THE RELATIONSHIP BETWEEN QUALITY OF LIFE (EORTC QLQ C-30) AND SURVIVAL AND TREATMENT IN PATIENTS WITH GASTRO-OESOPHAGEAL CANCER

by

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AJCC	American Joint Committee on Cancer
ASCO	American Society Clinical Oncology
AUGIS	Association of Upper Gastrointestinal Surgeons
BMI	Body Mass Index
CRP	C-reactive protein
CT	Computer Tomography
ECOG	Eastern Co-operative Oncology Group
EORTC	European Organisation for Research and Treatment of Cancer
KPS	Karnofsky Performance Status Scale Index
SAGOC	Scottish Audit of Gastric and Oesophageal cancer
SD	Standard Deviation
SIGN	Scottish Intercollegiate Guidelines Network
TNM	Tumour, Node, Metastases
QoL	Quality of Life
QLQ-C30	Quality of Life Questionnaire-Core 30
QLQ-OES18	Quality of Life Questionnaire-Oesophageal module 18
UICC	Union International Centre of Cancer
WHO	World Health Organisation
WHOQOL	World Health Organisation Quality of Life

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VI DECLARATION

The studies presented in this thesis reflect work carried out by myself except where indicated below, over the period of 1997-2005, whilst working as a research nurse in the Department of Surgery, Glasgow Royal Infirmary.

Routine measurements of serum albumin, C-reactive protein and white cell count were performed in the Institute of Biochemistry and Department of Haematology in Glasgow Royal Infirmary and the Southern General Hospital.

Pathology reports were discussed at the multi-disciplinary meeting and were forwarded to me by the pathology departments within Glasgow Royal Infirmary and the Southern General Hospital.

The statistical analysis was performed with the assistance of Dr Donald McMillan and Dr Wilson Angerson, University Department of Surgery, Glasgow Royal Infirmary, Glasgow.

List of publications arising from this thesis

1. M. McKernan., D.C. McMillan., J. Anderson., W. Angerson., R. Stuart. (2008). The relationship between quality of life (EORTC QLQ-C30) and survival in patients with gastro-oesophageal cancer. *British Journal of Cancer*, **98**, 888-893

2. M. McKernan., R. Stuart., J. Anderson., D.C. McMillan. (2008). A prospective longitudinal study of the impact of treatment on quality of life (EORTC QLQ-C30) in patients with gastric and oesophageal cancer. (Submitted to *European Journal of Cancer*, March 2008).

VII. SUMMARY

Gastro-oesophageal cancer is the third commonest cause of cancer death in the UK. Each year, there are approximately 16,500 new cases diagnosed and over 13,000 deaths attributable to the disease. Overall survival is poor with the majority of patients presenting with advanced, inoperable disease and less than 15% surviving 5 years, therefore ensuring the best quality of life is paramount for these patients.

The traditional end points of tumour response, toxicity and survival are limited in discerning differences between the various treatments for gastro-oesophageal cancer. Irrespective of treatment, the majority of patients with advanced disease do not achieve a response to treatment or an increased survival. Consequently, in the last decade, there has been considerable interest in including some measure of quality of life in the assessment of patients with cancer and their continuing aftercare, as it provides information on the patient's perception of their health and the effectiveness and side effects of their treatment.

Quality of life has been an implied outcome since the earlier days of health care. In 1947, the World Health Organisation defined health as "a state of complete physical, mental and social well-being and not merely the absence of disease". The first scale to quantify patient's activity level and capability was developed in 1948 by Karnofsky. Since that time, numerous scales have been developed to assess an individual's physical, psychological and social response to disease and its treatment.

The aim of this thesis is to examine the baseline relationship between clinico-pathological characteristics and quality of life in gastro-oesophageal cancer patients and to further assess the long-term effect of treatment (surgery, oncological treatment or supportive care).

For this study we have used the EORTC QLQ-C30, the ECOG performance status scale and the dysphagia score.

In Chapter 2, an assessment of quality of life, clinical and pathological variables was undertaken on 152 patients. This study demonstrated there were major differences in quality of life and symptom scores with increasing stage of disease. In particular, social functioning, fatigue, appetite loss and global quality of life were all impaired with increasing tumour stage. As might be expected in view of these associations, the majority

of quality of life and symptom scores predicted survival on univariate analysis. It was of interest, however, that appetite loss remained an independently significant prognostic factor even after adjustment for TNM stage and treatment.

Furthermore in the present study C-reactive protein concentrations were available in 94 (62%) patients, at the time of quality of life assessment. An elevated C-reactive protein concentration was associated with increased appetite loss and when included in the multivariate analysis, an elevated C-reactive protein concentration was independently associated with poorer cancer specific survival. However, even those patients without an elevated C-reactive protein concentration, reported some appetite loss and the independent prognostic value of appetite loss remained, thus confirming the importance of appetite loss in the multifactorial nature of weight loss and poor outcome in these patients.

The effect of treatment on aspects of quality of life including appetite loss has rarely been examined. Furthermore, there are, to our knowledge, no studies which have examined the effect of surgery on quality of life beyond 3 years. Therefore in Chapter 3 we examined the effect of treatment (surgery, oncological treatment or supportive care) on quality of life (EORTC QLQ-C30) for up to fours years post treatment in 160 patients. Patients who underwent surgery had, at study entry, better global quality life including better physical and role functioning and less fatigue and appetite loss compared with those patients who did not receive surgery. Furthermore, the effect of oesophageal surgery on global quality of life appeared to be more profound and persistent. In contrast, in patients with inoperable disease, the poor quality of life measures at study entry remained poor on follow-up whether patients received oncological input or supportive care.

In conclusion, the results of the present studies have indicated that appetite loss is important in determining quality of life in gastro-oesophageal cancer patients and is independently associated with poor survival. Furthermore, the effect of surgery has a long lasting and profound effect on quality of life in this cohort of patients.

Chapter 1

1. INTRODUCTION AND AIMS

1.1 Incidence and mortality of gastro-oesophageal cancer

1.1.1 Incidence and mortality world wide

In 2002, there were an estimated 11 million newly diagnosed cancer cases and 7 million cancer deaths reported worldwide. Furthermore, there were nearly 25 million persons living with cancer. Cancers of the lung, stomach, colon and rectum, liver and oesophagus are associated with the highest incidence worldwide; cancers of the lung, liver and oesophagus are associated with the highest mortality and are indicative of poor survival (Kamangar et al., 2006; Parkin et al., 2005). Lung, colorectal, stomach and breast cancers account for nearly all cancer deaths in Europe (Boyle and Ferlay, 2005; Parkin et al., 2005).

Worldwide gastric cancer was the fourth most common cancer with approximately 600,000 new cases among men and 330,000 new cases among women in 2002. It is the second most common cause of cancer death with approximately 700,000 deaths annually. Across continents incidence rates vary from 3.4 per 100,000 per year among females in North America to 26.9 per 100,000 per year among males in Asia. Overall the 5-year survival rates are approximately 20% in most areas of the world, except Japan where there are mass screening programs and survival rates are approximately 60% (Parkin et al., 2005).

Gastric cancer is declining in Switzerland and neighbouring countries, and the mortality fell by 60 % within one generation. It is said that if this trend continues, gastric cancer may in some world regions become a rare disease within the next 30 years (WHO global cancer rates, 2003). The incidence of non-cardia gastric cancer has declined in more developed countries over the last decade; this may be due to improved sanitation and improved diet and the decline of helicobacter infection. In contrast the incidence of cardia cancers have increased or remained constant, this may be due to smoking, the rise in obesity and reflux disease (Blot et al., 1991; Munoz and Francesci, 1997).

Worldwide oesophageal cancer is the eighth most common cancer and accounted for approximately 320,000 new cases among men and 150,000 new cases among women in 2002, it is the sixth most common cause of cancer death with approximately 386,000

deaths annually (Parkin et al., 2005). Overall incidence rates are two-fold higher in less developed countries compared with more developed countries (Kamangar et al., 2006). The majority of cases (80-85%) are diagnosed in developing countries where it is the fourth most common cancer in men and in most cases are squamous cancers (Brown and Devesa, 2002). It has also been reported that the highest incidence for oesophageal cancer is in the so-called Asian 'oesophageal cancer belt' which stretches from Turkey through Iran, Afghanistan and Russia to China, and where incidence rates rise steadily with age (Parkin, 2004). Oesophageal cancer tends to occur more often in the elderly, with the male to female ratio 3:1 (Keighley, 2003).

Over the last three decades the incidence of adenocarcinoma in the lower part of the oesophagus has been rising steadily, in contrast there has been a decline in squamous cancers. Wide variation has been reported both between countries and in different ethnic groups and populations within a country. For example, in the USA the incidence of squamous cancers is almost six times higher in black men than in white, and the incidence of adenocarcinoma is almost four times higher in white men than black men. It has been reported that the decline in the prevalence of squamous cancers is due partly to the decline in smoking and drinking, especially among men, and with the increased intake of fresh fruits and vegetables (Brown and Devesa, 2002). It has also been reported that the increasing incidence of adenocarcinoma is partly due to reflux disease and Barretts oesophagus (Blot et al., 1991).

Survival is universally poor worldwide, the majority of patients present with advanced or inoperable disease and mortality figures occasionally exceed the number of newly diagnosed cases per year. Furthermore, it has been reported that less than 15% of the people survive for at least five years after initial diagnosis (Keighley, 2003).

1.1.2 Incidence and mortality in the United kingdom

In 2002, in the United Kingdom there were approximately 17,000 new cases of gastro-oesophageal cancers diagnosed, and combined gastro-oesophageal cancer was the third most common cause of cancer death (Cancer Research UK, Information Resource Centre 2004 and Welsh Cancer Intelligence), with over 13,000 deaths attributed to the disease (Office for National Statistics, Cancer Statistics). Overall survival is poor with the

majority of patients presenting with advanced disease and less than 15% surviving 5 years (Cancer Research UK).

Gastric cancer accounted for 9,500 new cases and occurs more commonly in men, the male/ female ratio being 2:1, and has been reported to be the sixth most common cancer. Incidence rates rise steeply with increasing age, with the majority of cases being diagnosed from 60 years onwards.

Fifty years ago gastric cancer was reported to be the leading cause of death in Britain, since then there has been a dramatic decline in incidence and mortality, with current rates less than half of the 1950's. In addition there is evidence of increasing adenocarcinoma in the gastric cardia. It has been reported that this may be due to the rise in obesity and reflux disease, and in contrast there has been a decline in distal cancers, similar to the reported worldwide figures (Cancer Research UK).

The 5 year survival rate for advanced gastric cancer has increased over the last twenty years in many countries, figures from the United Kingdom are still poor compared to other countries and only 12% survive 5 years. Unfortunately, the majority of patients are diagnosed with advanced inoperable disease and the number of deaths per year is 15% less than the number of new cases diagnosed (Keighley, 2003).

Rates for oesophageal cancer in the United Kingdom are significantly higher than the European average, with the highest incidence occurring in Scotland and rank 34th out of 172 countries (Boyle and Ferlay, 2005). In 2002, oesophageal cancer accounted for 7,500 new cases, the male/ female ratio was 3:2, and has been reported to be the fifth most common cancer. Less than 10% of cases are diagnosed before the age of 55 and the rates increase steeply from the age of 60 onward. Unfortunately, even when diagnosed at an early stage, cancer of the oesophagus has a poor prognosis. Furthermore, adenocarcinoma is rising rapidly, partly due to reflux disease and Barretts oesophagus, particularly in men.

Oesophageal cancer has been reported to be the fourth most common cause of death in men and sixth in women and mortality rates have risen sharply over the last thirty years (Cancer Research UK). The 5-year survival rate for oesophageal cancer has recently been reported to be 9%. Similar to gastric cancer, the majority of patients are diagnosed with

advanced inoperable disease and the number of deaths per year is 9% less than the number of new cases diagnosed (Keighley, 2003).

Based on current evidence, both gastric and oesophageal cancer will remain as commonly fatal cancers with incidence only just greater than the mortality (Scottish Audit of Gastric and Oesophageal Cancer, 1997-2000). Furthermore, areas with high levels of deprivation are strongly associated with high rates of oesophageal cancer in men, and of gastric cancer in both men and women (McKinney et al., 1995).

From the above data it is evident that overall gastro-oesophageal cancer has a high incidence and mortality rate, as the majority are diagnosed at an advanced stage ensuring the best quality of life is paramount for these patients.

1.2 Pathology

The vast majority of gastric cancers within the United Kingdom are adenocarcinomas. Rare tumours such as adenosquamous or lymphomas are not considered typical and are not included in this thesis.

Jarva and Lauren (1951), established that the histological structure of gastric adenocarcinoma often displays features characteristic of intestinal mucosa and reported that at least 50% of gastric cancers arise from intestinal metaplasia in the stomach; gastric adenocarcinoma can also be described as a solid tumour. Lauren (1965) reported that gastric cancers could be divided into those with gland formation (intestinal type) and those without glandular characteristics (diffuse type). Intestinal type cancer occurs more commonly in older male patients, whereas diffuse type cancer has a constant rate worldwide and occurs in a younger age group (Lauren Classification, 1965). Lo and co-workers (1996) reported that the diffuse type tumours are predominate in younger patients and are associated with a worse prognosis (Lo et al., 1996). Early gastric cancer (EGC) was first defined in 1962 by the Japanese's Society of Gastroenterological Endoscopy, as adenocarcinoma confined to the mucosa or submucosa without penetration through the muscularis propria, irrespective of lymph node involvement (Murakami, 1971).

Tumours are also classified according to the Japanese Research Society Committee and are divided into papillary/well differentiated and tubular/moderately differentiated adenocarcinoma. It has been reported that the degree of differentiation is closely related to the depth of invasion, with poorer differentiation evident in submucosal and advanced cancers (Ferrari et al., 1992).

There are two main types of oesophageal cancer, squamous and adenocarcinoma due to the marked differences in the pathogenesis, tumour biology and characteristics of the affected patients they are treated as separate entities. Squamous cell cancer continues to be the most common histology and occurs more frequently in the upper two-thirds of the oesophagus, macroscopically there are ulcerated, polypoid and diffusely infiltrating forms, differentiation can differ in this tumour type (Vellone et al., 2006). However, in the last few years adenocarcinoma involving the distal oesophagus and gastro-oesophageal junction has increased in frequency.

Following a consensus conference of the International Gastric Cancer Association and International Society for Diseases of the Esophagus all participating experts agreed that there should be a clear definition and classification of tumours arising within the oesophagogastric junction (Siewert and Stein, 1998). Type; I/II/III, the most common is type I, adenocarcinoma of the distal oesophagus which can arise in Barretts oesophagus; and contains glandular epithelium, of which there are three types (metaplastic columnar, metaplastic glandular and metaplastic intestinal). Type II arises within the cardiac epithelium (cardia) or can be short segments with intestinal metaplasia at the gastro-oesophageal junction. Type III infiltrates the oesophagogastric junction and distal oesophagus from below. Dysplasia is more likely to develop in intestinal type mucosa (Siewert and Stein, 1998; Stein et al., 2001).

1.3 Aetiology

The large majority (approximately 90%) of gastric and oesophageal cancers are believed to be due to environmental factors and the remaining 10% having been linked to genetic factors.

1.3.1 Genetics

Researchers are beginning to identify genetic factors that contribute to the development of stomach cancer. Patients with blood relatives who have been diagnosed with stomach cancer are more likely to develop the disease, two Italian studies estimated that 8% of stomach cancer cases are due to inherited factors (Encyclopaedia of genetic disorders, 2006; Cancer consultants.com). In the United Kingdom approximately 10% of gastric cancers cluster in families, a family history of gastric cancer has been shown to marginally increase the risk of relatives developing cancer compared to that of the general population. Furthermore, it has been reported that environmental factors shared by family members may explain the clustering effect in families (Cancer Research UK).

A previous study in the USA reported that the risk of developing gastric cancer was elevated in patients who had a family history of the disease; in contrast there was no association to any form of oesophageal cancer. The authors have stated that the study has a number of limitations, most importantly that the potential for recall bias from patients can be poor and inaccurate (Dhillon et al., 2001).

1.3.2 Environment

In 2002 the World Health Organization and Food and Agriculture Organization stated that eating habits were the main factor involved in gastric and oesophageal cancer risk. Furthermore, as developing countries become urbanised the patterns of cancer shift towards those of more developed countries (WHO, 2003). There are geographic and ethnic differences in the incidence around the world. Furthermore, incidence patterns observed among immigrants change according to where they live (Tsugane and Sasazuki, 2007). All of these factors serve to indicate the close association of gastric and oesophageal cancer with factors such as diet and lifestyle changes.

Several case-controlled studies have been undertaken over the years to study the association between a poor diet and the diagnosis of gastric cancer. Low consumption of vegetables and fruits and a high intake of processed foods and salts have been highlighted as being predisposing factors in gastric cancer. One study by Tajima and Tominaga (1985) from Japan, reported that in gastric and colorectal cancer patients, a fondness for salty tastes, especially salted foods such as pickled hakusai (vegetable) and dried salted fish, which are typical traditional Japanese foods, showed a significantly positive association with gastric cancer. Conversely, the habit of eating a western style breakfast for greater than 10 years made a greater contribution to colon cancer, but a decreased risk in gastric cancer (Tajima and Tominaga, 1985).

Another study from Italy by Buiatta and co-workers (1989) reported on diet, between known gastric cancer patients and the general population, that a significant trend of increasing gastric cancer was found with an increased consumption of traditional soups, meats, salted/dried fish and a combination of cold cuts and seasoned cheeses. The habit of adding salt to food and the preference for salty foods were associated with an elevated risk of gastric cancer, while storing foods in the refrigerator and the availability of the freezer to store fresh unsalted foods lowered the risk, along with increasing the intake of raw vegetables and fresh fruit (Buiatti et al., 1989).

A case controlled study by Cook-Mozaffari and co-workers (1979) on oesophageal cancer patients in Iran, reported that there was a strong association between low-socio-economic class and a low intake of fresh fruit and vegetables. Furthermore, a second potential factor associated with socio-economic class is the continued use of traditional outmoded agricultural practices in separating and storing wheat, which could lead to a contamination of bread. The study concluded that a high-fat, low protein diet, low intake of fresh fruit and vegetables and also excessive drinking of hot liquids have also been shown to increase the risk of oesophageal cancer (Cook-Mozaffari et al., 1979).

Wu and co-workers (2007) reported recently that the intake of fibre had a significant impact on risk of oesophageal and gastric cardia adenocarcinoma. The study reported on dietary factors in oesophageal (n=206), gastric cardia (n=257), distal gastric (n=366) adenocarcinoma patients and 1,308 control subjects in Los Angeles. The study concluded that a high intake of fibre was associated with significant reduced risks of oesophageal and gastric cardia adenocarcinoma (Wu et al., 2007).

The incidence of oesophageal and gastric cardia adenocarcinoma has been rising steadily since the 1970's in obese patients. It is unclear to what extent the two are related; several authors have looked at the relation. One possible relation could be that patients with an increased girth are more susceptible to reflux; in turn this is known to predispose the risk of Barretts metaplasia. Vaughan and co-workers in the USA, (1994) undertook two case controlled studies on 404 gastric and oesophageal cancer patients. They reported that high body mass index was associated with an increase in adenocarcinomas of the oesophagus and cardia in 18% of patients, in contrast, patients with squamous cancer had consistently lower body mass indices than controls (Vaughan et al., 1994).

A further study by Lagergren and co-workers on Swedish patients (1999) measured patients BMI at diagnosis, and enquired about body weight 20 years before diagnosis, to assess latency between the critical effect of BMI on carcinogenics and the clinical manifestation of the tumours. The study concluded that the association between BMI and oesophageal adenocarcinoma was strong, and was independent of the presence of reflux symptoms or of Barretts metaplasia, furthermore the mechanism that would fully explain the carcinogenic effect remained to be identified (Lagergren et al., 1999).

In contrast, a study from China by Zhang and co-workers (2003) compared a healthy population of subjects and operable gastric cardia adenocarcinoma patients, BMI was recorded and it was reported that patients diagnosed were underweight. Furthermore, no underweight subject was found in the healthy cohort of patients. The study reported that the differences in results might be due to the genetic background of Chinese people, which differs greatly from Westerners (Zhang et al., 2003).

(Kubo and Corley, 2006) undertook a systematic review of observational studies from 1966 to 2005 and found 14 relevant studies which filled their criteria, which included body mass index and oesophageal and cardia cancers. The pooled results supported a positive association between increased BMI and the risk of oesophageal adenocarcinoma. The strength of the association increased with increasing BMI and there was a trend towards men compared with women. The results on gastric cardia association were weaker; furthermore, there was no clear association in cancer patients from China.

Another possible factor involved in the development of gastric cancer is Helicobacter-pylori (a spiral-shaped gram-negative bacillus) found in the stomach, which causes

inflammation of the mucous membrane, and is more often associated with diffuse and intestinal gastric cancers. In 1994, the International Agency for Research on Cancer, as part of the World Health Organization identified H-pylori as a definite biological carcinogen (Schwesinger, 1996). In 20% of patients this can induce gastric ulcers (Parsonnet, 1998), numerous studies have looked closely at the link to H-pylori and gastric adenocarcinoma, and there are conflicting outcomes to these studies. El-Omar and co-workers (2000), reported that helicobacter was present in approximately 50% of the world's population and infected patients have an increased risk of developing gastric cancer due to the histological and functional changes it causes, such as atrophic gastritis and hypochlorhydria. The study also reports that relatives of Scottish gastric cancer patients with H-pylori infection also have an increased prevalence of atrophy (52%) and hypochlorhydria (40%) and therefore an increased chance of them developing the disease (El-Omar et al., 2000). Ye and co-workers (2004) reported a reduced risk of oesophageal adenocarcinoma in Swedish patients with H-pylori and suggested that the H-pylori infection may have a protective effect in respect of this cancer (Ye et al., 2004).

A possible factor involved in the development of oesophageal cancer is chronic irritation of the mucosa related to acid reflux, which has been recognised to be a factor in developing Barretts oesophagus. Barretts oesophagus as detailed above develops in the distal part of the oesophagus in a subset of patients (approximately 1%) with chronic reflux. The epithelial surface is altered to become more like the lining of the stomach; a process called intestinal metaplasia, this condition requires endoscopic surveillance to detect any pre-cancerous changes (National Cancer Institute). In Scotland approximately 14% of oesophageal cancer patients had previously been diagnosed with Barretts oesophagus (SAGO C, 2002). A study by Chak and co-workers (2002) reported that patients with Barretts oesophagus or oesophageal adenocarcinoma are 12 times more likely to have a first or second degree relative with a history of Barretts and /or oesophageal adenocarcinoma and concluded that it is important to gather careful family history when screening patients with Barretts oesophagus for surveillance (Chak et al., 2002).

Toxins and chemicals have been reported to be significant in both gastric and oesophageal cancer. O'Neill and co-workers (1980) reported that there was a high incidence of oesophageal cancer in north-east Iran, where there is contaminated flour originating from a fine fibrous silica which is found in the weeds that contaminate the wheat (O'Neill et al., 1980).

Several studies regarding cigarette smoking and alcohol have been undertaken to demonstrate the association with gastro-oesophageal adenocarcinoma. Squamous cell cancers of the oesophagus have been long associated with cigarette smoking and/or excessive alcohol intake. Studies undertaken in Japan and Italy looked at gastric cancer patients and reported that there was no positive link between drinking and gastric cancer (Tajima and Tominaga, 1985; Buiatti et al., 1989). A more recent study, reported that combined high levels of tobacco and alcohol were more prevalent in patients with cardia, proximal and distal gastric cancers (Sung et al., 2007).

Vaughan and co-workers (1994) reported in their study of oesophageal cancer patients that cigarette smoking and alcohol accounted for 50% of adenocarcinomas and an elevated risk was found in patients who drank straight liquor. In comparison, cigarette smoking and alcohol alone accounted for 87% of the squamous cancers; the study concluded that there was no reason to believe that cigarettes and alcohol were associated with the rise in adenocarcinomas (Vaughan et al., 1994). A French study reported that for a given lifetime consumption of alcohol, a high intake during a shorter period carries a higher risk than a moderate intake during a longer period. Furthermore, the risk varied greatly according to the type of alcoholic beverage, the higher risks were associated with aniseed aperitifs, beer and hot spirits (especially hot Calvados) the study further suggested that 2⁄3 of the high incidence in the west of France and in rural populations could be due to the specific habit of drinking hot spirits (Launoy et al., 1997; Launoy et al., 1997).

The risk of gastric and oesophageal cancer in the workplace has been the focus of significant research, studies have looked at the exposure to toxins and chemicals in employees. The IARC recently considered that there is evidence, although not definitive, of an association between gastric cancer and coal, rubber, and leather industries and asphalt workings (International Agency for Research on Cancer, 1981).

A Danish study by Raaschou-Nielsen and colleagues (2003) reported that 1:8 of employees working with Trichloroethylene went on to develop oesophageal cancer. A further study by Yu and colleagues (2005) examined the relationship between silicosis and oesophageal cancer in Hong Kong and concluded that there was a greater risk in employees who worked in underground caissons after adjusting for cigarette smoke and alcohol (Raaschou-Neilsen et al., 2003; Yu et al., 2005). Raj and co-workers (2003) reviewed several previous studies and concluded, that it would be difficult to judge with confidence

whether some people are more at risk as a result of their occupation or their social class, when some occupations attract workers from certain classes and indeed occupations can define social classes (Raj et al., 2003).

Worldwide low socio-economic class has also been reported to be a risk factor in the development of gastric and oesophageal cancer and is more obvious in squamous oesophageal cancer, where environmental issues associated with poor housing, overcrowding and inadequate/unsanitary food preparation areas play an important role. Data from the United Kingdom also shows a strong association with social deprivation and gastric cancer and oesophageal squamous cancer, but no clear association with oesophageal adenocarcinoma **(**Cancer Research UK, 2004; SAGO C, 2002).

1.3.3 Inflammation

There is increasing evidence that the systematic inflammatory response, as evidenced by elevated circulating concentrations of C-reactive protein, often acts as a tumour promoter, resulting in aggressive cancerous growth and spread, normally the inflammation response is self limiting and ceases when healing occurs. However, continuing inflammatory response may occur in response to a tumour, releasing a number of substances, including pro-inflammatory cytokines (Argyles and Lopez-Soriano, 1998; MacDonald, 2007). A further study from Japan identified a decrease in survival in oesophageal cancer patients with an elevated C-reactive protein at the time of diagnosis (Nozoe et al., 2001). Recent studies by (Crumley et al., 2006; Deans et al., 2006; Wong et al., 2007) showed that the presence of an elevated C-reactive protein and hypoalbuminaemia, (using the Glasgow Prognostic score) highlighted that a systematic inflammatory response appears to be a useful outcome measurement of survival in patients with operable and inoperable gastric-oesophageal cancer. Furthermore, Crumley and co-workers (2007) reported in patients undergoing platinum based treatment that the presence of systemic inflammatory response appears to be superior to the subjective assessment of performance status (Crumley et al., 2007).

In summary, it would appear a healthy lifestyle i.e. not smoking, not consuming excess alcohol, avoiding obesity and maintaining a good dietary intake of fibre, fruit and vegetables is associated with reduced risk of both oesophageal and gastric cancer and should be encouraged (SIGN 87, 2006 Recommendation). It may be that such lifestyle

factors are associated with the elaboration of an inflammatory response that, in turn, promotes tumour formulation and progression (McMillan et al., 2006).

1.4 Staging of disease

Tumour staging is a method of describing cancer development. Gastric and oesophageal cancers are diagnosed and staged after a number of investigations are performed; accurate staging is essential in planning the surgical approach or oncological input and in determining the risk of tumour recurrence and overall prognosis. The Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland, (AUGIS, 2002) and more recently the Scottish Intercollegiate Guidelines Network (SIGN, 2006) developed guidelines after they undertook a systematic review of relevant literature.

1.4.1 Diagnosis

Initially, an endoscopy (flexible telescope is passed through the mouth into the stomach) should be performed and multiple biopsies taken for a pathological diagnosis. At the time of endoscopy, location, size and appearance of the tumour can also be ascertained. This procedure can be undertaken with or without a mild sedative. In some cases barium meals or swallows are still performed, as part of the diagnostic workup. In recent years endoscopy has become the preferred choice of initial assessment. Dooley and co-workers (1984) reported on randomly selected patients (n=100) who were examined with both double-contrast barium meal and endoscopy in a blinded prospective fashion and concluded, that endoscopy was reported to be more sensitive and specific than the double-contrast barium meal and further reported that endoscopy should be recommended for initial assessment (Dooley et al., 1984). AUGIS (2002) and SIGN (2006) guidelines recommended that the diagnosis of malignancy should be confirmed by endoscopy and pathologically (Alum et al., 2002; www.sign.ac.uk).

