC, 2003). Recently, there are no data regarding survival rate for head and neck cancer in Canada. Nonetheless, in Quebec, the five-year relative survival rate between 1984 and 1998 for men varies from 34 to 90% for oral cavity, 27 to 47% for pharynx, and 63 to 66% for larynx; for women the survival rate for these cancers vary respectively from 26 to 98%,
23 to 67%, and 65 to 72%. Equally important, these relative survival rates in men have not improved during this period; except for the survival rate of oral cavity cancer (i.e. tongue, salivary glands, gum, floor of the mouth) and larynx cancer, which improved by 3 to 12% (Louchini and Beaupré, 2003).

Furthermore, in addition to the short survival rates, head and neck cancer patients may have a poorer prognosis if the presence of distant metastasis and/or lymph node involvement is detected, with 5-year survival rates being 20% or lower for patients with distant metastasis and 40% or lower for patients with lymph node involvement (Wingo et al., 1995).

1.1.2 Aetiological and risk factors

1.1.2.1 Tobacco and alcohol

Tobacco and alcohol exposure have been repeatedly substantiated as the major determinants of head and neck cancer, especially in developed countries, the Caribbean and South American countries; with both, tobacco and alcohol exposure, showing dose-response relationships with the incidence of those cancers (Boffetta and Garfinkel, 1990; Kato et al., 1992; Lefebvre and Adenis, 1995; Macfarlane et al., 1996; Schlecht et al., 1999). Tabacco and alcohol consumption account for an average of three-quarters of all pharyngeal, laryngeal and oral cancers (Blot et al., 1988), and five- to 25- fold increase in the risk of cancer in heavy smokers compared to non-smokers (La Vecchia et al., 1999).

When analyzing alcohol consumption alone, strong trends in risk were observed for cancers of the oral cavity, pharynx, and larynx (Bagnardi et al., 2001; Blot et al., 1988;
Kato et al., 1992). The consumption of alcohol and the use of tobacco seem to interact in a multiplicative way, and their joint effects were also found to have a strong association with the development of second primary tumors. For patients with head and neck squamous cell carcinoma who were currently smokers the relative risk (RR) was 2.1 compared to non smokers, and for those who were alcohol consumers the RR was 1.3 compared to non alcohol consumers (Do et al., 2003). Similarly, a study conducted by Day et al. found that individuals with pharyngeal and oral cancer who smoke experience a four-fold increase in the risk of a second primary tumour when compared to non-smokers and former smokers (Day et al., 1994). Moreover, a case-control study conducted by Franco et al. also reported a strong association between tobacco and alcohol consumption and the risk of developing second primary cancers (Franco et al., 1991).

1.1.2.2 Other factors

Research evidence has brought support to the possibility of human papillomavirus (HPV) being an important causal agent in some of the head and neck cancer (i.e. oral cavity cancer), identifying the HPV-16 as the dominant causative type of papillomas (Capone et al., 2000; Forastiere et al., 2001; Gillison et al., 1999; Gillison and Shah, 2001; Miller and Johnstone, 2001). However, there is an inconsistency in prevalence estimates with the range varying from 8 to 100% in premalignant and malignant lesions (Bouda et al., 2000; Chang et al., 1991; Franceschi et al., 1996; Greer, Jr. et al., 1990; Holladay and Gerald, 1993; Miguel et al., 1998; Sand et al., 2000; Syrjanen et al., 1987). Such a wide range may be due to the different study designs used (e.g. detection and sampling methods), the reliability of the viral measurement, or the classification variety used to describe the lesion (Ha et al., 2002). In addition, malignant transformation in the mouth is rare and
much less frequent that the malignant transformation observed in the genital tract (Licitra et al., 2002; Licitra et al., 2003). Finally, some of these infections may reflect the latent form of the viral infection, although smoking and alcohol consumption are known to be cofactors for the promotion of the tumour (Gillison et al., 1999; Steinberg, 1995).

Malnutrition has been associated with high incidence rates of oral and pharyngeal cancer (Willett and Trichopoulous, 1996), and the intake of fruits and vegetables rich in vitamin A, C and fibers may be associated with a protective effect on the risk of developing head and neck cancer (Licitra et al., 2002; Llewellyn et al., 2003; McLaughlin et al., 1988; Petridou et al., 2002). Such protective effect was observed to be stronger particularly among men, smokers and heavy alcohol drinkers (Sanchez et al., 2003). In addition, the intake of salted fish seems to be an important risk factor for nasopharynx in some southern China and Inuit population. Meanwhile, no associations has been seen in relation to other dietary nutrients, such as vitamins E and B, iron, or folate; or the intake of smoked, charcoal grilled, or pickled meat (Gridley et al., 1990; Licitra et al., 2002; McLaughlin et al., 1988).

Until today, there have not been many genetic studies addressing head and neck cancer. Some researchers tended to associated the risk of head and neck cancer with the presence of enviromental factors among relatives. For example, a case-control study conducted by Goldstein et al. found a weak non-significant association between the risk of head and neck cancer and familial history of any cancer. After controlling for enviromental factors such as alcohol and tabacco consumption, as well as sociodemographic determinants, the odds ratio (OR) remained close to the null value (OR= 1.1 [95% confidence interval (CI)
0.9-1.3]. However, there is not enough information reporting the consumption of cigarettes and/or alcohol among the patient's relatives who had developed cancer (Goldstein et al., 1994). On the other hand, a case-control study conducted in Brazil involving 754 patients with head and neck squamous cell carcinoma found that family history of cancer was a risk factor for developing head and neck cancer. When controlling for smoking and tobacco habits, an individual with a first-degree relative who had head and neck cancer, was found to have 3.65 (95% CI: 1.97-6.76) higher chances of developing head and neck cancer compared with an individual with no familial history of cancer. For siblings as a first-degree relative with head and neck cancer, the RR was found to be as high as 8.57 (95% CI: 2.72-27.04); and among this group, larynx was the region with the highest risk (RR = 11.23; 95%CI: 2.90-43.50) (Foulkes et al., 1995). Furthermore, the risk of developing a second primary head and neck cancer is eight times higher in those individuals with a family history of head and neck cancer (Morita et al., 1994).

For work-related risk, Haguenoer et al. found significant associations between nasal cancer and woodwork, lip cancer and farming - mainly caused by sunlight exposure - (OR=5.3, 95% CI 1.1-26.8), pharyngeal cancer and textile-industry and building industry (OR 2.4, 95% CI 1.0-5.7 and OR 2.0, 95% CI 1.1-3.9 respectively). Coal miners showed the highest work-related risk for oral cavity and larynx cancer (OR=3.5, 95% CI 1.1-11.8 and OR=3.2, 95% CI 1.1-9.7 respectively) (Haguenoer et al., 1990). Furthermore, a case-control study conducted by Berrino et al. found significant effect of occupational exposure to solvents and asbestos, and the risk of hypopharyngeal/laryngeal cancer in European males (Berrino et al., 2003).
Despite evidence suggesting that poor oral health (e.g. ill-fitted dentures, poor oral hygiene) may be associated with oral cancer, the role of such factors in the etiology of oral cancer remains unclear. Graham et al (1977), Franco et al (1989), and Velly et al. (1998) reported poor dentition, lack of oral hygiene, infrequent tooth brushing, and ill-fitted dentures, being associated higher risk of developing oral cancer (Balaram et al., 2002; Franco et al., 1989; Graham et al., 1977; Velly et al., 1998). On the other hand, a study conducted with 400 oral cancer patients did not find an association between the use of ill-fitted dentures and oral cancer (Gorsky and Silverman S Jr, 1984).

1.1.3 Cancer treatment and side-effects

Head and neck cancer treatment requires multidisciplinary approaches and the use of combined procedures, which often renders it prolonged and aggressive. The selection of the treatment depends mainly on the stage and location of the tumour. The levels of problems associated with side-effects these individuals may have will depend mainly on the type and intensity of the treatment received, including radiation, surgery, and/or chemotherapy; the treatment dose received; and the area affected by radiation or surgery. Cancer treatment may cause acute side effects (usually happening during and immediately after treatment), and/or chronic side effects when they continue for months and years after the treatment; the chronic side effects will occur especially in patients with locally advanced disease, when usually high doses of radiation or combined treatment is used. Most of the problems which affect head and neck cancer appear during the first months after diagnosis and treatment, with little change occurring after 1 to 3 years after diagnosis (Hammerlid et al., 2001). Treatment-related problems have been shown to
affect the patient’s quality of life (Ohm et al., 2001), since the patient has to deal with acute toxicities, causing mild discomfort such as mucositis and difficulty chewing; to more serious debilitating symptoms such as pain, malnutrition and xerostomia (De Graeff et al., 1999; Epstein et al., 1999; Huguenin et al., 1999; List et al., 1997; Wijers et al., 2002). The latter is a major problem among patients who receive high-dose radiation, or who have one of the major salivary glands removed. In addition, as a result of extensive surgery and/or sequelae from radiotherapy and chemotherapy, the patient must cope with a wide range of other long-term problems that may have major impact on patient’s quality of life, such as limited diet (Huguenin et al., 1999; List et al., 1997), serious appearance damage (Rathmell et al., 1991; Rogers et al., 1999), functional impairment (e.g. hoarseness) (List et al., 1999), difficulty breathing (Gotay and Moore, 1992; Rogers et al., 1999) and reduced speech abilities (Epstein et al., 1999; Lazarus et al., 1996; Logemann et al., 1993; Pauloski et al., 1993; Rogers et al., 1999). For example, patients who undergo laryngectomy usually report problems related to speech, altered appearance and decreased perceived abilities when swallowing (de Boer et al., 1995). Financial concerns (Rogers et al., 1999; Terrell et al., 1999), changes in the body image (Gamba et al., 1992; Rogers et al., 1999), and negative reactions from the partner are also important issues that affect most of the head and neck patients, with some studies suggesting that most of these patients experience tensions in the family and sexual problems (e.g. worsened relationship with their partner, reduced sexuality) (de Boer et al., 1995; Gamba et al., 1992). Indeed, the changes in social relations (Epstein et al., 1999; Gritz et al., 1999; Terrell et al., 1999), the increased social isolation and the emotional distress caused by the cancer disease to the family members, may in fact further the family’s ability to support and help the patient (Gamba et al., 1992).
1.1.4 Psychological problems

1.1.4.1 Psychological consequences

Head and neck cancer is a threatening and traumatic disease which often devastates the patients’ life. Head and neck cancer patients not only have to cope with having a disease with a low survival rate, but also with the loss of considerable important functions, and the permanent threat of disease recurrence and death. These and other factors cause the patient to feel uncertain, vulnerable, influencing his/her physical and emotional integrity.

According to a recent literature review on physical and psychosocial aspects of head and neck cancer, anxiety, mood distress, depression, worry and fatigue were found to be the main problems among this population (de Boer et al., 1999; Pruyn et al., 1986). In spite of these problems, which are well-documented, there is still some debate on whether they are minimized or persist with time. Some studies suggest that, in the long-term, some patients with head and neck cancer tend to adapt to the disease and its treatment and to report fairly good overall quality of life (Hammerlid et al., 2001; List et al., 1999; List and Stracks, 2000; Murry et al., 1998). While, on the other hand, some studies have shown that with time, some physical and emotional functioning remains impaired or deteriorates (Pourcel et al., 2002). To illustrate this controversy, a prospective study involving 107 head and neck patients, reported that despite initial high level of depressive symptoms, the patients had gradual improvement in quality of life and psychological functioning over a period of three years follow-up (De Graeff et al., 2000a). In the same way, in a longitudinal prospective study of 357 head and neck patients Bjordal et al.
observed a general trend of significant deterioration on quality of life during treatment but a slow recovery during the 12 following months (Bjordal et al., 2001).

In contrast, a study conducted by Rapoport et al. among 55 head and neck patients does not support these findings. Although the authors found an improvement in the medical condition of most of the patients; the same was not observed in relation to psychological conditions. That is, the levels of depression and anxiety among those patients were seen to increase with time (Rapoport et al., 1993). This exacerbation of psychological symptoms may be due to chronic stress caused by the threatening presence of the disease and the distress caused by trying to maintain a normal and healthy appearance (de Boer et al., 1995). Similarly, a study conducted by De Boer et al. (1995) which supports the previous findings, found that over half of the patients who had undergone laryngectomy reported having their appearance highly damaged by such treatment, with the highest levels of complaints being among women. This study also showed that even 2 years after treatment, patients still reported feeling of uncertainty, low self-esteem, depression, anxiety, sexual problems and trouble managing their emotions (de Boer et al., 1995). Finally, Pourel et al. also suggested that in a long-term follow-up “emotional and social functioning remain profoundly impaired” in a group of 113 oropharynx cancer patients (Pourel et al., 2002). Among others, these are some of the reasons why head and neck cancer patients have one of the worse quality of life levels when compared to colon and lung cancer patients (Gritz et al., 1999), and why there is a need for psychosocial intervention in this group of cancer patients.

