Evaluation of Quality of Life in Greek Colorectal Cancer Survivors

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Georgia Doga

School of Health and Social Sciences
Middlesex University

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ABSTRACT

Survival from cancer is becoming a reality for more people in the world each year. Survival rate from colorectal cancer disease is approximately 80% one year after diagnosis, but falls to 62% at 5 years from diagnosis. Quality of life research in colorectal cancer to date has focused on investigating patients' experience during the diagnostic or treatment phase while the experiences of those who have survived this cancer have been ignored.

Based on the concept of Health-Related Quality of Life (HRQOL) this study was focused on understanding and assessing the impact of colorectal cancer disease and its treatment on Greek patients' HRQOL over time. Also, this study sought to identify multiple factors (related either to patient or disease characteristics) that contributed to patients' HRQOL in both specific and general domains. Age, gender, stage at diagnosis, time elapse since diagnosis, income, education, colostomy appliance, disease recurrence, depression and communication between couples were examined for their effect on HRQOL over time.

145 Greek outpatients (male 87, female 58) completed the Functional Assessment of Cancer Therapy-Colorectal (FACT-C) Quality of Life Instrument and the Mental Component of the Short Form 36 Health Survey questionnaire measuring both generic and disease-specific HRQOL, as well as the Center for Epidemiologic Studies Depression Scale (CES-D) to detect depressive symptoms, and the Enriching & Nurturing Relationship Issues, Communication & Happiness (ENRICH) scale to assess communication between couples, at an interval of either one year or more than 5 years since diagnosis. Statistical significance was set at ($p<0.05$) and data were analysed using the Statistical Package for the Social Sciences (SPSS).

The findings suggest that patients who survived colorectal cancer experienced an overall high quality of life independent of the stage of disease at diagnosis or time since diagnosis. Among those factors that had a negative effect on patients overall HRQOL over time depression was the most prevalent. Stoma patients experienced an overall lower HRQOL than non-stoma patients. Most domains of HRQOL assessment such as physical, emotional and role functioning of stoma patients were negatively affected, but these did not reach statistical significance. Notably, stoma patients in this sample showed significantly more dissatisfaction with body image than patients without a stoma - a finding that was more prevalent in women. This may suggest that stoma formation negatively affects sexual function and body image. Finally, patients with lower incomes and a recurrence or metastatic disease also experienced a poorer HRQOL.

It is recommended that a practice-based strategy is developed in Greece to assess the HRQOL and psychosocial functioning of these patients as well as the recommendation that in the preoperative stage, after surgery and in the rehabilitation phase for stoma patients to be assessed and supported by a specialist Stoma Care nurse. Other suggestions for future research are also proposed.

CHAPTER 1

INTRODUCTION

1.1 Background and Rationale of the Study

Colorectal cancer is a major health problem since it is the second leading cause of cancer mortality in many developed countries (Stewart, 2003). Approximately 1 million new cases of colorectal cancer occur in the world each year (Ferlay et al., 2001). In Greece, 1,670 new cases were officially registered in 1990 (Greek Cancer Registry Central Health Council, 2000), while in 2002 were estimated 3,769 new cases of cancer of colon and rectum according to GLOBOCAN figures (GLOBOCAN, 2002). The year 2004 the number of deaths by colorectal cancer was estimated to 2,126 people (WHO, 2004).

More men are affected by colorectal cancer than females (Fraser & Adelstein, 1982) while it is a disease that mainly affects the older adult population. So, more than half of patients are over 60 years old, with a peak incidence in people aged 70-80 years old (Engstrom et al., 1999; Jones, 1999).

The prognosis is influenced by a number of factors at the time of diagnosis including age, the type, size and position of the tumour, the extent to which the tumour has spread as well as the depth of penetration of the tumour through the bowel wall (Skibber et al., 2001). Survival rates are significantly

improved when a diagnosis of early stage (Dukes A and B) is made (Table 2.2).

The most common therapeutic choice for colorectal cancer remains surgery. It may be used alone or in combination with radiotherapy and chemotherapy. The location and the extent of the malignancy will determine the type of surgical resection (Skibber et al., 2001). Left hemicolectomy, right hemicolectomy and sigmoidectomy are types of surgery which are used in the treatment of colon cancer. During these surgical procedures the piece of bowel that contains the cancer is removed and the two open ends are rejoined. The abdominoperineal excision is a treatment of choice for rectal cancer when the tumour is situated in the lower part of the rectum, resulting in a permanent colostomy. The anterior resection is a therapeutic choice for rectal cancer when the tumour is not very close to the anal sphincter, resulting in the preservation of the sphincter function (Skibber et al., 2001; Hoebler, 1997).