1.4.2 Assessment and staging

After histological confirmation the next step is to assess the depth and spread of the tumour. Accurate staging is achieved by a combination of techniques. The recommended initial preferred mode of non invasive investigation staging assessment should include contrast enhanced computerised tomography scan of the thorax and abdomen to determine the presence or absence of metastatic disease. The neck and pelvis should be imaged at the same time to provide adequate staging. If at this time advanced or metastatic disease is

confirmed then no further investigation is required (Allum et al., 2002 and www.sign.ac.uk).

More recently, in the absence of metastatic disease, assessment of operability is preferably made by endoscopic ultrasound (EUS); which is performed with a small high frequency probe incorporated into the distal end of the endoscope. This technique more accurately assesses the depth of penetration of the tumour, but the ability to accurately stage nodal involvement is dependant upon the site of the tumour. Local nodes are usually well seen, but detection of more distant nodes is reduced by the limited ultrasound penetration (McLean and Fairclough, 1996). Endoscopic ultrasound also allows fine needle aspiration (FNA) of suspicious lymph nodes; this also improves the accuracy of nodal staging.

Magnetic resonance imaging (MRI) and Positron emission tomography (PET) are accurate for TNM staging, but are not routinely used, as CT and EUS can be as accurate in staging (www.sign.ac.uk).

Patients with gastric cancer and oesophageal tumours with a gastric component, if suitable for anaesthetic, will have a laparoscopy to detect any peritoneal deposits. Laparoscopy can be performed with or without ultrasound, and a peritoneal lavage will be carried out and sent to cytology to detect any peritoneal metastasis. Molloy and co-workers (1995) reported on the role of laparoscopy to detect inoperable advanced disease or to determine patients suitable for further resection, laparoscopy was performed on 244 patients and concluded that laparoscopy was a valuable investigation when used to assess the feasibility of resection (Molloy at al., 1995).

Patients with upper third oesophageal cancer may have a bronchoscopy to assess tracheobronchial invasion, again washings may be sent to cytology to assess any spread to the lung.

Tumours are then staged using TNM, edition of the international union against cancer (UICC) classification of malignant tumours, which defines the anatomical extent of the disease, (see appendix A 1.4). The (T) category is the depth of tumour infiltration and the relationship with neighbouring structures. The (N) category determines regional lymph node metastases and the (M) category reports on distant metastases or lymphatic invasion (UICC, 1997).

1.4.3 Symptom staging

Gastric and oesophageal cancer is often asymptomatic or causes mild symptoms in its early stages i.e. heartburn, indigestion and loss of appetite. It is usually only in later stages symptoms are more severe i.e. abdominal pain, nausea, vomiting, weight loss, weakness, fatigue, bleeding and dysphagia. A muticentre study of oesophageal cancer patients (n=5000) by Daly and co-workers between 1994-1997 reported that at diagnosis patient's most common symptoms were dysphagia (74%) and weight loss (57%). They concluded that patients tend to modify their diets for a long time before seeking attention and dysphagia may progress rapidly to a stage where patients are unable to swallow fluids or saliva (Daly et al., 2000). Therefore, the disease is usually advanced when the diagnosis is made. However, several studies have reported that the duration of symptoms does not predict survival (SAGOC 2002; Martin et al., 1997).

In potentially curative cancer patients the main symptom tool used is the ECOG performance status, lung function tests and, in some centres, the POSSUM score. A retrospective study of patients who underwent oesophagectomy reported that age, lung function, and performance status could be used to select patients who would benefit from pre-operative cardio pulmonary rehabilitation (Ferguson and Durkin, 2002). McCulloch and co-workers (2003) reported that after initial assessment 57% of gastric and oesophageal patients assessed for surgery were unfit for surgery due to chronic respiratory and cardiac conditions (McCulloch et al, 2003). One American study reported a stair climbing exercise offers an inexpensive means to predict potential post-operative cardiopulmonary complications after high-risk surgery (Girish et al, 2001). Therefore, TNM staging, age, performance status and co-morbidity need to be taken into consideration before deciding on the best treatment for the patient.

1.5 Treatment

Like any cancer, treatment is adapted to fit each person's individual needs and depends on tumour size, location, and extent of the tumour, the stage of disease and the patients general health, well being and patient preference to options available. Gastric and oesophageal cancer is difficult to cure unless it diagnosed at an early stage, unfortunately the majority of these cancers are advanced at time of presentation. Treatment options include surgery, chemotherapy, radiation therapy, endoscopic therapy, multimodality therapy, or palliative care.

Alici and co-workers (2006) reported that in patients with gastric cancer, the ideal approach to patient's treatment choice is to establish as many prognostic factors as possible before administering therapy, furthermore knowing the prognostic factors could therefore aid the physician in improving prognosis. Surgical complications and chemotherapy toxicity can also have an impact on overall survival time (Alici et al., 2006).

There are various treatments that can be offered to patients once prognostic factors have been determined. In patients who have potentially curable disease, the majority of cases will be offered surgery if fit enough. The extent of the resection undertaken will depend on tumour site, histology and stage. Although surgery confers the greatest chance of long-term cure and aims to maintain long-term quality of life it may be associated with significant morbidity.

Surgery for gastric cancer has the best chance of cure, two studies comparing distal gastrectomy and total gastrectomy for non cardia gastric cancers reported similar results on 5 year survival, morbidity and mortality and concluded that sub total gastrectomy was associated with a better nutritional status and quality of life and should be the procedure of choice, provided that the proximal margin of the resection falls in healthy tissue, the only adverse outcome of this type of operation is the chance of recurrence in the remaining stump (Gouzi et al., 1989; Bozzetti et al., 1999; Bae et al., 2006). (Hundahi et al., 2000) reported that in Japanese proximal and distal cancers, the patient's 5 year survival rate was approximately 20%/34% respectively five years after resection.

Surgery for oesophageal cancer is extensive and there is a greater chance of operative mortality and very seldom performed on patients with upper third cancer, Daly and co-

workers (2000) reported that on comparing transthoracic and transhiatal oesophagectomy, that hospital stay was similar, but post operative complications were more frequent in the later, furthermore at least one major postoperative complication occurred in 46% of patients (Daly et al., 2000). The 5-year survival rate for oesophageal cancer patients that undergo potentially curative resection has recently been reported to be 40% (Stein et al., 2005). Ancona and co-workers (2006) reported that postoperative complications after oesophagectomy did not affect the patient's long-term prognosis (Ancona et al., 2006). Important postoperative complications in both tumour sites include anastomotic leak, wound infection, cardiac and pulmonary complications and pneumonia.

If unfit for surgery but stage of disease is amenable for cure then chemotherapy agents can be administered, normally (ECF) Epirubicin, Cisplatin and 5-Fluorouracil (5-FU). Side effects (usually temporary) of chemotherapy may include a low blood count, hair loss, vomiting and diarrhoea and skin irritation. Chemotherapy can be combined with radiotherapy, particularly when cure is being sought in oesophageal cancer; Ross and co-workers reported an improved outcome in patients with loco-regional oesophageal disease (Ross et al., 1998).

Several studies have reported on the use of neo-adjuvant chemotherapy to downstage tumour. The United Kingdom MAGIC (MRC adjuvant gastric infusional chemotherapy) trial randomised gastric and oesophageal cancer patients (n=503) to pre-operative and post operative chemotherapy versus surgery alone, with a follow up period of three years. The results demonstrated a significant difference in favour of the surgery plus chemotherapy group with respect to resection rate and survival (Cunningham and W.A.S.S.S.W, 2005).

Radiotherapy may be used as a single modality radical treatment for patients with a small length of oesophageal cancer, to relieve dysphagia and control local disease. The main disadvantage of radiotherapy is the development of an oesophageal stricture or oesophagitis.

Endoscopic treatments offer an alternative to surgery, endoscopic mucosal resection (EMR) can be undertaken to remove an early tumour of less than 3cm in diameter in gastric and oesophageal cancer patients. The resected specimen will be sent to pathology where they will check the depth of invasion and if the margins are clear. EMR is suitable for elderly patients who are not fit enough to undergo surgery or able to cope with the side

effects of chemotherapy, this is performed under sedation at time of endoscopy; therefore the patient will not be subjected to a general anaesthetic. EMR has an advantage of low morbidity and mortality. A recent Japanese study reported that the 3 year residual/recurrence free survival rate after EMR was 92.5% and concluded should be the standard treatment for early cancers (Oda et al., 2006).

Patients who have advanced/metastatic disease will be offered palliative therapies directed towards alleviating symptoms. These palliative treatments can include surgery or by-pass but this is associated with high mortality and morbidity and less invasive options are currently used. There are a wide variety of palliative therapies suitable for this cohort of patients as outlined below. Daly (2000) reported that after clinical staging over 60% of patients had advanced disease and went on to receive palliative input (Daly et al., 2000). This result was replicated in another study by (Schlansky et al., 2005) where 89% of patients were clinically staged as advanced disease.

Palliative chemotherapy may be given with the intent to increase survival, sustain quality of life and improve dysphagia. Ross and co-workers (1998) reported that gastric cancer was one of the most chemo sensitive solid tumours of the gastrointestinal tract with the majority of patients being suitable for palliative chemotherapy. The ECF regimen was developed in the gastrointestinal unit of the Royal Marsden Hospital and first reported in 1991, in a prospective randomised trial. ECF was compared with the standard combination of 5-Fluorouracil, Adriamycin and Methotrexate (FAMTX) in patients with previously untreated gastric cancer, it was reported that the response rate and overall survival was significantly improved with the ECF regime (Ross et al., 1998). In recent years Mitomycin had been substituted for Epirubicin in the hope to reduce toxicity, Ross (2002) reported that on comparing ECF with MCF that there was a higher response rate and less toxicity with ECF and recommends that ECF should still be the treatment of choice for advanced gastro-oesophageal cancers (Ross et al., 2002). Currently there is limited evidence to support the efficacy of chemotherapy alone in oesophageal cancer patients (Conroy, 2006).

Palliation of advanced oesophageal cancer will be the main goal of treatment and will offer relief of mechanical obstruction and swallowing function (Kelsen, 1982), thus allow improved food intake. Caspers and co-workers (1988) reported that oesophageal cancers are often responsive to radiotherapy and has been shown to palliate symptoms of dysphagia, the study concluded that 70% of patients showed improvement in dysphagia

and furthermore, 54% remained palliated until time of death (Caspers et al., 1998). The potential side effect from this mode of treatment may be severe oesophagitis. There are no studies evaluating the use of radiotherapy alone in patients with gastric cancer, but it can be useful for pain control in patients with proven bone metastatic disease.

Palliation of dysphagia in oesophageal cancer patients is of high importance and there is a range of different endoscopic modalities that involve ablation or stenting. Ablation techniques include laser, argon plasma coagulation, alcohol injection and photodynamic therapy. The side effects from these treatments include perforation, haemorrhage, fistulas and stricture; these treatments are repeated until the patients' swallowing has improved. In a study by Mellow and Pinkas (1985) it was reported that 97% of oesophageal patients achieved luminal patency after an average of three laser treatments over seven days. Furthermore, there was also a marked improvement in nutritional input and performance status (Mellow and Pinkas, 1985).

Laser treatments are also extensively used in the treatment of gastric cancers and can provide good palliative results and contribute to a good quality of life (Wu et al., 1989). Mathus-Vliegen and Tytgat (1990), reported in patients with gastro-oesophageal cancer (n=42) who were mainly referred for bleeding or obstruction that laser palliation was successful in 81% and 86% of patients respectively. Argon plasma coagulation (APC) in which a current is applied to tissues by means of ionised argon gas was developed by Grund and co-workers (1991) in Germany and initially piloted on patients (n=102) with highly effective results and in Germany has became the preferred mode of ablation therapy (Grund et al., 1994).

The placement of a plastic or metal stent, offers rapid relief of dysphagia, although there can be retrosternal pain for the first few days, there can also be recurrent dysphagia due to stent migration or bolus obstruction. Dilatation with bougies or balloon can also relieve dysphagia temporarily and can, be repeated as required; it can also be used to allow access for laser therapy or the placement of the stent. The main complications from repeated dilatation are perforation and haemorrhage (Kavic and Basson, 2001).

Studies have compared laser treatment with stent placement; the results which have been reported are variable, Dallal and co-workers (2001) reported that survival was greater in patients who underwent laser ablation compared to patients who stent placement.

However, dysphagia relief was disappointing in both groups and overall deterioration of quality of life was more noticeable in the stent group. The aim of the above treatments are to restore and/or maintain an as normal as possible food intake and improve quality of life. These procedures avoid immediate morbidity associated with surgery, but should only be applied if they are effective in disease control and/or symptom control.

For some patients there is no appropriate treatment that can be offered or the patient may refuse treatment. McMillan nurses; clinical nurse specialists and hospices can offer supportive care to the patients and their families. This has been defined by (Ahmeddzai, 2001) as "Supportive care for cancer patients is the multi professional attention to the individual's overall physical, psychological, spiritual and cultural needs, and should be available at all stages of the illness, for patients of all ages regardless of the current intention of anti-cancer treatment". The philosophy as seeing the patient as a whole person is an acknowledgement that the effect of the disease will also impact on other parts of the patient's life and support needs to be offered.

It is acknowledged increasingly that in the process of weighing the benefits and side effects of treatment, the patient's perspective is of prime concern. Some patients are willing to go to extreme lengths to prolong survival, accepting treatments that severely impair quality of life. Other patients feel that they want to make the most of their remaining time and are unwilling to risk an inferior quality of life. A study by Voogt and co-workers (2005) concluded that attitudes toward medical treatment vary in cancer patients in whom the cancer is, in principle incurable. One third of the patients can be classified as striving for length of life, one third strived for quality of life and one third seemed unwilling or unable to express preference (Voogt et al., 2005).

In summary, the majority of patients with gastric and oesophageal cancer present late with a multitude of problems, some related to and some independent of the underlying disease and treatment should be adapted to fit each person's needs. Despite the advances of cancer therapy, cancer continues to be a life threatening illness with a poor survival rate and the newly diagnosed patient faces a crisis that emphasizes his or her mortality.

1.6 Weight loss, body composition and the systemic inflammatory response

The general poor outcome observed in patients with gastric and oesophageal cancer is related to the fact that most patients have locally/regionally advanced or disseminated disease at diagnosis (Blot and McLaughlin, 1999).

Malnutrition, weight loss, cachexia, reduced calorie intake and multiple vitamin deficiencies are a few of the symptoms often seen in patients with advanced cancer. Due to anorexia, maintaining and attaining a good nutritional state is frequently difficult to overcome (Laszlo and Spencer, 1953) all of these symptoms can in some way be related to one another.

Belghiti and co-workers (1987) conducted a study of squamous oesophageal cancer patients (n=50) and reported that 42% suffered from anorexia and further reported that malnutrition can be attributed to mechanical obstruction, widespread tumour or disseminated cancer. Therefore, nutritional status should be evaluated while evaluating for the suitability of surgery (Belghiti et al., 1987).

Fearon (1992) reported that patients with advanced cachexia are characterized by anorexia, early satiety and marked weight loss. The majority of patients present with advanced disease and it was recognised that morbidity and mortality are associated with cachexia (Fearon, 1992). Furthermore, Ovesen and co-workers (1993) noted that a deteriorating nutritional status and insufficient food intake in cancer patients with solid tumours, compromised their physical functional status even if the weight loss was minor to moderate and concluded that it was not possible to ascertain which symptom came first (Ovesen et al., 1993).

Bruera (1997) reported that more than 80% of patients with cancer develop cachexia before death and furthermore, 80% of patients with gastrointestinal cancers will have cachexia at the time of diagnosis. In general, patients with solid tumours (with the exception of breast cancer) have a higher frequency of cachexia and can become more pronounced as disease progresses. Patients with oesophageal cancer may suffer greatly from dysphagia, abnormalities of taste or chronic nausea, resulting in reduced caloric intake and anorexia (Bruera, 1997).

Argiles and Lopez-Soriano reported similar observations in that cachexia occurs because of alterations in metabolism caused by the tumour and that the body uses calories faster than they can be replaced, due to this the weight loss cannot be reversed simply by increasing calories. They suggested that appropriate treatment at onset of tumour growth, could improve on the patients clinical state and quality of life (Argilies and Lopez-Soriano, 1998).

Furthermore, Goldberg and Loprinzi, (1999) reported that cancer associated causes of reduced caloric intake can be separated into direct and indirect tumour effects. A direct tumour effect is a consequence of the presence of a tumour mass or tumour infiltration, from tumour encroachment of the gastrointestinal tract. The remote effects from treatments such as surgery, radiotherapy or chemotherapy are exemplified and the disinterest in food and reduced appetite can be due to poorly controlled pain, depression or from the oesophageal pain of mucositis, and that in patients with several months to live, therapy with progestational agents may be of benefit to aid an increase in appetite (Goldberg and Loprinzi, 1999).

Argiles and co-workers (2002) reported that the most relevant characteristics of cachexia is that of asthenia (or lack of muscle strength), which reflects the great muscle wasting that takes place, it is also characterized by general weakness as well as physical and mental fatigue (Argiles et al., 2002).

Although there is good evidence that weight loss, appetite loss, cachexia, performance status and the systemic inflammatory response in gastro-intestinal cancer patients are associated, it is also important to note that not all patients with weight loss demonstrate evidence of a systemic inflammatory response. Several authors have studied the potential relationship between the variables and concluded that although they are all related; the relationship remains complex and unclear (Fearon et al., 2006). Furthermore, it has also been reported that the loss of adipose tissue constitutes for the majority of weight loss; and it is thought that the depletion of skeletal muscle, which occurs later, is more significant in the survival of cancer patients. The development of nutritional therapies should aim at increasing weight gain and the preservation of skeletal mass and in turn improve the quality of life in these patients (McMillan et al., 1994; O'Gorman et al., 1999; Kotler, 2000; McMillan et al., 2001; Delano et al., 2006).

Persson and co-workers (2002) reported that gastric cancer patients who had nutritional support during their illness gained weight. Furthermore, appetite loss and fatigue decreased in the same cohort of patients. A further study undertaken by (Hopkinson et al., 2006) found that patients with advanced cancers, 17% of whom were gastrointestinal, had experienced weight loss and a decline in food intake and were concerned about their quality of life.

The majority of patients with oesophageal cancer suffer from dysphagia, which will normally be due to obstruction caused by the neoplasm. Dysphagia can occur at anytime during their illness and this can also result in marked weight loss. Palliation of dysphagia can be offered and relieving the dysphagia will help to improve quality of life.

Belghiti and co-workers (1987) conducted a study of squamous oesophageal cancer patients (n=50) and reported that all patients suffered from dysphagia with or without anorexia at some stage during their disease (Belghiti et al., 1987).

Spencer and Laszlo (1953) reported that contrary to the common belief, pain is not always associated with advanced cancer and pain medication is not a treatment for cancer. Furthermore, anxiety and fear are often mistaken for pain and are often treated with analgesics. A survey of advanced cancer patients reported that more than 50% of patients with advanced cancer were not in need of analgesics (Spencer and Laszlo, 1953).

(Foley, 1985) reported that severe intense and poorly controlled pain may be a primary reason for patients to abandon treatment. Furthermore, poorly controlled pain also impacts on mood, appetite and overall quality of life. Proper management of pain control should be sufficient to allow them to carry on with their daily activities and to die relatively free from pain. Two studies undertaken by Cleeland and Ryan (1989 and 1994*)* reported that many adults including patients with cancer function effectively with mild pain, as pain increases it can no longer be ignored as it may affect general well being. Many patients may not report an increase in pain as they would then have to acknowledge the spread of disease and they may be concerned that their physician will be diverted from the task of curing the tumour, it was also reported that 36% of patients with metastatic disease reported significant pain (Cleeland & Ryan, 1989; Cleeland et al., 1994).

A study was undertaken in the general population in primary care centres for the World Health Organization to assess the association between persistent pain and psychological illness, showed a 4-fold increase in patients also suffering with depression, anxiety and difficulty in coping with daily activities over those patients not affected by persistent pain (Gureje et al., 1998). It was reported that when pain is ongoing and uncontrolled it has a detrimental and deteriorative effect and it is apparent that it has a diminishing effect on quality of life; it produces emotional distress, undermines well being and interferes with general daily functioning. For patients with chronic pain opioid analgesics can improve quality of life (Katz, 2002).

Cancer related fatigue is an important rarely treated symptom in cancer today; this fact is probably due to improved management options for other symptoms associated with cancers and its treatment such as pain, depression, nausea and vomiting. However, though the problem is real, both patients and physicians may review cancer related fatigue as something to be endured, as treatment for cancer is foremost in the physicians and patients minds.

It has been reported that for most individuals fatigue is a protective response to physical and psychological stress, for patients with chronic disease it can become a distressing symptom with negative effects on daily functioning and quality of life (Glaus et al., 1994).

A panel of experts of the National Comprehensive Cancer Network (NCCN) defined fatigue as “a persistent subjective sensation of fatigue related to cancer and its treatments that interfere with the daily life activities of the patient” (Mock et al., 2000). Furthermore, cancer related fatigue has been described by Romanelli (2004) as general weakness, limb weariness and difficulty in finishing the daily activities, diminished concentration, sleep disturbances and a marked emotional reaction to fatigue (Romanelli et al., 2004).

(Servaes et al., 2000) reported in their study that one fifth of disease free patient’s still suffered from fatigue, psychological and physical problems long after treatment. It is frequently one of the initial symptoms experienced by patients and it tends to increase with the progression of cancer and its treatment. Furthermore, it is possible that fatigue is related to the psychological and physical problems. It has been reported that cancer related fatigue differs from normal fatigue, which can be due to overexertion or lack of sleep. In contrast, cancer related fatigue is characterized by feelings of tiredness and weakness

despite adequate amounts of sleep. In a study by Cella and co-workers (2001), 17% of patients who had completed treatment for more than 1 year, reported ongoing fatigue (Cella et al., 2001).

(Persson et al., 2002) reported that fatigue and appetite loss were closely linked with depression and anxiety, in which order they appear is more difficult to report, patients may worry over treatment and the anxiety and depression affect their appetite and contribute to the fatigue, or the fatigue may have compromised the ability to buy and cook food and adversely promote appetite loss.

Prue and co-workers (2006) undertook a literature search with fatigue and cancer as the main criteria, and reported that cancer related fatigue has a major impact on a sufferer's life with devastating social and economical consequences and can persist for months or even years following completion of treatment (Prue et al., 2006).

Depression and anxiety can be quite variable in cancer patients and may also be related to pain, reduced performance status and other physical symptoms such as dysphagia, which are difficult to palliate. Patients deal with depression in various ways depending on personality and coping ability and in some cases can improve and as their depression is appropriately treated.

A study undertaken by Schag and Heinrick (1989) reported that adults with cancer were subjected to a variety of potentially stressful medical situations, yet little attention has been paid to the impact of these situations on them. Anxiety and poor communication skills was an important finding; it could not be decided if anxiety was a consequence of a patient's inability to communicate effectively with physicians or whether the anxiety makes it more difficult to communicate (Schag and Heinrick, 1989).

In one study, patients who were deemed suitable for radiotherapy, were asked to complete a quality of life questionnaire, the study reported that 69% of patients had psychological distress, social dysfunction and reduced well being at onset of treatment; furthermore distress can evolve from unresolved symptoms and be associated with increased depression (Kaasa et al., 1993). Servaes and co-workers (2000) also reported that patients were still clinically depressed long after treatment had completed and this could be as a result of

being confronted with a life threatening illness or be anxious of disease recurrence (Servaes et al., 2000).

A study undertaken by (Lloyd-Williams et al., 2004) of patients attending a palliative care day unit, reported that depression is a symptom affecting approximately one in four patients receiving palliative care and that it is significantly associated with general quality of life and the presence of immobility, tiredness and pain in this population. Yan and Sellick, (2004) reported similar results in patients diagnosed with gastro-intestinal cancer, that 27% of patients suffered from depression and that depression and quality of life were strongly associated, particularly during the time of diagnosis and the commencement of treatment. This study further reported that younger patients demonstrated a higher level of depression (Yan and Sellick, 2004).

In summary, cancer is now often classified as a chronic illness and increasing survival can be accompanied by increased numbers of hospitalisations, complications and expense, furthermore symptom control and the dying process can be prolonged and arduous for all concerned. A number of publications have concluded that cancer and cancer treatments may affect the way in which patients perceive their quality of life and in particular, a deteriorated state of health and the adverse effects of treatments may influence reduced physical functioning.

1.7 Quality of life

Quality of life has been an implied outcome since the earlier days of health care. The ethical basis for cancer care treatment is provided by the well-known dictum *primum non-nocere*, which translated means first do no harm. Furthermore, the benefit of the treatment proposed must be greater than the suffering it entails; one of medicines time honoured precepts is to treat the patient and not only the disease (Greer, 1984).

The ethics of cancer treatment was summarised by Dr Neil Fiore, who had developed metastatic cancer as: "Fighting cancer must come to mean more than excising a tumour and focusing the latest weapon on the metastases. It must include recognition, by both the medical professionals and the patient, that the patient's mind and body are powerful factors in this fight. Failure to use these potential allies can mean losing them to the 'enemy' through patient resistance to treatment, depression and loss of the will to live. Effective cancer therapy must treat the healthy portion of the patient's body as well as combat the diseased cells" (Fiore, 1979).

(Slevin, 1992) reported that cancer and its treatment can create distress to the patient and their families, furthermore patients are often told "there is nothing we can do for you", it is therefore not surprising that patients with cancer often feel miserable and despondent and maintaining quality of life then becomes an issue.

Tradeoffs between quality of life and quantity of life are often found to be necessary in decision making Stiggelbout and co-workers (1996) found that younger cancer patients were more likely to strive for length of life, whereas older patients were more likely to strive for quality of life. Cancer patients who thought they would survive for at least 6 months were more likely to favour life-prolonging therapy over comfort care, than cancer patients who thought they had at least 10% chance of not surviving the next six months (Stiggelbout et al., 1996).

Quality of life is a phrase that covers a multitude of factors each contributing to the value of life perceived by the patient during their illness and treatment. Health-related quality of life is largely based upon a multidimensional perspective of health as physical, psychological, social functioning and general well being. In recent years improvements in cancer treatment have emphasised the importance to the short and long term implications

of therapy and it is important to the cancer patient that quality of life is maintained.

1.8 Definitions and dimensions of quality of life

There are differing opinions regarding what concepts of quality of life are important and this has hindered an agreement of the definition of "quality of life".

In 1947, the World Health Organisation defined health as "a state of complete physical, mental and social well-being and not merely the absence of disease" (World Health Organisation Constitution, 1947). In 1978 they reiterated, that individuals were entitled to an adequate quality of life, but they did not elaborate on what constituted an "adequate quality of life" (International Conference on Primary Health Care: WHO and UNICEF, 1978).

Gough and co-workers (1983) reported that the effectiveness for cancer treatment was usually measured on tumour response, toxicity and overall survival and the concept of quality of life had been too complex to be quantified, in their study of 100 advanced metastatic gastrointestinal and breast cancer patients, using 4 different questionnaires, they advocated that only one question need be asked to assess quality of life- on a ten centimetre analogue scale –"How would you rate your quality of life today?". They support their claim with evidence of a strong correlation between scores on this scale and on more elaborate sets of quality of life assessments and concluded that this question could be advocated for periodic assessment of patients with cancer, particularly in clinical trials (Gough et al., 1983).

Calman stated that quality of life was a difficult concept to define and to measure. It was suggested that quality of life should measure the difference, or the gap, at a particular period of time between the hopes and expectations of the individual and the individual's present experiences. Furthermore, it can only be described by the individual and must take into account many aspects of life. Quality of life extends not only to the impact of treatment and side effects but also to the recognition of the patient as an individual and as a whole person, body, mind and spirit (Calman, 1984).