1.1.4.2 Quality of life
The *Stedman’s Medical Dictionary* defines “quality of life” as “a patient’s general well-being, including mental status, stress level, sexual function and self-perceived health status.” (Lathrop S.T., 2000). Ferrans defined quality of life as “a person’s sense of well-being that stems from satisfaction or dissatisfaction with the areas of life that are important.” (Ferrans, 1990). While Morton et al. defined it as “the perceived discrepancy between the reality of what a person has and the concept of what that person wants, needs, or expects” (Morton and Izzard, 2003). Although it is an overall enjoyment of life, it is difficult to find a universal definition for quality of life, since it has a multidimensional nature and complex concepts.

Quality of life is known to be a very dynamic phenomenon, with some authors suggesting the involvement of constructs such as psychological, functional, physical, and social well-being (Gotay, 1996), as well as intimacy, spirituality, occupational functioning, and global quality of life (Cella and Tulsky, 1990). Due to its broad conceptualization, a measure with a multidimensional state of being is necessary to its accurate assessment (Allison et al., 1997; Cella and Tulsky, 1990; Cella and Tulsky, 1993).

Studies assessing quality of life in head and neck cancer have increased within the last decade. Before, most of the existing studies were cross-sectional or retrospective and described only few aspects of post-treatment situation (Gotay and Moore, 1992; Pruyn et al., 1986). Since then, the number of studies addressing quality of life among head and neck cancer patients have increased tremendously. A reason for that may be the changes that medicine and society have encountered. Whereas, before, cancer treatment was primarily focused on attempting to cure the cancer or to prolong the survival, now more
attention is being given to the broad outcome of health-related quality of life. Consequently, the idea of conceptualizing and evaluating the importance of having quality of life as an outcome in cancer treatment has increased.

Assessing quality of life in head and neck cancer is especially important, given the potential for disruption of some of the quality of life dimensions due to cancer and the high levels of morbidity associated with this disease. Head and neck cancer remains a highly psychologically traumatic type of illness, and it has been demonstrated that such illness can affect many fundamental aspects of life (Terrell et al., 1999), which may then have a dramatic effect on patients' quality of life and disease recovery. As an example, a study conducted in 1987 by Burns et al. (1987) with advanced head and neck cancer patients reported that 75% of the patients had problems eating and speaking, while 42% reported having no joy in their lives after cancer treatment (Burns et al., 1987).

Although quality of life has a strong correlation with functional domains, higher correlation has been seen for the emotional domains (Meyer and Mark, 1995; Spiegel et al., 1989; Terrell et al., 1999). As an example, despite some cancer patients reporting significant functional impairment, surprisingly high levels of quality of life has been observed (Ruhl et al., 1997). A cohort study with 153 head and neck patients found that high levels of depressive symptoms, low performance status, and combined modality treatment were significant predictors of poor functioning and psychological morbidity after treatment (De Graeff et al., 2000b). Similarly, Hammerlid et al. (2001) reported depression and physical functioning at diagnosis to be independent predictors of quality of life after three years (Hammerlid et al., 2001). At the same time that functional and
psychological problems may be strongly correlated to quality of life, there may also be some predictors of quality of life that may help identify those patients who are likely to encounter difficulty in their recovery. For instance, sociodemographic variables such as level of education (Bjordal et al., 1995; Sehlen et al., 2002), employment status (Allison et al., 1998; Sehlen et al., 2002), age, gender (Allison et al., 1998), and marital status (Long et al., 1996) have been shown to be strongly correlate to quality of life of head and neck cancer patients. Furthermore, Allison et al. (1999) suggested that the dental status may play an important role in the quality of life of head and neck cancer patients (Allison et al., 1999). Finally, support from the family, friends (Ruhl et al., 1997) and the family doctor (Mathieson et al., 1996), and the patients’ perception of the disease (i.e. state of mind and optimism) (Allison et al., 2000; Allison et al., 2003; Greer et al., 1992) may favorably influence the disease recovery and be of great value for the patients’ quality of life. For example, a study analysing how optimism and pessimism personality may affect the health-related quality of life among a group of head and neck cancer, reported that optimistic patients tended to score lower on symptom domains and higher on functional domains compared to pessimistic patients (Allison et al., 2000), leading to the idea that personality’s characteristic and patient reaction are linked, and that different behaviour and recovery may be expected.

1.1.4.3 Psychiatric morbidity

Psychiatric morbidity has been extensively assessed among head and neck cancer patients, with numerous studies finding high levels of mental distress and morbidity in this population (Bjordal and Kaasa, 1995; Hammerlid et al., 1999a; McDonough et al., 1996).
Most of the health-related quality of life problems experienced by this population will occur during and just after treatment, tending to reduce and eventually return to normality after one year (Hammerlid et al., 1997; Hammerlid et al., 1999a). Even so, exceptions may occur, and some patients may not have their problem levels return to pre-cancer treatment levels.

The majority of the head and neck cancer patients report higher levels of depression, anxiety and higher rates of suicide (Dropkin M.J., 1986; Faberow, 1997; Godding et al., 1995; Rapoport et al., 1993) compared to other cancer populations. Feelings of worry and loss (Rathmell et al., 1991), mood disorders (Breitbart, 1995; Bronheim et al., 1991a; Bronheim et al., 1991b; Rathmell et al., 1991), distress and stress (Langius et al., 1993), and anger (Gamba et al., 1992) has also been observed.

Different studies suggest that the rates of depression among this population are not constant across studies, varying from 18-53% (de Boer et al., 1995; de Boer et al., 1999; De Leeuw et al., 2000; Hammerlid et al., 2001; Morton et al., 1984; Rapoport et al., 1993; Zabora et al., 2001). Hammerlid et al conducted a prospective multicentre study in which anxiety and depression were accessed 6 times during the first year after cancer diagnosis. The results showed that up to one third of the head and neck cancer patients reported possible psychiatric disorder, with anxiety being most frequent at diagnosis and depression being most frequent during treatment. Although females reported higher levels of anxiety compared to males, and similarly younger patients tended to be more anxious than elderly patients, the same was not observed with respect to depression levels, neither
on one or three years follow-up (Hammerlid et al., 1999a; Hammerlid et al., 2001). The three years follow-up of this study found that women scored higher on 17 of the 28 domains measured, reaching over 10 points difference compared to men for dyspnea domain, leading to the idea that with time women may cope better than men. Younger patients also tended to have better rehabilitation potential compared to elderly patients (Hammerlid et al., 2001). An interesting fact is that, the only probable predictor found for such psychiatric problems was the anxiety and depression caused by the cancer diagnosis, whereas a prospective study conducted among 260 head and neck patients found a broad range of pretreatment symptoms (e.g. cancer stage, gender, depressive symptoms, physical symptoms, emotional support, family openness to discuss the illness in the family) to be correlated with the prediction of depressive symptoms up to three years after diagnosis. Physical and psychological factors predicted nearly 90% of the patients who became depressed, and women were the most affected (De Leeuw et al., 2000; De Leeuw et al., 2001). Nevertheless, when the scores at diagnosis were compared to those at three months, disease stage was also found to be a possible predictor for anxiety and depression (Hammerlid et al., 1999a). The same tendency was observed in a later study involving a larger group of patients (Hammerlid et al., 2001). It is clear that this may be due to treatment side-effects, since late stage cancer tends to have a much more invasive treatment compared to early stage cancer, which may also lead to more sequelae.

List et al. (1997) conducted a study on quality of life outcomes in head and neck cancer patients and found that 23% of the patients reported being depressed (although it was associated with past history of alcohol use). Moreover, following one year after treatment,
patients were still reporting functional problems due to treatment and disease side-effects (List et al., 1997).

1.1.5 Interventions

For the past 20 years, psychosocial intervention programs have been developed to help patients with cancer to better cope with the psychological consequences of cancer diagnosis and treatment, with some of these approaches focusing on behavioral and emotional aspects of dealing with cancer. These psychosocial intervention programs focus mainly on delivery of information, promotion of emotional and social support, stress management strategies, and teaching relaxation techniques, among others. By using these programs, individuals and their family members may gain emotional support to deal with their fears, and to reduce their stress and anxiety caused by the disease. Since the results of research on psychosocial intervention programs may be affected by small sample size or unrestricted selection of study subjects (e.g. patients in need of psychological support may have higher benefit from the intervention), the potential benefits of these intervention programs remain unclear.

Two randomized studies on psychosocial support conducted by Spiegel et al. and Fawzy et al. reported a strong positive effect of the intervention in prolonging survival for patients with cancer (Fawzy et al., 1993; Spiegel et al., 1989). However, both studies had a small number of subjects among whom most were breast cancer patients.

Newell et al. (2002) conducted a systematic review of psychological interventions for oncology patients, reviewing over 300 different intervention therapies (Newell et al.,
Although breast cancer was the most common type of cancer investigated, other cancers were also included. The authors reported only a very few studies having good quality, and few having fair-quality. Also, most of the recommendations were based on results from single studies (i.e. based on only one trial) rather than many. Among those good and fair quality studies, music therapy was recommended for reducing patients’ anxiety (Sabo and Michael, 1996) and general affect (Zimmerman et al., 1996). Group therapy was recommended for improving coping and control skill immediately after intervention (Fawzy et al., 1990; Greer et al., 1992). Counseling was recommended for general affect (Zimmerman et al., 1996), reducing distress/stress (Greer et al., 1992), improving quality of life, functional ability and social relationship (Linn et al., 1982; Maguire et al., 1983).

In particular, structured and unstructured counseling, cognitive behavioral, education, and group therapy provided potential benefits for most of the psychosocial interventions outcomes explored (e.g. depression, anxiety, general affect, quality of life, marital and social relationship). In addition, relaxation training and visualization/guided imagery showed to reduce most of the cancer treatment side-effects. For example, a randomized controlled trial conducted by Greer and colleagues showed the results of a psychological therapy focusing on the “personal meaning of cancer to the individual” and on the patient’s own coping strategies, delivered to patients with different types of cancer. In the aforementioned study, it was observed that after two and four months follow-up, the proportion of depressed and anxious patients dropped significantly in the intervention group, while the same was not observed in the control group (Greer et al., 1992). According to Newell’s review, long- and medium-term follow-up therapies were the most recommended therapies. Overall, the review suggested that some interventions may have
potential, however “no intervention strategies could be recommended for improving patient’s lengths of survival” (Newell et al., 2002).

The literature on psychosocial intervention among head and neck cancer is very limited. Currently, there are only three studies concerning psychosocial intervention among this population. All these three studies were pilot studies conducted in Sweden in the middle 90’s. The two first studies investigated: i) the effects of a long-term group psychological therapy for newly diagnosed head and neck cancer patients compared to a control group, and ii) the effects of a one-week psychoeducational intervention offered one year after the cancer diagnosis (Hammerlid et al., 1999b). Despite the small sample size (13 patients and 34 control for the first study, and 14 patients for the second study) in the above mentioned studies, and the high rates of drop-out among the group therapy (5 patients did not follow the group therapy), there was an improvement in psychosocial and emotional functioning among the group therapy patients compared to the control group. Furthermore, among the short-term intervention group, there was an improvement in most of the functions and symptoms after the intervention.

The third study investigated a supportive psychosocial program, and outcome data was compared to a control group. Although still limited by the small sample, this study involved a larger sample group (52 patients) compared to the previous studies. By the end of the study, the intervention group reported lower levels of quality of life compared to the control group. However, despite this lack of improvement in quality of life, the survival rate at the 3-year follow-up in the intervention group was higher than the control group (Petruson et al., 2003).
1.2 NUCARE INTERVENTION PROGRAM

The literature shows that there are many different types of intervention programs that have been applied to a variety of cancer patients. Most of these programs aim at improving the quality of life and/or psychological problems of cancer patients after disease diagnosis and treatment. The Nucare is one of these programs. We chose to apply the Nucare program among a population of head and neck cancer, because of its previous positive results among other cancer populations (Edgar et al., 1992; Edgar et al., 2001), and also because the people who created the Nucare program are located in Montreal.

The Nucare (an acronym for nursing, cancer and research) program is a short-term psycho-educational coping skills training intervention, whose aim is to instruct individuals with cancer in how to cope with this disease. It enhances mainly two areas: i) the sense of personal control, and ii) the learning of cognitive and instrumental coping responses. This intervention is based on two principles: 1) The Lazarus and Folkman’s model, which defines coping as behavioral and cognitive efforts used to deal with stressful demands (Lazarus and Folkman, 1984), where successful coping strategies may improve the patient’s emotional well being (e.g., anxiety, depression) (Endler and Parker, 1990); and 2) The McGill Model of Nursing which focuses on the relationship between the family and the patient, orienting their improvement in coping skills and behavioral understanding (Allen FM, 1977; Gottlieb and Rowat, 1987). This model’s objective is to improve the patient’s health through an interactive milieu, where the patient and his family are seen as a whole. For instance, it works according to the patients’ schedule, it provides feedback pointing to positive behaviours, and it emphasizes the individuals’
strength. In particular, the patient will acquire, based on his own resources and strengths, necessary tools to reach good coping, and hence, better health (Edgar et al., 2001).

In order to address these issues, the Nucare program consists of the following eight components:

1) Good Coping. Through the psychosocial, biological and sociological aspects of life, patients learn how to effectively cope with the daily life stress and the changes cause by the cancer.