Adjuvant therapy, chemotherapy or radiotherapy, is commonly given after surgery to eliminate any residual cancer and to reduce the risk of the cancer reoccurring. Also, they can be used with patients who may have a poor prognosis (Giles & Venables, 1994), or with patients who have developed secondary cancer in other parts of the body (Cancer BACUP, 2001). The effectiveness of chemotherapy and radiation therapy depends on some factors such as disease stage, methods of treatment, but before any conclusion is made, further research is required.

The early detection of the disease, as well as the modern achievements in medicine and technology that have contributed to the development of new

therapeutic interventions, prolongs patients' survival changing colorectal cancer from being regarded as a life threatening illness to a chronic disease, for many patients. Across all disease stages, approximately 80% of patients now survive the first year after diagnosis from colorectal cancer and approximately 62% survive 5 years and beyond (Brenner, 2002).

Although much work has been undertaken investigating people's experience of cancer during the diagnostic or treatment phase, little work had been done investigating people's experience of cancer and quality of life after treatment. The improvements in survival have required attention to explore the needs of patients as they enter the post-treatment/survivorship phase of their cancer journey (Zebrack, 2000; Given et al., 1997). It is becoming increasingly recognized that the survivorship phase is often a difficult and complex journey for many, with no guarantee that those surviving cancer will return to a state of "normal" health similar to the one experienced before their diagnosis of cancer or similar to healthy peers (Schag et al., 1994). This has resulted in increasing attention on the challenges faced by patients as they move into their post-treatment/survivorship phase with particular focus on understanding and assessing the impact of cancer survival on quality of life.

The term Quality of Life (QOL) correlated with a broad range of conditions of life that result to a "good life", "well-being", "happiness", or "life satisfaction". These conditions of life include social indicators (wealth, safety), physical conditions, health satisfaction, or personal resources (including mental health and life perspective) (Rapley, 2003; Cella et al., 2002). The WHOQOL Group (1993, p. 1) defines QOL as "*An individual's*

perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations values and concerns". Important QOL dimensions are: physical health, psychological state, level of independence, social relationship, personal beliefs and relationship to the environment (WHOQOL, 1993). Health outcomes research narrows the field to those domains or components of QOL that are important to patients and are experienced as a result of illness and medical procedures. Patients give their subjective information about perceived health and quality of life while a number of terms have been adopted into the literature to describe the Health Related Quality of Life (HRQOL) from patients' perspective (Sullivan, 2003; Cella et al., 2002). There is now consensus that the HRQOL should be an end point of concern alongside more objective measures (e.g. 5 year survival) in new cancer trials and intervention studies. Although there is not now an agreed definition of HRQOL, a definition accepted by David Cella has guided the assessment of this study and understanding of basic concepts. According to this definition *"Health-Related Quality of Life is a subjective and multidimensional concept that refers to the extent to which one's -usual or expected- physical, emotional, social well-being are affected by a medical condition or its treatment"* (Cella, et al., 2002, p. 11). For the cancer survivor, assessment of HRQOL should not only consider living with cancer symptoms (e.g. pain and fatigue) and treatment side-effects, such as a living with a colostomy, lymphoedema, amputation but also the broader aspects of the individual's psychological and social well-being.

Research suggests that although the physical functioning of cancer survivors varies from site to site over time, the impairment of psychosocial

functioning of their quality of life and depression are common. A study by Schag et al. (1994) concludes that patients who survived lung, colon and prostate cancer all had psychological distress in the disease-free phase of their illness. Other issues purported to affect cancer survivors include fears of recurrence, metastases, and death, dependence on caregivers, survivor guilt and negative effects on the family (Barsevick et al., 1997).

Especially for colorectal cancer, both surgical procedures, either low anterior resection or abdominoperineal excision necessitate dissections that may result in changing patients' physical and sexual functioning; very often with long-term impact. Particularly, anterior resection may damage the pelvic nerves that are involved in sexual functioning. Furthermore, with this technique, internal anal and sphincter control may be impaired (Skibber et al., 2001; Sprangers et al., 1995). During abdominoperineal procedure in men some nerve fibers are destroyed that are vital to the genital system, causing sexual dysfunction and impotence (Grumann et al., 2001; Allal et al., 2000; Hoebler, 1997; Sprangers et al., 1995). Sexual functioning is not the only area that is affected by the illness and its treatment. A variety of physical side-effects may still impair a patient's life after the surgery phase including diarrhoea, faecal leakage, frequencies of bowel movement, urinary problems and disturbed sleep (Lewis et al., 1995; Sprangers et al., 1995; Williams & Johnston, 1983). The degree to which these symptoms are experienced in stoma and non-stoma patients varies. On the other hand, the colostomy appliance is a consequence of surgery that is expected to cause considerable problems such as physical and social limitations, as well as psychological distress in patients' lives over time (Camilleri-Brennan &

Steele, 1998; Sprangers et al., 1995; McDonald and Anderson, 1984; Williams and Johnston, 1983).