Ware (1987) attempted to bring some order to the range of variables employed in health and quality of life and stated standards would need to be adhered to for judging the content validity. Five generic health concepts were defined as: physical health, mental health, social functioning, and role functioning and general health perceptions. Items from widely

used health measures were presented to clarify distinctions among these concepts and the different health states they encompass. It was recommended that labels be assigned to health measures in a manner consistent with their content and other evidence of validity (Ware, 1987).

In 1993, the Health Services Research Committee of the American Society of Clinical Oncology (ASCO) organised a working group to define outcomes, focusing on cancer treatments and concluded that survival should be the most important final outcome of cancer treatment. In contrast, patients with metastatic disease should still be offered treatment if it improves quality of life, and should encompass physical, psychological and social dimensions. Cancer related quality of life is important because it is the patient's evaluation of how cancer and its treatment affect the physical, psychological and social aspects of their life and concluded that reliable, valid measurements must be used (ASCO, 1996).

The need to objectively measure quality of life is now widely recognised as being an important outcome in clinical trials, several authors have highlighted the importance of outcome measures in addition to the traditional end points, such as survival time, morbidity, nutritional function and relief of dysphagia, as they fail to take into account the broader effects of both the illness and intervention on the patient with gastric and oesophageal cancer. More recently, quality of life has become an outcome measure for patients after the diagnosis and treatments in and out with trials (Blazeby et al., 1995; O'Hanlon et al., 1995; Coates et al., 1997; Zieren et al., 1998; Vickery et al., 2000).

The fundamental question of who should measure quality of life remains. Quality of life is an individual and personal experience; clinicians prefer scales where they can use their clinical judgement. However, when patients complete the questionnaires results may differ from a clinician's perspective, a study reported by Slevin and co-workers found a poor correlation between patients and doctors quality of life scores and led him to believe that assessments should be completed by patients themselves (Slevin et al., 1988).

1.9 Quality of life assessments

There is no gold standard measure of quality of life; several authors have highlighted the importance of establishing the validity and reliability of any assessment tool being used. Validity reflects the degree to which the tool measures what it claims to measure and it must cover construct, content and criterion validity, this can be assessed by comparing the results with another accepted tool. Reliability reflects the consistency of the information being collected. There are numerous quality of life tools available, which measure aspects of quality of life in relation to health care. However, there is no agreement on which tools are most effective. No single tool satisfies all dimensions for assessing quality of life and the use of numerous assessments can be impractical for seriously ill patients. Investigators need to clearly define the aims of their investigation and use the most appropriate assessment tool available.

Outlined below are some of the instruments used on assessing patient's performance status/quality of life.

1.9.1 Karnofsky Performance Scale

The Karnofsky performance scale (KPS) is a widely accepted tool, it was originally developed by Karnofsky and co-workers in 1948 to document physical function and the need for assistance in advanced lung cancer patients, it assesses the patient's performance on a numerical scale from 0-100 representing a patient's ability to perform normal activity, the ability to do normal work and the need for assistance with daily living (Karnofsky et al., 1949). The performance status is assessed by direct observation; the same observer should complete the scale to confirm continuity. It is also used to evaluate response to treatment. Studies evaluating the reliability of the scale came to different conclusions; Conill (1990) reported significant correlation between physician's scores and also between physician and patient score. Schagg (1984) reported that physician's reported higher scores than mental health professionals and concluded that further research was required (Schag et al., 1984; Conill et al., 1990). The major disadvantages of the KPS are that it has a limited content and is normally scored by a physician and it is subjective in nature, which does not reflect the patients' attitude.

1.9.2 Zubrod Scale, or the Eastern Cooperative Oncology Group Performance Scale: (ECOG)

A condensed version of the Karnofsky scale was developed in 1960 for use with cancer patients, and is known as the Zubrod Scale or the Eastern Cooperative Oncology Group Performance Scale (ECOG) (Zubrod et al., 1960). It is a measure of performance and a predictor of functional outcome of tumour treatment. It is an observer- rated scale that ranges from 0 to 4 (see appendix B 2.2). A study by (Verger et al., 1992) compared Karnofsky with ECOG in 150 cancer patients and reported that both scales where highly correlated, but caution should be used when using either scale as there is a wide spread in the lower performance status range.

Karnofsky and ECOG performance scales are both widely accepted tools, but neither scale measures any psychosocial indices (Bowling, 1995). Furthermore, disease specific aspects of a questionnaire would provide detailed information about the patients' perception of their health.

1.9.3 General Health Questionnaire

The General Health Questionnaire was first published in 1972, as a 60 item questionnaire (Goldberg, 1972) and subsequently shorter versions have been introduced. The version most frequently used is the 28 item version (GHQ-28), it has four subscales assessing somatic or physical symptoms, anxiety / insomnia, depression and social dysfunction, and it is a self report questionnaire in which patients are asked to respond to each question by comparing their present experience to their usual state. Four possible response options are provided and can be scored in two ways, firstly by employing the Likert type severity score, which is a psychometric response scale and is most widely used in survey research (Likert, 1932) or by using the general health questionnaire scoring. Goldberg and Hillier (1979) tested the validity of this assessment to discriminate between patients with and without mental illness and reported no advantage in using the Likert scale; however it is useful for indicating patients with severe psychological disturbance. This questionnaire was developed for research purposes (Goldberg, 1991; Bowling, 1991). There would appear to be no reliability testing reported on the use of the GHQ-28.

1.9.4 SF-36

The SF-36 was developed in 1988, as a multi-purpose, short-form health survey with 36 questions, it is suitable for self-administration or by a trained interviewer; it was constructed to satisfy minimum psychometric standards necessary for group comparisons, it is a generic measure, as opposed to one that targets a specific disease. Eight health concepts were chosen from a possible 40, those chosen represent the most frequently measured concepts used that can measure health affected by disease and treatment, these include: physical, role, social and emotional functioning, bodily pain, general health, vitality and mental health. Reliability has been estimated using both internal consistency and test-re-test measures; with rare exceptions published material has exceeded the minimum standard of 0.70 (McHorney et al., 2000).

1.9.5 WHOQOL-100

In 1991 the WHOQOL-group launched a program to define and measure the quality of life and proceeded to develop an instrument to assess overall quality of life and general health, it consists of six broad domains: physical, psychological, environmental, spiritual, levels of development and social relationships, there are a total of 100 items in the assessment and all items are rated on a five point scale. The WHO groups' initiative to develop a quality of life assessment, arose from a need for an international measure, and the commitment to the continued promotion of a holistic approach to health and health care. The WHOQOL-group undertook a pilot study and reliability studies during the development process. In 1998 the development of the WHOQOL-BREF, an abbreviated version of the WHOQOL-100 was constructed and validated as a reliable alternative to the previous assessment. It was envisaged that the WHOQOL-BREF would be most useful in large epidemiological studies and clinical trials. In addition, the WHOQOL-BREF may be of use to health professionals in the assessment and evaluation of treatment efficacy (WHOQOL, 1999).

1.9.6 Dysphagia Score

The first formal attempt to measure dysphagia was not made until 1976 when DeMeester devised a simple classification system, based on patients swallowing abilities (DeMeester et al., 1976). There have been attempts by other authors to further express dysphagia in numerical terms using a dysphagia scale graded from 1 to 5, (see appendix B 2.3) as well

as a diet scale **(**Goldschmid et al., 1989). (Van Knippenberg et al., 1992) adapted the Rotterdam Symptom check list to include dysphagia and eating scale for Dutch patients undergoing oesophageal surgery. The M. D. Anderson Dysphagia Inventory (MDADI) also included global, emotional, functional, and physical subscales. The MDADI was the first validated and reliable self-administered questionnaire designed specifically for evaluating the impact of dysphagia on the quality of life of patients with head and neck cancer (Chen et al., 2001). More recently a site specific oesophageal questionnaire module was developed by the EORTC (QLQ-OES18) to measure dysphagia in an objective fashion, and test its correlation with subjective estimates of dysphagia, the OES18 demonstrated good psychometric and clinical validity and should be used with the core C30 questionnaire (Blazeby et al., 2003).

1.10 EORTC QLQ-C30

(Aaronson, 1991) reported that at that time there was a large pool of instruments available for assessing health related quality of life and suggested that additional efforts at re-inventing the wheel might not be particularly useful, rather it would be more fruitful to maximise existing tools and apply modifications where needed. Furthermore, future efforts for designing assessments should be directed towards examining the relevance of the instruments in the clinical setting. The most serious limitation of a generic measurement, that when applied in the oncology setting, fails to address the disease specific aspects of treatment.

In 1986, the European Organisation for Research and Treatment of Cancer (EORTC) initiated a research programme to develop an integrated, modular approach for evaluating the quality of life of patients participating in international clinical trials. The 36 item version (see appendix B 2.1) was widely tested in 1991 and was shortened to 30 items. The QLQ-C30 incorporates nine multi-item scales: five functional scales (physical, role, cognitive, emotional and social); three symptom scales (fatigue, pain, and nausea/vomiting); and a global health and quality of life scale. Several single item symptom measures are also included. The response to questions are in the format of dichotomous (yes-no) and Likert-scale and asks patients to respond to items using a time frame of the “the past week”. The average time to complete the questionnaire is 10-12 minutes and no significant difference has been reported in the results whether it has been self completed or completed by interview.

Validity and reliability was performed following an international field study on the initial core questionnaire, with 300 non-resectable lung cancer patients from 13 countries. Clinical variables assessed included; weight loss, performance status and stage of disease. The internal consistency of the items produced reliability coefficients of 0.52-0.89. With the exception of role function status, the EORTC tool was shown to be reliable in assessing many dimensions of quality of life and it has been proposed that quality of life assessment promotes a patient centred approach and has the ability to influence cancer care. The results of the study concluded that the tool was reliable and a valid measure of quality of life in clinical research settings (Aaronson et al., 1993).

The EORTC study group provides written guidelines, which details the scoring procedure required (see appendix C 3.1). Once the questionnaire has been completed the sum of items in each category is added and the total divided by the number of questions in the category. A linear transformation is then undertaken to convert this to a percentage scale with a higher score representing a higher response level. Thus a high score for functional scale represents a high/healthy level of functioning. A high score for the global health status/ quality of life represents a high quality of life. In reverse a high score for the symptom scale represents a higher level of symptoms / problems (Aaronson et al., 1993).

The EORTC QLQ-C30 was recommended by Bowling (1995) as the best developed quality of life measures for use with cancer patients (Bowling, 1995).

The QLQ-C30 has been widely applied, during the year 2000 alone; 590 academic users and 45 pharmaceutical companies signed agreements with EORTC to use the questionnaire (EORTC, 2001). Several authors have looked at quality of life in reference to gastro-oesophageal cancer, in surgical and palliative patients in the short term. There are, to our knowledge, no studies which have examined the effect of surgery on quality of life beyond 3 years. A number of workers (Blazeby et al., 2000; 2001; 2005: Chau et al., 2004; Vigano et al., 2004; Reynolds et al., 2006; Viklund et al., 2006; Avery et al., 2007) have reported that the EORTC QLQ-C30 measurement of quality of life may have prognostic value in patients with gastro-oesophageal cancer and furthermore, a decrease in functional scales in the short term have been reported.

1.11 Quality of life summary

No single quality of life tool satisfies all dimensions for assessing quality of life and the use of numerous assessments can be impractical for seriously ill patients. Investigators need to clearly define the aims of their investigation and use the most appropriate assessment tool available.

For this study we have used the EORTC QLQ-C30 (Aaronson et al., 1993) as outlined above as it has passed numerous validity and reliability tests, the ECOG performance status scale (Zubrod, 1960) and the dysphagia score.

1.12 Aims of thesis

The prognosis of patients with gastric and oesophageal cancer remains poor and are commonly fatal cancers with incidence only just greater than the mortality. Traditionally various factors have been linked to poor survival rate; these include stage of disease, performance status, weight loss and inflammatory response, as the majority of patients are diagnosed at an advanced stage. Therefore, ensuring the best quality of life is paramount. Aaronson (1993) and Vickery (2000) reported the importance of quality of life as an outcome in addition to survival as debilitating problems with nutrition; pain and fatigue are predominant after surgery. Furthermore, in patients undergoing palliative treatment, symptom relief must be weighed against treatment toxicity and therefore recording ongoing quality of life in these patients is of considerable importance (Aaronson et al., 1993; Vickery et al., 2000).

It has also been reported that, in a few studies, the EORTC QLQ-C30 measurement of quality of life may have prognostic value in patients with gastro-oesophageal cancer (Conroy et al., 2006).

Clearly, further investigation is required in this area and this thesis will examine:-

1. The relationship between quality of life (EORTC QLQ-C30) and survival in patients with gastro-oesophageal cancer.

2. The longitudinal impact of treatment on quality of life (EORTC QLQ-C30) in patients with gastric and oesophageal cancer.

Chapter 2

2. The relationship between quality of life (EORTC QLQ-C30) and survival in patients with gastro-oesophageal cancer

2.1 Introduction

Gastro-oesophageal cancer is the third commonest cause of cancer death in the UK. Each year, there are approximately 16,500 new cases and over 13,000 deaths attributable to the disease. Overall survival is poor with the majority of patients presenting with advanced, inoperable disease and less than 15% surviving 5 years (Cancerstats, 2004;). Although there have been improvements in survival following surgery (Ando et al., 2000; Hundahl et al., 2000; Hofstetter et al., 2002; von Rahden et al., 2004), for the majority of patients current treatment offers little in terms of improved survival. As a result quality of life in these patients is likely to be of considerable importance (Aaronson, Bullinger and Ahmedzai, 1988; Aaronson et al., 1993).

The European Organisation for Research and Treatment of Cancer have developed and validated the EORTC-QLQ-C30 questionnaire designed to assess the quality of life of cancer patients (Aaronson et al., 1993). Disease specific aspects of the questionnaire provide detailed information about the patients' perception of their health. Moreover, it has been reported that, in a few studies, the EORTC QLQ-C30 measurement of quality of life may have prognostic value in patients with gastro-oesophageal cancer (Conroy et al., 2006).

Blazeby and co-workers (2001) reported that, in addition to age and TNM stage, physical function or emotional function had independent prognostic value in 92 patients with oesophageal cancer. However, treatment (whether or not the patient underwent surgery) was not included in the model (Blazeby et al., 2001).

Fang and co-workers (2003) studied 110 patients with squamous oesophageal cancer and concluded that there was evidence to support the correlation of patient-reported QOL scores with survival; therefore, pre-treatment physical functioning might be a surrogate marker of an unrecognised biological prognostic factor. Although performance status was significant on univariate analysis it was not significant on multivariate analysis, whereas physical functioning was significant (Fang et al., 2003).

In contrast, in a study of more than 1000 patients with inoperable gastro-oesophageal cancer, entering 3 randomised clinical trials, Chau and colleagues (2004) reported that no aspect of the QLQ-C30 had independent prognostic value when performance status was considered. However, physical function, role function and global quality of life were associated with survival on univariate analysis. There were no survival differences among patients with oesophageal or gastric cancer (Chau et al., 2004). However, this study was retrospective and included selected cohorts of patients.

Therefore, from the above it remains unclear whether any aspect of quality of life other than physical function has a role in predicting survival in an unselected cohort of patients with gastro-oesophageal cancer. The aim of the present study was to examine the relationship between quality of life (EORTC QLQ-C30), clinico-pathological characteristics and survival in patients with gastro-oesophageal cancer.

2.2 Patients and Methods

Patients

Patients presenting with adenocarcinoma or squamous carcinoma of the gastric or oesophageal tract at the Royal Infirmary and Southern General Hospital, Glasgow between November 1997 and December 2002 (n=152) participated in a quality of life study, using the EORTC QLQ-C30 core questionnaire.

The extent of tumour spread was recorded using the TNM 5th edition classification (Sobin and Wittekind, 1997). Tumours around the gastro-oesophageal junction were further classified according to tumour site, using the Siewert system; type 1 and 2 lesions of the gastro-oesophageal junction were designated as cancers of the oesophagus. Type 3 tumours of the cardia were designated as gastric cancers (Siewert and Stein, 1998).

For gastric cancers, tumour node metastasis (TNM) stage I–III tumours were considered to be potentially amenable to curative surgical resection. For oesophageal cancers, TNM stage I–III tumours, excluding T4, were deemed to be potentially amenable to curative surgical resection. Patients who had stage 1 and 2 disease but whose performance status was poor or who had significant co-morbidity were deemed not suitable for surgery and went forward for active palliative treatment or supportive care. There were 152 patients included in the study, 69 patients underwent surgery and 83 patients received active palliative treatment or supportive care.

The study was approved by the Research Ethics Committee of the Royal Infirmary and Southern General Hospital, Glasgow.

Methods

Clinical and demographic variables were recorded at the patient's initial presentation and included age, sex, tumour type, site and length, TNM stage, ECOG performance status, weight loss and dysphagia.

Following diagnosis but prior to treatment the lead clinician approached patients as to whether they would participate in a study to examine their quality of life. If they gave informed consent they were given the EORTC QLQ-C30 questionnaire to complete.

Different aspects of quality of life were assessed using this cancer specific 30-item questionnaire, which has six functional scales (physical, role, emotional, cognitive, social, global health status) and several questions relating to a range of physical symptoms (Aaronson et al., 1993). Patients marked to what extent each statement applied to them. A number of patients were excluded because they were unlikely to understand the questionnaire either due to language, brain metastases, delirium or confusion. Neither age nor performance status were considered when offering the patient questionnaire. Few subjects were excluded (less than 10 patients) and therefore in those patients offered the questionnaire the bias was likely to be small.

2.3 Statistics

Scoring algorithms have been produced by the EORTC Quality of Life Study Group. The sum of items in each category is added and the total divided by the number of questions in the category. A linear transformation is then undertaken to convert this to a percentage scale with a higher score representing a higher response level. Thus a high score for functional scale represents a high/healthy level of functioning. A high score for the global health status/quality of life represents a high quality of life. In contrast, a high score for the symptom scale represents a higher level of symptoms / problems (Aaronson et al., 1993).

Data are presented as the median and range. Survival was determined from the time of biopsy proven diagnosis, and the endpoint for survival analysis was cancer-specific death. Patients were followed up at their clinic or endoscopy appointments and information on date and cause of death was checked with that received by the cancer registration system through the Registrar General (Scotland). Deaths up to the end of April 2007 were included in the analysis.

Univariate and multivariate survival analysis and calculation of hazard ratios (HR) were performed using a Cox regression model. For simplicity of presentation, a single hazard ratio was calculated for each ordered categorical variable, corresponding to the relative risk between adjacent categories. Hazard ratios for EORTC quality of life and symptom scores relate to a one-percentage point increase in the score. Owing to the large number of covariates examined, only those that were significant on univariate analysis were included in the multivariate analysis, and only main effects were considered. The analysis was performed using a backward stepwise procedure to derive a final model of the variables that had a significant relationship with survival. To remove a variable from the model, the corresponding P-value had to be greater than 0.05. The proportional hazards assumption was checked using log minus log plots.

Comparison of the association between tumour site, TNM stage, treatment and the functional (physical, role, emotional, cognitive, social, global health status) and physical symptoms (fatigue, pain and appetite loss) scales of the EORTC-QLQ-C30 quality of life questionnaire was carried out using the X^2-test or Mann-Whitney U-test where appropriate. Analysis was performed using SPSS software (SPSS Inc, Chicago, IL, USA).

2.4 Results

Patient characteristics and cancer specific survival analysis of patients with gastro-oesophageal cancer (n=152) are shown in Table 2.1. The minimum follow up period was 54 months or until date of death, the median follow up for survivors was 81 months, one patient was lost to follow up and one patient withdrew from the study. During this period 106 (70%) patients died from their disease and 14 (9%) died from co-morbid disease.

The majority of patients were over the age of 65 years (57%), male (68%) and had adenocarcinomas (84%). The majority of patients presented with weight loss (66%), had little or no dysphagia, and a near normal performance status (ECOG-ps, 71%). The majority of patients had EORTC QLQ-C30 function scores above 50 (physical functioning 100%, role functioning 65%, emotional functioning 74%, cognitive functioning 83%, social a functioning 79% and global quality of life 56%) and symptom scores below 50 (fatigue 69%, nausea/vomiting 85%, pain 86%, dyspnoea 79%, sleep disturbance 69%, appetite loss 64%, constipation 76%, diarrhoea 95% and financial difficulties 89%) and therefore had apparently normal quality of life (Table 2.1).

On univariate analysis, age ($P<0.01$), tumour length ($P<0.0001$), TNM stage ($P<0.0001$), weight loss ($P<0.0001$), dysphagia score ($P<0.001$), performance status ($P <0.1$) and treatment ($P<0.0001$) were significantly associated with cancer specific survival. EORTC QLQ-C30, physical functioning ($P<0.0001$), role functioning ($P<0.001$), cognitive functioning ($P<0.1$), social functioning ($P<0.0001$), global quality of life ($P<0.0001$), fatigue ($P<0.0001$), nausea/ vomiting ($P<0.01$), pain ($P<0.001$), dyspnoea ($P<0.0001$), appetite loss ($P<0.0001$) and constipation ($P<0.01$) were also significantly associated with cancer specific survival.

On multivariate analysis, tumour stage ($P<0.001$), treatment ($P<0.0001$) and appetite loss ($P<0.0001$) were significantly independent predictors of cancer specific survival. The relationship between appetite loss and cancer specific survival in patients with gastro-oesophageal cancer is shown in Figure 2.1.

When appetite loss was rescaled so that the four categories were represented by an integer score of 0 to 3 (rather than a percentage score), the unadjusted hazard ratio comparing adjacent categories was 2.06 (95% CI 1.72 – 2.48, p<0.0001). When adjusted for stage and treatment, it was 1.72 (95% CI 1.41 – 2.08, p<0.0001). When adjusted for stage, treatment and remaining clinico-pathological variables, it was 2.07 (95% CI 1.61 – 2.67, p<0.0001). When adjusted for stage, treatment, remaining clinico-pathological variables and quality of life and symptom scores, it was 2.03 (95% CI 1.40 – 2.94, P=0.0002).

In the present study C-reactive protein concentrations, at the time of quality of life assessment, were available in 94 patients (57 patients <10mg/l, 37 patients >10mg/l) and were significantly associated with poorer cancer specific survival (P<0.0001). Therefore we included C-reactive protein in addition to TNM stage, treatment and appetite loss in the multivariate survival model. TNM stage (HR 1.37, 95%CI 1.01-1.87, P=0.0426), treatment (HR 3.67, 95%CI 1.74-7.75, P=0.0006), appetite loss (HR 1.02, 95%CI 1.01-1.03, P<0.0001) and C-reactive protein (HR 2.15, 95%CI 1.21-3.83, P=0.0091) were independently associated with cancer specific survival.

The relationship between tumour site, clinico-pathological characteristics and quality of life in patients with gastro-oesophageal cancer is shown in Table 2.2. Compared with the gastric cancer patients, oesophageal cancer patients were older (P<0.01), had more dysphagia (P<0.001) and a poorer ECOG-ps (P<0.05). In terms of quality of life, compared with the gastric cancer patients, oesophageal cancer patients had higher emotional functioning (P<0.01), cognitive functioning (P<0.05), less nausea and vomiting (P<0.05).

The relationship between TNM stage and clinico-pathological and quality of life characteristics in patients with gastric-oesophageal cancer is shown in Table 2.3. With increasing TNM stage patients had greater weight loss (P<0.01) and were less likely to have had surgery (P<0.001). In terms of quality of life, with increasing TNM stage there was poorer physical functioning (P<0.05), emotional functioning (P<0.05), social functioning (P<0.01) and global quality of life (P<0.01). In terms of symptoms, with increasing TNM stage there was more fatigue (P<0.01), appetite loss (P<0.001), dyspnoea (P<0.05) and constipation (P<0.05).

The relationship between appetite loss, clinico-pathological characteristics and quality of life in patients with gastric-oesophageal cancer is shown in Table 2.4. Increasing appetite loss was associated with greater tumour length ($P<0.05$), TNM stage ($P<0.001$) and the operability of the tumour ($P<0.001$). Also, increasing appetite loss was associated with weight loss ($P<0.001$) and dysphagia ($P<0.001$). In terms of quality of life, increasing appetite loss was associated with poorer physical ($P<0.001$), role ($P<0.001$), emotional ($P<0.01$), cognitive ($P<0.01$), social ($P<0.001$) and global quality of life ($P<0.001$) functioning. In terms of symptoms, with increasing appetite loss there was more fatigue ($P<0.01$), nausea and vomiting ($P<0.001$), pain ($P<0.001$), sleep disturbance (<0.05) and constipation ($P<0.001$).

The relationship between systemic inflammatory response, as evidenced by elevated C-reactive protein, clinico-pathological and quality of life characteristics in patients with gastric-oesophageal cancer is shown in Table 2.5. An elevated C-reactive protein was associated with greater tumour length ($P<0.01$), advanced TNM stage ($P<0.01$) and the operability of the tumour ($P<0.001$) and a poorer ECOG-ps ($P<0.05$). In terms of quality of life, an elevated C-reactive protein was associated with poorer physical ($P<0.01$), role ($P<0.05$) and social ($P<0.05$) functioning. In terms of symptoms, with an elevated C-reactive protein was associated with more fatigue ($P<0.01$), pain ($P<0.05$) and appetite loss ($P<0.01$).

2.5 Discussion

In the present study tumour site was not associated with major differences in EORTC QLQ-C30 quality of life function or symptom scores. However, there were major differences in quality of life and symptom scores with increasing stage of disease. In particular, social functioning, fatigue, appetite loss and global quality of life were all impaired with increasing tumour stage.

As might be expected in view of these associations with tumour stage, the majority of quality of life and symptom scores predicted survival on univariate analysis. It was of interest, however, that appetite loss remained an independently significant prognostic factor even after adjustment for TNM stage and treatment. Furthermore, the predictive value of appetite loss was maintained even after adjustment for all other clinico-pathological variables and quality of life and symptom scores. Taken together the results of the present study highlight the importance of appetite loss as a presenting symptom in patients with gastro-oesophageal cancer.

Few studies have examined the relationship between aspects of quality of life and survival in patients with gastro-oesophageal cancer. The results of the present study are consistent with the report of Fang and co-workers (2003) who reported that appetite loss was associated with poorer survival in 110 patients with oesophageal cancer. However, the association was much weaker than that of the present study and was not significant in multivariate analysis. Furthermore, the follow-up period and the numbers of patients who died of their disease was not defined. Blazeby and colleagues (1995), in a smaller study of 59 patients with oesophageal cancer, also reported that appetite loss was associated with poorer survival (Blazeby et al., 1995).

The basis of the relationship between appetite loss and poorer cancer specific survival cannot be determined by the present cross sectional study. However, it was of interest that appetite loss was closely associated with nausea and vomiting, dysphagia and weight loss and therefore it may be that these symptoms result in appetite loss and the consequent loss of weight, which has long been recognised to impact on outcome (DeWys et al., 1980).

A number of workers have implicated the systemic inflammatory response in this process (Kotler, 2000; MacDonald, 2007). O'Gorman and co-workers (1998), in a cross sectional

study, showed that in addition to appetite loss and weight loss, the systemic inflammatory response was an important factor in determining patients' quality of life (EORTC QLQ-C30) in gastro-intestinal cancer patients (O'Gorman et al., 1998). Therefore, it is of interest that two recent studies have shown that the presence of a systemic inflammatory response, as evidenced by an elevated C-reactive protein, predicts survival in both operable (Crumley et al., 2006a) and inoperable (Crumley et al., 2006b) gastro-oesophageal cancer patients. In the present study C-reactive protein concentrations, at the time of quality of life assessment, were available in 94 (62%) patients. Consistent with previous work an elevated C-reactive protein concentration was associated with increased appetite loss and when included in the multivariate analysis, an elevated C-reactive protein concentration was independently associated with poorer cancer specific survival. However, even those patients without an elevated C-reactive protein concentration reported some appetite loss and the independent prognostic value of appetite loss remained, thus confirming the importance of appetite loss in the multifactorial nature of weight loss and poor outcome in these patients (MacDonald, 2007).

In summary, in patients with gastro-oesophageal cancer, routinely used prognostic factors are based predominantly on clinical and pathological findings. The present study highlights the importance of quality of life (EORTC QLQ-C30) measures, in particular appetite loss, as prognostic factors in these patients.