2) Ways of thinking. It gives emphasis on the patient’s own ways of thinking, and how these thoughts could affect his/her feelings. The patient is taught to identify patterns that may lead to negative mood, and also to reappraise negative thoughts making them less distressing. It emphasizes that optimistic thinking leads to good feelings, enhancing the patient’ sense of personal control.

3) Communication. It is an important and basic skill for all human being. This section of the Nucare program brings a list of tools and techniques for successful communication. It shows the importance of the “I” statement when disclosing thoughts or feelings, in order to develop positive behaviors. Family and doctor-patient communication is also emphasized in this section.

4) Effective Use of Social Support. This section emphasizes the benefits of receiving and offering social support, it also teaches the patient in how to identify and acquire sources of information, and how to better use social support.

5) Problem-Solving Techniques. Patients are taught specific series of steps that lead to good problem-solving. There are examples illustrating common situations faced by
cancer patients, where the patient can practice before applying the technique on his/her own problem.

6) Goal Setting. Patient is encouraged to set short or long-term goals. Setting attainable goals constitutes a realistic way of achieving tasks that are important and timely. It also gives self-esteem and self-confidence to the patients, arousing a sense of personal control.

7) Healthy Lifestyle. It emphasizes the benefits of exercising (encouraging the patient to practice physical activities that he/she enjoys), good nutrition (stimulating the use of a variety of different foods everyday), good sense of humor (including a list of positive thoughts), dealing with feelings of fatigue (through a list of restorative activities, such as gardening, reading, listening to music), and also the benefits of having hope and spirituality.

8) Relaxation Training. The relaxation training gives, in steps, quick and useful relaxation techniques, allowing the patient to learn to relax to the degree that he chooses, and to gain the most from it.

The didactic material that patients receive comprises a workbook describing the eight components above mentioned; and a cassette or CD with instructions to guide the patient through the workbook and music to accompany the relaxation training component. For this study, this intervention was delivered over a maximum period of 4 weeks and it was offered in three different formats: 1) small group format (meaning a group of 3 or 4 people only), 2) one-to-one format, or 3) home format. Both small group and one-to-one format is conducted by a trained therapist, in two or three sessions of one to two hours long. For the home format, patients may have assistance through the telephone, but there is no therapist.
2 RATIONALE AND OBJECTIVES

2.1 Rationale

Despite enormous research investment and advances in cancer treatment over the past years, head and neck cancer survival has remained largely unchanged. In addition, reduced quality of life, high rates of anxiety and depression, and the presence of psychological distress caused by disease-related symptoms and patients' disease perception (e.g. emotional and physical) and stigma is highly prevalent in head and neck cancer. Also, despite many studies assessing the impact of psychological intervention in patients with cancer and demonstrating an improvement in quality of life and reduction in the levels of depression in these patients, little research has been done on means of addressing the effects of psychosocial problems in patients with head and neck cancer. Furthermore, many studies have shown evidence of the benefits of good coping in reducing emotional distress and enhancing positive psychological aspects (Dunkel-Schetter et al., 1992; Petrosky and Birkimer, 1991). Therefore, nowadays, in addition to survival improvement, researchers are investigating means of improving patients' quality of life, and also trying to better understand the role of psychological factors in cancer survival.

The Nucare program has been applied to over 480 breast and colonic cancer patients and it has shown significant results in improving coping skills among those patients (Edgar et al., 1992; Edgar et al., 2001). Likewise, this intervention was considered to have potential effectiveness managing treatment distressing side-effects when it was delivered during
the course of cancer treatment (Irvine D. and Lum L., 1997). Furthermore, the Nucare program has been cited in numerous reviews as an effective psycho-educational therapeutic intervention for patients with cancer (Andersen et al., 1994; Andersen, 1994; Fawzy et al., 1995; Meyer and Mark, 1995). Finally, according to a systematic review of psychological therapies for cancer patients conducted by Newell et al, the Nucare program contains elements which may improve some aspects of the patient’s quality of life, such as group therapy and cognitive behavioral therapy for medium- and long-term benefits; as well as relaxation training for minimizing side-effects outcomes (Newell et al., 2002). Therefore, the Nucare program has the potential to improve head and neck cancer patients’ coping strategies. Overall, the aforementioned information not only suggest a strong demand for research in this area but also confirm that patients with head and neck cancer may benefit from the Nucare program.

2.2 Objectives

First, the main aim of this feasibility study was to compare outcomes data from subjects who received the Nucare intervention program to control subjects who did not receive it. Second, as part of a pilot study, we aimed at collect preliminary outcomes data prior to a Randomized Clinical Trial to test the effectiveness of the intervention program.

2.3 Hypothesis

We hypothesized that subjects who received the Nucare intervention will have better health related quality of life and lower levels of anxiety and depression than those who did not receive the intervention.
3 METHODOLOGY

3.1 Study design

This project used a prospective, non-randomized, quasi-experimental study design.

3.1.1 Selection criteria

Eligible intervention and control subjects were those newly diagnosed with a first primary cancer of the head and neck region including lip, tongue, gum, floor of the mouth; other parts of the mouth, including cheek mucosa, vestibule of mouth, palate, retromolar area, and uvula; oropharynx; nasopharynx; hypopharynx; other sites within the lip, oral cavity, and pharynx; upper jaw bone; mandibular bone; and cancer of the larynx. Also, cancer of the salivary glands, which includes parotid, submandibular, sublingual, and other minor salivary glands; nose; ethmoid; sphenoid carcinoma and neck unknown primary. Subjects must have up to 36 months following the disease diagnosis. All had finished their cancer treatment, and were able to understand and complete the study questionnaires. Subjects who had poor physical or mental condition, who were severely debilitated or unable to give reliable answers to the questionnaires, or who were in palliative or terminal care were not included in the study, either as a case or a control.

3.1.2 Intervention

The intervention used was the Nucare program, which is a short-term psycho-educational intervention program aiming to instruct individuals with cancer in how to cope with that disease. It comprises a workbook which describes the following 8 components: good coping, ways of thinking, communication, effective use of social support, problem
solving techniques, goal setting, healthy lifestyle, relaxation training. There is also a cassette or CD to guide the patient through the workbook, and music to accompany the relaxation training component. There were three different delivery formats of the Nucare offered: i) small group format, in which the subjects received group sessions, involving a minimum of three and a maximum of four people, with a trained therapist, ii) one-to-one format, in which the sessions with the therapist were individually, or iii) home format, in which subjects received written information and a cassette to use at home. The two therapists involved in this study had experience applying the Nucare program in both English and French language. The intervention took place at the hospital (group and one-to-one format) or at the subject’s home (home format), and the subjects were allocated to the different intervention formats based on their own choice. The group format and the one-to-one format were carried out by one of the two trained therapists, in two or three 1-2 hour sessions, and the intervention was given during a period of four weeks maximum. For the home format, as with the group and one-to-one format, subjects received a workbook explaining the steps of the intervention; and a cassette or CD with oral information to guide subjects through the workbook, and music for the relaxation training part. However there was no therapist, but a phone number to assist those who opted for the home format.

3.1.3 Study subjects

We used a convenience sample in this study, where intervention and control subjects were recruited as they went to their appointment in the out-patient Head and Neck Oncology Clinic at the Sir Mortimer B. Davis-Jewish General Hospital in Montreal, Quebec, Canada.
The intervention subjects were those offered the Nucare program. Whereas control subjects received normal care, which is oral and written information concerning support groups existing at the Jewish General Hospital and in the local community.

3.1.4 Recruitment and data collection sequence

The baseline questionnaires with sociodemographic and clinical questions, plus the questionnaires measuring quality of life, depression and anxiety were delivered to subjects in person when they went to the hospital for their appointment at the head and neck oncology clinic. The follow-up took place at the head and neck hospital clinic 3-4 months after the first approach. Those patients who were not going to the hospital clinic during that period of time, received the follow-up questionnaire by mail. Although the control subjects' recruitment started 10 months after the cases were collected, both cases and controls were recruited at the hospital clinic.

Data from intervention subjects were collected at baseline, 6 weeks (i.e. 2 weeks after intervention) and 3-4 months after baseline approach. However, for statistical analysis purposes, only baseline and 3-4 months follow-up were considered.

Data from control subjects were collected at baseline and 3-4 months after baseline approach. The control subjects were matched to the intervention subjects by time since the diagnosis (± 2 months), and stage of cancer, which was dichotomized into early and late stage (respectively: stage I or II; and stage II or IV).
3.2 Consent form

Once the eligible subjects received complete explanation of the study project, they were asked to sign a written consent form upon agreement in participating in the study.

3.3 Ethical considerations

This study was approved by the Institutional Review Board of McGill University (appendix 1), and that of the participating hospital, and by patients with consent. Subjects were contacted after having full knowledge of the nature of their disease, and were introduced to the study by trained personnel. Subjects were aware that there were no direct personal benefits for participating in the study, and those who agreed to participate, after reading and signing the informed consent were recruited. English and French versions of informed consent for intervention subjects and control subjects are included in appendices 2 and 3. All the questionnaire answers are kept confidential, and names and other information cannot be linked to the data files.

3.4 Sample size

For the intervention group 128 patients were approached, 66 agreed to participate, baseline data are available on 59 and outcomes data are available on 45. For the control group 89 patients were approached, 72 agreed to participate, baseline data are available on 66 subjects and outcomes data are available on 56.

3.5 Clinical information (independent variables)

Clinical information was obtained from the medical chart and interview with the subjects. The following information was assessed: cancer site, cancer stage, time since diagnosis,
time since cancer treatment, type of treatment received, presence of comorbidity, personal history of previous cancer, and history of cancer recurrence.

3.6 Sociodemographic information (independent variables)

Baseline information on socio-demographic characteristics was obtained at the baseline interview with the subject. The variables measured were: age, gender, level of education, living arrangements, and employment status.

3.7 Outcome variables

Outcomes on health related quality of life (HRQL) as measured by the European Organization for Research and Treatment of Cancer (EORTC) core quality of life questionnaire (QLQ-C30); and anxiety and depression as measured by the Hospital Anxiety and Depression Scale (HADS). Both EORTC QLQ-C30 (Aaronson et al., 1993; Bjordal et al., 1999; Bjordal et al., 2000; Bjordal and Kaasa, 1992; King, 1996; Zigmond and Snaith, 1983) and HADS (Hammerlid et al., 1997; Hammerlid et al., 1999a; Kugaya et al., 2000; Zigmond and Snaith, 1983) have been tested and validated in many languages including English and French, and have been shown to provide respectively: a valid tool for the assessment of health-related quality of life (HRQL), and measurement of depression and anxiety symptoms in head and neck cancer amongst other cancer sites.

3.7.1 Health-related quality of life

The EORTC QLQ-C30 is a self-complete generic quality of life instrument used worldwide for measuring HRQL in patients with head and neck cancer amongst other cancer sites. It has shown satisfactory psychometric qualities (Aaronson et al., 1993). It
contains five functional scales: physical, role, emotional, cognitive, and social functioning. Three symptoms scales: fatigue, pain, nausea and vomiting. It also comprises six single-items: dyspnea, appetite loss, sleep disturbance, financial difficulties, diarrhea, and constipation and also a global health and quality of life scale. The scales and single-items scores are transformed into a 0 to 100 scale, with higher scores for functional scales and the global health and quality of life scale representing higher or better levels of functioning and quality of life, whereas higher scores for symptoms scales represent higher levels of symptoms and problems.

Due to its multiple domain scores, this questionnaire is able to provide individual score for the different aspects of quality of life instead of an overall score, and also to detect an intervention’s effects on each domain of the individual’s quality of life.

3.7.2 Anxiety and depression

HADS is a measurement tool designed to investigate rates of depressive symptoms and anxiety in hospital patients. It has been used extensively among a variety of cancers including head and neck cancer (Berard et al., 1998; Hammerlid et al., 2001; Hopwood et al., 1998; Katz et al., 2004; Petruson et al., 2003; Zigmond and Snaith, 1983). It is a 14-item questionnaire consisting of two scales which are equally divided in seven items for anxiety and seven for depression, giving a total score when adding both scales. Each item has a Likert four-response categorical scale, with a higher score indicating higher severity of problem. The scores for each of the two scales range from 0 to 21. Scoring 11 or more in each of the anxiety and depression scales is an indicative of “probable” problems, while scoring between 8 and 10 indicates "possible" problems, and scoring between 0 and
7 is considered "normal". These scores have also been established in a dichotomous way: the patient is considered normal for scores below eight, and possibly depressed if scores are equal or greater than eight (Julious et al., 1997).

3.8 Statistical analysis

SAS software was used to conduct the analysis for this study. First, univariate analysis summarizing the baseline and follow-up scores was conducted among the intervention and control groups.

3.8.1 Descriptive statistics

In order to describe the differences between intervention and control groups in relation to frequency distributions, means, standard deviations (SD), and medians, descriptive statistics were conducted on all socio-demographic and clinical characteristics, and on EORTC QLQ-C30 and HADS scores. Subsequently we compared 1) test and control groups (within groups) characteristics at baseline and follow-up, and 2) baseline characteristics between the groups, using Chi-square test for categorical variables with only 2 answers options (e.g. gender: male or female), Fischer's exact test for categorical variables with more than 2 answers options (e.g. cohabitation: with partner, with friends, alone or in communal accommodation), and Wilcoxon rank sum test for continuous variables (i.e. age). After, we also dichotomized age, cohabitation, occupation, level of education, stage, time since treatment and time since diagnosis, and used Chi-square test to compare between the intervention and intervention groups.