It is also well regarded that treatment should not be the only factor to shape people's perception of their HRQOL and cancer experience during the post-treatment/ survivorship phase. Delvin et al. (1971) many years ago showed that people from a lower social class, with lower income, and poorer education experienced poorer quality of life. Ramsey et al. (2000) concluded that low income status is associated with worse outcomes for some aspects of HRQOL. Also, tumour factors such as location of tumour and stage of disease may interact with treatment determining HRQOL over time.

Furthermore Health-Related Quality of Life is seen as a dynamic concept which can change over time as people change perceptions about their health outcome, or change their expectations in terms of specific life circumstances (often referred to as response shift bias) (Carr, 2001; Sprangers, 1999; Calman, 1984). Therefore, an important area of consideration is how HRQOL changes during the post-treatment /survivorship phase. Deficits in peoples' HRQOL are experienced in emotional, physical, social functioning, and fatigue after six months and 1 year survival when compared with healthy populations (Arndt et al., 2004; Kopp et al., 2004). Regarding long-term survivors, findings are very limited, and little if any work has examined the HRQOL of cancer survivors from Greece.

Two recent studies (Rauch et al., 2004; Mosconi et al., 2002) have compared the long-term HRQOL of colorectal cancer survivors with those of the general population. These studies show that colorectal survivors reported a satisfied HRQOL, very often comparable with those of the general population in most QOL domains.

Knowledge of the experience of cancer over time is useful to clinicians to prevent possible late effects of the disease during follow-up evaluations, or to policy makers to plan specific health programs.

Having identified the need for further research in relation to the colorectal cancer experience and its impact on quality of life of patients, years after the treatment and rehabilitation stage, the literature in this area was reviewed. Key areas were considered relevant to explore. Firstly, to identify the current evidence relating to the quality of life of patients who had survived colorectal cancer and the factors that contribute to the current quality of life status; secondly, to explore the evidence relating to the comparison of quality of life of these people with those of the general population.
Such a review reveals that most studies on colorectal cancer at present have used HRQOL as an outcome of clinical trials but not as a primary end point of concern while studies that have evaluated long-term effect of colorectal cancer disease on HRQOL are very limited. Also, very few measure global HRQOL using validated disease-specific instruments. There appears to be no study that measures quality of life with a disease-specific measure such as FACT-C (Appendix 9) that comes from USA developers, in European population.

1.2 Greek Patients with Colorectal Cancer

In Greece, there is a mixed system of public-private funding and provision of health care services. Its development is based, to a large extent, on social

insurance. The Greek health care system constitutes three subsystems, which operate almost independently: (a) the National Health System, which comprises public hospitals, health centres, and the National Centre of Emergency Assistance, (b) the Social Security Institution and other Social insurance Funds, and (c) the private sector, with numerous diagnostic centres, private clinics, and laboratories. Colorectal cancer patients are treated in both public and private hospitals. Socio-economic status is the main factor that distinguishes cancer patients who seek medical care in the private hospitals in which they have to pay from those who are hospitalized in the public free hospitals.

Regarding the care and information disclosure for cancer patients in Greece, withholding the truth from a cancer patient appears common. Only 25% of physicians admit that they reveal the diagnosis or prognosis to the patient with cancer (Mystakidou, et al., 1999). A recent study (Mystakidou et al., 2002) found that only a small percentage (23%) of relatives of cancer patients believe that the diagnosis and prognosis should be revealed to the patients, while the majority (54%) of relatives believes that only "sometimes" they would agree for the patient to be informed. However, they are also of the opinion that patients should be given information on possible treatment choices (71%), and the complications or side effects of treatment (53%). It seems that caregivers take all the responsibilities, or even decide on the patients' behalf, and the person remains in ignorance. Although in most European countries, doctors tend to reveal the truth directly to patients, without the family's consent, this is not yet common practice in Greece; possibly as a result of strong family bonds. Strong family relations in Greek society, which are still traditional and collectivist, help parents with health

problems restore their morale by getting support from their adult children, and feeling useful to them. Thus, in the face of adversity, family members maintain their subjective quality of life through supportive family relationships, and may experience higher levels of life satisfaction (Efklides, Kalaitzidou, & Chakin, 2003).

Regarding the psychosocial factors that may contribute to the adjustment of Greek cancer patients to their disease, Spanea, Anagnostopoulos, Kalantzi-Azizi, and Skarlos (2005) have found that no medical (e.g disease stage at diagnosis, type of surgery), demographic (e.g., age, education), or psychological (e.g., coping strategies) variables were associated with psychosocial adjustment (mental health functioning). The exception was anxious preoccupation (characterized by constant preoccupation with cancer and feelings of devastation, anxiety, tears and apprehension) which negatively influenced psychological well-being and adjustment.