Table 2.1 The relationship between clinico-pathological characteristics, quality of life and cancer specific survival in patients with gastro-oesophageal cancer (n=152)

	Patients (n=152)	Univariate analysis HR (95% CI)	P-value	Multivariate analysis HR (95% CI)	P-value
Age:(<65/65-74/≥75)	66/56/30	1.46 (1.14-1.89)	0.0033		
Sex:(male/female)	104/48	0.84 (0.55-1.30)	0.4377		
Tumour type:(adeno/squam)	127/25	1.40 (0.83-2.36)	0.2016		
Tumour site:(oesoph/gastric)	70/82	0.88 (0.60-1.29)	0.5163		
Tumour length:(<5/510/>10cm)	60/70/12	2.37 (1.71-3.27)	<0.0001		
TNM stage:(I/II/III/IV)	28/46/34/41	2.29 (1.84-2.83)	<0.0001	1.65 (1.25-2.18)	<0.0004
Weight loss:(no/yes)	51/101	3.08 (1.94-4.89)	<0.0001		
Dysphagia score:(1/2/3/4/5)	81/23/32/15/1	1.37 (1.16-1.63)	0.0003		
ECOG:(0-1/2/3-4)	108/38/6	1.61 (1.14-2.27)	0.0069		
Treatment:(operable/inoperable)	69/83	8.12 (5.06-13.03)	<0.0001	5.29 (2.80-9.97)	<0.0001
EORTC QLQ-C30 (0-100)*	Median (range)				
Physical functioning	93 (66.7-100)	0.96 (0.94-0.98)	0.0001		
Role functioning	66.7 (0-100)	0.99 (0.99-1.00)	0.0006		
Emotional functioning	66.7 (0-100	1.00 (0.99-1.00)	0.1302		
Cognitive functioning	83.3 (0-100)	0.99 (0.98-0.99)	0.0051		
Social functioning	83.3 (0-100)	0.99 (0.98-0.99)	<0.0001		
Global quality of life	50 (0-100)	0.98 (0.97-0.99)	<0.0001		
Fatigue	33.3 (0-100)	1.02 (1.01-1.02)	<0.0001		
Nausea and vomiting	16.7 (0-100)	1.01 (1.00-1.02)	0.0067		
Pain	16.7 (0-100)	1.01 (1.01-1.02)	0.0002		
Dyspnoea	0 (0-100)	1.01 (1.01-1.02)	0.0001		
Sleep disturbance	33.3 (0-100)	1.00 (0.99-1.01)	0.1558		
Appetite loss	33.3 (0-100)	1.02 (1.02-1.03)	<0.0001	1.02 (1.01-1.03)	<0.0001
Constipation	33.3 (0-100)	1.01 (1.00-1.02)	0.0007		
Diarrhoea	0 (0-100)	1.00 (0.99-1.01)	0.9586		
Financial difficulty	0 (0-100)	1.01 (1.00-1.01)	0.0932		

Table 2.2 The relationship between tumour site, clinico-pathological characteristics and quality of life in patients with gastro-oesophageal cancer (n=152)

	Gastric (n=82)	Oesophageal (n=70)	P-value
Age:(<65 yrs/ 65-74yrs/≥75 yrs)	41/29/12	25/27/18	0.0041
Sex:(male/female)	53/29	51/19	0.279
Type:(squam/adeno)	1/81	24/46	<0.001
Tumour length:(<5cm/5-10cm/>10cm)	33/33/7	27/37/5	0.724
Tumour stage:(I/II/III/IV)	22/13/18/28	6/33/16/13	0.528
Dysphagia score:(1/2/3/4/5)	64/9/8/1/0	17/14/24/1	<0.001
Weight loss:(yes/no)	53/29	48/22	0.610
ECOG:(0-1/2/3-4)	64/17/1	44/21/5	0.018
Treatment:(operable/inoperable)	38/44	31/39	0.800
EORTC QLQ-C30 (0-100)	Median (range)	Median (range)	
Physical functioning	93.3 (66.7-100)	93.3 (66.7-100)	0.733
Role functioning	66.7 (0-100)	66.7 (0-100)	0.923
Emotional functioning	66.7 (0-100)	83.3 (0-100)	0.007
Cognitive functioning	83.3 (0-100)	83.3 (0-100)	0.038
Social functioning	83.3 (0-100)	75 (0-100)	0.964
Global quality of life	50 (0-100)	50 (0-100)	0.284
Fatigue	33.3 (0-100)	22.2 (0-100)	0.077
Nausea and vomiting	16.7 (0-100)	0 (0-100)	0.036
Pain	16.7 (0-100)	16.7 (0-100)	0.716
Dyspnoea	33.3 (0-100)	0 (0-100)	0.123
Sleep disturbance	33.3 (0-100)	33.3 (0-100)	0.360
Appetite loss	33.3 (0-100)	33.3 (0-100)	0.624
Constipation	33.3 (0-100)	33.3 (0-100)	0.031
Diarrhoea	0 (0-100)	0 (0-100)	0.802
Financial difficulty	0 (0-100)	0 (0-66.7)	0.098

Table 2.3 The relationship between TNM stage and clinico-pathological characteristics and quality of life in patients with gastro-oesophageal cancer (n=149)

	TNM I (n=28)	TNM II (n=46)	TNM III (n=34)	TNM IV (n=41)	P-value
Age:(<65 yrs/ 65-74yrs/≥75 yrs)	15/12/1	23/21/2	18/9/7	18/13/10	0.482
Sex:(male/female)	17/11	33/13	20/14	31/10	0.387
Tumour type:(squam/adeno)	2/26	13/33	6/28	4/37	0.576
Tumour site:(oesophagus/gastric)	6/22	33/13	16/18	13/28	0.528
Tumour length:(<5cm/5-10cm/>10cm)	19/7/0	21/22/3	10/19/3	8/22/6	<0.001
Weight loss:(yes/no)	14/14	29/17	23/11	34/7	0.004
Dysphagia score:(1/2/3/4/5)	22/3/3/0/0	20/10/9/7/0	14/5/9/5/1	23/5/10/3/0	0.130
ECOG:(0-1/2/3-4)	22/6/0	33/11/2	27/6/1	24/15/2	0.099
Treatment:(operable/inoperable)	25/3	26/20	15/19	1/40	<0.001
EORTC QLQ-C30 (0-100)	Median (range)	Median (range)	Median (range)	Median (range)	
Physical functioning	93.3 (73.3-100)	100 (66.7-100)	100 (73.3-100)	86.7 (66.7-100)	0.023
Role functioning	66.7 (0-100)	66.7 (0-100)	66.7 (0-100)	50 (0-100)	0.058
Emotional functioning	66.7 (8.3-100)	75 (25-100)	83.3 (0-100)	58.3 (0-100)	0.042
Cognitive functioning	83.3 (50-100)	83.3 (33.3-100)	83.3 (16.7-100)	75 (0-100)	0.042
Social functioning	100 (33.3-100)	83.3 (0-100)	66.7 (0-100)	50 (0-100)	0.002
Global quality of life	66.7 (8.3-100)	66.7 (0-100)	50 (16.7-100)	41.7 (0-100)	0.001
Fatigue	27.8 (0-66.7)	22.2 (0-88.9)	33.3 (0-100)	55.6 (0-100)	0.002
Nausea and vomiting	16.7 (0-100)	0 (0-100)	16.7 (0-100)	16.7 (0-100)	0.553
Pain	16.7 (0-66.7)	16.7 (0-100)	33.3 (0-100)	16.7 (0-100)	0.098
Dyspnoea	16.7 (0-100)	0 (0-100)	0 (0-100)	33.3 (0-100)	0.014
Sleep disturbance	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	66.7 (0-100)	0.689
Appetite loss	0 (0-100)	33.3 (0-100)	33.3 (0-100)	66.7 (0-100)	<0.001
Constipation	33.3 (0-66.7)	16.7 (0-100)	0 (0-100)	33.3 (0-100)	0.013
Diarrhoea	0 (0-100)	0 (0-100)	0 (0-33.3)	0 (0-66.7)	0.601
Financial difficulty	0 (0-66.7)	0 (0-100)	0 (0-66.7)	0 (0-100)	0.306

Table 2.4 The relationship between appetite loss, clinico-pathological characteristics and quality of life in patients with gastro-oesophageal cancer (n=152)

	Not at all (n=55)	A little (n=43)	Quite a bit (n=26)	Very much (n=28)	P-value
Age:(<65 yrs/ 65-74yrs/≥75 yrs)	27/18/10	18/15/10	8/15/3	13/8/7	0.540
Sex:(male/female)	43/12	26/17	15/11	20/8	0.312
Tumour type:(squam/adeno)	7/48	5/38	7/19	6/22	0.138
Tumour site:(oesophagus/gastric)	25/30	17/26	15/11	13/15	0.603
Tumour length:(<5cm/5-10cm/ >10cm)	27/20/4	18/21/2	9/15/2	6/14/4	0.016
TNM stage:(I/II/III/IV)	16/17/13/8	8/17/9/9	3/8/7/8	1/4/5/16	<0.001
Weight loss:(yes/no)	26/29	27/16	22/4	26/2	<0.001
Dysphagia score:(1/2/3/4/5)	37/10/6/2/0	24/6/10/3/0	9/4/9/3/1	11/3/7/7/0	<0.001
ECOG:(0-1/2/3-4)	39/14/2	34/8/1	18/7/1	17/9/2	0.281
Treatment:(operable/inoperable)	35/20	20/23	11/15	3/25	<0.001
EORTC QLQ-C30 (0-100)	Median (range)	Median (range)	Median (range)	Median (range)	
Physical functioning	100 (73.3-100)	100 (73.3-100)	86.7 (66.7-100)	80 (66.7-100)	<0.001
Role functioning	100 (0-100)	66.7 (0-100)	58.3 (0-100)	33.3 (0-100)	<0.001
Emotional functioning	75 (73.3-100)	66.7 (0-100)	83.3 (8.3-100)	58.3 (0-96.7)	0.003
Cognitive functioning	83.3 (16.7-100)	83.3 (0-100)	83.3 (50-100)	66.7(0-100)	0.001
Social functioning	100 (0-100)	83.3 (0-100)	66.7 (0-100)	50 (0-100)	<0.001
Global quality of life	66.7 (16.7-100)	50 (0-100)	45.8(16.7-100)	29.1 (0-66.7)	<0.001
Fatigue	11.1 (0-88.9)	33.3 (0-83.2)	33.3 (0-100)	77.7 (22.2-100)	<0.001
Nausea and vomiting	0 (0-100)	16.7 (0-100)	16.7 (0-100)	41.7 (0-100)	<0.001
Pain	16.7 (0-100)	16.7 (0-83.3)	33.3 (0-100)	25 (0-100)	<0.001
Dyspnoea	0 (0-66.7)	0 (0-100)	0 (0-100)	50 (0-100)	<0.001
Sleep disturbance	0 (0-100)	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	0.044
Constipation	0 (0-100)	33.3 (0-100)	33.3 (0-100)	66.7 (0-100)	<0.001
Diarrhoea	0 (0-100)	0 (0-66.7)	0 (0-100)	0 (0-100)	0.512
Financial difficulty	0 (0-66.7)	0 (0-100)	0 (0-100)	0 (0-100)	0.296

Table 2.5 The relationship between systemic inflammatory response, as evidenced by elevated C-reactive protein, clinico-pathological and quality of life characteristics in patients with gastric-oesophageal cancer (n=94)

	CRP≤10 (n=57)	CRP>10 (n=37)	P value
Age:(<65 yrs/65-74yrs/≥75yrs)	34/16/7	18/12/7	0.258
Sex:(male/female)	38/19	27/10	0.520
Tumour type:(adeno/squam)	48/9	30/7	0.695
Tumour site:(oesoph/gastric)	23/34	20/17	0.195
Tumour length:(<5cm/5-10cm/>10cm)	35/17/2	11/20/3	0.005
Tumour stage:(I/II/III/IV)	15/20/13/8	4/10/10/13	0.006
Weight loss:(yes/no)	31/16	27/10	0.072
Dysphagia score:(1/2/3/4/5)	29/14/11/3/0	18/6/10/2/1	0.390
ECOG:(0-1/2/3-4)	52/5/0	27/10/0	0.019
Treatment:(operable/inoperable)	40/17	8/29	<0.001
EORTC:(0-100)	Median (range)	Median (range)	
Physical functioning	100 (73-100)	86.7 (66.7-100)	0.001
Role functioning	66.7 (0-100)	66.7 (0-100)	0.040
Emotional functioning	66.7 (0-100)	70.8 (0-100)	0.343
Cognitive functioning	83.3 (16.7-100)	83.3 (33.3-100)	0.875
Social functioning	83.3 (0-100)	66.7 (0-100)	0.045
Global quality of life	66.7 (0-100)	50 (0-100)	0.068
Fatigue	33.3 (0-100)	44.4 (0-88.9)	0.003
Nausea and vomiting	16.7 (0-100)	16.7 (0-100)	0.152
Pain	16.7 (0-100)	16.7 (0-100)	0.040
Appetite loss	33.3 (0-100)	66.7 (0-100)	0.001
Dyspnoea	0 (0-100)	0 (0-100)	0.055
Sleep disturbance	33.3 (0-100)	33.3 (0-100)	0.518
Constipation	0 (0-100)	33.3 (0-100)	0.142
Diarrhoea	0 (0-66.7)	0 (0-100)	0.304
Financial difficulty	0 (0-100)	0 (0-100)	0.362

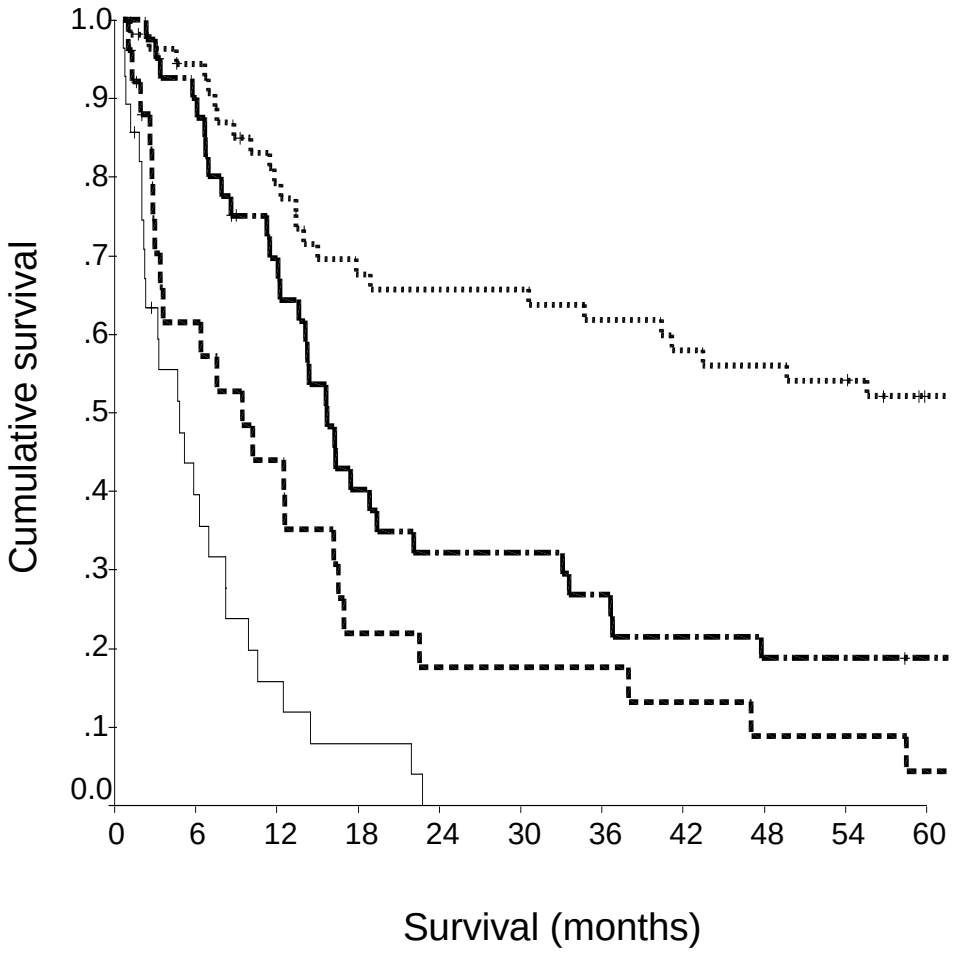

Figure 2.1 The relationship between appetite loss (None, A little, Quite a bit, Very much, from top to bottom) and cancer specific survival in patients with gastro-oesophageal cancer.

Chapter 3

3. A prospective longitudinal study of the impact of treatment on quality of life (EORTC QLQ-C30) in patients with gastric and oesophageal cancer

3.1 Introduction

In the United Kingdom gastric and oesophageal cancer are the sixth and fifth most common cause of cancer respectively and each year, there are approximately 17,000 new cases diagnosed. Combined gastro-oesophageal cancer is the third commonest cause of cancer death in the UK with over 13,000 deaths attributable to the disease. Overall survival is poor with the majority of patients presenting with advanced, inoperable disease and less than 15% surviving 5 years (Cancerstats, 2004). Although there has been improvements in survival following surgery long term outcome is still poor. Even in those who undergo potentially curative resection for gastric cancer, less than 30% survive 5 years (Hundahl et al., 2000). Survival for oesophageal cancer who undergo potentially curative resection has recently been reported to be 40% (Stein et al., 2005).

Therefore, although surgery confers the greatest chance of long-term cure it should also aim to maintain long-term quality of life. In the last decade or so there has been considerable interest in including some measure of quality of life in the assessment and follow up of patients with cancer and their continuing aftercare, as it provides information on the patient's perception of their health and the effectiveness and side effects of their treatment.

A number of workers have reported the importance of quality of life as an outcome measure, in addition to survival, as debilitating problems with nutrition, pain and fatigue are common after surgery. Furthermore, in patients undergoing palliative treatment symptom relief must be weighed against treatment toxicity and therefore recording ongoing quality of life in these patients is of considerable importance (Aaronson et al., 1993; Vickery et al., 2000).

We have recently reported that in an unselected cohort of patients with gastro-oesophageal cancer (McKernan et al., 2008) that appetite loss was a significant prognostic factor even after adjustment for TNM stage and the systemic inflammatory response. Furthermore, when the baseline relationship between appetite loss and the other quality of life functions or symptom scores were examined, it was clear that appetite loss was closely related to

these measures, in particular; appetite loss was closely associated with global quality of life, fatigue and dysphagia. However, the effect of treatment on aspects of quality of life including appetite loss has rarely been examined.

A study by Thybusch-Bernhardt and co-workers (1999) reported that in patients (n=62) undergoing gastric surgery, comparing total gastrectomy with extended gastrectomy, the global quality of life during the first 12 months was poor; thereafter there were no significant differences over the following 2 years (Thybusch-Bernhardt et al., 1999). However, in their study there were no baseline pre-operative quality of life measurements and therefore it is unclear if the patients already had underlying poor quality of life prior to surgery.

A later study by Blazeby and co-workers (2000) reported similar results in patients (n=55) with oesophageal cancer. They reported that six weeks after oesophagectomy, patients reported worse functional, symptom, and global quality of life scores than before treatment. Furthermore, it was reported that quality of life scores returned to preoperative levels within 9 months, dysphagia improved after surgery and the improvement was maintained until death or for the duration of the study. In the same study it was reported that there was gradual deterioration in most aspects of quality of life until death in patients (n=37) undergoing palliative treatment (Blazeby et al., 2000).

Bamias and colleagues (1996) reported that in oesophageal cancer patients (n=235) receiving palliative chemotherapy, the quality of life assessments showed a transient deterioration in physical and role functioning and provided good symptomatic control of pain (Bamias et al., 1996).

Glimelius and co-workers (1997) reported that in a randomised trial comparing chemotherapy and best supportive care in patients (n=55) with advanced gastric cancer, chemotherapy appeared to improve quality of life compared with patients in the supportive care group at the four month evaluation (Glimelius et al., 1997).

The aim of the present longitudinal study was to examine the effect of treatment (surgery, oncological treatment or supportive care) on quality of life (EORTC QLQ-C30) in patients with gastric and oesophageal cancer.

3.2 Patients and methods

Patients

Patients presenting with adenocarcinoma or squamous carcinoma of the gastric or oesophageal tract at the Royal Infirmary and Southern General Hospital, Glasgow between November 1997 and December 2002 (n=160) participated in a quality of life study, using the EORTC QLQ-C30 core questionnaire.

The extent of tumour spread was recorded using the UICC TNM 5th edition classification, as this was the edition in use at the commencement of the study (Sobin and Wittekind, 1997). Tumours around the gastro-oesophageal junction were further classified according to tumour site, using the Siewert system; type 1 and 2 lesions of the gastro-oesophageal junction were designated as cancers of the oesophagus. Type 3 tumours of the cardia were designated as gastric cancers (Siewert and Stein, 1998).

For gastric cancers, tumour node metastasis (TNM) stage I–III tumours were considered to be amenable to curative surgical resection. For oesophageal cancers, TNM stage I–III tumours, excluding T4, were deemed to be amenable to curative surgical resection.

Patients who had TNM stage I and II disease but their performance status and significant co-morbid disease was poor were not deemed suitable for surgery and went forward for active palliative oncological treatment or supportive care, which included endoscopic input. There were 160 patients included in the study, 35 patients were suitable for gastrectomy and 34 patients were suitable for oesophageactomy. Due to stage of disease or co-morbid disease, 91 patients were inoperable of which 38 received chemotherapy, radiotherapy or combined treatment, the further 53 patients received supportive care which may have included therapeutic endoscopic input.

The study was approved by the Research Ethics Committee of the Royal Infirmary and Southern General Hospital, Glasgow.

Methods

Clinical and demographic variables were recorded at the patient's initial presentation and included age, sex, tumour type (only adenocarcinoma or squamous cancers were included in the study), site and length, UICC TNM stage, ECOG performance status, weight loss, dysphagia and treatment.

Following diagnosis but prior to treatment the lead clinician approached patients as to whether they would participate in a study to examine their quality of life. If they gave informed consent they were given the EORTC QLQ-C30 questionnaire to complete.

Different aspects of quality of life were assessed using this cancer specific 30-item questionnaire, which has six functional scales (physical, role, emotional, cognitive, social, global health status) and several questions relating to a range of physical symptoms (Aaronson et al, 1993). Patients marked to what extent each statement applied to them. In the present study a number of patients (less than 10 patients) were excluded because they were unlikely to understand the language, had brain metastases, delirium or confusion. Neither age nor performance status were considered when offering the patient questionnaire. Patients were not randomised.

Questionnaires were completed at baseline 3, 6, 9 and 12 months, then 6 monthly until year 4 and the last questionnaire was at the end of year 5. Following the baseline assessment, questionnaires were posted out to patients in a self addressed, stamped envelope, with covering letter to re-iterate the reason for the assessment, or were conducted whilst the patient was attending a clinic or endoscopy appointment. The dysphagia score was recorded at time of the patients' routine clinic or endoscopic assessment.

As a result of loss of patients to follow-up, predominantly due to death, those patients who underwent surgery had questionnaires at baseline, 3 and 6 months and years 1, 2, 3 and 4 analysed. In those patients who received oncological treatment or supportive care had questionnaires at baseline, 3 and 6 months analysed.

3.3 Statistics

Data are presented as the median and range. Scoring algorithms produced by the EORTC Quality of Life Study Group were used. The sum of items in each category is added and the total divided by the number of questions in the category. A linear transformation is then undertaken to convert this to a percentage scale with a higher score representing a higher response level. Thus a high score for functional scale represents a high/healthy level of functioning. A high score for the global health status/quality of life represents a high quality of life. In contrast, a high score for the symptom scale represents a higher level of symptoms/ problems (Aaronson et al., 1993).

Data from different patient groups were tested for statistical significance using ANOVA (Kruskal–Wallis) and the Mann-Whitney U-test was used to compare two patient groups. Analysis of data from different time periods within each group were tested for statistical significance using the Freidman test, and when appropriate comparisons of data from different time periods were carried out using the Wilcoxon signed rank test. Analysis was performed using SPSS software (SPSS Inc, Chicago, IL, USA).

3.4 Results

The minimum follow up period was 54 months or until date of death, the median follow up for survivors was 81 months, one patient was lost to follow up and one patient withdrew from the study. During this period 112 (70%) patients died from their disease and 18 (11%) died from co-morbid disease. Deaths and patients who did not return questionnaires at each time point have been reported in each table.

The relationship between clinico-pathological and quality of life (EORTC QLQ-C30) characteristics in patients with operable gastric and oesophageal cancer and inoperable gastric and oesophageal cancer are shown in Table 3.1.

At study entry, there were significant differences in age ($P<0.001$), sex ($P<0.01$), tumour type ($P<0.01$), tumour length ($P<0.001$), TNM stage ($P<0.001$), dysphagia score ($P<0.001$), weight loss ($P<0.001$) and performance status ($P<0.001$) between the 4 groups. With reference to quality of life, there were significant differences in physical functioning ($P<0.01$), role functioning ($P<0.01$), cognitive functioning ($P<0.05$), social functioning ($P<0.05$), global quality of life ($P<0.01$), fatigue ($P<0.001$), nausea and vomiting ($P<0.01$), appetite loss ($P<0.001$) and dyspnoea ($P<0.001$) between the 4 groups.

Patients undergoing gastrectomy or oesophagectomy were more likely to be younger ($P<0.01$) had less advanced TNM stage ($P<0.001$) and had less dysphagia ($P<0.01$) and weight loss ($P<0.001$) and better performance status ($P<0.001$) compared with those patients who were inoperable or receiving supportive care. Furthermore, they reported better physical functioning ($P<0.01$), role functioning ($P<0.01$), social functioning ($P<0.01$) and global quality life ($P<0.01$) and less fatigue ($P<0.01$), nausea and vomiting ($P<0.05$), appetite loss ($P<0.001$) and dyspnoea ($P<0.01$) compared with those patients who were inoperable or receiving supportive care.

In those patients amenable to surgery, the patients undergoing oesophagectomy had fewer females ($P<0.05$), more adenocarcinomas ($P<0.001$), more dysphagia ($P<0.001$) but better emotional ($P<0.05$) and cognitive functioning ($P<0.05$) and had better symptom scores for fatigue ($P<0.01$), nausea/vomiting ($P<0.01$) and dyspnoea ($P<0.05$) compared with patients undergoing gastrectomy. In those patients deemed inoperable, patients who received supportive care were more likely to be older ($P<0.001$), female ($P<0.01$), and had poorer

performance status (P<0.001) than patients who were offered oncological treatment. Also higher symptom scores for fatigue (P<0.05) was seen in the patients receiving supportive care compared with those patients receiving oncological treatment.

The longitudinal measurement at baseline, 3 and 6 months, 1, 2, 3 and 4 years, of the dysphagia score and quality of life EORTC QLQ-C30 in patients who underwent a gastrectomy are shown in Table 3.2. Social functioning (P<0.01) was significantly poorer following surgery and persisted throughout the follow-up period. Also the symptom score for pain (P<0.05) increased following surgery and failed to return to pre-treatment levels (Figures 3.1-3.2).

The longitudinal measurement at baseline, 3 and 6 months, 1, 2, 3 and 4 years, of the dysphagia score and quality of life EORTC QLQ-C30 in patients who underwent oesophagectomy are shown in Table 3.3. Physical (P<0.001), role (P<0.001) and social (P<0.01) functioning and global quality of life (P<0.05) were significantly poorer following surgery and persisted throughout most of the follow-up period, gradually returning to near baseline levels after 2 years. Following oesophagectomy dysphagia (P<0.001) improved, fatigue (P<0.001) increased following surgery and failed to return to pre-treatment levels. However, following surgery there was a transient increase in nausea and vomiting (P<0.05), dyspnoea (P<0.01) and diarrhoea (P<0.01), which appeared to resolve slowly during follow-up (Figures 3.3-3.11).

The longitudinal measurement at baseline, 3 and 6 months, of the dysphagia score and quality of life EORTC QLQ-C30 in patients who had oncological treatment are shown in Table 3.4. Dysphagia (P<0.01) resolved gradually, physical functioning (P<0.001) had a transient change at 3 months and fatigue (P<0.01) increased during the follow-up period (Figures 3.12-3.14).

The longitudinal measurement at baseline, 3 and 6 months, of the dysphagia score and quality of life EORTC QLQ-C30 in patients who were offered supportive care are shown in Table 3.5. Dysphagia (P<0.05) and cognitive functioning (P<0.05) were shown to be significant during the follow-up period (Figures 3.15-3.16).