3.8.2 Analysis of means
We performed analysis of means on HADS and EORTC QLQ-C30 domain scores in intervention and control groups. Due to non-normal distribution of the data, non-parametric Wilcoxon matched-pairs signed-rank tests were used to compare differences in scores between the intervention and control groups.

First, we obtained a mean score for each domain of the questionnaires at baseline and follow-up for the intervention and control groups. Thereafter, for each subject, a difference from baseline to follow-up for each of the EORTC QLQ-C30 and HADS questionnaires’ domains was obtained (e.g. subject “x” scores 10 on the depression scale at baseline, and 7 on the follow-up. Therefore the difference obtained for subject “x” is -3). This process was repeated for all subjects in the intervention and control groups. Then a mean difference score for each of the domain of EORTC QLQ-C30 and HADS questionnaires for the intervention and control groups was generated. Finally, a difference of means between intervention and control groups (i.e. intervention – control) for each domain of the questionnaires was obtained by subtracting the mean difference scores of the control group from that of the intervention group (e.g. for the intervention group the fatigue mean difference score was -10, and for the control group the fatigue mean difference score was -2. Therefore the difference of mean between intervention and control is -8). This procedure was repeated for all the domains, and statistical non-parametric Wilcoxon matched-pairs signed-rank tests were used to analyse the differences above mentioned.

4 RESULTS
4.1 Descriptive characteristics

4.1.1 Intervention group

For the intervention group, there were 128 subjects invited to participate in this study, and 66 (51.6%) agreed to participate. The subjects who refused to participate tended to be older than those who accepted to participate (mean age 64 vs. 57; p-value<0.05). There is no information regarding the gender of the subjects who refused to participate. The reasons for refusal were diverse, however most of the people who refused to participate - 27 (43.5%) - said having no interest in participating in the study, while 22 (35.5%) people said “I’m ok, thanks”, the other 13 individuals said they were too physically (9.4%) or socially (11.6%) impaired.

Of the remaining 66 subjects, 21 dropped-out during the study, therefore outcome data are available for 45. Comparing those who participated throughout the study and those who dropped-out during the follow-up period, there were no significant differences in the mean age, nor on gender, occupation, comorbidity, time since diagnosis and time since treatment. However significant difference was observed on level of education, cancer site, cancer stage, and cancer treatment. Those who dropped out were more likely to have lower level of education (65.2% vs. 57.8%; p-value<0.05), to have other than pharyngeal cancer (71.2% vs. 66.7%; p-value<0.05) to be in early stage of disease (44% vs. 33.3%; p-value<0.05), and to have had only surgery as treatment modality (13.6% vs. 4.4%; p-value<0.05).

4.1.2 Control group
For the control group, 89 subjects were invited to take part in this study and 72 (80.9%) agreed to it. Out of the 17 subjects who refused to participate, 13 (76.5%) were male. Most of the subjects refused to participate in the study because of having no interest for it. There is no information regarding the age of the invited patients who refused to participate in the control group. Of the remaining 72 subjects, 5 withdrew before or during the first questionnaire, 1 passed-away during the follow-up period, and 10 did not reply to the follow-up questionnaire. Therefore baseline data are available for 66 subjects and outcome data are available for 56. Comparing those who participated throughout the study and those who dropped-out during the follow-up period, there were no significant differences in mean age, gender, occupation status, level of education, cohabitation, comorbidity, cancer stage, cancer site, the time since the diagnosis, the time since treatment, the treatment modality, history of cancer, or recurrence.

4.1.3 Both groups

Thus a total of 217 subjects were invited to participate in this study. Of the 138 subjects who consented to participate either in the control or intervention group, final data are available for 101. Table 1 shows the distribution of socio-demographic characteristics according to group. Comparing subjects' characteristics between baseline and follow-up, among those subjects who followed throughout the study, the proportion of males was higher among the intervention group compared to the control group (80.0% vs. 69.6% respectively; p-value<0.0001). Intervention subjects were on average younger than controls (mean age 57.3 vs. 63.9 respectively; p-value<0.05). Also the majority of control subjects were older than 55 years (75.4% for baseline, and 71.4% for follow-up), while for the intervention group the distribution between those below 55 years old and those
Table 1. Descriptive analysis of study subjects according to socio-demographic characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline N=66 (%)</td>
<td>Follow-up N=45 (%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>52 (78.8)</td>
<td>36 (80.0)</td>
</tr>
<tr>
<td>Female</td>
<td>14 (21.2)</td>
<td>9 (20.0)</td>
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<tr>
<td>Mean age</td>
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<td>57.3 (30-84)</td>
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<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Up to 55 years old</td>
<td>34 (51.5)</td>
<td>22 (48.9)</td>
</tr>
<tr>
<td>More than 55 years old</td>
<td>32 (48.5)</td>
<td>23 (51.1)</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retired or working</td>
<td>43 (65.1)</td>
<td>32 (70.1)</td>
</tr>
<tr>
<td>Unemployed or on sick leave</td>
<td>23 (34.9)</td>
<td>13 (29.9)</td>
</tr>
<tr>
<td>Level of education*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school or less</td>
<td>43 (65.2)</td>
<td>26 (57.8)</td>
</tr>
<tr>
<td>College or University</td>
<td>23 (34.8)</td>
<td>19 (42.2)</td>
</tr>
<tr>
<td>Cohabitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With partner or relative</td>
<td>46 (69.7)</td>
<td>37 (84.1)</td>
</tr>
<tr>
<td>Alone or communal accommodation</td>
<td>20 (30.3)</td>
<td>7 (15.9)</td>
</tr>
</tbody>
</table>

*P-value < 0.05 for comparison within the intervention group (from baseline to follow-up)
† P-value < 0.0001 for comparison between intervention and control
‡ P-value < 0.05 for comparison between intervention and control
above it (respectively 51.5% vs. 48.4% for baseline, and 48.9% vs. 51.1% for follow-up) was more balanced. Table 2 shows the distribution of clinical characteristics of intervention and control groups. Among the variables addressed in Table 2, intervention subjects differed from control subjects with respect to time since diagnosis and treatment received. For the intervention group, there was a balance in the time since diagnosis when comparing those diagnosed up to 12 months and between 13 to 36 months (46.7% and 53.3% respectively), while for the control subjects, most of the subjects were approached between 1 to 12 months since diagnosis (62.5%) compared to 13 to 36 months since diagnosis (37.5%). With respect to treatment modality received, 55.6% of the intervention subjects who followed the study received some sort of combined treatment (i.e. more than one treatment modality), compared to 73.2% of the control subjects; and 40.0% received only radiotherapy, compared to 21.4% of the control subjects.

Table 3 summarizes the EORTC QLQ-C30 domain scores for the intervention group. Analysing the baseline information separately, the compliant group (i.e. subjects who participated throughout the study, from baseline to follow-up) scored slightly better (i.e. higher scores) on all of the functioning scales compared to the complete group (i.e. subjects who provided baseline information only), however such differences were not found to be significant. A similar trend was observed among the symptoms scale, with the compliant group scoring better (i.e. lower scores) than the complete group on most of the domains, with exception for the financial impact domain. Comparing the baseline scores of the compliant group to their follow-up scores, there seems to have been an improvement in most of the variables scores, with significant changes occurring to physical and social functioning, global quality of life, fatigue, and sleep disturbance.
Table 2a. Descriptive analysis of study subjects according to clinical characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Follow-up</td>
</tr>
<tr>
<td></td>
<td>N= 66 (%)</td>
<td>N= 45 (%)</td>
</tr>
<tr>
<td>Co-morbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence</td>
<td>24 (36.4)</td>
<td>17 (37.8)</td>
</tr>
<tr>
<td>Absence</td>
<td>42 (63.6)</td>
<td>28 (62.2)</td>
</tr>
<tr>
<td>Stage*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early</td>
<td>29 (44.0)</td>
<td>15 (33.3)</td>
</tr>
<tr>
<td>Late</td>
<td>37 (56.0)</td>
<td>30 (66.7)</td>
</tr>
<tr>
<td>Site**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral cavity</td>
<td>14 (21.1)</td>
<td>8 (17.8)</td>
</tr>
<tr>
<td>Pharyngeal</td>
<td>19 (28.8)</td>
<td>18 (40.0)</td>
</tr>
<tr>
<td>Larynx</td>
<td>20 (30.3)</td>
<td>11 (24.4)</td>
</tr>
<tr>
<td>Other</td>
<td>13 (19.7)</td>
<td>8 (17.8)</td>
</tr>
<tr>
<td>Time since diagnosis†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Up to 12 months</td>
<td>32 (48.5)</td>
<td>20 (44.4)</td>
</tr>
<tr>
<td>12-36 months</td>
<td>34 (51.5)</td>
<td>25 (55.6)</td>
</tr>
<tr>
<td>Time since treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Up to 6 months</td>
<td>30 (45.5)</td>
<td>19 (42.2)</td>
</tr>
<tr>
<td>More than 6 months</td>
<td>36 (54.5)</td>
<td>26 (57.8)</td>
</tr>
</tbody>
</table>

* P-value < 0.05 for comparison within the intervention group.

** P-value < 0.05 for the intervention group when comparing the pharyngeal cancer with all the other cancers (i.e. oral cavity, larynx and other).

† P-value < 0.07 for comparison of baseline values between intervention and control group.
Table 2b. Descriptive analysis of study subjects according to clinical characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Follow-up</td>
</tr>
<tr>
<td></td>
<td>N= 66 (%)</td>
<td>N= 45 (%)</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>25 (37.9)</td>
<td>18 (40.0)</td>
</tr>
<tr>
<td>Surgery</td>
<td>9 (14.6)</td>
<td>2 (4.4)</td>
</tr>
<tr>
<td>Combination</td>
<td>32 (48.5)</td>
<td>25 (55.6)</td>
</tr>
<tr>
<td>History of cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence</td>
<td>8 (9.1)</td>
<td>4 (8.9)</td>
</tr>
<tr>
<td>Absence</td>
<td>60 (90.9)</td>
<td>41 (91.1)</td>
</tr>
<tr>
<td>Recurrence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence</td>
<td>8 (12.1)</td>
<td>4 (8.9)</td>
</tr>
<tr>
<td>Absence</td>
<td>58 (87.9)</td>
<td>41 (91.1)</td>
</tr>
</tbody>
</table>

*P-value < 0.06 for comparison of baseline values between intervention and control group.*
Table 3. Mean and standard deviation (SD) for EORTC QLQ-C30 variables: Results for the intervention group.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Intervention group</th>
<th></th>
<th></th>
<th>Change†</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Complete N= 66</td>
<td>Compliant N= 45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Functioning Scales</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical</td>
<td>87.0 (16.8)</td>
<td>88.6 (14.6)</td>
<td>91.7 (11.0)</td>
<td>3.09 (11.1)</td>
<td>0.05</td>
</tr>
<tr>
<td>Role</td>
<td>84.7 (24.6)</td>
<td>87.0 (22.7)</td>
<td>90.0 (16.8)</td>
<td>2.94 (24.7)</td>
<td>0.32</td>
</tr>
<tr>
<td>Emotional</td>
<td>75.8 (24.0)</td>
<td>78.9 (20.4)</td>
<td>79.6 (20.2)</td>
<td>0.72 (17.2)</td>
<td>0.57</td>
</tr>
<tr>
<td>Cognitive</td>
<td>81.3 (24.4)</td>
<td>84.4 (21.7)</td>
<td>83.7 (19.3)</td>
<td>-0.74 (15.5)</td>
<td>0.57</td>
</tr>
<tr>
<td>Social</td>
<td>81.1 (24.3)</td>
<td>81.8 (22.1)</td>
<td>89.6 (18.2)</td>
<td>7.78 (22.6)</td>
<td>0.02</td>
</tr>
<tr>
<td>Global</td>
<td>65.4 (22.7)</td>
<td>66.6 (20.2)</td>
<td>75.8 (17.3)</td>
<td>9.14 (20.6)</td>
<td>0.002</td>
</tr>
<tr>
<td>Symptom Scales</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>31.6 (26.7)</td>
<td>27.6 (23.4)</td>
<td>22.0 (20.0)</td>
<td>-5.68 (19.2)</td>
<td>0.04</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>5.1 (14.0)</td>
<td>2.6 (7.0)</td>
<td>1.1 (5.5)</td>
<td>-1.48 (7.8)</td>
<td>0.18</td>
</tr>
<tr>
<td>Pain</td>
<td>15.1 (23.2)</td>
<td>10.7 (17.8)</td>
<td>12.2 (19.9)</td>
<td>1.48 (19.7)</td>
<td>0.59</td>
</tr>
<tr>
<td>Single-item Scales</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>19.2 (27.5)</td>
<td>16.3 (26.2)</td>
<td>14.1 (23.0)</td>
<td>-2.22 (25.0)</td>
<td>0.47</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>34.3 (37.0)</td>
<td>29.6 (34.2)</td>
<td>21.5 (31.1)</td>
<td>-8.15 (28.6)</td>
<td>0.03</td>
</tr>
<tr>
<td>Appetite loss</td>
<td>17.7 (31.1)</td>
<td>13.3 (27.0)</td>
<td>13.3 (29.6)</td>
<td>0.00 (23.6)</td>
<td>0.87</td>
</tr>
<tr>
<td>Constipation</td>
<td>13.6 (24.1)</td>
<td>11.1 (22.5)</td>
<td>11.1 (22.5)</td>
<td>0.00 (22.5)</td>
<td>1.00</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3.03 (9.7)</td>
<td>2.2 (8.4)</td>
<td>4.6 (13.8)</td>
<td>2.33 (15.3)</td>
<td>0.53</td>
</tr>
<tr>
<td>Financial impact</td>
<td>23.2 (33.6)</td>
<td>25.2 (36.3)</td>
<td>21.5 (34.9)</td>
<td>-3.70 (29.5)</td>
<td>0.44</td>
</tr>
</tbody>
</table>

†Change within paired observation= [follow-up (intervention)- baseline (intervention)]. *P-value obtained from non-parametric Wilcoxon matched-pairs signed-ranks test. †Scores range from 0 to 100 with a higher score representing a higher level of functioning. ‡Scores range from 0 to 100 with a higher score representing a greater degree of symptoms.
The HADS domain scores are summarized on Table 4. Although follow-up compliant subjects reported lower levels of anxiety and depression at baseline compared to the complete group, such differences were not found to be significant. Meanwhile, small improvements were observed on all of the HADS variables after the intervention, however only depression scores had significant changes.