1.3 Objectives

The present study provides an insight into a specific cultural group of colorectal cancer survivors that have not been investigated before.

It attempts to evaluate specific dimensions of HRQOL and overall HRQOL of Greek Colorectal cancer survivors after the treatment phase of their cancer journey to mid/long term survival. It also identifies those factors (clinical, demographic) contributing to the current state of the HRQOL at one year after diagnosis and beyond.

1.4 Basic Research Questions

The present study was designed to answer the following questions:

1. How do Greek colorectal cancer patients perceive their HRQOL during the post-treatment /survivorship phase?

2. What factors (clinical, demographic) influence colorectal cancer patients' HRQOL?

3. How do HRQOL measures change for patients with colorectal cancer of different stages at diagnosis, and at different times since diagnosis?

1.5 Overview of the Study

Chapter 1 includes an introduction to the study that consists of general information about the problem of colorectal cancer. The problem of those people who have survived cancer of colon and rectum, the rationale, and the significance of the study, the cancer experience within the Greek context, and the study's objectives are also provided.

Chapter 2 describes the problem of colorectal cancer emphasizing the epidemiology, etiology, symptoms and curative procedures.

In Chapter 3 the relevant literature review examines the need and demand for consideration of HRQOL in colorectal cancer survivors as well as the effect that the disease and treatment have on patients' quality of life years after diagnosis. It specifically describes differences that were observed over time in quality of life between stoma and non-stoma patients.

In chapter 4 the literature review describes the conceptual basis of QOL and how it has been constructed and debated into the literature. Also, it examines

the need and demand for HRQOL assessment in the context of the cancer experience as well as the current methods of HRQOL assessment in cancer patients.

Chapter 5 consists of the methodology of the research and presents the procedures and design used in this study. It focuses on investigating Greek patients' cancer experience through a subjective assessment of their HRQOL. It presents the main objectives, research questions and the hypotheses of the study. Also included are a description and selection of the populations and the sample, description and validation of the criteria instruments and description of data collection. The techniques for data analysis are also included.

The findings of the study are presented in chapter 6.

The discussion of the findings, implications, and recommendations for further related research are presented in chapter 7.

Chapter 8 includes the conclusions, and the final section contains the selected bibliography and appendices.

CHAPTER 2

COLORECTAL CANCER

2.1 Introduction

This chapter gives an introduction to colorectal cancer. Consideration of the epidemiology, symptomatology, diagnostic techniques, staging and therapy of the disease are presented. An overview is also given of current screening perspectives for early detection of risk factors for individuals.

2.2 Epidemiology of Colorectal Cancer

Colorectal cancer, also known as large bowel cancer, refers to cancer of the colon and rectum.

The epidemiology of colorectal cancer has generated more interest recently, because this disease may provide a particularly good model for the study of interactions of genes and environment in the aetiology of cancer (Skibber et al., 2001).

Colorectal cancer is the third most commonly diagnosed malignancy in the U.S for both women and men after breast and lung cancer and prostate and lung cancer respectively (Jemal et al., 2003). In 2003, more than 130,000 new cases of colorectal cancer were diagnosed in the U.S. (Jemal et al., 2003).

Almost one million new cases occur in the world each year (Ferlay et al., 2001).

In 2004 in Europe the most common form of cancer was lung cancer (13.3% of all incident cases), followed by colorectal cancer with 376,400 incident cases (13.2%) and 203,700 (11.9%) was the number of colorectal cancer deaths in Europe the same year (Boyle & Ferlay, 2005).

In the United Kingdom it is reported to be the second most common cause of cancer disease after lung cancer with 30,000 people diagnosed each year from which approximately 18,000 will die (Scottish Cancer Therapy Network, 2000).

In Greece colorectal cancer is the fourth most commonly diagnosed malignancy for men after lung, prostate, and bladder cancer and the fourth cause of death after lung, prostate and liver cancer (GLOBOCAN, 2002). For women colorectal cancer is the second most commonly diagnosed malignancy after breast cancer and the second cause of death after breast cancer (GLOBOCAN, 2002). While in 1990 1,670 new cases were registered in Greece (Greek Cancer Registry Central Health Council, 2000), according to GLOBOCAN figures for Greece in the year 2002, 3,769 new cases of cancer of colon and rectum were registered, and in the same year the number of deaths by colorectal cancer was 2,031 (GLOBOCAN, 2002). A Similar number of deaths -2,126 deaths-from colorectal cancer was reported for Greece in the year 2004 by WHO data (WHO, 2004).