3.5 Discussion

In the present cross sectional and longitudinal study, patients who underwent surgery had, at study entry, better global quality life including better physical and role functioning and less fatigue and appetite loss compared with those patients who did not receive surgery. Furthermore, the effect of oesophageal surgery on global quality of life appeared to be more profound and persistent, in particular patients went on to have poorer physical and role functioning and more fatigue. In contrast, in patients with inoperable disease, the poor quality of life measures at study entry remained poor on follow-up whether patients received oncological input or supportive care. Therefore, these longitudinal data from an unselected cohort of patients with gastric and oesophageal cancer further inform the treatment decision making process. In particular, it is clear that oesophageal surgery has a profound and long lasting effect on quality of life.

We have previously reported (McKernan et al., 2008) that appetite loss at study entry was independently associated with poorer survival and associated with other quality of life parameters such as global quality of life, fatigue and dysphagia. In the present longitudinal study appetite loss did not appear to be significantly altered on follow-up or on whether patients had gastric or oesophageal cancer or were operable or not. Even in those patients with oesophagectomy who reported an improvement in their dysphagia there was only a transient alteration in appetite loss. Therefore, it would appear that the degree of appetite loss is determined at an early stage in the disease process and is not related simply to obstruction of the gastro-oesophageal tract.

The results of the present study are consistent with the previous studies of Thybusch-Bernhardt and co-workers (1999) in gastric cancer patients. Similarly the results of the present study are consistent with those of Viklund and co-workers (2006) who compared oesophageal cancer patients (n=282) undergoing resection to the general population and reported that, at 6 months following oesophagectomy, patients had significantly worse quality of life including most functioning and symptom scales (Viklund et al., 2006). However, similar to the Thybusch-Bernhardt study there were no baseline pre-operative quality of life measurements recorded.

In the present study there were persistent reductions in physical, role and social functioning and fatigue in oesophageactomy patients up to 4 years following surgery. There are, to our

knowledge, no studies which have examined the effect of surgery on quality of life beyond 3 years. Previous studies by (Blazeby et al., 2000 and 2005; Reynolds et al., 2006) in oesophageal cancer patients have reported transient changes in dysphagia and some functional scales and global quality of life in the first year following oesophagectomy. Blazeby and co-workers also reported that patients who died within 2 years of surgery did not appear to regain their quality of life.

In the present study, in the oncological treatment and supportive care patient groups most function and symptom scales were poor at study entry and remained poor during the follow-up period. However, in a larger palliative cohort of oesophageal cancer patients (n=209) receiving brachytherapy or stent Homs and co-workers (2004) reported that there was a deterioration in all functional scales and an increase in symptom scales particularly pain.

In summary, the results of the present study suggest that surgery for oesophageal cancer, compared with that for gastric cancer, has a more profound and long lasting effect on quality of life, especially physical, role and social functioning and fatigue symptoms. In contrast, patients with inoperable gastro-oesophageal cancer have poor quality of life and oncological treatment or supportive care appears to have little further impact on their quality of life.

Table 3.1: The relationship between clinico-pathological and quality of life (EORTC QLQ-C30) characteristics in patients with operable gastric and oesophageal cancer and inoperable gastric and oesophageal cancer

	Operable Gastrectomy (n=35)	Operable Oesophagectomy (n=34)	Inoperable Oncology (n=38)	Inoperable Supportive care (n=53)	P value
Age:(<65yrs/65-74yrs/≥75yrs)	16/7/2	21/10/3	22/13/3	9/22/22***	<0.001
Sex:(male/female)	19/16	27/7*	33/5	32/21**	0.005
Type:(squam/adeno)	0/35	23/11***	11/27	7/46	0.001
Tumour length:(<5cm/5-10cm/>10cm)	20/11/1	22/11/0	6/25/7	14/27/6	<0.001
Tumour stage:(I-II/III/IV)	29/4/1	22/11/0	11/12/13	15/9/28	<0.001
Dysphagia score:(1/2/3/4/5)	30/3/2/0/0	12/10/9/3/0***	15/8/9/5/1	26/4/14/9/0	<0.001
Weight loss:(yes/no)	18/17	15/19	32/6	43/10	<0.001
ECOG:(0-1/2/3-4)	30/5/0	29/5/0	27/11/0	23/24/6***	<0.001
EORTC: QLQ-C30 (0-100)					
Physical functioning	100 (73.3-100)	100 (73.3-100)	86.7 (66.7-100)	86.7 (66.7-100)	0.006
Role functioning	66.7 (0-100)	100 (0-100)	66.7 (0-100)	50 (0-100)	0.003
Emotional functioning	66.7 (8.3-100)	83.3 (33.3-100)*	75 (0-100)	66.7 (0-100)	0.191
Cognitive functioning	83.3 (16.7-100)	100 (50.100)*	83.3 (16.7-100)	83.3 (0-100)	0.037
Social functioning	91.6 (0-100)	100 (0-100)	66.7 (0-100)	66.7 (0-100)	0.013
Global quality of life	50 (8.3-100)	66.7 (25-100)	50 (0-100)	50 (0-100)	0.002
Fatigue	33.3 (0-83.2)	11.1 (0-88.9)**	33.3 (0-100)	44.4 (0-100) *	<0.001
Nausea and vomiting	16.7 (0-100)	0 (0-50)**	16.7 (0-100)	16.7 (0-100)	0.002
Pain	16.7 (0-83.3)	16.7 (0-66.7)	16.7 (0-100)	16.7 (0-100)	0.444
Appetite loss	33.3 (0-100)	0 (0-100)	33.3 (0-100)	66.7 (0-100)	<0.001
Dyspnoea	0 (0-100)	0 (0-66.7) *	33.3 (0-100)	33.3 (0-100)	<0.001
Sleep disturbance	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	0.715
Constipation	0 (0-100)	0 (0-100)	33.3 (0-100)	33.3 (0-100)	0.104
Diarrhoea	0 (0-100)	0 (0-33.3)	0 (0-100)	0 (0-100)	0.881
Financial difficulty	0 (0-100)	0 (0-100)	0 (0-100)	0 (0-100)	0.444

* p<0.05, ** p<0.01, ***p<0.001 compared with gastrectomy

* p<0.05, ** p<0.01, ***p<0.001 compared with inoperable oncology

Table 3.2 Longitudinal dysphagia score and quality of life EORTC QLQ-C30 in patients after gastrectomy at baseline, 3 and 6 months, 1, 2, 3 and 4 years.

	Baseline (n=35)	3 month (n=28)[a]	6 month (n=26)[b]	1 year (n=24)[c]	2 year (n=21)[d]	3 year (n=15)[e]	4 year (n=15)[f]	P- value
Dysphagia score (1-5)	1 (1-3)	1 (1-3)	1 (1-2)	1 (1-2)	1 (1-2)	1 (1-3)	1 (1)	0.228
EORTC:(0-100)								
Physical functioning	100 (73.3-100)	86.7 (66.7-100)	80 (66.7-100)	86.7 (66.7-100)	80 (60-100)	86.7 (66.7-100)	86.7 (73.3-100)	0.822
Role functioning	66.7 (0-100)	41.6 (0-100)	41.6 (0-100)	58.3 (0-100)	50 (0-100)	50 (0-100)	33.3 (16.7-100)	0.253
Emotional functioning	66.7 (8.3-100)	66.7 (0-100)	70.8 (16.7-100)	50 (0-100)	66.7 (8.3-100)	83.3 (8.3-100)	66.7 (0-100)	0.787
Cognitive functioning	83.3(16.7-100)	83.3 (0-100)	75 (16.7-100)	58.3 (0-100)	66.7 (16.7-100)	83.3 (16.7-100)	66.7 (16.7-100)	0.112
Social functioning	91.6 (0-100)	50 (0-100)**	66.7 (0-100)*	66.7 (0-100)***	66.7 (0-100)**	66.7 (16.7-100) [n/s]	50 (0-100)**	0.008
Global quality of life	50 (8.3-100)	50 (0-100)	58.3 (16.7-100)	50 (0-83.3)	58.3 (0-83.3)	50 (0-100)	50 (8.3-75)	0.541
Fatigue	33.3 (0-83.2)	50 (0-100)	50 (0-100)	44.4 (0-100)	38.3 (0-100)	44.4 (0-77.8)	33.3 (11.1-100)	0.513
Nausea and vomiting	16.7 (0-100)	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	16.7 (0-100)	16.7 (0-100)	33.3 (0-83.3)	0.098
Pain	16.7 (0-88.3)	33.3 (0-100)**	33.3 (0-100)*	33.3 (0-100)**	33.3 (0-83.3)*	33.3 (0-83.3)**	50 (0-100)**	0.021
Appetite loss	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	0.260
Dyspnoea	0 (0-100)	33.3 (0-100)	16.5 (0-100)	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	0.350
Sleep disturbance	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	66.7 (0-100)	33.3 (0-100)	33.3 (0-100)	66.7 (0-100)	0.718
Constipation	0 (0-100)	0 (0-100)	0 (0-33.3)	0 (0-66.7)*	0 (0-33.3)	0 (0-100)	0 (0-33.3)	0.473
Diarrhoea	0 (0-100)	33.3 (0-100)	33.3 (0-100)	0 (0-66.7)	0 (0-100)	0 (0-100)	33.3 (0-100)	0.306
Financial difficulty	0 (0-100)	33.3 (0-100)	0 (0-100)	0 (0-100)	33.3 (0-100)	33.3 (0-66.7)	0 (0-100)	0.276

a. 7 not returned
b. 1 too ill to complete questionnaire, 8 not returned
c. 2 patients died, 5 too ill to complete questionnaire, 4 not returned
d. 8 further patients died, 4 not returned
e. 2 further patients died, 1 not returned
f. 3 further patients died, 5 not returned

* $p<0.05$, ** $p<0.01$, ***$p<0.001$ compared with baseline

Table 3.3 Longitudinal dysphagia score and quality of life EORTC QLQ-C30 in patients after oesophagectomy at baseline, 3 and 6 months, 1, 2, 3 and 4 years.

	Baseline (n=34)	3 month (n=25)[a]	6 month (n=23)[b]	1 year (n=23)[c]	2 year (n=19)[d]	3 year (n=15)[e]	4 year (n=14)[f]	P-value
Dysphagia score (1-5)	2 (1-4)	2 (1-3)*	2 (1-3)**	1 (1-3)**	1 (1)**	1 (1)**	1 (1)**	<0.001
EORTC:(0-100)								
Physical functioning	100 (73.3-100)	86.7 (53.3-100)***	86.7 (66.7-100)***	86.7 (66.7-100)**	93.3 (73.3-100)*	93.3 (73.3-100)*	93.3 (73.3-100)*	<0.001
Role functioning	100 (0-100)	33.3 (0-100)**	33.3 (0-100)**	66.7 (0-100)[n/s]	66.7 (0-100)[n/s]	83.3 (0-100)[n/s]	91.7 (0-100)*	<0.001
Emotional functioning	83.3 (33.3-100)	83.3 (16.7-100)	83.3 (0-100)	91.7 (25-100)	91.7 (0-100)	100 (0-100)	95.8 (0-100)	0.447
Cognitive functioning	100 (50-100)	83.3 (50-100)	91.7 (0-100)	100 (33.3-100)	100 (33.3-100)	83.3 (0-100)	100 (0-100)	0.523
Social functioning	100 (0-100)	41.7 (0-100)***	66.7 (0-100)**	75 (25-100)*	66.7 (0-100)*	83.3 (0-100)*	91.7 (0-100)*	0.002
Global quality of life	66.7 (25-100)	58.3 (16.7-91.7)**	54.1 (0-91.7)**	66.7 (33.3-100)[n/s]	75 (33.3-100)[n/s]	66.7 (33.3-100)[n/s]	75 (33.3-100)[n/s]	0.033
Fatigue	11.1 (0-88.9)	33.3 (0-88.9)***	33.3 (0-100)***	33.3 (0-88.9)**	33.3 (0-100)**	33.3 (0-77.8)**	33.3 (0-88.9)**	<0.001
Nausea and vomiting	0 (0-50)	16.7 (0-100)**	16.7 (0-100)**	16.7 (0-66.7)[n/s]	0 (0-100)[n/s]	0 (0-66.7)[n/s]	0 (0-83.3)[n/s]	0.018
Pain	16.7 (0-66.7)	33.3 (0-100)	33.3 (0-100)	16.7 (0-100)	33.3 (0-100)	16.7 (0-100)	8.3 (0-83.3)	0.638
Appetite loss	0 (0-100)	33.3 (0-100)	33.3 (0-100)	0 (0-66.7)	0 (0-100)	0 (0-66.7)	0 (0-66.7)	0.182
Dyspnoea	0 (0-66.7)	33.3 (0-100)***	33.3 (0-100)**	33.3 (0-100)**	33.3.(0-100)**	0 (0-100)*	16.7 (0-100)*	0.009
Sleep disturbance	33.3 (0-100)	33.3 (0-100)	50 (0-100)	0 (0-100)	33.3 (0-100)	0 (0-100)	0 (0-100)	0.790
Constipation	0 (0-66.7)	0 (0-100)	0 (0-100)	0 (0-100)	0 (0-100)	0 (0-33.3)	0 (0-100)	0.893
Diarrhoea	0 (0-33.3)	33.3 (0-100)**	33.3 (0-100)**	0 (0-66.7)**	0 (0-66.7)[n/s]	33.3 (0-66.7)[n/s]	0 (0-33.3)[n/s]	0.003
Financial difficulty	0 (0-100)	16.7 (0-100)	33.3 (0-100)	0 (0-100)	0 (0-100)	0 (0-100)	0 (0-100)	0.103

a. 3 patients died, 2 too ill to complete questionnaire, 4 not returned
b. 1 further patient died, 1 too ill to complete questionnaire, 6 not returned
c. 4 further patients died, 1 too ill to complete questionnaire, 2 not returned
d. 5 further patients died, 2 not returned
e. 3 further patients died, 1 too ill to complete questionnaire, 2 not returned
f. 1 further patient died, 1 too ill to complete questionnaire, 2 not returned

* $p<0.05$, ** $p<0.01$, ***$p<0.001$ compared with baseline

Table 3.4 Longitudinal dysphagia score and quality of life EORTC QLQ-C30 in patients with gastro-oesophageal cancer receiving oncological treatment at baseline, 3 and 6 months.

	Baseline (n=38)	3 month (n=31)[a]	6 month (n=15)[b]	P-value
Dysphagia (1-5)	1 (1-5)	1 (1-2)*	1 (1-2)**	0.007
EORTC:(0-100)				
Physical functioning	86.7 (66.7-100)	80 (66.7-100)***	86.7 (66.7-100)**	<0.001
Role functioning	66.7 (0-100)	33.3 (0-100)	66.7 (0-100)	0.191
Emotional functioning	75 (0-100)	75 (25-100)	91.7 (0-100)	0.846
Cognitive functioning	83.3 (16.7-100)	66.7 (16.7-100)	50 (16.7-100)	0.052
Social functioning	66.7 (0-100)	66.7 (0-100)	66.7 (0-100)	0.281
Global quality of life	50 (0-100)	50 (0-83.3)	50 (0-91.7)	0.813
Fatigue	33.3 (0-100)	50 (0-100)**	55.6 (11.1-100)*	0.005
Nausea and vomiting	16.7 (0-100)	16.7 (0-100)	16.7 (0-66.7)	0.756
Pain	16.7 (0-100)	33.3-(0-100)	33.3-(0-100)	0.102
Appetite loss	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	0.614
Dyspnoea	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	0.091
Sleep disturbance	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	0.223
Constipation	33.3 (0-100)	33.3 (0-100)	0 (0-100)	0.784
Diarrhoea	0 (0-100)	0 (0-66.7)	0 (0-66.7)	0.646
Financial difficulty	0 (0-100)	16.7 (0-100)	33.3 (0-100)	0.507

a. 6 patients died, 1 too ill to complete questionnaire,
b. 6 further patients died, 6 too ill to complete questionnaire, 5 not returned

* $p<0.05$, ** $p<0.01$, ***$p<0.001$ compared with baseline

Table 3.5 Longitudinal dysphagia score and quality of life EORTC QLQ-C30 in patients with gastro-oesophageal cancer receiving supportive care at baseline, 3 and 6 months.

	Baseline (n=53)	3 month (n=23)[a]	6 month (n13)[b]	P-value
Dysphagia (1-5)	1 (1-4)	1 (1-3)**	1 (1-4)*	0.025
EORTC:(0-100)				
Physical functioning	86.7 (66.7-100)	80 (66.7-100)	80 (66.7-100)	0.214
Role functioning	50 (0-100)	41.7 (0-100)	33.3 (0-100)	0.562
Emotional functioning	66.7 (0-100)	66.7 (0-100)	66.7 (0-100)	0.337
Cognitive functioning	83.3 (0-100)	83.3 (33.3-100)[n/s]	83.3 (0-100) [n/s]	0.050
Social functioning	66.7 (0-100)	50 (0-100)	66.7 (0-100)	0.717
Global quality of life	50 (0-100)	50 (0-83.3)	50 (0-83.3)	0.590
Fatigue	44.4 (0-100)	61.1 (0-100)	66.7 (11.1-100)	0.500
Nausea and vomiting	16.7 (0-100)	16.7 (0-66.7)	0 (0-100)	0.508
Pain	16.7 (0-100)	33.3-(0-100)	33.3-(0-100)	0.519
Appetite loss	66.7 (0-100)	33.3 (0-100)	33.3 (0-100)	0.368
Dyspnoea	33.3 (0-100)	66.7 (0-100)	66.7 (0-100)	0.121
Sleep disturbance	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	0.394
Constipation	33.3 (0-100)	33.3 (0-100)	33.3 (0-100)	0.834
Diarrhoea	0 (0-100)	0 (0-66.7)	0 (0-100)	0.368
Financial difficulty	0 (0-100)	0 (0-100)	0 (0-100)	0.779

a. 19 patients died, 6 too ill to complete questionnaire, 5 not returned
b. 8 further patients died, 6 too ill to complete questionnaire, 7 not returned

* $p<0.05$, ** $p<0.01$, ***$p<0.001$ compared with baseline

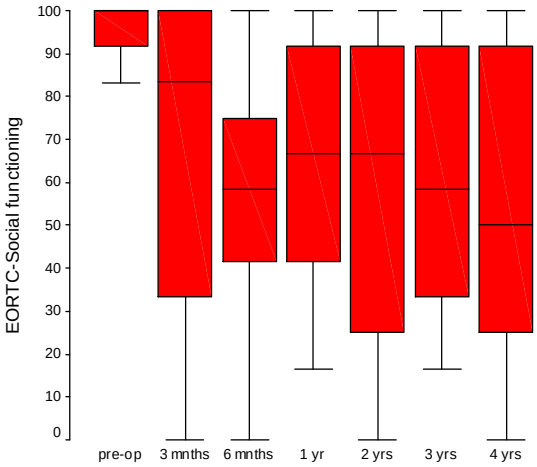

Figure 3.1 Changes in quality of life following gastrectomy; social functioning

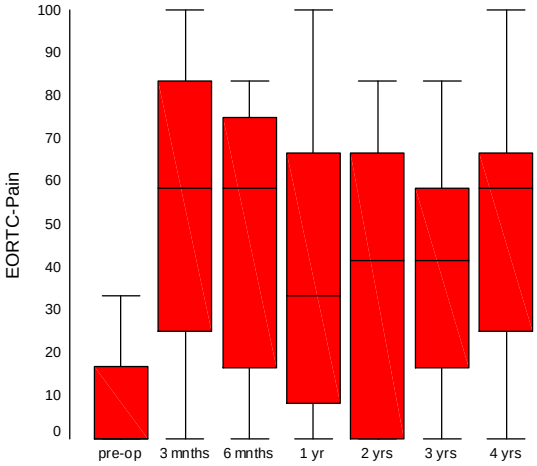

Figure 3.2. Changes in quality of life following gastrectomy; pain

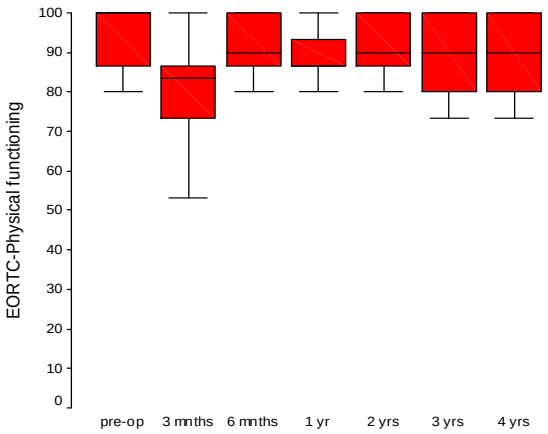

Figure 3.3 Changes in quality of life following oesophagectomy; physical functioning

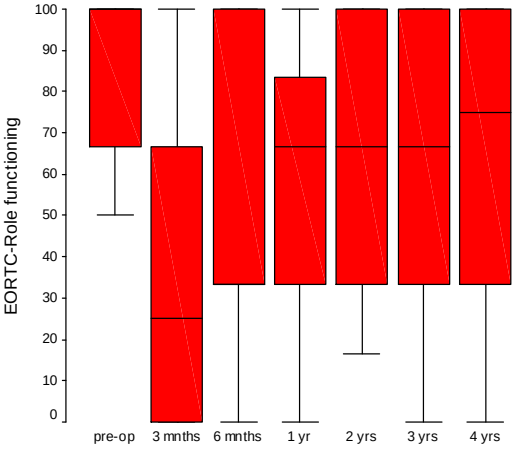

Figure 3.4 Changes in quality of life following oesophagectomy; role functioning

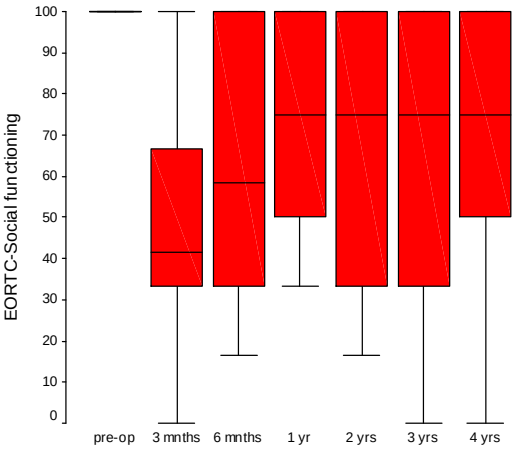

Figure 3.5 Changes in quality of life following oesophagectomy; social functioning

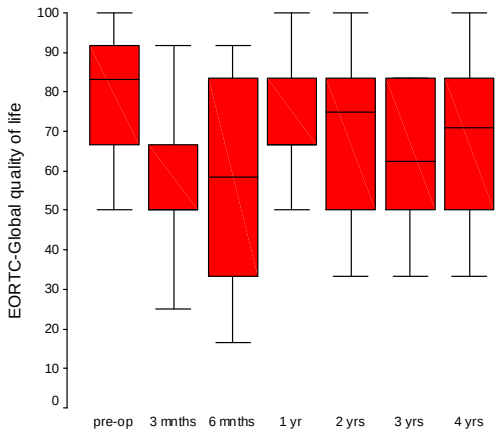

Figure 3.6 Changes in quality of life following oesophagectomy; global quality of life

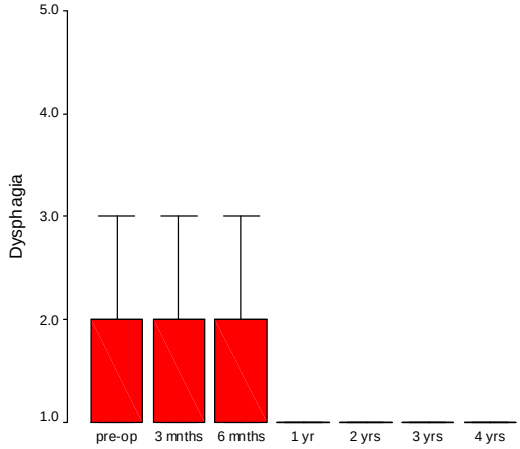

Figure 3.7 Changes in quality of life following oesophagectomy; dysphagia

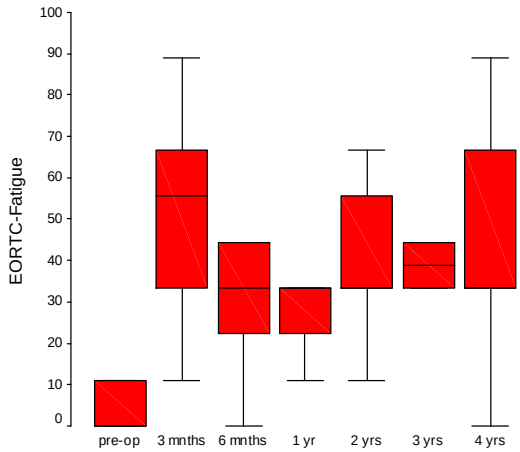

Figure 3.8 Changes in quality of life following oesophagectomy; fatigue

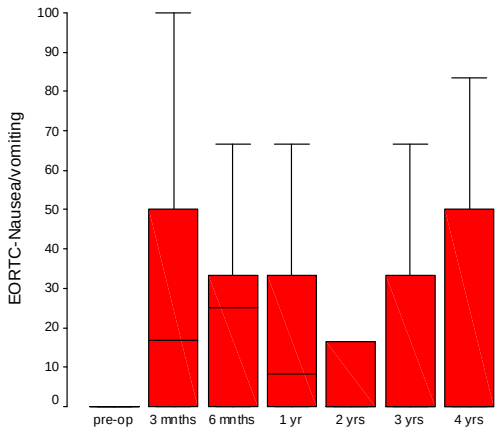

Figure 3.9 Changes in quality of life following oesophagectomy; nausea/vomiting

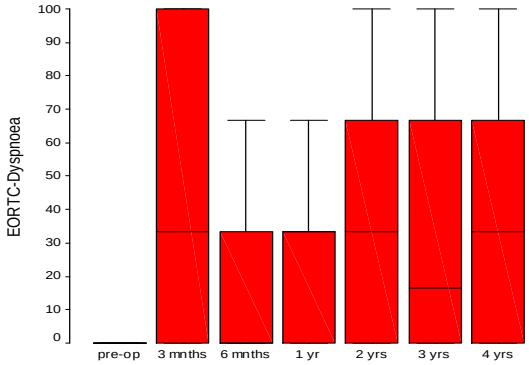

Figure 3.10 Changes in quality of life following oesophagectomy; dyspnoea

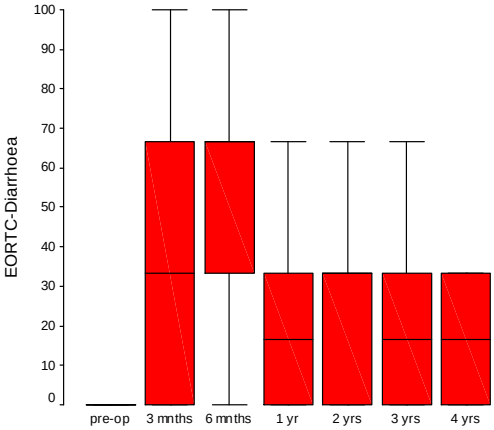

Figure 3.11 Changes in quality of life following oesophagectomy; diarrhoea

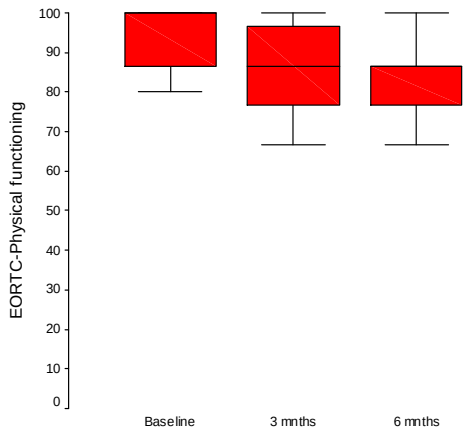

Figure 3.12 Changes in quality of life following oncological treatment; physical functioning

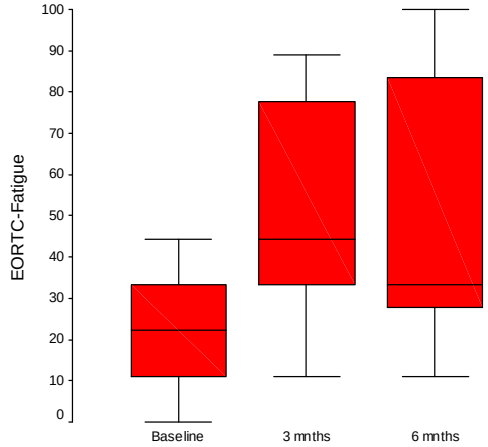

Figure 3.13 Changes in quality of life following oncological treatment; fatigue

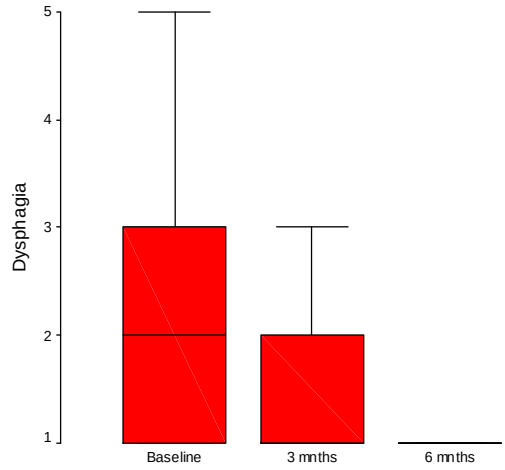

Figure 3.14 Changes in quality of life following oncological treatment; dysphagia

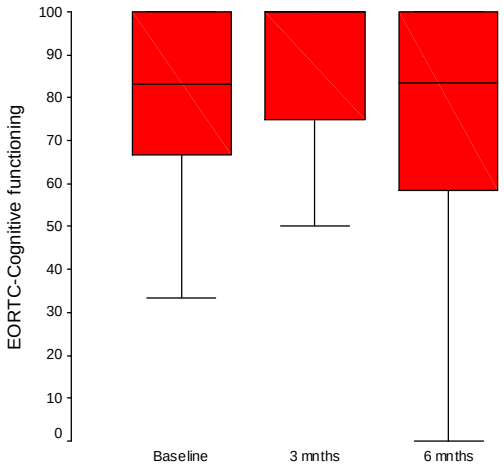

Figure 3.15 Changes in quality of life during supportive care; cognitive functioning

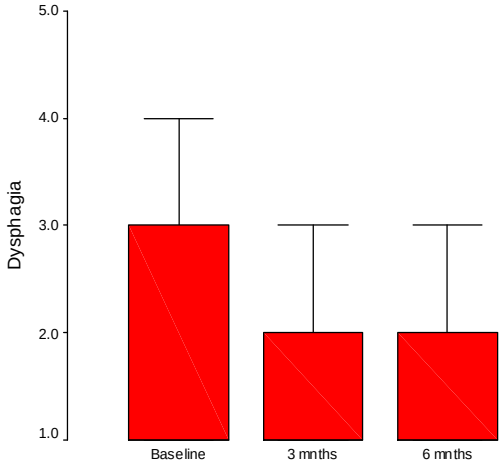

Figure 3.16 Changes in quality of life during supportive care; dysphagia

Chapter 4

4. CONCLUSIONS

4.1 Introduction

In Chapter 1 the aims of this thesis were defined as follows:

1. To examine the relationship between quality of life (EORTC QLQ-C30) and survival in patients with gastro-oesophageal cancer.