Although we preferred to use non-parametric Wilcoxon matched-pairs signed-rank tests to analyse the changes in scores from baseline to follow-up, some of the histograms presented in Figure 1 show that most of the score changes followed a normal distribution.

Table 5 summarizes the EORTC QLQ-C30 domain scores for the control group. For the baseline scores, the compliant group scored lower on half of the functioning scales compared to the complete group, however such differences were not significant. Comparing the symptom scales scores between compliant and complete groups, the compliant group scored lower (i.e. lower levels of symptoms) on the majority of the domains. The nausea and vomiting, dyspnea, and constipation symptoms were the exceptions, as they were higher among the compliant group. Comparing the baseline scores of the compliant group to their follow-up scores, most of the functioning scales show a small increase in the scores, on the other hand, most of the symptoms scales show a small decrease in the scores. However, none of these changes were statistically significant.
Table 4. Mean and standard deviation (SD) for HADS variables: Results for the intervention group.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline Complete group N= 66</th>
<th>Baseline Compliant group N= 45</th>
<th>Follow-up N= 45</th>
<th>Change†</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>6.1 (3.7)</td>
<td>5.8 (3.2)</td>
<td>5.5 (3.51)</td>
<td>-0.33 (3.8)</td>
<td>0.62</td>
</tr>
<tr>
<td>Depression</td>
<td>5.2 (4.0)</td>
<td>4.7 (3.8)</td>
<td>3.5 (3.25)</td>
<td>-1.18 (3.6)</td>
<td>0.01</td>
</tr>
<tr>
<td>Total HADS</td>
<td>11.35 (6.9)</td>
<td>10.5 (6.5)</td>
<td>9.0 (6.19)</td>
<td>-1.47 (6.7)</td>
<td>0.10</td>
</tr>
</tbody>
</table>

†Change within paired observation = [follow-up (intervention) - baseline (intervention)]

*P-value obtained from non-parametric Wilcoxon matched-pairs signed-ranks test.

Higher scores represent worse problems.
Figure 1. Histogram representing changes (from baseline to follow-up) in some of the EORTC QLQ-C30 and HADS domain scores within paired observations: Results for the intervention group.
Table 5. Mean and standard deviation (SD) for EORTC QLQ-C30 variables: Results for the control group.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline Complete N= 65</th>
<th>Baseline Compliant N= 56</th>
<th>Follow-up N= 56</th>
<th>Change†</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Functioning Scales</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical</td>
<td>84.0 (19.0)</td>
<td>83.3 (19.5)</td>
<td>83.0 (18.2)</td>
<td>-0.36 (12.3)</td>
<td>0.55</td>
</tr>
<tr>
<td>Role</td>
<td>81.0 (26.0)</td>
<td>79.8 (26.9)</td>
<td>84.5 (23.5)</td>
<td>4.76 (26.3)</td>
<td>0.28</td>
</tr>
<tr>
<td>Emotional</td>
<td>75.9 (28.1)</td>
<td>76.8 (27.9)</td>
<td>79.3 (26.1)</td>
<td>2.53 (17.3)</td>
<td>0.36</td>
</tr>
<tr>
<td>Cognitive</td>
<td>84.4 (21.4)</td>
<td>86.0 (17.6)</td>
<td>85.4 (19.6)</td>
<td>-0.59 (17.1)</td>
<td>0.83</td>
</tr>
<tr>
<td>Social</td>
<td>80.8 (23.2)</td>
<td>80.1 (23.6)</td>
<td>82.7 (24.8)</td>
<td>2.68 (22.9)</td>
<td>0.42</td>
</tr>
<tr>
<td>Global</td>
<td>71.0 (24.8)</td>
<td>71.7 (24.0)</td>
<td>72.5 (22.6)</td>
<td>0.74 (19.9)</td>
<td>0.53</td>
</tr>
<tr>
<td><strong>Symptom Scales</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>33.0 (31.4)</td>
<td>32.2 (31.2)</td>
<td>33.2 (27.1)</td>
<td>0.98 (37.0)</td>
<td>0.85</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>5.6 (17.0)</td>
<td>6.2 (18.1)</td>
<td>4.2 (10.2)</td>
<td>-2.08 (17.4)</td>
<td>0.71</td>
</tr>
<tr>
<td>Pain</td>
<td>20.5 (27.9)</td>
<td>20.2 (26.7)</td>
<td>17.8 (24.6)</td>
<td>-2.38 (26.1)</td>
<td>0.59</td>
</tr>
<tr>
<td><strong>Single-item Scales</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>15.4 (22.1)</td>
<td>16.1 (22.9)</td>
<td>15.3 (22.8)</td>
<td>-0.74 (18.6)</td>
<td>0.66</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>20.0 (25.5)</td>
<td>18.4 (23.7)</td>
<td>17.8 (25.4)</td>
<td>-0.60 (22.5)</td>
<td>0.51</td>
</tr>
<tr>
<td>Appetite loss</td>
<td>15.6 (27.8)</td>
<td>13.3 (25.3)</td>
<td>16.7 (26.9)</td>
<td>3.64 (23.7)</td>
<td>0.21</td>
</tr>
<tr>
<td>Constipation</td>
<td>9.7 (17.4)</td>
<td>10.12 (17.9)</td>
<td>12.5 (23.4)</td>
<td>2.42 (20.9)</td>
<td>0.53</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>8.2 (21.3)</td>
<td>7.7 (22.0)</td>
<td>12.5 (24.2)</td>
<td>4.76 (28.0)</td>
<td>0.20</td>
</tr>
<tr>
<td>Financial impact</td>
<td>13.8 (26.9)</td>
<td>13.7 (26.0)</td>
<td>14.9 (23.7)</td>
<td>1.22 (19.0)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

†Change within paired observation= [follow-up (control)- baseline (control)]. *P-value obtained from non-parametric Wilcoxon matched-pairs signed-ranks test. ¹Scores range from 0 to 100 with a higher score representing a higher level of functioning. ²Scores range from 0 to 100 with a higher score representing a greater degree of symptoms.
With respect to baseline outcome variables, although we observed differences when comparing baseline scores of intervention group (Table 3) with those of control group (Table 5), such differences were not statistically significant at 5% level.

Table 6 summarizes the HADS variables scores for the control group. The compliant group reported, although not significant, lower levels of anxiety and depression at baseline compared to the complete group. Such levels tended to slightly increase after the follow-up period. However no significant difference was observed.

Figure 2 shows some of the histograms with the distribution of changes in scores from the baseline subjects to the follow-up for the control group. As can be seen, most of the distributions approximates to normality, however since the initial data was not normally distributed, we opted to use non-parametric Wilcoxon matched-pairs signed-ranks test to do the analyses.

The final analysis carried out was to calculate the net response attributable to the intervention program. This is, the observed difference from baseline to follow-up among the intervention group minus the observed difference from baseline to follow-up among the control group. Such results are summarized in Table 7. To be able to analyse the net response attributable to the intervention program, the intervention and control subjects had to be matched one-to-one (i.e. each intervention subject had to be matched to one control subject). Out of the 45 subjects in the intervention group, 4 did not have any matched control subject. Consequently, for analysis purposes, only 82 subjects (41 intervention subjects and 41 control subjects) could be kept for this analysis.
Table 6. Mean and standard deviation (SD) for HADS variables: Results for the control group.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline Complete group (N=65)</th>
<th>Baseline Compliant group (N=56)</th>
<th>Follow-up (N=56)</th>
<th>Change† (N=56)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HADS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>5.5 (4.7)</td>
<td>5.2 (4.6)</td>
<td>5.4 (4.1)</td>
<td>0.20 (3.0)</td>
<td>0.71</td>
</tr>
<tr>
<td>Depression</td>
<td>3.9 (4.0)</td>
<td>3.8 (4.1)</td>
<td>4.0 (4.0)</td>
<td>0.14 (2.6)</td>
<td>0.94</td>
</tr>
<tr>
<td>Total HADS</td>
<td>9.4 (7.9)</td>
<td>9.1 (7.8)</td>
<td>9.5 (7.3)</td>
<td>0.41 (4.7)</td>
<td>0.79</td>
</tr>
</tbody>
</table>

†Change within paired observation= [follow-up (control)- baseline (control)]

*P-value obtained from non-parametric Wilcoxon matched-pairs signed-ranks test
Figure 2. Histogram representing changes (from baseline to follow-up) in some of the EORTC QLQ-C30 and HADS domain scores within paired observations: Results for the control group.
Table 7. Net response attributable to the intervention program (N=41).

<table>
<thead>
<tr>
<th>Variables</th>
<th>†Diff. of Means (SD)</th>
<th>Median</th>
<th>P-value*</th>
<th>P-value**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>EORTC QLQ-C30</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical</td>
<td>+1.3 (15.8)</td>
<td>0.00</td>
<td>0.57</td>
<td>0.61</td>
</tr>
<tr>
<td>Role</td>
<td>-2.9 (36.0)</td>
<td>0.00</td>
<td>0.78</td>
<td>0.61</td>
</tr>
<tr>
<td>Emotional</td>
<td>-1.5 (27.6)</td>
<td>0.00</td>
<td>0.85</td>
<td>0.74</td>
</tr>
<tr>
<td>Cognitive</td>
<td>-1.2 (26.2)</td>
<td>0.00</td>
<td>0.51</td>
<td>0.77</td>
</tr>
<tr>
<td>Social</td>
<td>+5.7 (30.4)</td>
<td>0.00</td>
<td>0.22</td>
<td>0.24</td>
</tr>
<tr>
<td>Global</td>
<td>+10.0 (28.6)</td>
<td>8.34</td>
<td>0.03</td>
<td>0.03</td>
</tr>
<tr>
<td>Fatigue</td>
<td>-5.4 (37.7)</td>
<td>-11.1</td>
<td>0.18</td>
<td>0.36</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>-0.8 (15.4)</td>
<td>0.00</td>
<td>0.75</td>
<td>0.74</td>
</tr>
<tr>
<td>Pain</td>
<td>+4.5 (31.2)</td>
<td>0.00</td>
<td>0.33</td>
<td>0.36</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>+2.6 (28.3)</td>
<td>0.00</td>
<td>0.59</td>
<td>0.56</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>-7.3 (37.7)</td>
<td>0.00</td>
<td>0.71</td>
<td>0.22</td>
</tr>
<tr>
<td>Appetite loss</td>
<td>-4.9 (36.2)</td>
<td>0.00</td>
<td>0.42</td>
<td>0.39</td>
</tr>
<tr>
<td>Constipation</td>
<td>-4.1 (33.5)</td>
<td>0.00</td>
<td>0.47</td>
<td>0.44</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>-6.0 (38.9)</td>
<td>0.00</td>
<td>0.21</td>
<td>0.34</td>
</tr>
<tr>
<td>Financial impact</td>
<td>-4.9 (33.8)</td>
<td>0.00</td>
<td>0.20</td>
<td>0.36</td>
</tr>
<tr>
<td><strong>HADS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>-0.6 (5.0)</td>
<td>-1.00</td>
<td>0.59</td>
<td>0.46</td>
</tr>
<tr>
<td>Depression</td>
<td>-1.4 (4.5)</td>
<td>-1.00</td>
<td>0.06</td>
<td>0.07</td>
</tr>
<tr>
<td>Total HADS</td>
<td>-2.0 (8.3)</td>
<td>-2.00</td>
<td>0.14</td>
<td>0.13</td>
</tr>
</tbody>
</table>

†Difference of means= [follow-up (interv.)- baseline (interv.)]- [followup (control)- baseline (control)]. For functioning domains of EORTC QLQ-C30 positive values means the intervention group did better than the control group. For symptoms and single-items of EORTC QLQ-C30, and HADS domains negative values means the intervention did better than the control group.