The incidence of colorectal cancer is higher in North America, Western Europe, Australia and New Zealand, whereas the age–standardized incidence rate of colorectal carcinoma is very low in India and Africa. Sharp

increases in incidence have been seen in Eastern Europe and Japan and the incidence rates vary tenfold between developed and developing countries (Skibber et al., 2001).

The dramatic rise in incidence in some countries points to environmental rather than genetic factors (Skibber et al., 2001; Wilmink, 1997). Immigration from a low-incidence to a high incidence environment will increase a person's risk (Skibber et al., 2001).

Advances in treatment increase the number of colorectal survivors over time. Across all disease stages, approximately 80% of patients now survive beyond the first years after diagnosis (Brenner, 2002). A 5-year survival rate of 61% is reported by the U.S. (Skibber et al., 2001). In Greece 10,253 people survived 5-years after the time of diagnosis according the GLOBOCAN figures for the year 2002 (GLOBOCAN, 2002). The survival rate is around 41% to 42% in European and Indian registries (Skibber et al., 2001). Lower survival rate of 32% and 38% are reported in China and developing countries respectively (Skibber et al., 2001).The lowest estimated survival rate of 30% is in Eastern Europe (Skibber et al., 2001). Survival rates are significantly improved when a diagnosis of early stage (Dukes A and B) is made.

Male incidence adjusted for age and ethnicity, appears greater than female rates (Skibber et al., 2001). Age- specific registration rates of colon and rectal cancer show a 6.7 % increase for males and a 0.7 % increase for females in the Birmingham Cancer Registry per five year period during the period 1970 to 1987 in England (Wilmink, 1997). In Greece 1,937 men and

1,832 women diagnosed during the year 2002 with colorectal cancer (GLOBOCAN, 2002).

It is suggested that women tend to be younger than men at diagnosis with mean ages of 55.1 years and 58.6 years respectively (Dukes, 1940). Also, women have been found to have a better prognosis than men depending on whether they have had children; nulliparous women having the same prognosis as men (Koch, McPherson & Egedahl, 1982).

Colorectal cancer is a disease of elderly people. Less than 5% of colorectal cancer patients are under the age of 40, while more than half are over 60; with a peak incidence in people aged 70-80 years old (Jones, 1999).

2.3 Aetiology and Risk Factors of the Disease.

Colorectal cancer has long been recognized to have a familial component. Two features of colorectal cancer have been fundamental in the recent progress in understanding its genetics basis. First, the majority of colorectal cancer arises from premalignant adenomatous polyps and has a monoclonal composition. Second, there are two well-defined inherited syndromes that predispose to colorectal cancer although the number of hereditary colon cancer syndromes has been expanding rapidly. These are the classic familial adenomatosis polyposis (FAP) syndrome and hereditary nonpolyposis colorectal cancer (HNPCC) syndrome (Won-Seok Jo & Chung, 2004).

The FAP is characterized by the development of multiple colonic adenomas and is caused by mutations in the tumor suppressor gene (APC gene) on chromosome 5. Although it is responsible for only 1% of colorectal cancers it has 100% lifetime risk for developing colorectal cancer before the age of 40 years (Won-Seok Jo & Chung, 2005). The HNPCC may account for as

much as 6 % of the patients with colorectal cancer whilst the individuals who have nonpolyposis syndrome are considered to be at 80% risk for developing colon cancer by age of 50 (Bell, 2005; Bromer &Weinberg, 2005; Won-Seok Jo & Chung, 2005;).

Epidemiological factors have provided initial evidence about the specific factors that initiate the process of carcinogenesis in the large bowel mucosa. Amstrong and Doll (1975) first described the high correlations of incidences and mortality rate of colorectal cancer with the consumption of meat, animal protein and fat. Diets high in fat increase the production and change the compositions of bile salts. These altered bile salts are converted into potential carcinogens by intestinal flora (Hoebler, 1997). Among the risk factors studied are also the intake of red meats cooked at high temperatures due to neterocyclic amines that are then present. On the other hand dietary fiber has been found to protect against colorectal cancer (Skibber et al., 2001).

Patients with chronic ulcerative colitis have an increased risk of colorectal cancer (Bernhard & Hunry, 1998; Wilmink, 1997). Two independent risk factors for cancer among these patients have been well documented: younger age at diagnosis and extent of disease at diagnosis. The increased risk of patients with Crohn's disease (CD) is considered less certain (Wilmink, 1997).

Identification of colorectal cancer-related syndromes, as well as identification of all the other colorectal cancer-related factors, is very

important for a new approach to cancer risk assessment and cancer screening for affected individuals and their families, or for the general population. Table 2.1 demonstrates risk categories for colorectal cancer disease and screening recommendations.