2. To examine the longitudinal impact of treatment on quality of life (EORTC QLQ-C30) in patients with gastric and oesophageal cancer.

4.2 Aim 1

It had been previously reported that few aspects of quality of life had a role in predicting survival in an unselected cohort of patients with gastro-oesophageal cancer.

Fang and co-workers (2003) reported that there was evidence to support the correlation of patient-reported QOL scores with survival; in particular physical functioning might be a surrogate marker of an unrecognised biological prognostic factor. In contrast, Chau and colleagues (2004) reported that no aspect of the quality of life (QLQ-C30) had independent prognostic value when performance status was considered.

The results of the present work (Chapter 2) demonstrate there were major differences in quality of life and symptom scores with increasing stage of disease. In particular, social functioning, fatigue, appetite loss and global quality of life were all impaired with increasing tumour stage. Furthermore, appetite loss remained an independently significant prognostic factor even after adjustment for TNM stage and treatment. It was of interest that appetite loss was closely associated with nausea and vomiting, dysphagia and weight loss and therefore it may be that these symptoms result in appetite loss and the consequent loss of weight, which has long been recognised to impact on outcome. These findings are consistent with Blazeby (1995) who reported that appetite loss was associated with poorer survival.

A number of workers (O'Gorman et al., 1998; Kotler, 2000; Scott et al., 2003; MacDonald, 2007). Previously reported the systemic inflammatory response also had an important

factor in determining patients' quality of life (QLQ-C30) in gastro-intestinal and lung cancer patients. Consistent with previous work, the present study suggests that an elevated C-reactive protein concentration was associated with increased appetite loss. Nevertheless, even those patients without an elevated C-reactive protein concentration, reported some appetite loss and both were independently associated with poorer cancer specific survival.

In order to take this work forward it will be important to examine the effect of targeting the systemic inflammatory response, using anti-inflammatory agents **(**MacDonald, 2007), targeting appetite loss using appetite stimulants **(**McMillan et al., 1998; Goldberg and Loprinzi, 1999; Tomiska et al., 2003) and quality of life in patients with gastric and oesophageal cancer.

4.3 Aim 2

There are, to our knowledge, no studies, which have examined the effect of surgery on quality of life beyond 3 years. Therefore, the aim of the present longitudinal study was to examine the effect of treatment (surgery, oncological treatment or supportive care) on quality of life.

In the present work (Chapter 3), at study entry, patients who underwent surgery had better quality of life (QLQ-C30) scores, in particular; physical, role and social functioning and global quality life and less fatigue, nausea and appetite loss, compared with those patients with inoperable disease, where the poor quality of life measures at study entry remained poor on follow-up, whether patients received oncological input or supportive care.

The effect of oesophageactomy reported persistent and profound reductions in physical, role and social functioning and fatigue in patients up to 4 years following surgery. In contrast, in patients with inoperable disease, the poor quality of life measures at study entry remained poor on follow-up whether patients received oncological input or supportive care.

Furthermore, in the present longitudinal study appetite loss did not appear to be significantly altered on follow-up, even in those patients with oesophagectomy there was only a transient alteration in appetite loss. Therefore, it would appear that the degree of

appetite loss is determined at an early stage in the disease process and is not related simply to obstruction of the gastro-oesophageal tract.

In conclusion, the results of the present thesis show that host (appetite loss, systemic inflammation), tumour (stage, type), and treatment (surgery, chemotherapy) factors are important in determining quality of life in patients with gastric and oesophageal cancer. It is therefore important that these factors are taken into account when considering how to improve quality of life.

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APPENDICES

APPENDIX A

Appendix 1.1

TNM classification of gastric tumours

T – Primary Tumour

TX Primary tumour cannot be assessed

T0 No evidence of primary tumour

Tis Carcinoma in situ: intraepithelial tumour without invasion of the lamina propria

T1 Tumour invades lamina propria or submucosa

T2 Tumour invades muscularis propria or subserosa

T3 Tumour penetrates serosa (visceral peritoneum) without invasion of adjacent structures

T4 Tumour invades adjacent structures

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Metastasis in 1 to 6 regional lymph nodes

N2 Metastasis in 7 to 15 regional lymph nodes

N3 Metastasis in more than 15 regional lymph nodes

M – Distant Metastasis

MX Distant metastasis cannot be assessed

M0 No distant metastasis

M1 Distant metastasis

Stage Grouping

Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T1	N1	M0
	T2	N0	M0
Stage II	T1	N2	M0
	T2	N1	M0
	T3	N0	M0
Stage IIIA	T2	N2	M0
	T3	N1	M0
	T4	N0	M0
Stage IIIB	T3	N2	M0
Stage IV	T4	N1, N2, N3	M0
	T1, T2, T3	N3	M0
	Any T	Any N	M1

Appendix 1.1 continued

TNM classification of oesophageal tumours

T – Primary Tumour

TX Primary tumour cannot be assessed

T0 No evidence of primary tumour

Tis Carcinoma in situ

T1 Tumour invades lamina propria or submucosa

T2 Tumour invades muscularis propria

T3 Tumour invades adventitia

T4 Tumour invades adjacent structures

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Regional lymph node metastasis

M – Distant Metastasis

MX Distant metastasis cannot be assessed

M0 No distant metastasis

M1 Distant metastasis-For tumours of lower thoracic oesophagus

M1a Metastasis in coeliac lymph nodes

M1b Other distant metastasis-For tumours of upper thoracic oesophagus

M1a Metastasis in cervical lymph nodes

M1b Other distant metastasis-For tumours of mid-thoracic oesophagus

M1a Not applicable

M1b Non-regional lymph node or other distant metastasis

Stage Grouping

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T2	N0	M0
	T3	N0	M0
Stage IIB	T1	N1	M0
	T2	N1	M0
Stage III	T3	N1	M0
	T4	Any N	M0
Stage IVA	Any T	Any N	M1a
Stage IVB	Any T	Any N	M1b

APPENDIX B

Appendix 2.1

EORTC QLQ-C30 (version 2.0)

We are interested in some things about you and your health. Please answer all of 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.
Please fill in your initials: _____
Your birth date (Day, Month, Year): _____
Today's date (Day, Month, Year): _____

	No	Yes
1. Do you have any trouble doing strenuous activities like carrying a heavy shopping bag or a suitcase?	1	2
2. Do you have any trouble taking a long walk?	1	2
3. Do you have any trouble taking a short walk outside of the house?	1	2
4. Do you need to stay in bed or a chair during the day?	1	2
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2

During the past week:	**Not at All**	**A Little**	**Quite a Bit**	**Very Much**
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4

Please go on to the next page

Appendix 2.1 continued

During the past week:	Not at All	A Little	Quite a Bit	Very Much
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

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?

1 2 3 4 5 6 7

Very poor Excellent

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

1 2 3 4 5 6 7

Very poor Excellent

Appendix 2.2

WHO/ECOG Performance Status:

Code	Description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, eg light housework, office work
2	Ambulatory and capable of self care but unable to carry out any work activities: up and about more than 50% of waking hours
3	Capable of only limited self care, confined to bed or chair more than 50% of waking hours
4	Completely disabled, cannot carry on any self care, totally confined to bed or chair
9	Unknown (not recorded)

Appendix 2.3

Dysphagia Score:

0 = able to eat normal diet / no dysphagia.

1 = able to swallow some solid foods

2 = able to swallow only semi solid foods

3 = able to swallow liquids only

4 = unable to swallow anything / total dysphagia

APPENDIX C

Appendix 3.1

EORTC QLQ-C30 Scoring Sheet

Physical functioning (PF) = (Q1+Q2+Q3+Q4+Q5)/5

Linear transformation to convert to a 0 to 100 scale (XPF) =100 - [(PF-1) × 100]

Role functioning (RF) = (Q6+Q7)/2

Linear transformation to convert to a 0 to 100 scale (XRF) =100 - [(RF-1) ×100/3]

Emotional functioning (EF) = (Q21+Q22+Q23+Q24)/4

Linear transformation to convert to a 0 to 100 scale (XEF) =100 - [(EF-1) ×100/3]

Cognitive functioning (CF) = (Q20+Q25)/2

Linear transformation to convert to a 0 to 100 scale (XCF) =100 - [(CF-1) ×100/3]

Social functioning (SF) = (Q26+Q27)/2

Linear transformation to convert to a 0 to 100 scale (XSF) =100 - [(SF-1) × 100/3]

Quality of Life (QL) = (Q29+Q30)/2

Linear transformation to convert to a 0 to 100 scale (XQL) = (QL-1) × 100/6

Fatigue (FA) = (Q10+Q12+Q18)/3

Linear transformation to convert to a 0 to 100 scale (XFA) = (FA-1) × 100/3

Nausea and Vomiting (NV) = (Q14+Q15)/2

Linear transformation to convert to a 0 to 100 scale (XNV) = (NV-1) × 100/3

Pain (PA) = (Q9+Q19)/2

Linear transformation to convert to a 0 to 100 scale (XPA) = (PA-1) × 100/3

The remaining questions are single items and are also converted to a 0-100 scale

Dyspnoea (Q8=DY) Linear transformation (XDY) = (DY-1) × 100/3
Sleep Disturbance (Q11=SL) Linear transformation (XSL) = (SL-1) × 100/3
Appetite loss (Q13=AP) Linear transformation (XAP) = (AP-1) × 100/3
Constipation (Q16=CO) Linear transformation (XCO) = (CO-1) × 100/3
Diarrhoea (Q17=DI) Linear transformation (XDI) = (DI-1) × 100/3
Financial Difficulty (Q28=FI) Linear transformation (XFI) = (FI-1) × 100/3

APPENDIX D

Appendix 4.1 Quality of life in gastric and oesophageal cancer patients at baseline

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
1	66.7	0	8.3	50	33.3	0	100	50	66.7	100	66.7	0	66.7	0	66.7	1
2	93.3	66.7	100	100	100	100	11.1	16.7	0	66.7	0	0	66.7	0	0	1
3	100	50	91.7	100	83.3	66.7	22.2	0	0	0	100	0	100	0	0	1
4	100	0	0	100	33.3	25	55.6	33.3	100	0	0	100	0	0	0	1
5	100	66.7	83.3	100	83.3	83.3	22.2	16.7	0	0	33.3	33.3	33.3	0	33.3	4
6	100	100	100	83.3	100	83.3	11.1	0	16.7	0	0	0	33.3	0	33.3	1
7	100	100	41.7	100	100	667	0	0	0	0	33.3	0	0	0	0	2
8	93.3	100	100	83.3	100	100	0	33.3	16.7	0	0	0	0	0	33.3	3
9	100	100	91.7	100	100	50	33.3	66.7	50	0	66.7	33.3	100	0	0	1
10	100	100	91.7	83.3	100	83.3	0	0	0	0	0	0	0	33.3	0	1
11	93.3	16.7	50	50	33.3	50	55.6	0	33.3	33.3	0	0	0	0	33.3	1
12	73.3	0	8.3	16.7	0	16.7	77.8	16.7	100	33.3	100	100	100	0	33.3	3
13	66.7	0	25	33.3	0	16.7	88.9	66.7	66.7	100	100	100	100	33.3	100	1
14	100	100	75	100	100	50	22.2	16.7	0	33.3	33.3	33.3	0	0	0	1
15	100	100	100	50	100	100	22.2	0	16.7	66.7	0	0	66.7	0	0	1
16	100	66.7	0	0	33.3	0	55.6	50	33.3	66.7	33.3	0	33.3	0	100	1
17	86.7	66.7	66.7	66.7	66.7	33.3	33.3	0	33.3	33.3	66.7	66.7	33.3	33.3	0	1
18	73.3	33.3	41.7	16.7	66.7	66.7	77.8	16.7	0	100	33.3	0	0	0	33.3	1
19	86.7	83.3	41.7	66.7	33.3	41.7	44.4	0	0	33.3	100	33.3	*	*	66.7	4
20	86.7	33.3	66.7	83.3	50	33.3	55.6	66.7	50	0	33.3	66.7	66.7	0	33.3	1
21	100	83.3	83.3	100	100	50	11.1	50	0	0	33.3	100	0	*	0	4
22	100	0	91.7	100	0	41.7	22.2	0	50	0	33.3	33.3	33.3	0	0	3
23	93.3	66.7	100	100	66.7	58.3	22.2	0	0	0	0	33.3	66.7	0	0	3
24	86.7	50	25	83.3	66.7	41.7	66.7	83.3	66.7	100	100	0	66.7	0	0	1
25	93.3	0	100	100	33.3	50	44.4	16.7	0	0	33.3	0	33.3	0	0	3
26	100	83.3	66.7	83.3	66.7	33.3	33.3	0	33.3	0	0	0	33.3	33.3	0	2
27	73.3	16.7	66.7	66.7	50	50	77.8	66.7	100	33.3	100	33.3	66.7	0	66.7	4
28	100	100	91.7	100	100	58.3	0	0	33.3	0	33.3	33.3	33.3	0	0	2

Appendix 4.1 continued Quality of life in gastric and oesophageal cancer patients at baseline

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
29	86.7	33.3	91.7	66.7	83.3	58.3	44.4	0	66.7	0	66.7	0	33.3	0	0	1
30	93.3	33.3	66.7	100	16.7	100	33.3	16.7	0	0	66.7	100	0	33.3	0	4
31	93.3	66.7	50	66.7	100	50	55.6	50	16.7	66.7	0	100	33.3	100	0	1
32	100	83.3	50	100	16.7	41.7	11.1	0	16.7	0	0	333	33.3	33.3	0	3
33	100	33.3	83.3	100	83.3	66.7	0	16.7	16.7	0	66.7	0	33.3	0	0	3
34	100	0	66.7	66.7	16.7	16.7	77.8	16.7	83.3	33.3	66.7	100	33.3	33.3	33.3	1
35	66.7	0	91.7	100	0	16.7	100	83.3	16.7	100	100	0	33.3	33.3		4
36	100	0	83.3	100	100	83.3	11.1	16.7	0	0	66.7	0	0	0	0	4
37	100	0	75	66.7	0	33.3	22.2	66.7	0	0	0	33.3	0	0	0	4
38	100	100	100	100	100	100	0	0	0	0	0	0	0	0	0	4
39	86.7	66.7	66.7	66.7	50	50	55.6	0	33.3	100	33.3	0	33.3	0	0	3
40	73.3	33.3	41.7	33.3	16.7	16.7	77.8	16.7	16.7	100	100	0	66.7	0	66.7	4
41	86.7	50	66.7	100	83.3	41.7	55.6	16.7	0	33.3	100	0	66.7	0	0	1
42	100	0	0	0	0	0	100	100	100	33.3	100	100	33.3	0	0	3
43	73.3	66.7	8.3	50	83.3	8.33	22.2	100	33.3	0	66.7	66.7	66.7	33.3	66.7	1
44	66.7	0	41.7	50	0	0	66.7	50	100	100	66.7	66.7	0	0	66.7	3
45	86.7	16.7	*	100	83.3	83.3	22.2	0	16.7	33.3	0	0	33.3	0	0	1
46	80	33.3	50	66.7	66.7	66.7	77.8	0	100	33.3	100	66.7	33.3	0	33.3	1
47	93.3	83.3	25	50	50	33.3	44.4	33.3	33.3	33.3	66.7	66.7	33.3	*	33.3	1
48	86.7	0	75	66.7	33.3	50	44.4	0	16.7	100	100	100	66.7	0	0	1
49	100	50	100	100	100	66.7	11.1	0	16.7	0	0	33.3	33.3	0	0	1
50	86.7	50	100	100	16.5	50	55.6	50	0	33.3	33.3	66.7	33.3	0	*	1
51	100	100	83.3	83.3	100	83.3	22.2	0	16.7	0	66.7	33.3	0	0	0	2
52	86.7	100	91.7	83.3	100	91.7	33.3	0	0	0	33.3	33.3	0	0	0	3
53	93.3	50	33.3	66.7	50	25	66.7	100	66.7	33.3	100	33.3	100	0	33.3	1
54	100	33.3	100	66.7	83.3	66.7	0	0	16.7	0	0	0	0	33.3	0	1
55	86.7	16.7	58.3	*	66.7	41.7	66.7	33.3	83.3	0	33.3	0	33.3	0	0	1

Appendix 4.1 continued Quality of life in gastric and oesophageal cancer patients at baseline

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
56	100	100	83.3	100	100	66.7	0	50	0	0	33.3	0	0	0	0	3
57	93.3	100	25	83.3	100	66.7	55.6	8	0	0	0	33.3	100	0	33.3	1
58	73.3	16.7	*	*	*	16.7	22.2	33.3	16.7	66.7	0	66.7	*	*	*	1
59	86.7	100	66.7	83.3	100	50	33.3	0	0	33.3	33.3	0	0	33.3	0	1
60	80	83.3	33.3	83.3	100	33.3	33.3	16.7	33.3	0	33.3	66.7	33.3	0	0	1
61	93.3	100	91.7	100	100	83.3	0	0	0	0	0	0	0	33.3	0	1
62	100	100	100	83.3	100	100	0	0	0	0	0	0	33.3	0	0	1
63	93.3	33.3	83.3	83.3	66.7	50	55.6	0	16.7	0	100	33.3	33.3	0	0	2
64	100	0	91.7	100	100	100	11.1	16.7	16.7	*	0	33.3	0	33.3	0	2
65	80	66.7	33.3	83.3	66.7	66.7	88.9	16.7	50	66.7	0	66.7	66.7	33.3	33.3	1
66	100	100	58.3	100	100	66.7	22.2	16.7	16.7	0	100	0	0	0	0	3
67	100	100	75	83.3	100	66.7	0	0	16.7	33.3	33.3	0	33.3	0	0	1
68	100	100	41.7	83.3	66.7	66.7	33.3	16.7	33.3	33.3	33.3	33.3	33.3	0	0	1
69	80	66.7	66.7	66.7	100	33.3	44.4	0	33.3	66.7	0	33.3	33.3	0	66.7	1
70	86.7	16.7	75	100	66.7	33.3	33.3	33.3	0	66.7	100	66.7	33.3	0	0	4
71	100	100	66.7	66.7	100	41.7	11.1	0	16.7	0	33.3	0	0	0	33.3	3
72	86.7	66.7	75	83.3	83.3	66.7	33.3	66.7	33.3	33.3	33.3	0	0	33.3	0	3
73	100	100	83.3	83.3	100	83.3	0	0	16.7	0	0	0	0	0	0	2
74	86.7	100	91.7	100	100	50	33.3	66.7	50	100	66.7	0	66.6	0	33.3	3
75	80	66.7	100	66.7	66.7	50	44.4	0	50	0	66.7	33.3	66.7	33.3	33.3	4
76	100	100	100	100	100	100	0	0	0	0	0	0	33.3	0	0	1
77	100	100	100	100	66.7	41.7	33.3	0	50	0	66.7	66.7	33.3	0	0	3
78	100	100	66.7	100	100	66.7	11.1	0	16.7	33.3	0	33.3	0	0	0	3
79	86.7	100	91.7	100	100	66.7	11.1	0	0	0	0	0	0	0	0	1
80	86.7	33.3	66.7	100	50	50	66.7	16.7	33.3	33.3	66.7	33.3	33.3	0	0	3
81	86.7	33.3	58.3	83.3	33.3	25	66.7	16.7	66.7	*	66.7	66.7	66.7	0	0	3
82	73.3	16.7	91.7	50	33.3	16.7	77.8	66.7	50	66.7	100	100	66.7	33.3	66.7	3
83	100	0	91.7	100	50	33.3	11.1	16.7	33.3	0	66.7	66.7	66.7	0	0	2

Appendix 4.1 continued Quality of life in gastric and oesophageal cancer patients at baseline

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
84	93.3	66.7	75	83.3	100	83.3	44.4	0	0	33.3	0	66.7	0	0	0	1
85	100	33.3	58.3	83.3	100	50	55.6	16.7	16.7	100	33.3	66.7	33.3	0	33.3	1
86	100	100	16.7	50	100	66.7	22.2	0	0	0	0	66.7	33.3	0	33.3	1
87	100	100	75	83.3	83.3	66.7	33.3	16.7	50	0	0	33.3	33.3	0	33.3	1
88	100	100	58.3	100	66.7	83.3	0	0	0	0	0	0	0	0	0	2
89	100	100	66.7	100	100	83.3	44.4	33.3	0	0	0	0	33.3	0	0	1
90	100	66.7	83.3	100	100	91.7	33.3	16.7	50	0	33.3	0	0	0	0	1
91	100	0	83.3	100	0	33.3	0	0	16.7	0	0	0	0	0	0	1
92	86.7	83.3	66.7	100	66.7	50	55.6	33.3	50	0	66.7	66.7	66.7	0	0	2
93	100	100	83.3	100	100	83.3	0	0	0	0	0	33.3	0	0	0	1
94	73.3	66.7	58.3	50	33.3	33.3	44.4	0	33.3	33.3	0	66.7	33.3	0	33.3	1
95	86.7	66.7	58.3	66.7	83.3	50	33.3	0	66.7	33.3	0	33.3	33.3	0	33.3	2
96	100	100	66.7	83.3	100	75	0	0	0	0	0	0	0	0	0	1
97	100	100	83.3	100	83.3	83.3	11.1	16.7	16.7	0	0	0	0	0	0	1
98	100	66.7	91.7	83.3	100	33.3	33.3	16.7	0	33.3	100	0	0	0	0	4
99	100	100	50	83.3	0	33.3	11.1	0	16.7	0	33.3	66.7	0	0	0	3
100	100	100	66.7	83.3	100	50	11.1	*	16.7	33.3	0	33.3	0	0	33.3	1
101	86.7	50	83.3	83.3	66.7	33.3	33.3	0	33.3	33.3	66.7	33.3	0	0	0	3
102	80	0	41.6	83.3	0	50	83.2	100	16.7	66.7	33.3	33.3	100	0	33.3	1
103	100	100	91.6	83.3	100	83.3	0	0	0	0	0	0	0	0	0	1
104	80	50	58.3	83.3	100	0	77.8	50	0	100	100	0	100	0	0	1
105	100	66.7	33.3	83.3	66.7	33.	22.2	16.7	16.7	0	33.3	0	0	33.3	33.3	4
106	100	100	66.7	66.7	83.3	66.7	33.3	16.7	0	33.3	33.3	33.3	33.3	33.3	33.3	1
107	93.3	83.3	66.7	50	66.7	41.7	33.3	50	0	33.3	33.3	0	33.3	0	66.7	1
108	86.7	0	66.7	33.3	50	0	88.9	50	16.7	100	100	33.3	33.3	100	0	2
109	66.7	0	66.7	100	0	0	88.9	50	66.7	100	66.7	33.3	33.3	100	100	1
110	86.7	66.7	91.7	66.7	33.3	33.3	33.3	0	33.3	0	66.7	0	0	0	33.3	3
111	100	100	100	100	100	66.7	11.1	0	16.7	33.3	33.3	0	0	33.3	0	2

Appendix 4.1 continued Quality of life in gastric and oesophageal cancer patients at baseline

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
112	86.7	33.3	83.3	83.3	83.3	83.3	33.3	33.3	16.7	33.3	33.3	66.7	33.3	0	33.3	2
113	100	100	100	83.3	100	91.7	0	0	0	0	0	33.3	0	0	33.3	2
114	100	100	100	100	66.7	91.7	0	0	0	0	0	0	0	0	0	1
115	80	66.7	75	83.3	83.3	50	55.6	0	0	33.3	66.7	0	33.3	66.7	0	2
116	93.3	0	83.3	66.7	16.7	41.7	44.4	0	0	33.3	66.7	33.3	100	0	33.3	5
117	100	100	100	100	100	100	0	0	0	0	0	0	0	0	0	3
118	100	33.3	58.3	66.7	0	33.3	33.3	16.7	0	0	33.3	33.3	33.3	0	0	1
119	86.7	66.7	50	83.3	33.3	50	55.6	33.3	50	0	33.3	66.7	66.7	0	33.3	3
120	80	0	41.7	83.3	33.3	66.7	44.4	0	33.3	33.3	33.3	100	33.3	0	0	2
121	73.3	100	50	50	16.7	25	44.4	0	0	0	0	66.7	0	0	0	2
122	80	66.7	75	33.3	66.7	0	66.7	33.3	33.3	33.3	100	0	33.3	0	0	4
123	100	100	83.3	83.3	100	100	0	0	16.7	0	33.3	33.3	0	0	0	1
124	73.3	16.7	66.7	83.3	33.3	41.7	55.6	100	16.7	66.7	0	100	0	0	0	3
125	100	100	100	100	100	91.7	0	0	0	0	0	0	0	0	0	1
126	73.3	33.3	0	50	66.7	0	77.8	100	66.7	66.7	100	100	100	66.7	33.3	2
127	100	100	66.7	100	100	83.3	11.1	0	0	0	0	0	0	33.3	0	2
128	100	100	83.3	100	100	100	0	16.7	16.7	0	33.3	0	0	0	0	1
129	100	50	75	83.3	83.3	66.7	22.2	16.7	16.7	0	100	0	0	0	0	1
130	86.7	83.3	8.33	66.7	66.7	50	33.3	33.3	0	33.3	33.3	66.7	0	0	33.3	1
131	80	83.3	58.3	83.3	50	41.7	11.1	0	0	33.3	0	66.7	33.3	0	33.3	2
132	93.3	83.3	0	66.7	83.3	66.7	11.1	0	33.3	0	33.3	100	*	0	33.3	2
133	86.7	83.3	75	83.3	100	83.3	11.1	0	33.3	33.3	33.3	0	33.3	0	0	1
134	86.7	83.3	91.7	100	83.3	83.3	33.3	0	16.7	0	66.7	100	33.3	0	0	1
135	80	33.3	0	16.7	33.3	16.7	100	100	100	66.7	100	100	0	0	66.7	3
136	86.7	100	41.7	83.3	50	16.7	33.3	16.7	0	0	33.3	0	66.7	0	33.3	1
137	80	0	0	66.7	0	0	88.9	66.7	66.7	100	100	100	100	0	0	3
138	80	33.3	100	*	*	16.7	22.2	66.7	66.7	0	0	33.3	66.7	0	*	1
139	73.3	0	16.7	50	16.7	0	88.9	83.3	100	66.7	100	100	66.7	66.7	100	3