*P-value obtained from non-parametric Wilcoxon matched-pairs signed-rank tests

**P-value obtained from Student t-tests
Among the EORTC QLQ C-30 domain, the intervention seemed to have stronger positive effect on Global quality of life, with a 10 point improvement, followed by diarrhea (6 points improvement), social functioning (5.7 points improvement), fatigue (5.4 points improvement), appetite loss (4.9 points improvement) and financial impact (4.9 points improvement) among others. Yet, only the global quality of life response attributable to the intervention was found to be significant. Among the HADS domain, the intervention also had positive effects reducing the levels of anxiety and depression, however only the improvements observed on depression levels approximated to significance.

The histograms in figure 3 show the distribution of the observed difference from baseline to follow-up among the intervention group minus the observed difference from baseline to follow-up among the control group. Once again, most of the distribution approximated to normality. Therefore, we opted to carry out this analysis with non-parametric Wilcoxon matched-pairs signed-rank tests and also with Student t-tests. And to confirm our assertion, the p-value obtained from the non-parametric Wilcoxon matched-pairs signed-rank tests was very similar to the p-value obtained from parametric Student t-tests.
Figure 3. Histogram representing the change (net response attributable to the intervention) in some of the EORTC QLQ-C30 and HADS variables score within paired observations.
DISCUSSION

Primarily, this study aimed at comparing outcomes from patients who received the Nucare intervention program to control subjects who did not receive it, and at the same time collect outcomes data prior to a randomized clinical trial. Our hypothesis was that subjects who received the Nucare intervention would have better quality of life and lower levels of depressive symptoms compared to those who did not receive the intervention. The results support our hypothesis, suggesting that the Nucare program may improve quality of life and reduce depressive symptoms among head and neck cancer patients. However, the non-experimental design restricts our ability to draw firm conclusions.

Previously published studies suggest that cancer patients may benefit from education-based interventions which facilitate the individual's initial adjustment to the illness (Gray et al., 2000; Hammerlid et al., 1999b; Newell et al., 2002). However, most of those studies were mainly delivered to breast cancer patients, and only a very few were delivered to head and neck cancer patients. When compared to breast cancer, head and neck cancer has a very different profile, since it affects mostly men, and it is mainly caused by cigarette smoking and abusive alcohol drinking. Therefore, the comparison between our study and previous published studies will be very limited.

5.1 Recruitment and refusal

The recruitment of intervention and control subjects was done at different points in time, without randomization. This may raise the discussion about possible selection bias. However, besides using the matching process to reduce the inequalities among the subjects, intervention and control subjects were all recruited from the same hospital.
clinic, which is a clinic of reference for head and neck cancer treatment in Montreal. Therefore, we expect the intervention and control groups to have fairly similar characteristics.

Regarding the refusal rate, although it was higher among the intervention group compared to the control group (49.6% vs. 19.1% respectively), the main reason for subjects refusing to participate in the study was predominantly the same in both groups (i.e. no interest in participating in the study). The reasons for those people having no interest in participating in the study may be many. For instance, for the control group, it may be probably due to the fact that there was no direct benefit for those individuals. While for the intervention group, it may be difficult for some individuals to share their own experience or to talk about their feelings in front of other people. At the same time, some individuals may be too weak, or too depressed to feel motivated to take part in this study. Previous studies on head and neck cancer showed refusal rate varying from 32% to 70% (Hammerlid et al., 1999b; Petruson et al., 2003), and the refusal rate in the intervention group of our study fall within this range.

We did not obtain all clinical and sociodemographic information from those subjects who refused to take part in this study, making it difficult to make comparisons between those subjects who refused and those who accept to enter in the study. As a result, we were unable to know if these two groups were different in regard to clinical and sociodemographic characteristics nor if there was some sort of selection bias.

5.2 Sociodemographics and clinical characteristics
Being a non-randomized study, small differences in baseline sociodemographic and clinical characteristics of the test and control groups, as well as differences in baseline dependent variable scores are expected. Regarding the differences in sociodemographic characteristics between intervention and control groups, there was a significant difference only for age and gender distribution. Although the majority of the intervention and control group were predominantly males, the proportion of males in the intervention group was higher. These results contradict with the ones found by Petruson et al. (Petruson et al., 2003) and Hammerlid et al. (Hammerlid et al., 1999b), which are, to my knowledge, the only published studies on psychosocial interventions among head and neck cancer patients. With respect to age, the intervention group in our study had lower average age compared to the control group. The same was observed in the above mentioned studies.

Since women tend to score worse on psychosocial outcomes compared to men, and young patients tend to do better after cancer treatment compared to elderly patients (Bebbington et al., 1998), one may say that the aforementioned sociodemographic differences between the groups may have played an important role in the differences found on baseline outcome scores between intervention and control groups. Nevertheless, the differences found on baseline outcome scores between the two groups were not statistically significant.

Regarding the differences in clinical characteristics, time since diagnosis and treatment modality were the only variables found to be slightly different, although statistically significant, in their distribution between intervention and control groups. Most of the
subjects in the intervention group had more than 12 months since their cancer diagnosis, and that may have helped the intervention group to score slightly better on most of the baseline scores compared to the control group.

Despite the fact that intervention and control subjects were matched by stage and time since diagnosis, we observed a difference in the distribution of time since diagnosis when comparing 45 intervention subjects to 56 control subjects. The majority of the intervention group had more than 12 months since diagnosis, while the majority of the control group had less than 12 months since diagnosis. Since we compared 45 intervention subjects with 56 control subjects, it is possible that the difference found in the time since diagnosis distribution was due to the irregular matching (i.e. some intervention subjects are matched one-to-one to the control subjects, some are matched one-to-two, and some are not matched at all). As can be noted, there are at least 11 subjects in the control group that were the second match of the intervention subjects. We hypothesize that most of those 11 control subjects would have less than 12 months since diagnosis, which would have caused the imbalance between the intervention and control groups. To confirm this hypothesis, we ran descriptive analyses with only 41 exactly-matched pairs of subjects (i.e. one intervention subject matched for one control subject), and the results suggested that the distribution of time since diagnosis for the intervention group and for the control group were very similar [up to 12 months since diagnosis: 21 (51.2%) vs. 22 subjects (53.7%) for intervention and control group respectively], confirming the matching process.

5.3 EORTC QLQ-C30 and HADS domains
This study provides slightly higher scores for both the intervention and control groups with respect to EORTC QLQ-C30 functioning scales scores at baseline, when compared to previously published studies involving head and neck cancer patients (Bjordal et al., 2001; Hammerlid et al., 1999b; Petruson et al., 2003). The same trend was observed for the symptoms and single-items scales scores at baseline, with the majority of the subjects in our study scoring slightly better on most of the those scales compared to previous studies (Bjordal et al., 2001; Hammerlid et al., 1999b; Petruson et al., 2003). Consequently, we were unable to observe great changes in the outcome variable scores from baseline to follow-up.

In addition, as previously mentioned, we observed differences in baseline outcome scores between intervention and control groups. However, it is unlikely that these differences contributed substantially to our study results.

With respect to those subjects who dropped-out of the study during the follow-up period, it is clear that they were more likely to have scored worse in most of the domains (although no difference was significant). Since the studies on psychosocial intervention conducted by Hammerlid et al. and Petruson et al. did not provide outcome information regarding those subjects who did not complete the study, it is impossible to make any comparison. Nonetheless, a prospective study measuring the quality of life of head and neck cancer patients at different points in time (Bjordal et al., 2001) reported that those who dropped-out of the study during the follow-up period were more likely to have lower functioning scores compared to those who remained in the study, supporting our study results.
For the HADS domains we observed in our study a similar trend as for the EORTC QLQ-C30 domains, with most of the subjects having very low scores for depression and anxiety scales at baseline when compared to other studies in head and neck population (De Leeuw et al., 2001; Hammerlid et al., 1999a). Moreover, as for the EORTC QLQ-C30 domains, those who complied and followed throughout our study were more likely to score lower (i.e. to have lower depressive symptoms) at baseline of the HADS questionnaire compared to those who dropped-out of the study.

Although it is unclear the reasons for finding such results in our study, we have a few suggestions for such occurrence. The literature describes gender as playing an important role among cancer patients with depressive symptoms, and women have been reported as having higher prevalence of depressive symptoms compared to men (Bebbington et al., 1998; Cassileth et al., 1986). Likewise, age is another important factor that may affect depressive symptoms, with some studies suggesting that older patients may suffer more from treatment side-effects and may present more depressive symptoms (Bennahum et al., 1997; De Leeuw et al., 2000; McGuirt and Davis, III, 1995).

Despite the observation that the prevalence of head and neck cancer among women had increased in the past years (McGuirt, 1986; NCIC, 2003), it is known that this type of cancer affects mostly men. Perhaps the reason our study subjects present reasonably good scores for most of the EORTC QLQ-C30 domains, and low scores for HADS domains compared to previous studies, may be the fact that, in this study, comparing the proportion of males and females, there was a high Male:Female ratio of 4:1 for the
intervention, and 2.3:1 for the control group. In addition, we had a fairly young intervention group (mean age = 57), and most of the subjects in both groups were living with partner or a relative, which has been shown to affect the patient's quality of life and emotional response to the cancer.

It is known that most psychological symptoms have their highest peak after diagnosis, during and right after treatment (Bjordal et al., 2001; List et al., 1999). More than 50% of the intervention group had more than one year since the cancer diagnosis and treatment, and more than 50% of the control group had more than one year since treatment. Thus, it is possible that most of the subjects might have adapted themselves to the illness and have also their emotional feelings and psychological behavior more established, compared to those recently diagnosed or treated for the cancer. Therefore, this may help explain the reasonably good scores we obtained at baseline for our study population.

On the other hand, these results may also suggest that those who agreed to participate in the study tended to score slightly better on EORTC QLQ-C30 and HADS questionnaires compared to those who dropped-out.

Finally, since we used a convenience sample, the representativeness is not very good. As one of the consequences of having a convenience sample, we obtained, by chance, a sample group in whom the majority does not have major depressive symptomatology and who possibly do not need psychological help. If that is the case, a larger sample size and the use of a screening program for psychological disorders would probably help us target a population in need of psychological help.
5.4 The Nucare effect

The results of this study showed that, although intervention and control subjects slightly differ on baseline scores, most of those subjects scored well on EORTC QLQ-C30 domains and were also considered having no depression or anxiety symptoms at baseline. Nevertheless, we observed that after the follow-up period the intervention group had improved on most of the domains, scoring reasonably better than the control group for most of the functioning, symptoms, and single-items scales, as well as on anxiety and depression scales. Some of the domains such as global quality of life, fatigue and sleep disturbance, which had the worse scores at baseline, were the ones we observed the greatest improvement in the intervention group, we also observed significant improvement on social and physical functioning. As for the control group, the same trend could not be observed. Although the highest improvement for the control group was observed on role functioning (4.7 points), there were no significant changes in any of the questionnaire domains.

When analyzing the changes occurring in dependent variable scores in the intervention and control groups from baseline to follow-up scores, the intervention group did better on 10 out of 15 domains of the EORTC QLQ-C30 questionnaire, and 3 out of 3 of the HADS questionnaire. Global quality of life, with 10 points difference, was the domain with the greatest difference between the intervention and control, followed by sleep disturbance, diarrhea, social functioning, fatigue, appetite loss and financial impact, constipation and physical functioning respectively (only global functioning was significant). In addition,
the intervention group also did better on HADS depression and anxiety scales. However, only depression changes were significant.

The Nucare intervention program has as its main aim to improve the quality of life of cancer patients and reduce their depression and anxiety levels, through the use of better coping techniques (e.g. better use of social support, and relaxation). Due to the nature of this psychoeducational intervention, one may expect this program to have stronger effects on domains such as global quality of life, social functioning, anxiety and depression. However it is somewhat surprising that the intervention also positively affected other domains such as diarrhea, constipation, financial impact, and fatigue symptoms.

As mentioned before, the Nucare program has already been applied to other cancer populations, and despite different cancer profiles, the results of those previous studies coincide with our study results. One of the previous applications of the Nucare program was a clinical trial with over 220 newly diagnosed breast and colon cancer patients (Edgar et al., 2001). In this study patients were allocated to one of the 4 different formats (individual Nucare, group Nucare, supportive unstructured support group, or a no intervention control), and those receiving the intervention were invited to participate in five sessions of ninety minutes each within a 6 months period. Improvements in functional, physical, emotional and general well-being, as well as depression, were observed throughout the study period. Overall, the individual format was more effective and provided more significant improvements compared to the other formats. It is not unexpected to see no significant improvements in the control and unstructured support.
groups. Nonetheless, some studies suggested that subjects may have more benefits from group-format compared to individual sessions (Newell et al., 2002).