Table 2.1: Current Recommendations for CRC Screening for High-Risk, Intermediate-Risk and Average (Low)-Risk Individuals

Risk Categories	Screening Recommendations
High-Risk Category	
- Patients with Familial Adenomatous Syndrome (FAP)	- If genetic test is positive: annual Flexible Sigmoidoscopy (FS) beginning at age 10-12 years; if no polyps, annual FS to age 40, then 3-5 years thereafter; for patients with attenuated FAP (AFAP) (characterized by germline APC mutation, but fewer polyps) annual colonoscopy initiated by the age 25 years. If genetic test is negative: FS in all potentially affected relatives like Intermediate Risk Category for family history of colorectal cancer or Adenomatus Polyps.
- Patients with Hereditary Nonpolyposis Syndrome (HNPCC)	- Colonoscopy every 1-2 years beginning at age 25, or 10 years before the earliest case within the family, whichever comes first, annual screening after age 40.
-MYH Polyposis Syndrom	- No official guidelines; like recommendations for screening in attenuated FAP.
Intermediate-Risk Category	
- Peutz-Jegher's Syndrome (PJS)	- Colonoscopy every 3 years starting at age 18 years.
- Juvenile Polyposis Syndrome (JPS)	- Colonoscopy every 1 to 2 years starting at age 15 to 18 years.
- Hyperplastic Polyposis Syndrome (HPS)	- Colonoscopy 1 year after diagnosis and then every 2 to 3 years.
- Patients with personal History of Adenomatous Polyps	- Colonoscopy every 3 to 5 years.

- Patients with personal History of Colorectal Cancer	- Colonoscopy 12 months follow resection; subsequently every 3 years.
- Personal history of Inflammatory Bowel Disease - Uncerative Pancolitis > 8 years - Crohn's Pancolitis >8 years -Left-sided ulcerative colitis >15 years -Personal history of Colonic Adenomas	-Colonoscopy with 4 quadrant biopsies every 10 cm to rule out dysplasis every 1 to 2 years.
- Family history of Colorectal Cancer or Adenomatous Polyps: first-degree relatives with sporadic CRC or adenomas prior to age 60 or multiple first-degree relatives with CRC or adenomas); -Second or third-degree relatives with sporadic CRC or Adenomatous Polyps.	- Colonoscopy beginning at age 40, or 10 years younger than the age at diagnosis of the youngest affected relative. The interval between normal colonoscopies should be 5 years in this setting. -Recommendations like average-risk category for general population
Average-Risk Category or Low Risk Category - Bloom's Syndrome	- Colonoscopy starting in the early third decade of life.
- I1307K APC Polymorphism	- Genetic test has little impact upon clinical management.
-"Breast-colon cancer" syndrome (BRCA1)	- Screening is not recommented.
- General population at age 50 without: previous history of colorectal cancer or adenoma, one or more first-degree relatives	Colonoscopy is considered the "gold standard". It is recommended every 10 years. Other recommended techniques include: Fecal Occult Blood Testing (FOBT), Flexible Sigmoidoscopy (FS), Double-Contrast Barium Enema (DCBE), Stool-Based DNA Testing.

Won-Seok Jo & Chung, 2004; Bromer & Weinberg, 2004

2.4 Symptoms of Colorectal Cancer

The symptoms of colorectal cancer depend on the stage of the disease and the area of the colon that is involved. The problem with colorectal cancer is that it may present with no symptoms at all in early stages, or its symptoms are also found in other conditions such as ulcers, gallstones, haemorrhoids or reactions to certain foods - conditions far less serious than colorectal cancer. The majority of patients present either with abdominal symptoms such as abdominal discomfort, a persistent (6 weeks) change in bowel habits, particularly looser stools or increased frequency, or symptoms of anaemia such as weakness and fatigue, rectal bleeding (especially if it is not associated with anal symptoms such as itching, pain or soreness) or mucus discharge per rectum. Persons whose cancer involves the rectum may experience a feeling of rectal fullness, painful spasms, change in bowel movements, and change in the diameter of stools. Pain, diarrhoea or vomiting may be other symptoms of colorectal cancer (Thompson & Wells, 2006; Bell, 2005; Skibber et al.,, 2001; Hoebler, 1997).

2.5 Diagnosis of Colorectal Cancer

Early diagnosis is essential in maximizing the chance of survival (Bernhard & Hunry, 1998). Unfortunately, the diagnosis of colorectal cancer is often delayed due to the wide range of gastrointestinal problems common to the general population (Holliday & Hardcastle, 1979) as most symptoms are concerned with elderly populations (Curless, et al., 1994). The main diagnostic and screening method for colorectal carcinoma is colonoscopy.