Appendix 4.1 continued Quality of life in gastric and oesophageal cancer patients at baseline

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
140	100	66.7	83.3	100	100	66.7	22.2	33.3	16.7	0	33.3	0	33.3	0	0	1
141	80	66.7	66.7	66.7	83.3	50	22.2	0	16.7	33.3	0	33.3	33.3	0	33.3	1
142	73.3	33.3	83.3	50	83.3	50	66.7	100	33.3	0	100	66.7	66.7	0	33.3	1
143	100	66.7	91.7	100	66.7	58.3	22.2	0	0	33.3	0	0	0	0	0	1
144	100	100	66.7	100	100	83.3	22.2	66.7	16.7	0	0	0	0	0	0	1
145	100	0	33.3	16.7	0	25	55.6	16.7	50	0	0	100	66.7	0	66.7	2
146	80	16.7	25	50	16.7	33.3	77.8	33.3	16.7	66.7	100	33.3	0	0	0	1
147	86.7	66.7	83.3	66.7	100	50	44.4	66.7	16.7	33.3	66.7	66.7	33.3	0	33.3	3
148	86.7	33.3	100	100	100	100	11.1	33.3	0	33.3	0	33.3	33.3	33.3	0	1
149	86.7	66.7	100	100	100	50	66.7	0	0	33.3	33.3	66.7	66.7	0	0	1
150	100	66.7	66.7	83.3	33.3	50	22.2	16.7	33.3	0	33.3	33.3	0	0	0	3
151	73.3	16.7	33.3	66.7	0	0	66.7	0	0	100	33.3	33.3	0	66.7	0	1
152	100	50	58.3	100	100	91.7	0	0	0	0	0	0	0	0	0	1
153	100	100	100	100	83.3	91.7	0	16.7	0	100	33.3	33.3	33.3	66.7	0	4
154	100	33.3	67	83.3	83.3	66.7	16.7	33.3	16.7	33.3	33.3	*	0	0	0	2
155	100	100	91.7	100	100	83.3	0	16.7	0	100	0	0	0	0	0	2
156	80	83.3	91.7	100	100	*	22.2	33.3	16.7	83.1	33.3	0	0	0	0	0
157	80	0	100	83.3	33.3	33.3	33.3	33.3	50	0	66.7	33.3	66.7	0	33.3	3
158	100	66.7	66.7	100	100	75	33.3	0	16.7	66.7	0	0	33.3	0	0	1
159	86.7	83.3	83.3	100	100	66.7	11.1	0	0	33.3	33.3	33.3	66.7	0	66.7	3
160	80	100	91.7	100	66.7	50	44.4	0	0	33.3	100	33.3	0	0	0	4
Median	90.7	59.5	66.7	79	67.2	53	36.1	23	25	26.7	39.2	33.8	30.6	8.8	0	2
Range	66.7-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	1-5

* not obtained/ patient deceased

Appendix 4.2 Quality of life in gastric and oesophageal cancer patients at 3 months

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
1	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
2	86.7	0	50	33.3	83.3	41.7	66.7	0	33.3	100	33.3	66.7	100	0	0	1
3	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
4	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
5	80	100	83.3	100	33.3	66.7	33.3	0	16.7	0	0	0	33.3	0	33.3	1
6	86.7	50	50	83.3	100	50	66.7	16.7	66.7	0	100	33.3	0	100	0	1
7	100	100	66.7	100	100	66.7	11.1	0	16.7	0	0	0	0	0	0	2
8	73.3	0	100	66.7	50	58.3	77.8	66.7	83.3	100	33.3	33.3	66.7	33.3	0	3
9	66.7	0	91.7	33.3	0	50	100	0	0	0	66.7	0	66.7	0	0	1
10	100	33.3	66.7	100	50	50	66.7	16.7	0	33.3	100	0	33.3	0	0	1
11	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
12	73.3	0	66.6	33.3	33.3	41.6	100	33.3	100	33.3	33.3	100	33.3	0	66.6	3
13	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
14	93.3	100	91.7	100	100	50	0	0	16.7	33.3	0	33.3	0	0	0	1
15	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
16	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
17	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
18	93.3	50	75	50	66.7	66.7	33.3	66.7	0	0	33.3	33.3	33.3	0	66.7	1
19	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
20	86.7	66.7	66.7	33.3	100	83.3	33.3	16.7	16.7	66.7	100	66.7	66.7	0	0	1
21	100	66.7	100	100	100	75	0	0	0	0	33.3	33.3	0	100	0	1
22	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
23	80	0	91.7	83.3	66.7	50	55.6	0	50	66.7	33.3	66.7	0	0	0	1
24	80	33.3	0	0	0	33.3	44.4	100	100	66.7	100	33.3	100	66.7	66.7	1
25	86.7	50	100	100	66.7	75	22.2	33.3	16.7	0	0	33.3	0	0	33.3	3
26	93.3	16.7	0	16.7	50	41.7	77.8	16.7	66.7	33.3	66.7	0	66.7	667	*	4
27	86.7	0	16.7	33.3	0	0	100	66.7	100	66.7	100	100	100	0	33.3	4

Appendix 4.2 continued Quality of life in gastric and oesophageal cancer patients at 3 months

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
28	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
29	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
30	73.3	50	33.3	83.3	50	16.7	22.2	16.7	0	0	66.7	66.7	0	0	0	3
31	86.7	50	66.7	50	83.3	41.7	77.8	100	50	33.3	100	100	33.3	33.3	33.3	1
32	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
33	80	83.3	75	100	66.7	58.3	44.4	0	66.7	0	66.7	0	100	0	0	2
34	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
35	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
36	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	2
37	80	0	100	100	0	41.7	77.8	33.3	33.3	66.7	33.3	0	33.3	0	0	2
38	73.3	100	*	*	*	0	11.1	50	0	0	0	0	0	0	0	1
39	73.3	0	58.3	50	33.3	50	100	66.7	50	100	66.7	33.3	33.3	0	0	1
40	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	3
41	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
42	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
43	80	16.7	16.7	33.3	50	16.7	77.8	50	100	0	33.3	66.7	0	33.3	33.3	1
44	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
45	73.3	33.3	25	66.7	16.7	58.3	66.7	50	66.7	33.3	66.7	100	33.3	66.7	66.7	1
46	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
47	80	66.7	41.7	66.7	50	25	66.7	33.3	66.7	66.7	66.7	33.3	33.3	0	33.3	2
48	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
49	100	66.7	100	100	100	66.7	0	33.3	0	33.3	33.3	0	33.3	33.3	0	3
50	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
51	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
52	73.3	83.3	66.7	66.7	33.3	50	88.9	16.7	0	100	100	100	33.3	0	0	1
53	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	2
54	86.7	66.7	91.7	100	66.7	75	22.2	0	33.3	0	0	33.3	0	0	0	2
55	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.2 continued Quality of life in gastric and oesophageal cancer patients at 3 months

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
56	86.7	0	16.7	100	16.7	25	77.8	33.3	50	66.7	66.7	100	33.3	0	100	1
57	86.7	50	41.7	83.3	83.3	50	44.4	16.7	50	0	33.3	66.7	0	66.7	0	1
58	73.3	33.3	*	*	*	*	100	16.7	66.7	66.7	33.3	33.3	*	*	*	3
59	80	0	66.7	66.7	100	66.7	77.8	33.3	33.3	100	33.3	33.3	33.3	66.7	0	1
60	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
61	93.3	100	100	100	100	83.3	11.1	16.7	0	33.3	0	0	0	33.3	0	1
62	100	100	100	100	83.3	75	0	33.3	16.7	0	33.3	33.3	0	0	0	1
63	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
64	100	100	91.7	833	100	66.7	22.2	16.7	0	33.3	0	0	0	0	0	1
65	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	2
66	86.7	0	66.7	83.3	33.3	50	55.6	33.3	33.3	66.7	33.3	66.7	0	33.3	0	1
67	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
68	86.7	50	41.7	66.7	66.7	58.3	33.3	16.7	33.3	0	0	0	0	0	0	1
69	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
70	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	2
71	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	3
72	80	33.3	66.7	83.3	83.3	50	77.8	50	83.3	66.7	100	33.3	0	66.7	0	2
73	93.3	0	66.7	100	50	50	33.3	16.7	0	0	33.3	0	0	0	0	2
74	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
75	80	16.7	100	66.7	33.3	50	55.6	50	66.7	33.3	0	33.3	33.3	66.7	66.7	1
76	93.3	*	100	100	100	58.3	33.3	0	0	66.7	0	0	100	0	0	1
77	80	0	91.7	66.7	0	16.7	88.9	33.3	66.7	100	66.7	33.3	0	33.3	33.3	1
78	66.7	33.3	25	33.3	16.7	41.7	88.9	16.7	33.3	100	66.7	100	33.3	0	100	3
79	73.3	0	91.7	100	0	50	55. 6	0	16.7	33.3	66.7	0	33.3	33.3	0	1
80	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
81	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	2
82	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
83	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.2 continued Quality of life in gastric and oesophageal cancer patients at 3 months

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
84	80	50	75	100	100	50	55.6	0	33.3	100	0	33.3	0	0	33.3	1
85	100	66.7	100	83.3	66.7	83.3	33.3	0	16.7	33.3	0	66.7	0	0	0	1
86	80	33.3	41.7	66.7	16.7	41.7	44.4	66.7	66.7	33.3	100	33.3	33.3	33.3	66.7	1
87	86.7	16.7	41.7	50	16.7	33.3	100	33.3	100	100	0	66.7	33.3	33.3	66.7	1
88	93.3	66.7	100	100	83.3	83.3	33.3	0	0	0	0	0	0	33.3	33.3	2
89	73.3	0	0	83.3	0	0	100	100	100	0	66.7	100	0	33.3	100	1
90	86.7	83.3	91. 7	100	66.7	75	44.4	16.7	50	0	33.3	0	33.3	0	0	1
91	80	0	83.3	100	16.7	41.7	55.6	33.3	50	0	33.3	0	0	33.3	66.7	1
92	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
93	86.7	66.7	91.7	66.7	83.3	66.7	33.3	0	0	0	0	0	33.3	0	66.7	1
94	66.7	33.3	66.7	66.7	0	50	55.6	66.7	66.7	66.7	66.7	66.7	33.3	66.7	33.3	1
95	86.7	33.3	58.3	50	33.3	50	66.7	0	33.3	66.7	33.3	33.3	33.3	66.7	66.7	2
96	86.7	66.7	66.7	66.7	66.7	66.7	33.3	16.7	33.3	33.3	33.3	33.3	33.3	0	33.3	2
97	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	2
98	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
99	86.7	50	75	83.3	33.3	66.7	33.3	0	33.3	0	100	33.3	0	0	0	1
100	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
101	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
102	86.7	0	33.3	66.7	0	33.3	77.8	83.3	66.7	66.7	0	33.3	0	100	100	1
103	93.3	100	75	66.7	83.3	75	33.3	0	0	33.3	33.3	0	33.3	0	0	1
104	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
105	80	0	33.3	33.3	0	16.7	77.8	100	83.3	0	66.7	33.3	0	0	100	1
106	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
107	73.3	0	41.7	33.3	16.7	8.33	88.9	50	66.7	66.7	100	33.3	0	100	33.3	1
108	80	33.3	91.7	33.3	83.3	25	77.8	16.7	33.3	100	100	33.3	100	0	0	3
109	73.3	0	100	100	0	58.3	66.7	0	0	100	0	0	0	0	0	1
110	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.2 continued Quality of life in gastric and oesophageal cancer patients at 3 months

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
111	80	33.3	100	100	50	33.3	44.4	16.7	16.7	100	66.7	0	0	33.3	66.7	1
112	86.7	33.3	100	83.3	50	66.7	55.6	83.3	16.7	33.3	66.7	33.3	33.3	66.7	33.3	1
113	100	66.7	100	83.3	66.7	66.7	22.2	0	33.3	33.3	33.3	33.3	0	66.7	0	1
114	80	33.3	66.7	50	50	50	44.4	16.7	33.3	33.3	66.7	33.3	0	0	100	1
115	73.3	33.3	83.3	83.3	33.3	41.7	66.7	33.3	33.3	33.3	33.3	0	0	100	33.3	1
116	86.7	100	91.7	50	66.7	33.3	66.7	0	50	33.3	0	33.3	66.7	33.3	0	1
117	86.7	100	100	100	66.7	91.7	33.3	16.7	33.3	33.3	0	0	0	33.3	0	2
118	93.3	66.7	66.7	83.3	83.3	58.3	33.3	16.7	0	0	33.3	33.3	33.3	0	0	1
119	73.3	33.3	33.3	33.3	33.3	50	100	66.7	66.7	33.3	100	100	66.7	33.3	66.7	1
120	73.3	0	58.3	66.7	0	33.3	66.7	66.7	100	66.7	33.3	100	100	0	100	1
121	66.7	50	50	50	66.7	25	44.4	0	33.3	33.3	0	66.7	0	0	0	2
122	73.3	0	0	50	0	0	100	66.7	100	66.7	100	100	33.3	33.3	0	1
123	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
124	73.3	0	33.3	33.3	16.7	16.7	100	33.3	100	100	0	0	66.7	33.3	33.3	1
125	93.3	100	75	100	100	66.7	33.3	16.7	16.7	0	0	66.7	0	0	0	1
126	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
127	53.3	33.3	33.3	50	33.3	33.3	66.7	33.3	0	100	66.7	66.7	0	33.3	66.7	1
128	100	66.7	83.3	66.7	100	75	44.4	0	66.7	0	66.7	0	0	0	0	1
129	66.7	0	66.7	50	16.7	41.6	88.9	66.7	33.3	0	66.7	66.7	33.3	33.3	100	1
130	73.3	66.7	33.3	66.7	66.7	66.7	33.3	0	0	33.3	0	66.7	0	0	0	1
131	80	16.7	25	50	50	50	44.4	66.7	33.3	33.3	33.3	100	667	0	33.3	1
132	86.7	83.3	75	83.3	83.3	66.7	33.3	0	0	0	0	0	0	0	0	1
133	66.7	33.3	66.7	66.7	50	66.7	44.4	16.7	33.3	66.7	33.3	33.3	66.7	33.3	66.7	1
134	66.7	0	83.3	100	0	33.3	100	50	33.3	100	100	66.7	100	0	100	1
135	80	66.7	50	33.3	83.3	41.7	77.8	83.3	16.7	66.7	100	100	100	100	0	3
136	73.3	33.3	25	33.3	66.7	33.3	77.8	0	50	0	0	100	33.3	0	66.7	1
137	73.3	33.3	8.33	66.7	33.3	33.3	44.4	50	16.7	33.3	100	66.7	33.3	33.3	100	1
138	73.3	16.7	50	50	33.3	0	88.9	100	83.3	66.7	100	66.7	33.3	0	66.7	3

Appendix 4.2 continued Quality of life in gastric and oesophageal cancer patients at 3 months

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
139	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
140	93.3	100	100	83.3	100	100	22.2	0	0	0	0	0	0	33.3	0	1
141	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
142	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
143	100	100	91.7	100	83.3	66.7	11.1	0	0	0	0	66.7	0	0	0	1
144	100	83.3	100	83.3	66.7	100	33.3	0	0	0	0	0	0	0	0	1
145	66.7	0	16.7	16.7	0	16.7	100	83.3	33.3	66.7	66.7	0	33.3	100	100	1
146	73.3	33.3	66.7	66.7	16.7	33.3	55.6	16.7	0	0	66.7	33.3	66.7	0	66.7	1
147	73.3	33.3	16.7	0	50	50	55.6	50	0	33.3	100	100	0	0	66.7	1
148	100	100	75	83.3	100	100	0	0	0	0	0	0	0	33.3	0	1
149	86.7	100	100	100	100	100	33.3	0	0	0	0	0	0	0	0	1
150	86.7	66.7	66.7	83.3	16.7	41.7	44.4	50	33.3	0	33.3	33.3	0	33.3	0	1
151	86.7	50	83.3	100	50	16.7	33.3	0	0	66.7	0	33.3	0	66.7	0	1
152	66.7	0	16.7	66.7	16.7	25	88.9	100	66. 7	100	66.7	100	0	100	100	1
153	93.3	83.3	100	100	100	66.7	0	0	33.3	0	0	100	0	0	0	2
154	93.3	83.3	75	100	100	75	22.2	33.3	16.7	33.3	33.3	0	0	0	0	2
155	100	100	91.7	100	100	83.3	22.2	0	16.7	0	0	0	33.3	0	0	2
156	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
157	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	3
158	100	66.7	75	83.3	83.3	66.7	33.3	33.3	0	33.3	0	0	0	0	0	2
159	86.7	83.3	91.7	100	0	83.3	22.2	0	16.7	33.3	33.3	0	0	0	0	3
160	66.7	33.3	33.3	16.7	100	0	100	66.7	100	100	100	33.3	66.7	0	100	3
Median	82.5	42.7	64.8	70	51.3	49.4	54.9	30.2	36.3	39.3	42.9	39.6	26.3	24.7	29.6	1.4
Range	53.3-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	1-4

* not obtained/ patient deceased

Appendix 4.3 Quality of life in gastric and oesophageal cancer patients at 6 months

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
1	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
2	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
3	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
4	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
5	86.7	100	91.7	100	100	83.3	22.2	0	0	0	0	33.3	0	0	0	2
6	93.3	83.3	100	83.3	83.3	66.7	11.1	0	0	0	0	0	0	66.7	0	1
7	100	100	75	100	100	91.7	0	0	0	0	0	0	33.3	0	0	1
8	86.7	33.3	100	100	16.7	66.7	100	100	33.3	33.3	100	100	0	100	0	3
9	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
10	100	100	100	100	100	66.7	33.3	0	0	0	66.7	0	0	0	0	1
11	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
12	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	3
13	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
14	100	100	75	100	100	50	11.1	0	16.7	33.3	0	33.3	33.3	0	0	1
15	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
16	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
17	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
18	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
19	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
20	80	33.3	100	83.3	50	25	66.7	0	50	100	33.3	33.3	33.3	0	66.7	1
21	66.7	0	41.7	33.3	0	0	100	33.3	100	100	100	33.3	100	0	33.3	1
22	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
23	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
24	80	33.3	33.3	66.7	66.7	50	88.9	16.7	33.3	66.7	33.3	66.7	0	33.3	66.7	1
25	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
26	86.7	50	55.5	100	16.7	50	33.3	0	33.3	0	33.3	0	100	0	0	2
27	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
28	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	4

Appendix 4.3 continued Quality of life in gastric and oesophageal cancer patients at 6 months

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
29	86.7	33.3	75	50	66.7	33.3	66.7	0	66.7	0	100	33.3	66.7	0	0	2
30	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
31	80	16.7	33.3	66.7	50	41.7	88.9	100	66.7	66.7	33.3	66.7	33.3	0	0	1
32	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
33	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
34	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
35	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
36	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
37	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	2
38	80	33.3	100	100	66.7	91.7	55.6	16.7	0	33.3	33.3	66.7	0	0	0	1
39	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
40	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	3
41	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
42	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
43	73.3	0	25	16.7	33.3	25	77.8	33.3	83.3	100	33.3	66.7	33.3	0	66.7	1
44	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
45	80	33.3	41.7	50	33.3	33.3	55.6	33.3	50	66.7	33.3	66.7	33.3	33.3	100	1
46	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
47	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	2
48	73.3	16.7	83.3	66.7	0	58.3	55.6	0	50	66.7	100	66.7	0	0	0	1
49	100	83.3	91.7	100	83.3	66.7	0	0	0	0	33.3	33.3	0	33.3	0	3
50	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
51	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
52	73.3	0	66.7	50	83.3	50	77.8	0	0	66.7	100	0	33.3	33.3	0	1
53	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
54	86.7	66.7	*	*	*	0	0	0	16.7	0	0	0	0	0	*	1
55	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
56	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1

Appendix 4.3 continued Quality of life in gastric and oesophageal cancer patients at 6 months

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
57	93.3	66.7	25	66.7	66.7	50	22.2	0	50	0	33.3	66.7	0	66.7	33.3	1
58	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	2
59	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
60	73.3	33.3	75	83.3	83.3	66.7	44.4	0	33.3	33.3	0	33.3	0	33.3	0	1
61	100	83.3	100	100	100	83.3	11.1	0	16.7	0	0	0	0	0	0	1
62	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
63	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
64	100	100	91.7	100	100	66.7	11.1	16.7	0	0	0	33.3	0	33.3	0	1
65	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	2
66	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
67	66.7	0	41.7	83.3	0	0	100	83.3	100	100	100	100	100	100	66.7	1
68	80	0	16.7	33.3	16.7	25	100	50	100	0	66.7	100	0	100	33.3	1
69	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
70	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
71	73.3	0	66.7	66.7	66.7	91.7	11.1	33.3	33.3	33.3	100	33.3	0	33.3	0	1
72	73.3	33.3	66.7	66.7	50	8.3	88.9	16.7	83.3	66.7	100	66.7	33.3	33.3	0	1
73	93.3	33.3	91.7	100	66.7	50	33.3	16.7	0	0	33.3	33.3	0	33.3	0	2
74	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
75	80	33.33	100	83.3	66.7	33.3	33.3	0	33.3	0	0	33.3	0	66.7	33.3	2
76	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
77	93.3	16.7	83.3	83.3	0	33.3	88.9	66.7	33.3	66.7	100	33.3	0	33.3	0	1
78	66.7	16.7	66.7	50	50	50	100	33.3	66.7	66.7	100	100	100	0	33.3	3
79	86.7	16.7	91.7	66.7	33.3	33.3	33.3	0	0	66.7	66.7	0	33.3	66.7	33.3	1
80	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
81	86.7	16.7	83.3	100	33.3	50	88.9	0	66.7	33.3	33.3	33.3	0	100	33.3	1
82	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
83	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
84	73.3	50	50	100	100	58.3	44.4	16.7	66.7	66.7	100	66.7	0	0	33.3	1

Appendix 4.3 continued Quality of life in gastric and oesophageal cancer patients at 6 months

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
85	100	100	66.7	83.3	100	58.3	33.3	16.7	50	0	0	33.3	0	0	0	1
86	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
87	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
88	93.3	66.7	100	100	66.7	83.3	33.3	16.7	50	0	0	0	33.3	33.3	33.3	1
89	86.7	33.3	91.7	66.7	50	66.7	88.9	83.3	83.3	0	66.7	100	0	0	66.7	1
90	100	83.3	91.7	100	100	66.7	44.4	16.7	16.7	0	0	0	33.3	33.3	0	1
91	80	66.7	75	100	50	58.3	55.6	0	33.3	0	0	0	0	33.3	66.7	1
92	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
93	100	100	91.7	100	100	83.3	11.1	33.3	33.3	0	0	0	0	0	0	1
94	66.7	0	0	16.7	0	0	100	66.7	100	66.7	100	100	0	33.3	66.7	1
95	86.7	66.7	66.7	66.7	50	66.7	33.3	33.3	50	33.3	33.3	0	33.3	33.3	66.7	2
96	93.3	66.7	66.7	66.7	66.7	66.7	33.3	33.3	0	33.3	33.3	33.3	0	33.3	33.3	2
97	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	2
98	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
99	93.3	50	41.7	100	50	58.3	33.3	0	16.7	0	66.7	0	0	0	0	1
100	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
101	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
102	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
103	100	100	91.7	83.3	100	83.3	22.2	0	0	0	0	0	0	0	0	1
104	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
105	86.7	83.3	50	50	50	25	55.6	33.3	0	33.3	33.3	33.3	0	0	100	1
106	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
107	73.3	0	33.3	33.3	0	16.7	88.9	66.7	66.7	66.7	100	66.7	0	66.7	0	2
108	80	16.7	91.7	50	66.7	33.3	77.8	16.7	50	100	100	0	33.3	0	33.3	1
109	73.3	16.7	75	100	0	50	66.7	16. 7	33.3	100	0	33.3	0	0	0	1
110	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
111	86.7	66.7	91.7	100	83.3	66.7	11.1	50	33.3	33.3	0	33.3	0	33.3	0	1

Appendix 4.3 continued Quality of life in gastric and oesophageal cancer patients at 6 months

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
112	66.7	50	33.3	33.3	33.3	33.3	55.6	66. 7	33.3	33.3	66. 7	66.7	33.3	33.3	33.3	2
113	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
114	93.3	66.7	66.7	83.3	83.3	58.3	33.3	16.7	16.7	33.3	0	33.3	0	0	0	1
115	80	33.3	91.7	83.3	66.7	50	66.7	66.7	16.7	0	100	33.3	33.3	33.3	0	1
116	86.7	66.7	100	100	83.3	66.7	33.3	0	0	33.3	0	33.3	0	0	0	1
117	100	100	91.7	100	100	91.7	22.2		16.7	0	0	0	0	66.7	0	1
118	86.7	66.7	83.3	83.3	66.7	75	33.3	0	0	0	0	33.3	33.3	0	0	1
119	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
120	73.3	0	58.3	66.7	50	50	66.7	66.7	100	66.7	66.7	100	66.7	33.3	100	1
121	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	2
122	73.3	0	0	0	0	41.7	100	100	0	66.7	100	66.7	33.3	0	0	*
123	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
124	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
125	100	83.3	75	100	100	58.3	33.3	50	83.3	0	100	33.3	0	0	33.3	1
126	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
127	100	33.3	83.3	83.3	33.3	50	44.4	33.3	50	0	33.3	33.3	0	66.7	66.7	1
128	100	100	100	100	100	91.7	22.2	0	0	0	33.3	0	0	0	0	1
129	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
130	73.3	0	0	16.67	0	0	100	66.7	100	66.7	100	0	0	0	33.3	1
131	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
132	86.7	50	66.7	66.7	66.7	75	33.3	0	33.3	0	0	33.3	33.3	0	0	1
133	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
134	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
135	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	3
136	80	33.3	33.3	50	66.7	41.7	55.6	0	33.3	0	0	66.7	0	0	33.3	1
137	80	0	0	33.3	16.7	0	77.8	33.3	33.3	100	33.3	66.7	0	33.3	100	1
138	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1

Appendix 4.3 continued Quality of life in gastric and oesophageal cancer patients at 6 months

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
139	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
140	100	100	100	100	100	100	0	0	0	0	0	0	0	0	0	1
141	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
142	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	
143	86.7	66.7	100	100	50	66.7	33.3	0	0	0	66.7	33.3	66.7	0	0	1
144	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
145	80	16.7	66.7	33.3	0	33.3	88.9	50	33.3	66.7	33.3	33.3	33.3	66.7	100	1
146	66.7	0	33.3	16.7	0	0	100	66.7	66.7	66.7	100	33.3	0	66.7	66.7	1
147	80	33.3	25	16.7	50	66.7	55.6	33.3	33.3	33.3	100	33.3	0	33.3	66.7	1
148	93.3	50	66.7	66.7	66.7	33.3	44.4	33.3	33.3	33.3	0	33.3	0	33.3	33.3	1
149	93.3	100	83.3	83.3	100	100	11.1	0	0	0	0	0	0	0	0	1
150	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
151	86.7	66.7	75	83.3	33.3	50	33.3	0	0	33.3	0	33.3	0	33.3	0	1
152	86.7	0	0	0	33.3	16.7	100	66.7	66.7	100	33.3	100	33.3	100	100	2
153	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
154	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
155	100	100	83.3	100	100	75	22.2	0	33.3	0		*	33.3	0	0	1
156	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
157	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
158	86.7	66.7	83.3	100	100	66.7	33.3	16.7	0	33.3	*	*	33.3	0	0	2
159	66.7	0	33.3	16.7	0	16.7	88.9	33.3	100	66.7	*	*	0	0	66.7	*
160	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	3
Median	85.2	46.6	67.1	72.1	56.4	51.1	51.2	25.9	35.8	33.3	42.8	37.4	17.1	25.7	25.6	1.3
Range	66.7-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	1-4