A more recent application of the Nucare program consists of a one day problem-focusing and emotional-focusing coping strategies workshop for breast cancer patients completing their cancer treatment. Although this clinical trial had a different design compared to our study, its results also reported similar positive outcomes, with most of the subjects benefiting from the program (Rosberger et al., 2002).

With respect to other psychosocial interventions among head and neck cancer, the only published study, which showed positive results is the one conducted by Hammerlid and colleagues (Hammerlid et al., 1999b). In the latter study, two different interventions were applied. The first one comprises a long-term group psychological therapy, while the second one is a one week psychoeducational rehabilitation program. In spite of the control group scoring worse than the intervention group at baseline, the intervention group which received the long-term therapy had the greatest improvements observed on emotional and social functioning, global quality of life, and reduction of depression and anxiety levels. For the psychoeducational rehabilitation, although the majority of the domains did not have great changes before and after the one week rehabilitation program, they observed an improvement on most of the functioning and symptoms domains, as well as a reduction in the number of patients considered having possible anxiety disorder. These results show similarities to our study, except that most of our subjects scored low on depression and anxiety domains, therefore we could not find great changes as observed by Hammerlid and colleagues. Indeed, the subjects in our study generally scored well on
most of the EORTC QLQ-C30 domains at baseline, making improvements following the intervention more difficult to achieve. Still, the changes observed in the intervention group were greater than the ones observed in the control group. The same patterns, especially for global quality of life and depression, were observed when analyzing the EORTC QLQ-C30 and the HADS.

On the other hand, a study conducted by Petruson and colleagues (Petruson et al., 2003) did not find, after a supportive psychosocial program, improvement in the quality of life of head and neck cancer patients. Nonetheless, compared to the control group, the intervention group had higher survival rate at the 3-year follow-up. The authors pointed to a few things that may have played an important role for such lack of improvements in the quality of life of head and neck cancer patients. For example, to consider 10 points difference as clinically significant (King, 1996) may be too large for a quality of life score difference between two measure points. Also, 39% of the patients in the intervention group were living alone, compared to 29% in the control group. In addition, the author also pointed that the subjects in the intervention group may have developed “a dependent relationship with the counselors”. The results of the aforementioned study contradict with our study results.

5.5 Methodology issues, limitations and suggestions

Being a feasibility study, the reported research had many limitations, such as the small sample size, and the losses due to follow-up. However, we recognize the study limitations and weakness.
5.5.1 Sample size

In spite of our effort to collect the most subjects we could, the time limitation did not permit a larger sample size. Furthermore, the patient's commitment to participate in the intervention and the time they would have to spend completing the questionnaires may have affected their choice of participating in the study or/and completing the study.

Due to small size, our study did not have enough power to detect many differences after the follow-up period between intervention and control groups. We also observed a large variance in most of the baseline and follow-up scores, as well as in the mean changes. Moreover, due to the small sample size, we were unable to conduct multivariate analyses.

5.5.2 Bias

Bias was another limitation in this study, mainly because of the many sampling weaknesses and time constraints.

In the present study, we were unable to approach the subjects in a systematic way, where all the patients from the head and neck oncology clinic would be systematically included in the study. Instead, we used a convenience sample, where only those patients going to their appointment in the clinic were offered to participate in the study. Consequently, our results can not be generalized to all head and neck cancer patients, and one may expect sample bias to occur. A study involving a more representative sample may allow the results to be more generalized, giving a better idea of the quality of life and depressive symptoms outcomes in the head and neck population, and how the psychoeducational intervention may affect those outcomes.
Selection bias may have occurred, since subjects were not randomized to the groups, and intervention and control subjects were recruited at different time period. Therefore a randomized study where control and intervention subjects are recruited at the same time would minimize such bias.

5.5.3 Losses to follow-up

As part of a follow-up study, losses due to follow-up and consequently significant reduction on the study sample size are inevitable. The problem with subjects lost due to follow-up is that a particular group (e.g. those more depressed) may be more likely to withdraw thereby biasing the results. Being a pilot study, we did not have the required resources, such as making phone calls and/or mailing the subjects to remind them to answer the questionnaires. Nevertheless, as previously stated, the proportion of subjects who withdrew from our study was similar to previous studies (Hammerlid et al., 1999b; Petruson et al., 2003).

5.5.4 Different intervention delivery formats and deliverers

The Nucare program was offered in 3 different formats (individual, group, and home format). Most of the subjects opted either for individual or home format, and very few opted for the group format. The question why most of our subjects were not interested in the group format is still unclear. Nonetheless, a few suggestions are made: i) it is possible that the study did not have a sample size large enough to form the group intervention; ii) some patients do not feel comfortable to express their emotions in front of other peers;
and iii) sometimes “peers are not the most helpful source of emotional support for those subjects who have a rich and full emotional support network” (Edgar et al., 2001).

Due to the small number of subjects on each group, we analyzed all intervention subjects together. As a result, we were unable to analyze the individual effect of each delivery format, nor the subjects’ response to the format they chose. In addition, it is possible that the results obtained from one format may cancel the effect of other.

Also, we had two therapists delivering the Nucare program. Although they were both trained, the intervention delivery and the subjects’ perception of it may be slightly different from one therapist to another, possibly affecting our study results.

5.5.5 Other limitations

As mentioned previously, our study subjects were not screened for depressive symptoms, and this may have influenced the fact that our study subjects generally scored high on EORTC QLQ-C30 functioning domains and low symptoms and single items domains, as well as on HADS domains. Therefore, the use of a screening program prior to the subjects’ recruitment may highlight those who need help. However, offering the study to the entire population of head and neck cancer patients during the study period helps to minimize selection bias that may occurs when patients are pre-selected in some way.

5.6 Study strengths
Although this study was a feasibility study, with recognized limitations, it also had some strength. We matched intervention and control subjects. In addition, we used valid instruments which are well recognized outcome indicators of health-related quality of life and psychological distress.

6 SUMMARY AND CONCLUSION

Progress in treatment of head and neck cancer has been slow and challenging, and the survival rates of this disease have remained unchanged. Given the importance of psychological symptoms to cancer survival, the need to reduce depressive symptoms and to improve post-treatment health-related quality of life among head and neck patients has become an important issue in public health and oncology.

This study was conducted in order to test, for the first time, the feasibility of delivering the Nucare intervention program among head and neck cancer patients. The overall results of this short-term psychoeducational program demonstrated that the program is feasible and it may have a positive effect in improving the quality of life and reducing the levels of depression among head and neck cancer patients.

We recognize the limitations of this study. However it fulfilled the requirements for a feasibility study. In order to confirm the effectiveness of the Nucare intervention in improving quality of life and reducing depressive symptoms in head and neck cancer, a randomized controlled trial with an appropriate sample size is required.


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APPENDIX 1:

Ethical approval
APPENDIX 2:

English version of the consent form for patients
Coping with head and neck cancer

Drs. Paul Allison, Eduardo Franco and Larissa Vilela
McGill University

Purpose of the Study
The teaching hospitals of McGill University that provide treatment for cancer offer a range of services and resources to people who are diagnosed with cancer. Previous research has shown that patients who have been recently diagnosed with cancer may benefit from learning new coping skills. Good coping skills lead to reduced emotional stress and a faster return to a usual lifestyle. We therefore want to know about the quality of life and well-being of people diagnosed with a cancer of the mouth or throat.

Study procedures
The study will measure the quality of life of people who have had mouth and/or throat cancer. If you agree to participate, we will collect some information from your medical records, and also ask you to complete two short questionnaires with questions related to how you are coping with your life. It will take no longer than 15 minutes to complete both questionnaires. You will be completing the questionnaires today, and once again in 3 months.

Potential benefits
Participants will not benefit directly from their participation in this study. However, the results from this study may contribute to help us and other researches to provide better coping skills strategies for head and neck cancer patients.

Risks and discomforts
There are no potential risks associated with participating in this study. It involves no treatment or procedures that can cause harm, injuries or discomfort. It involves only collection of data by means of a self-complete questionnaire and medical files.

Confidentiality
In order to participate in this research project, it is necessary for the research staff to review your medical records as they relate to the study. You will be assigned a code to protect your identity from being revealed. Any information collected about you will be held in strict confidence and stored in a locked filing cabinet. Findings from this study may be presented at meetings and may be published, but your identity will never be revealed.

Your Rights as a Research Volunteer
Your participation is voluntary. Although you are encouraged to answer all the questions in the questionnaires, you are not obliged to do so. You are free to refuse to participate or to withdraw your consent at any time. Your care and medical treatment will not be affected in any way.
APPENDIX 3:

French version of the consent form for patients
L’adaptation au cancer de la bouche et de la gorge
Drs. Paul Allison, Eduardo Franco et Larissa Vilela
Université McGill

Objectif de l’étude
Les hôpitaux d’enseignement de l’Université McGill qui dispensent des traitements pour le cancer offrent une panoplie de services et de ressources pour les personnes diagnostiquées avec le cancer. Des recherches antérieures ont démontré que les patients récemment diagnostiqués avec le cancer bénéficient de l’apprentissage de nouvelles habiletés d’adaptation à la maladie. De bonnes habiletés d’adaptation mènent à une réduction du stress émotif et à un retour plus rapide à un style de vie habituel. Nous cherchons donc actuellement à en savoir davantage à propos de la qualité de vie et du bien-être des personnes diagnostiquées avec un cancer de la bouche et/ou de la gorge.

Modalités et Procédures
L’étude vise à mesurer la qualité de vie de personnes qui ont eu un cancer de la bouche et/ou de la gorge. Si vous acceptez de participer à cette recherche, Nous allons recueillir quelques renseignements à même votre dossier médical et nous vous demanderons de répondre à deux questionnaires qui traitent de comment vous vous adaptez à votre vie. 15 minutes de votre temps devraient suffire pour compléter les deux questionnaires. Vous remplirez les questionnaires aujourd’hui et une seconde fois dans environ 3 mois.

Bénéfices potentiels
Les participants ne bénéficieront pas directement de leur participation à cette étude. Cependant, les résultats de cette recherche pourraient contribuer à nous aider à développer de meilleures stratégies d’adaptation au cancer de la bouche et de la gorge.

Risques et inconforts
Il n’y a pas de risque associé à votre participation à cette étude. Elle n’implique aucun traitement ou procédure qui puisse vous causer du mal, des blessures ou de l’inconfort. Elle implique seulement la cueillette de données à partir de votre dossier médical et de questionnaires auto administrés.

Confidentialité
Afin de vous permettre de participer à ce projet, il est nécessaire que le personnel de recherche consulte vos dossiers médicaux puisque ces derniers renferment des renseignements pertinents pour la réalisation de l’étude. Afin de protéger votre identité et de l’empêcher d’être révélée, un code vous sera assigné et toute information recueillie vous concernant sera tenue strictement confidentielle et conservée dans une filière sous-clé. Des résultats de cette étude pourront être présentés lors de réunions et pourraient être publiés mais votre identité ne sera jamais révélée.
APPENDIX 4:

English version of the baseline information, EORTC QLQ-C30 and HADS
questionnaires
Baseline Data Sheet

1. Patient’s name: ____________________________________________
2. Patient’s initials/Chart number: _______________________________

3. Subject study code number: __________
4. Date baseline data entered: d/_____/m_____/_y_____

5. Gender: Male [ ] Female [ ]
6. Date of birth: d/_____/m_____/_y_____ 
7. Age (at baseline): _______yrs

8. Living arrangements:
   With partner [ ]
   With other family [ ]
   Alone [ ]
   In communal accommodation [ ]

9. Principal occupation:
   Retired [ ]
   Housewife [ ]
   Unemployed [ ]
   Working [ ]
   On sick leave [ ]

10. Maximum education level attained:
    Did not graduate at high school [ ]
    High school graduate [ ]
    College/CEGEP [ ]
    University [ ]
11. Personal history of previous cancer (of any sort): Yes ☐ No ☐

12. Co-morbidity: Yes ☐ No ☐

If yes, specify _____________________________________________

13. Initial cancer diagnosis:

13a. Cancer site (main): lip ☐ pharynx ☐

oral cavity ☐ larynx ☐

other ☐ (specify) _______________________

13b. Histological diagnosis: scc ☐ other ☐ (specify) _______________________

13c. TNM stage: T _____  N _____  M ____ (Source: _______________________

Overall stage ______

14. Date of initial diagnosis: d/ _____ /m. _____ /y. _____ (Source: _______________________

15. Time since diagnosis (at baseline): _______ months

16. Initial Treatment modality(ies)

16a. Surgery Only ☐

16b. Radiotherapy Only ☐

16c. Combination ☐ i.e. (a.+b., or Chemotherapy + a. and/or b.)