Colonoscopy has the advantage of visual examination of the entire colon with the option of biopsies to be taken or polyps to be removed at the time of the procedure. This examination may be suggested after positive results obtained by other diagnostic tests (Bell, 2005; Bromer & Weinberg, 2005). Fecal Occult Blood Testing is usually used for detecting hidden blood in the stool. It has advantage that it is inexpensive and easy to accomplish but is not sensitive enough for detecting polyps and colorectal cancers since at many times both produce false positive and false negative results (Bromer & Weinberg, 2005; Hoebler, 1997).

Flexible Sigmoidoscopy is also a visual examination of the rectum and lower third of the colon. The double-contrast barium enema is also a valuable diagnostic procedure of colorectal cancer and has a rate greater than 90% accuracy for detecting colon cancer and polyps 6 to 10 mm (Bromer & Weinberg, 2004).

More recently, genetic tests that detect DNA alterations are used in the screening of the high-risk groups (Bromer & Weinberg, 2005; Won-Seok Jo & Chung, 2005).

2.6 Staging Classifications and Prognostic Features

The need for a staging system which would determine the treatment choice, allow comparisons among different surgical treatments, and determine prognosis, led to the first classification system which was introduced by Dukes in the 1930s (Table 3.2). Dukes' staging system has been modified many times over the years in order to include additional prognostic factors beyond the depth of tumor invasion and extent of lymph node metastases (Skibber et al., 2001; Hoebler, 1997).The American Joint Committee on

Cancer (AJCC) has developed the Tumour, Node, Metastasis (TNM) staging system for colorectal cancer that is compatible with Dukes system but it adds greater precision in identification of prognostic subgroups (Table 3.3). The TNM system describes the degree the tumour - usually started as a polyp and change in situ carcinoma – extent of invasion into gastrointestinal mucosa, the number and site of regional lymph nodes involved, as well as the spread of the cancer to other areas of the body. The TNM system also classifies a tumour based on histological grade, including four levels from well-differentiated to undifferentiated.

As with most cancers, the stage of colorectal cancer at the time of diagnosis or at the time that treatment started is the most reliable prognostic factor. Furthermore, other independent prognostic factors for survival have been identified such as age, gender, carcinoembryonic antigen (CEA) level, vascular invasion, DNA content, tumour grade, (Skibber et al., 2001).

Table 2.2: Dukes' classification and corresponding five-year survival rate

Dukes' Stage	Pathological description	Five- year survival rate
A	Cancer confined to mucosa and submucosa	>90%
B1	Cancer extends into the muscularis	85%
B2	Cancer extends into or through the serosa	70%-85%
C	Cancer involves the regional lymph nodes	30%-60%
D	Cancer has metastasized to distant organs or structures	5%

Source: Mayer RJ :Tumours of the large and small intestine. In Isseibacher KJ, Braunwald E, Wilson JD, et al (Eds): Harrison's Principles of Internal Medicine (ed 13). New York, McGraw-Hill,1994,p 1428

Table 2.3: Colorectal cancer stage classification and grouping. American Joint Committee on Cancer (AJCC), (1997).

Pathologic description	AJCC (1997)	Astler-Coller Modification Duke's Stage
Carcinoma in situ (Tis) N0: No regional lymph node metastasis. M0: No distant metastasis	Stage 0:Tis, NO, MO	Stage 0
Tumour invades submucosa (T1)	Stage I:T1, NO,MO	Stage I-A
Tumour invades muscularis propria (T2)	Stage I:T2, NO, MO	StageI-B1
Tumour invades muscularis propria into subserosa or nonperitonealized perirectal tissues (T3)	StageII:T3, NO, MO	Stage II-B2
Tumour directly invades other organs or structures or perforates visceral peritoneum (or both) (T4)	StageII:T4, NO,MO	Stage II-B3
Any degree of bowel wall invasion with regional node metastasis, without distant metastasis (Any T) N1: Metastasis in 1 to 3 pericolic or perirectal lymph nodes N2: Metastasis in 4 or more pericolic or perirectal lymph nodes N3: Metastasis in any lymph nodes along the course of a named vascular trunk	Stage III: Any T, N1-3,MO	Stage III-C1,C2
Any degree of bowel invasion with or without nodal metastasis but with any distant metastasis M1: Distant metastasis	Stage IV: any T, any N, any M1	Stage IV-D

2.7 Curative Procedures for Colorectal Cancer

Surgical intervention is the first line treatment of cancer of the colon and rectum. The location and the extent of the malignancy will determine the type of surgical resection (Skibber et al., 2001; Zaheer et al., 1998; Steele & Osteen, 1986). It can be used alone or in combination with radiotherapy and chemotherapy (CancerBACUP, 2001).

The usual surgical intervention of tumour in the cecum and ascending colon is the high hemicolectomy, whereas carcinoma of the descending and sigmoid colon is surgically resected by left hemicolectomy. A transverse colectomy is the procedure of choice when the lesion involves the middle and left transverse colon (CancerBUCUP, 2001; Hoebler, 1997).