* not obtained/ patient deceased

Appendix 4.4 Quality of life in gastric and oesophageal cancer patients at 1 year

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
1	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
2	100	66.7	100	83.3	91.7	91.7	11.1	0	0	33.3	0	0	0	0	0	1
3	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
4	86.7	66.7	50	33.3	33.3	33.3	44.4	16.7	66.7	100	66.7	33.3	33.3	0	0	1
5	66.7	0	0	33.3	0	0	100	66.7	100	66.7	100	100	100	*	100	1
6	86.7	83.3	83.3	83.3	66.7	66.7	22.2	0	16.7	0	0	0	0	66.7	0	2
7	100	100	75	100	91.7	91.7	0	0	0	0	0	0	33.3	0	0	1
8	80	33.3	75	83.3	58.3	58.3	55.6	33.3	66.7	33.3	33.3	33.3	66.7	33.3	0	1
9	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
10	100	83.3	100	100	75	75	33.3	0	0	0	33.3	0	33.3	0	0	1
11	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
12	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
13	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
14	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
15	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
16	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
17	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
18	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
19	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
20	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
21	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
22	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
23	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
24	86.7	33.3	41.7	66.7	33.3	33.3	66.7	33.3	66.7	66.7	33.3	66.7	33.3	33.3	33.3	1
25	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
26	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
27	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.4 continued Quality of life in gastric and oesophageal cancer patients at 1 year

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
28	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
29	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
30	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
31	86.7	66.7	41.7	50	58.3	58.3	44.4	50	33.3	66.7	66.7	100	66.7	0	0	1
32	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
33	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
34	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
35	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
36	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
37	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
38	73.3	50	91.7	100	91.7	91.7	44.4	0	0	66.7	0	0	0	0	0	1
39	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
40	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
41	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
42	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
43	73.3	0	8.33	0	8.33	8.33	100	83.3	100	100	100	100	33.3	0	66.7	1
44	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
45	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
46	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
47	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
48	66.7	0	91.7	16.7	41.7	41.7	100	0	100	33.3	100	0	0	0	0	2
49	80	16.7	83.3	100	58.3	58.3	33.3	0	33.3	0	0	100	0	0	0	3
50	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
51	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
52	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
53	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
54	100	66.7	100	83.3	66.7	66.7	0	0	0	0	0	0	0	0	0	1
55	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.4 continued Quality of life in gastric and oesophageal cancer patients at 1 year

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
56	100	83.3	91.7	100	50	50	22.2	16.7	16. 7	33.3	33.3	0	0	0	66.7	1
57	80	50	25	50	50	50	33.3	0	33.3	0	0	100	0	33.3	0	1
58	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
59	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
60	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
61	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
62	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
63	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
64	100	100	100	83.3	75	75	0	16.7	0	0	0	0	0	33.3	0	1
65	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
66	66.7	66.7	58.3	66.7	50	50	55.6	33.3	50	66.7	33.3	33.3	100	33.3	33.3	1
67	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
68	86.7	66.7	50	50	66.7	66.7	33.3	16.7	33.3	0	0	33.3	0	0	33.3	1
69	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
70	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
71	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	2
72	73.3	0	50	100	58.3	58.3	100	100	33.3	100	33.3	100	0	33.3	0	1
73	93.3	66.7	100	100	83.3	83.3	33.3	0	0	0	0	33.3	0	0	0	1
74	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
75	73.3	33.3	91.7	66.7	66.7	66.7	33.3	0	66.7	33.3	0	0	0	33.3	33.3	1
76	100	100	100	100	100	100	0	0	0	0	0	0	0	0	0	1
77	73.3	16.7	75	33.3	33.3	33.3	88.9	66.7	100	33.3	33.3	100	0	0	33.3	1
78	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
79	86.7	83.3	100	100	66.7	66.7	33.3	0	0	33.3	33.3	0	0	0	0	2
80	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
81	86.7	33.3	100	100	50	50	44.4	0	50	0	33.3	33.3	0	66.7	0	1
82	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
83	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.4 continued Quality of life in gastric and oesophageal cancer patients at 1 year

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
84	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	
85	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
86	93.3	50	33.3	66.7	50	50	77.8	33.3	0	66.7	100	0	0	66.7	33.3	1
87	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
88	100	100	91.7	100	91.7	91.7	22.2	16.7	16.7	0	0	0	0	33.3	0	1
89	80	0	8.33	83.3	0	0	77.8	100	100	33.3	66.7	66.7	0	33.3	66.7	1
90	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
91	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
92	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	2
93	100	100	100	100	66.7	66.7	22.2	0	16.7	0	0	0	0	0	33.3	1
94	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
95	86.7	33.3	83.3	66.7	66.7	66.7	11.1	33.3	33.3	33.3	66.7	33.3	33.3	66.7	33.3	1
96	100	100	100	100	66.7	66.7	0	0	0	0	33.3	33.3	0	0	0	1
97	93.3	83.3	100	66.7	83.3	83.3	33.3	0	16.7	33.3	0	0	0	33.3	0	1
98	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
99	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
100	86.7	66.7	75	66.7	50	50	33.3	33.3	50	66.7	33.3	66.7	0	0	0	1
101	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
102	80	33.3	0	33.3	25	25	55.6	50	50	66.7	33.3	66.7	0	66.7	33.3	1
103	100	100	100	83.3	83.3	83.3	22.2	0	0	0	0	0	0	0	0	1
104	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
105	93.3	33.3	58.3	66.7	33.3	33.3	22.2	0	0	66.7	0	0	0	0	100	1
106	86.7	83.3	100	50	50	50	11.1	33.3	0	33.3	0	33.3	0	0	33.3	1
107	80	33.3	75	50	33.3	33.3	66.7	16.7	33.3	33.3	66.7	66.7	0	66.7	0	1
108	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
109	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
110	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.4 continued Quality of life in gastric and oesophageal cancer patients at 1 year

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
111	93.3	66.7	91.7	100	58.3	58.3	11.1	0	50	33.3	0	33.3	0	33.3	0	1
112	80	33.3	25	16.7	16.7	16.7	88.9	83.3	66.7	33.3	100	66.7	0	0	66.7	1
113	100	100	100	83.3	100	100	0	16.7	16.7	0	33.3	0	0	33.3	0	1
114	100	100	58.3	100	83.3	83.3	33.3	0	16.7	33.3	0	33.3	0	0	33.3	1
115	73.3	50	58.3	83.3	25	25	55.6	50	33.3	33.3	66.7	100	0	0	0	1
116	86.7	66.7	83.3	100	66.7	66.7	22.2	0	0	33.3	0	0	0	0	0	1
117	93.3	66.7	100	100	100	100	22.2	33.3	33.3	33.3	0	33.3	0	0	0	1
118	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
119	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
120	86.7	50	83.3	83.3	75	75	33.3	33.3	66.7	33.3	0	100	0	0	33.3	1
121	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
122	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
123	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
124	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
125	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
126	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
127	86.7	66.7	83.3	100	66.7	66.7	33.3	16.7	16.7	66.7	0	0	0	33.3	66.7	1
128	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
129	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
130	86.7	33.3	16.7	66.7	50	50	66.7	33.3	0	66.7	66.7	100	0	33.3	0	1
131	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
132	66.7	0	25	33.3	0	0	100	83.3	100	66.7	100	33.3	100	0	0	1
133	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
134	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
135	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
136	80	33.3	33.3	66.7	50	50	66.7	0	66.7	0	66.7	66.7	0	0	0	1
137	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
138	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.4 continued Quality of life in gastric and oesophageal cancer patients at 1 year

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
139	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
140	93.3	100	8.33	50	50	50	11.1	0	50	0	0	0	33.3	0	0	1
141	86.7	50	50	66.7	66.7	66.7	44.4	0	33.3	66.7	0	100	0	0	0	1
142	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
143	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
144	100	100	100	83.3	83.3	83.3	33.3	16.7	0	0	33.3	0	33.3	0	0	1
145	86.7	66.7	16.7	50	25	25	100	33.3	50	33.3	66.7	66.7	0	66.7	100	1
146	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
147	66.7	0	0	33.3	16.7	16.7	100	66.7	33.3	33.3	100	33.3	0	33.3	33.3	1
148	93.3	100	50	100	50	50	33.3	0	0	0	33.3	66.7	0	0	0	1
149	93.3	100	91.7	83.3	83.3	83.3	22.2	0	0	0	0	0	0	0	0	1
150	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
151	86.7	66.7	83.3	83.3	50	50	22.2	0	0	33.3	0	33.3	0	33.3	0	1
152	86.7	0	25	33.3	50	50	77.8	66.7	16.7	100	33.3	66.7	0	33.3	100	2
153	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
154	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
155	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
156	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
157	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
158	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
159	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
160	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Median	86.9	57.2	66.5	72.2	56.5	56.5	41.7	23.1	32.2	33.3	30.5	37.8	10.5	17.5	19.4	1.1
Range	66.7-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-66.7	0-100	1-3

* not obtained/ patient deceased

Appendix 4.5 Quality of life in gastric and oesophageal cancer patients at 2 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
1	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
2	100	83.3	100	83.3	100	75	0	0	0	33.3	0	0	0	0	0	1
3	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
4	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
5	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
6	86.7	83.3	83.3	83.3	50	50	33.3	0	0	0	33.3	33.3	33.3	66.7	0	1
7	100	100	66.7	100	100	83.3	0	0	0	0	0	0	0	0	33.3	1
8	86.7	16.7	25	33.3	33.3	33.3	100	100	66.7	100	33.3	66.7	0	0	0	1
9	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
10	73.3	0	100	100	66.7	0	100	33.3	0	100	100	0	33.3	66.7	0	1
11	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
12	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
13	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
14	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
15	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
16	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
17	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
18	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
19	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
20	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
21	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
22	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
23	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
24	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
25	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
26	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
27	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
28	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.5 continued Quality of life in gastric and oesophageal cancer patients at 2 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
29	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
30	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
31	80	50	50	50	33	33.3	77.8	100	50	100	33.3	100	0	100	0	1
32	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
33	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
34	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
35	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
36	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
37	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
38	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
39	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
40	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
41	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
42	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
43	80	83.3	41.7	100	66.7	25	33.3	0	50	33.3	0	66.7	0	0	33.3	1
44	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
45	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
46	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
47	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
48	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
49	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
50	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
51	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
52	93.3	66.7	100	83.3	66.7	75	33.3	0	50	0	33.3	33.3	0	0	0	1
53	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
54	93.3	66.7	100	83.3	66.7	75	33.3	0	50	0	33.3	33.3	0	0	0	1
55	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
56	86.7	33.3	75	83.3	33.3	41.7	55.6	16.7	50	66.7	100	33.3	33.3	0	66.7	1

Appendix 4.5 continued Quality of life in gastric and oesophageal cancer patients at 2 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
57	93.3	66.7	41.7	66.7	66.7	66.7	44.4	0	33.3	0	66.7	33.3	0	0	33.3	1
58	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
59	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
60	66.7	50	75	83.3	66.7	33.3	33.3	0	16.7	33.3	33.3	33.3	0	33.3	0	1
61	100	100	100	100	100	100	0	0	0	0	0	33.3	0	0	0	1
62	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
63	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
64	93.3	100	100	100	100	75	22.2	33.3	0	0	0	66.7	33.3	33.3	0	1
65	73.3	0	91.7	100	0	50	88.9	16.7	100	100	33.3	66.7	100	0	66.7	1
66	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
67	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
68	80	50	41.7	66.7	50	58.3	33.3	16.7	50	0	0	66.7	0	0	33.3	1
69	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
70	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
71	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
72	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
73	93.3	66.7	100	100	66.7	83.3	33.3	0	0	0	0	33.3	0	0	0	1
74	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
75	80	33.3	91.7	66.7	33.3	50	55.6	16.7	50	0	0	33.3	33.3	66.7	33.3	1
76	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
77	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
78	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
79	80	66.7	100	100	33.3	50	33.3	0	0	33.3	0	0	0	33.3	0	1
80	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
81	80	16.7	83.3	100	16.7	33.3	77.8	33.3	83.3	66.7	33.3	66.7	0	66.7	0	1
82	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
83	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
84	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.5 continued Quality of life in gastric and oesophageal cancer patients at 2 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
85	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
86	80	33.3	8.33	50	0	66.7	77.8	33.3	50	33.3	100	0	33.3	100	100	1
87	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
88	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
89	80	66.7	33.3	33.3	0	33.3	77.8	50	83.3	0	33.3	100	33.3	0	100	1
90	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
91	100	83.3	83.3	100	66.7	75	33.3	0	16.7	33.3	0	0	0	0	33.3	1
92	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
93	100	100	100	100	100	83.3	33.3	0	0	0	0	33.3	0	0	0	1
94	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
95	86.7	100	100	83.3	83.3	83.3	33.3	16.7	33.3	33.3	33.3	0	33.3	33.3	0	1
96	100	100	100	100	100	83.3	0	0	0	0	0	0	0	0	0	1
97	100	100	100	83.3	100	83.3	11.1	0	16.7	0	0	0	0	33.3	0	1
98	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
99	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
100	86.7	50	91.7	83.3	50	50	44.4	33.3	33.3	33.3	33.3	66.7	33.3	0	33.3	1
101	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
102	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
103	100	100	100	83.3	100	100	0	0	0	0	0	0	0	0	0	1
104	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
105	86.7	66.7	83.3	100	66.7	33.3	33.3	0	0	66.7	0	0	0	0	66.7	1
106	93.3	100	100	50	66.7	66.7	33.3	33.3	0	0	33.3	33.3	0	33.3	33.3	1
107	73.3	33.3	41.7	16.7	0	16.7	100	16.7	83.3	66.7	66.7	100	0	66.7	0	1
108	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
109	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
110	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
111	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.5 continued Quality of life in gastric and oesophageal cancer patients at 2 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
112	80	50	33.3	50	100	41.7	66.7	66.7	50	66.7	66.7	33.3	33.3	33.3	33.3	1
113	100	100	100	100	100	83.3	0	0	0	0	0	0	0	0	0	1
114	100	50	66.7	66.7	66.7	75	33.3	0	33.3	33.3	0	0	0	0	66.7	1
115	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
116	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
117	100	100	83.3	100	100	100	11.1	0	33.3	66.7	0	0	0	66.7	0	1
118	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
119	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
120	86.7	50	75	100	66.7	66.7	33.3	16.7	33.3	33.3	0	100	100	0	66.7	1
121	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
122	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
123	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
124	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
125	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
126	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
127	100	66.7	91.7	83.3	100	66.7	44.4	0	16.7	33.3	0	33.3	0	33.3	33.3	1
128	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
129	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
130	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
131	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
132	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
133	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
134	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
135	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
136	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
137	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
138	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
139	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.5 continued Quality of life in gastric and oesophageal cancer patients at 2 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
140	100	83.3	100	83.3	100	83.3	0	0	16.7	0	0	0	0	0	0	1
141	80	33.3	33.3	33.3	50	58.3	77.8	0	50	100	33.3	100	33.3	33.3	0	1
142	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
143	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
144	100	100	75	83.3	83.3	66.7	0	16.7	0	0	33.3	0	33.3	0	0	1
145	60	16.7	33.3	33.3	0	16.7	77.8	33.3	50	66.7	66.7	66.7	0	66.7	100	1
146	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
147	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
148	100	100	66.7	83.3	100	66.7	11.1	0	0	33.3	0	0	0	0	0	1
149	93.3	83.3	83.3	66.7	100	83.3	11.1	0	0	0	0	0	0	0	0	1
150	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
151	86.7	66.7	83.3	83.3	66.7	50	22.2	0	0	33.3	0	33.3	0	33.3	33.3	1
152	86.7	16.7	0	33.3	16.7	50	66.7	66.7	66.7	66.7	33.3	100	66.7	33.3	100	1
153	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
154	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
155	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
156	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
157	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
158	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
159	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
160	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Median	87.8	62.5	71	75.8	60.8	58.5	43.3	18.7	31.7	33.3	25.8	37.5	17.1	25	25	1
Range	60-100	16.7-100	0-100	16.7-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	1

* not obtained/ patient deceased

Appendix 4.6 Quality of life in gastric and oesophageal cancer patients at 3 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
1	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
2	86.7	83.3	83.3	83.3	66.7	58.3	33.3	0	33.3	66.7	0	33.3	0	0	33.3	1
3	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
4	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
5	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
6	86.7	50	66.7	83.3	33.3	50	44.4	0	33.3	0	33.3	33.3	0	33.3	0	1
7	100	100	66.7	100	100	83.3	11.1	0	16.7	33.3	0	0	33.3	0	0	1
8	73.3	0	0	0	0	33.3	77.8	50	100	66.7	33.3	100	33.3	33.3	66.7	1
9	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
10	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
11	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
12	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
13	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
14	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
15	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
16	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
17	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
18	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
19	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
20	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
21	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
22	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
23	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
24	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
25	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
26	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
27	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
28	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.6 continued Quality of life in gastric and oesophageal cancer patients at 3 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
29	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
30	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
31	86.7	50	33.3	50	83.3	25	55.6	33.3	66.7	100	66.7	33.3	0	100	0	1
32	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
33	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
34	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
35	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
36	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
37	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
38	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
39	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
40	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
41	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
42	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
43	80	0	25	167	50	0	77.8	100	83.3	66.7	100	66.7	0	0	33.3	1
44	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
45	73.3	16.7	33.3	66.7	33.3	50	66.7	50	50	33.3	33.3	66.7	0	33.3	66.7	1
46	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
47	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
48	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
49	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
50	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
51	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
52	100	83.3	100	100	100	100	0	0	16.7	0	0	0	0	0	0	1
53	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
54	100	83.3	100	100	100	100	0	0	16.7	0	0	0	0	0	0	1
55	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
56	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.6 continued Quality of life in gastric and oesophageal cancer patients at 3 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
57	86.7	50	8.3	66.7	66.7	50	66.7	0	50	100	33.3	66.7	0	66.7	33.3	1
58	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
59	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
60	66.7	0	83.3	100	100	33.3	55.6	33.3	50	66.7	33.3	33.3	0	33.3	0	3
61	100	100	100	100	100	83.3	0	0	0	0	0	0	0	0	0	1
62	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
63	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
64	93.3	100	100	83.3	100	75	33.3	16.7	0	0	0	33.3	0	33.3	0	1
65	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
66	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
67	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
68	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
69	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
70	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
71	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
72	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
73	93.3	83.3	100	100	83.3	83.3	33.3	0	0	0	0	33.3	0	0	0	1
74	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
75	80	33.3	100	83.3	33.3	58.3	44.4	0	33.3	0	0	0	33.3	33.3	66.7	1
76	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
77	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
78	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
79	80	50	100	100	50	50	44.4	0	0	0	33.3	0	0	33.3	0	1
80	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
81	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
82	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
83	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
84	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.6 continued Quality of life in gastric and oesophageal cancer patients at 3 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
85	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
86	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
87	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
88	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
89	80	8.33	8.33	66.7	16.7	16.7	55.6	66.7	50	0	66.7	100	33.3	33.3	66.7	1
90	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
91	100	100	91.7	100	66.7	83.3	11.1	0	16.7	0	0	0	0	0	66.7	1
92	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
93	100	100	100	83.3	100	83.3	33.3	0	0	0	0	0	33.3	0	0	1
94	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
95	80	66.7	66.7	66.7	33.3	58.3	44.4	33.3	50	66.7	66.7	33.3	0	66.7	33.3	1
96	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
97	86.7	83.3	100	83.3	100	66.7	22.2	0	33.3	0	33.3	0	0	33.3	0	1
98	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
99	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
100	86.7	33.3	91.7	83.3	100	83.3	22.2	33.3	33.3	33.3	33.3	33.3	0	0	33.3	1
101	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
102	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
103	100	100	100	83.3	100	100	0	0	0	0	0	0	0	0	0	1
104	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
105	93.3	66.7	66.7	100	66.7	50	33.3	0	0	66.7	33.3	33..3	0	33.3	66.7	1
106	86.7	66.7	100	50	66.7	66.7	11.1	0	0	0	0	33.3	0	0	33.3	1
107	73.3	33.3	50	33.3	33.3	16.7	77.8	50	33.3	66.7	100	66.7	0	33.3	33.3	1
108	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
109	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
110	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
111	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.6 continued Quality of life in gastric and oesophageal cancer patients at 3 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
112	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
113	100	100	100	100	100	83.3	0	16.7	0	0	0	0	0	33.3	0	1
114	100	66.7	83.3	83.3	100	33.3	33.3	16.7	0	33.3	0	0	0	0	33.3	1
115	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
116	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
117	100	100	83.3	100	100	83.3	11.1	0	0	33.3	0	0	0	33.3	0	1
118	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
119	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
120	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
121	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
122	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
123	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
124	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
125	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
126	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
127	100	66.7	75	100	83.3	66.7	33.3	0	33.3	0	0	66.7	0	0	66.7	1
128	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
129	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
130	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
131	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
132	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
133	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
134	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
135	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
136	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
137	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
138	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
139	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.6 continued Quality of life in gastric and oesophageal cancer patients at 3 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
140	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
141	86.7	33.3	41.7	66.7	66.7	50	44.4	16.7	33.3	66.7	0	33.3	100	0	33.3	1
142	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
143	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
144	100	66.7	100	83.3	100	83.3	33.3	33.3	16.7	0	33.3	33.3	66.7	0	0	1
145	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	1
146	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
147	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
148	100	100	100	83.3	100	100	22.2	16.7	0	33.3	0	33.3	0	0	0	1
149	93.3	100	100	100	100	100	0	0	0	0	0	0	0	0	0	1
150	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
151	80	50	66.7	83.3	66.7	50	44.4	16.7	16.7	66.7	33.3	33.3	33.3	33.3	33.3	1
152	86.7	16.7	16.7	16.7	66.7	50	66.7	66.7	33.3	100	0	100	33.3	0	100	1
153	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
154	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
155	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
156	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
157	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
158	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
159	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
160	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Median	88.7	61.1	70.8	75	72.2	60.5	37.8	21.1	27.8	30	23.3	33.3	12.2	21.1	25.5	1.1
Range	66.7-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	0-100	1-3

* not obtained/ patient deceased

Appendix 4.7 Quality of life in gastric and oesophageal cancer patients at 4 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
1	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
2	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
3	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
4	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
5	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
6	86.7	50	75	83.3	33.3	50	33.3	0	66.7	0	0	33.3	0	66.7	0	1
7	100	100	66.7	100	83.3	83.3	11.1	0	0	0	0	0	33.3	0	0	1
8	73.3	0	8.3	0	0	33.3	88.9	16.7	33.3	66.7	66.7	100	100	0	33.3	1
9	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
10	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
11	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
12	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
13	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
14	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
15	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
16	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
17	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
18	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
19	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
20	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
21	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
22	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
23	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
24	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
25	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
26	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
27	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
28	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.7 continued Quality of life in gastric and oesophageal cancer patients at 4 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
29	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
30	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
31	80	16.7	25	66.7	83.3	50	66.7	33.3	66.7	33.3	33.3	66.7	0	66.7	0	1
32	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
33	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
34	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
35	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
36	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
37	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
38	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
39	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
40	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
41	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
42	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
43	80	16.7	16.7	33.3	50	25	100	83.3	100	66.7	66.7	100	33.3	0	33.3	1
44	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
45	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
46	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
47	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
48	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
49	73.3	0	91.7	100	0	66.7	22.2	0	83.3	0	0	33.3	0	0	0	1
50	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
51	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
52	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
53	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
54	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
55	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
56	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.7 continued Quality of life in gastric and oesophageal cancer patients at 4 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
57	86.7	66.7	50	66.7	50	33.3	33.3	16.7	50	0	0	100	0	66.7	33.3	1
58	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
59	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
60	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
61	100	100	83.3	100	100	83.3	11.1	16.7	16.7	0	0	0	0	0	0	1
62	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
63	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
64	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
65	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
66	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
67	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
68	86.7	50	66.7	83.3	50	75	11.1	0	16.7	33.3	0	66.7	0	0	0	1
69	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
70	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
71	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
72	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
73	93.3	83.3	100	100	100	83.3	33.3	0	0	0	0	0	0	0	0	1
74	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
75	80	16.7	66.7	50	50	50	66.7	50	33.3	33.3	66.7	66.7	33.3	33.3	33.3	1
76	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
77	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
78	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
79	80	50	100	100	66.7	50	33.3	0	16.7	33.3	0	0	0	0	0	1
80	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
81	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
82	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
83	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
84	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.7 continued Quality of life in gastric and oesophageal cancer patients at 4 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
85	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
86	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
87	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
88	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
89	86.7	33.3	25	66.7	16.7	8.33	77.8	50	66.7	0	100	100	33.3	0	100	1
90	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
91	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
92	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
93	100	100	100	100	100	83.3	33.3	0	0	0	0	0	0	33.3	0	1
94	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
95	86.7	66.7	66.7	66.7	66.7	58.3	66.7	50	33.3	100	33.3	66.7	33.3	33.3	33.3	1
96	100	100	100	100	100	100	0	0	0	0	0	0	0	0	0	1
97	93.3	100	100	83.3	100	66.7	22.2	0	0	33.3	0	0	0	33.3	0	1
98	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
99	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
100	86.7	16.7	66.7	50	33.3	33.3	66.7	33.3	83.3	33.3	66.7	100	33.3	0	33.3	1
101	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
102	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
103	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
104	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
105	93.3	66.7	91.7	83.3	66.7	33.3	33.3	0	0	33.3	33.3	33.3	0	0	66.7	1
106	86.7	50	100	50	66.7	58.3	22.2	0	0	33.3	33.3	0	0	0	33.3	1
107	80	33.3	50	16.7	0	25	88.9	33.3	50	100	100	100	0	100	0	1
108	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
109	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
110	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
111	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.7 continued Quality of life in gastric and oesophageal cancer patients at 4 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
112	86.7	33.3	66.7	50	50	41.7	66.7	33.3	50	33.3	66.7	66.7	33.3	33.3	33.3	1
113	100	100	100	100	100	83.3	0	0	0	0	0	0	0	0	0	1
114	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
115	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
116	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
117	100	100	75	100	100	100	33.3	0	33.3	33.3	0	0	0	33.3	0	1
118	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
119	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
120	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
121	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
122	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
123	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
124	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
125	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
126	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
127	100	100	100	100	100	83.3	0	0	0	0	0	0	0	0	0	1
128	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
129	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
130	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
131	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
132	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
133	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
134	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
135	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
136	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
137	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
138	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
139	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Appendix 4.7 continued Quality of life in gastric and oesophageal cancer patients at 4 years

EORTC QLQ-C30

Study No	Physical function	Role function	Emotional function	Cognitive function	Social function	Quality of Life	Fatigue	Nausea	Pain	Dyspnoea	Appetite loss	Sleep disturbance	Constipation	Diarrhoea	Financial difficulty	Dysphagia
140	86.7	33.3	58.3	33.3	66.7	50	33.3	0	50	100	33.3	33.3	0	66.7	0	1
141	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
142	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
143	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
144	100	100	100	66.7	100	66.7	33.3	50	0	0	33.3	0	33.3	33.3	0	1
145	73.3	16.7	41.7	33.3	0	33.3	77.8	33.3	33.3	66.7	66.7	100	0	66.7	100	1
146	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
147	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
148	100	100	66.7	83.3	100	66.7	11.1	0	0	33.3	0	0	0	0	0	1
149	93.3	100	100	100	100	66.7	11.1	0	0	0	0	0	33.3	0	0	1
150	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
151	73.3	16.7	50	50	16.7	50	66.7	33.3	0	100	0	100	33.3	3.3	66.7	1
152	86.7	33.3	0	16.7	0	50	77.8	83.3	50	100	0	100	0	33.3	100	1
153	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
154	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
155	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
156	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
157	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
158	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
159	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
160	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Median	88.5	57.5	68.4	68.9	60.9	57.7	42.1	19.5	31.6	32.2	26.4	42.5	13.8	24.1	19.5	1
Range	73.3-100	0-100	0-100	0-100	0-100	8.3-100	0-100	0-83.3	0-100	0-100	0-100	0-100	0-100	0-100	0-100	1-3

* not obtained/ patient deceased