17. Is this cancer recurrent? Yes ☐ No ☐ Don’t know ☐

18. Time in relation to treatment (at baseline): _______ months
A: EORTC QLQ-C30

We are interested in some things about you and your health. Please answer all the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?  
   Not at All  A Little  Quite a Bit  Very Much  
   1  2  3  4

2. Do you have any trouble taking a long walk?  
   Not at All  A Little  Quite a Bit  Very Much  
   1  2  3  4

3. Do you have any trouble taking a short walk outside of the house?  
   Not at All  A Little  Quite a Bit  Very Much  
   1  2  3  4

4. Do you need to stay in bed or a chair during the day?  
   Not at All  A Little  Quite a Bit  Very Much  
   1  2  3  4

5. Do you need help with eating, dressing, washing yourself or using the toilet?  
   Not at All  A Little  Quite a Bit  Very Much  
   1  2  3  4

   During the past week:

6. Were you limited in doing either your work or other daily activities?  
   Not at All  A Little  Quite a Bit  Very Much  
   1  2  3  4

7. Were you limited in pursuing your hobbies or other leisure time activities?  
   Not at All  A Little  Quite a Bit  Very Much  
   1  2  3  4

8. Were you short of breath?  
   Not at All  A Little  Quite a Bit  Very Much  
   1  2  3  4

9. Have you had pain?  
   Not at All  A Little  Quite a Bit  Very Much  
   1  2  3  4

10. Did you need to rest?  
    Not at All  A Little  Quite a Bit  Very Much  
    1  2  3  4

11. Have you had trouble sleeping?  
    Not at All  A Little  Quite a Bit  Very Much  
    1  2  3  4

12. Have you felt weak?  
    Not at All  A Little  Quite a Bit  Very Much  
    1  2  3  4

13. Have you lacked appetite?  
    Not at All  A Little  Quite a Bit  Very Much  
    1  2  3  4

14. Have you felt nauseated?  
    Not at All  A Little  Quite a Bit  Very Much  
    1  2  3  4
During the past week:

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at All</th>
<th>A Little</th>
<th>Quite a Bit</th>
<th>Very Much</th>
</tr>
</thead>
<tbody>
<tr>
<td>15. Have you vomited?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>16. Have you been constipated?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>17. Have you had diarrhoea?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>18. Were you tired?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>19. Did pain interfere with your daily activities?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>21. Did you feel tense?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>22. Did you worry?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>23. Did you feel irritable?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>24. Did you feel depressed?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>25. Have you had difficulty remembering things?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>26. Has your physical condition or medical treatment interfered with your family life?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>27. Has your physical condition or medical treatment interfered with your social activities?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>28. Has your physical condition or medical treatment caused you financial difficulties?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past week?

<table>
<thead>
<tr>
<th>Rating</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very poor</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Excellent</td>
<td>7</td>
</tr>
</tbody>
</table>

30. How would you rate your overall quality of life during the past week?

<table>
<thead>
<tr>
<th>Rating</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very poor</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3</td>
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<tr>
<td></td>
<td>4</td>
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<tr>
<td></td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Excellent</td>
<td>7</td>
</tr>
</tbody>
</table>
B: HADS

Please choose one phrase for each question that best applies to you, right now.

1. (A) I feel tense or "wound up":
   a) □ Most of the time
   b) □ A lot of the time
   c) □ From time to time, occasionally
   d) □ Not at all

2. (D) I still enjoy the things I used to enjoy:
   a) □ Definitely as much
   b) □ Not quite so much
   c) □ Only a little
   d) □ Hardly at all

3. (A) I get a sort of frightened feeling as if something awful is about to happen:
   a) □ Very definitely and quite badly
   b) □ Yes, but not too badly
   c) □ A little, but it doesn’t worry me
   d) □ Not at all

4. (D) I can laugh and see the funny side of things:
   a) □ As much as I always could
   b) □ Not quite so much now
   c) □ Definitely not so much now
   d) □ Not at all

5. (A) Worrying thoughts go through my mind:
   a) □ A great deal of the time
   b) □ A lot of the time
   c) □ From time to time but not too often
   d) □ Occasionally
6. (D) I feel cheerful:
   a) □ Not at all
   b) □ Not often
   c) □ Sometimes
   d) □ Most of the time

7. (A) I can sit at ease and feel relaxed:
   a) □ Definitely
   b) □ Usually
   c) □ Not often
   d) □ Not at all

8. (D) I feel as if I am slowed down:
   a) □ Nearly all the time
   b) □ Very often
   c) □ Sometimes
   d) □ Not at all

9. (A) I get a sort of frightened feeling like “butterflies” in the stomach:
   a) □ Not at all
   b) □ Occasionally
   c) □ Quite often
   d) □ Very often

10. (D) I have lost interest in my appearance:
    a) □ Definitely
    b) □ I don’t take as much care as I should
    c) □ I may not take quite as much care
    d) □ I take just as much care as ever
11. (A) I feel restless as if I have to be on the move:
   a) □ Very much indeed
   b) □ Quite a lot
   c) □ Not very much
   d) □ Not at all

12. (D) I look forward with enjoyment to things:
   a) □ As much as ever
   b) □ Rather less than I used to
   c) □ Definitely less than I used to
   d) □ Hardly at all

13. (A) I get sudden feelings of panic:
   a) □ Very often indeed
   b) □ Quite often
   c) □ Not very often
   d) □ Not at all

14. (D) I can enjoy a good book or radio or TV program:
   a) □ Often
   b) □ Sometimes
   c) □ Not often
   d) □ Very seldom
APPENDIX 6:

French version of the baseline information, EORTC QLQ-C30 and HADS questionnaires
Données de base

11. Nom du (de la) patient(e): ____________________________________________

12. Initiales du (de la) patient(e) /Numéro de dossier: ______________________

13. Code du sujet: __________

14. Date d’entrée des données de base : /j_____/m_____a_____

15. Sexe:  Homme ☐  Femme ☐

16. Date de naissance: /j_____/m_____a_____

17. Age (au T de base): _______ans

18. Type de ménage:
   Avec conjoint(e) ☐
   Avec autre(s) membre(s) de la famille ☐
   Seul(e) ☐
   En communauté ☐

19. Occupation principale:
   Retraité(e) ☐
   Tient maison ☐
   Sans emploi ☐
   Au travail ☐
   En congé de maladie ☐

20. Niveau maximal d’études complété:
   N’a pas terminé le secondaire ☐
   Secondaire ☐
   CEGEP ☐
   Université ☐
11. Antécédents de cancer (de n'importe quel type): Oui □ Non □

12. Co-morbidité: Oui □ Non □
   Si oui, spécifier ________________________

13. Diagnostic initial de cancer
   13a. Site du cancer: lèvre □ pharynx □
   cavité orale □ larynx □
   autre □ (spécifier) ________________________
   13b. Diagnostic histologique: scc □ autre □ (spécifier) ________________________
   13c. Stade TNM: T ___ N ___ M ___ (Source: ____________)
   Stade global __

14. Date du diagnostic: __/___/_____ (Source: ________________)

15. Temps écoulé depuis le diagnostic (au T de base): _______mois

16. Modalité(s) de traitement initiales
   16a. Chirurgie Oui □ Non □
   16b. Radiothérapie seulement Oui □ Non □
   16c. Combinaison Oui □ Non □ (i.e. a+b, ou Chimiothérapie + a, et/ou b.)

17. Ce cancer récidive t-il? Oui □ Non □ Ne sais pas □

18. Temps v/s traitement (au T de base): _______ mois
A: EORTC QLQ-C30

Nous nous intéressons à vous et à votre santé. Répondez en indiquant le chiffre qui correspond le mieux à votre situation. Il n'y a pas de « bonne » ou de « mauvaise » réponse. Ces informations sont strictement confidentielles.

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
<th>Pas du tout</th>
<th>Un Peu</th>
<th>Assez</th>
<th>Beaucoup</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Avez-vous des difficultés à faire certains efforts physiques pénibles comme porter un sac à provisions chargé ou une valise?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>Avez-vous des difficultés à faire une longue promenade?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>Avez-vous des difficultés à faire un petit tour dehors?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>Etes-vous obligé(e) de rester au lit ou dans un fauteuil pendant la journée?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>Avez-vous besoin d’aide pour manger, vous habiller, faire votre toilette ou aller aux W.C.?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

Au cours de la semaine passée:  

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
<th>Pas du tout</th>
<th>Un Peu</th>
<th>Assez</th>
<th>Beaucoup</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Avez-vous été gêné pour faire votre travail ou vos activités de tous les jours?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>Avez-vous été gêné dans vos activités de loisirs?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8</td>
<td>Avez-vous eu le souffle court?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>9</td>
<td>Avez-vous eu mal?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>10</td>
<td>Avez-vous eu besoin de repos?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>11</td>
<td>Avez-vous eu des difficultés pour dormir?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>12</td>
<td>Vous êtes-vous senti(e) faible?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>13</td>
<td>Avez-vous manqué d’appétit?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>14</td>
<td>Avez-vous eu des nausées?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Au cours de la semaine passée:</td>
<td>Pas du tout</td>
<td>Un Peu</td>
<td>Assez</td>
<td>Beaucoup</td>
<td></td>
</tr>
<tr>
<td>-----------------------------------------------------------------------------------------------</td>
<td>-------------</td>
<td>--------</td>
<td>-------</td>
<td>-----------</td>
<td></td>
</tr>
<tr>
<td>15. Avez-vous vomi?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>16. Avez-vous été constipé(e)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>17. Avez-vous eu la diarrhée?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>18. Etiez-vous fatigué(e)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>19. Des douleurs ont-elles perturbé vos activités quotidiennes?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>20. Avez-vous eu des difficultés à vous concentrer sur certaines choses par exemple pour lire le journal ou regarder la télévision?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>21. Vous êtes-vous senti(e) tendu(e)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>22. Vous êtes-vous fait du souci?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>23. Vous êtes-vous senti(e) irritable?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>24. Vous êtes-vous senti(e) déprimé(e)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>25. Avez-vous eu des difficultés pour vous souvenir de certaines choses?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>26. Votre état physique ou votre traitement médical vous ont-ils gêné(e) dans votre vie familiale ?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>27. Votre état physique ou votre traitement médical vous ont-ils gêné(e) dans vos activités sociales (par exemple sortir avec des amis, aller au cinéma...)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>28. Votre état physique ou votre traitement médical vous ont-ils causé des problèmes financiers?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>
Pour les questions suivantes, veuillez répondre en indiquant le chiffre entre 1 et 7 qui s’applique le mieux à votre situation

29. Comment évalueriez-vous votre état de santé au cours de la semaine passée?

   1  2  3  4  5  6  7
Très mauvais                                Excellente

30. Comment évalueriez-vous l’ensemble de votre qualité de vie au cours de la semaine passée?

   1  2  3  4  5  6  7
Très mauvaise                                Excellente
B: HADS

Pour chaque question, s'il vous plaît indiquer la case qui s'applique le mieux à vous, en ce moment.

1. (A) Je suis tendu(e):
   a) □ La plupart du temps
   b) □ Très souvent
   c) □ De temps en temps
   d) □ Jamais

2. (D) Je prends plaisir aux mêmes choses qu'autrefois:
   a) □ Oui, tout à fait
   b) □ Pas autant
   c) □ Un peu seulement
   d) □ Presque pas du tout

3. (A) J'ai l'impression que quelque chose d'horrible va m'arriver:
   a) □ Oui, très nettement
   b) □ Oui, mais ce n'est pas trop grave
   c) □ Un peu, mais cela ne m'inquiète pas
   d) □ Pas du tout

4. (D) Je ris facilement et vois le bon coté des choses:
   a) □ Autant que par le passé
   b) □ Plus autant maintenant
   c) □ Vraiment moins qu'avant
   d) □ Pas du tout

5. (A) Je me fais du souci:
   a) □ Très souvent
   b) □ Assez souvent
   c) □ De temps en temps
d) □ Parfois

6. (D) Je suis de bonne humeur:
   a) □ Jamais
   b) □ Pas souvent
   c) □ Parfois
   d) □ La plupart du temps

7. (A) Je peux rester assis(e) et me sentir décontracté(e):
   a) □ Oui
   b) □ En général
   c) □ Pas souvent
   d) □ Jamais

8. (D) J’ai l’impression de ne fonctionner qu’à vitesse réduite:
   a) □ Presque toujours
   b) □ Très souvent
   c) □ Parfois
   d) □ Pas du tout

9. (A) J’éprouve des sensations de peur:
   a) □ Jamais
   b) □ Parfois
   c) □ Assez souvent
   d) □ Très souvent

10. (D) Je ne m’intéresse plus à mon apparence:
    a) □ Pas du tout
    b) □ Je n’y accorde pas autant d’attention que je le devrais
    c) □ Il se peut que je n’y fasse pas autant attention
    d) □ J’y prête autant d’attention que par le passé
11. (A) J’ai la bougeotte et n’arrive pas à tenir en place:
   a) □ Oui, beaucoup
   b) □ Assez
   c) □ Pas beaucoup
   d) □ Jamais

12. (D) Je me réjouis à l’avance de certains événements de la vie:
   a) □ Autant qu’auparavant
   b) □ Un peu moins qu’avant
   c) □ Bien moins qu’avant
   d) □ Presque jamais

13. (A) J’éprouve des sensations soudaines de panique:
   a) □ Vraiment très souvent
   b) □ Assez souvent
   c) □ Pas très souvent
   d) □ Jamais

14. (D) Je peux prendre plaisir à un bon livre ou à une émission de radio ou de télévision:
   a) □ Souvent
   b) □ Parfois
   c) □ Peu souvent
   d) □ Très rarement