The surgical intervention for rectal carcinoma has changed during the last decade. For proximal and midrectal adenocarcinomas, a low anterior resection has become the technique of choice as sphincter function is preserved (Skibber et al., 2001; Hoebler, 1997; Sprangers et al., 1995). Tumours situated in the lower part of the rectum (i.e., 0-5cm from the anal verge) usually require abdominoperineal resection resulting in a permanent colostomy. In the past few years advances in surgical techniques have resulted in the decrease of the number of patients requiring a permanent colostomy (Sprangers et al., 1995; Heald, 1980). Often a colostomy is temporary and usually a second operation carried out for rejoining the two open ends (O' Leary et al., 2001).

Lately, prophylactic surgery has been suggested for those patients with confirmed family adenomatous polyposis. Several surgical options are suggested such as proctocolectomy with an ileostomy, proctocolectomy with an ileoanal pouch reconstruction or colectomy without removing the rectum and an ileorectal anastomosis (Thompson & Wells, 2006).

The surgical treatment for colorectal cancer is used either with curative or palliative intervention. Palliative surgery involves different techniques such as surgical bypass, loop colostomy or loop ileostomy, and stent placement (Thompson & Wells, 2006).

Adjuvant therapy, such as chemotherapy is offered to colon cancer patients for eliminating the probability of disease relapse, palliative symptoms and cancer-related death. Although a series of large randomized studies have shown that adjuvant chemotherapy reduces recurrence and improves survival in patients with stage III disease, much debate exists of patients' benefit in stage II disease. Since the results remain controversial in stage II patients with high-risk characteristics, adjuvant therapy can reasonably be offered (Chau & Cunningham, 2002). Concerning advanced (metastatic) colorectal cancer the situation has changed dramatically over the years. New drugs such as cytoxic agents (irinotecan, oxaliplatin, oral fluoropyrimidines) have contributed to improved outcomes for patients with metastatic colorectal cancer, while agents acting on novel targets or molecular markers might play a role in the treatment of advanced colon cancer (Cutsem & Verslype, 2002).

Combined modality therapy (chemotherapy plus concurrent pelvic radiation) is the standard postoperative adjuvant therapy for rectal cancer patients with

T3 and or N1 to N2 stage disease (National Institute of Health Consensus Conference, 1990). Such a combination decreases local recurrence and improves overall survival (Wolmark et al., 1990). Also, in other therapeutic settings adjuvant combined modality therapy used preoperatively in T3 rectal cancer increase the chance of sphincter preservation (Minsky, 2002).

2.8 Summary and Conclusions

Colorectal cancer remains one of the most commonly diagnosed malignancies in US as in Europe with about one million new cases in the world each year. In Greece, colorectal cancer with 3,769 incident cases and 2,031 deaths in 2002 remains an important public health problem.
Factors that contribute to the pathogenesis of the disease are many. Age, genetics, diet, environment, inflammatory bowel conditions are known risk factors for colorectal cancer.

Current screening mechanisms for detecting high, intermediate and low risk people for colorectal cancer, as well as modern surgical interventions, have contributed significantly to improved long-term survival and enhanced quality of life. Improvements in survival have required attention to explore the experience as well as the needs of patients after they have finished treatment for their disease. Surgical techniques, in particular, remain the main therapeutic choice for colorectal cancer, and have contributed to changes in patients' physical and sexual functioning; very often with long-term impact on their overall quality of life.

In chapter 3 the relevant literature is reviewed for an in depth understanding of the long-term impact of the disease and its treatment on patients who survive colorectal cancer. It explains why it is important to explore the perceived quality of life of Greek colorectal cancer patients.

CHAPTER 3

HEALTH-RELATED QUALITY OF LIFE IN LONG-TERM COLORECTAL CANCER SURVIVORS: LITERATURE REVIEW

3.1 Introduction

Critical examination of the literature is a crucial point in starting to set the objectives of this study. Understanding the HRQOL of colorectal cancer survivors is important for the understanding of the full impact of the disease on patients and their families. Despite the prevalence of colorectal cancer in the western world, the knowledge about the patients' HRQOL over time and the late-effects of colorectal cancer treatment is very limited. Most studies until now have focused on examining the HRQOL in colorectal cancer patients within one year post-surgery. The data available on the quality of life of this population beyond one year post-surgery is less obvious (Ramsey et al., 2000; Sahay et al., 2000).

Three key objectives will be considered by this review: First, it will identify the major predictors associated with HRQOL of colorectal cancer patients over time. Second, it will describe the main dimensions of HRQOL as they are experienced by survivors. Third, it will examine how the survivors perceive their overall HRQOL in comparison with a healthy population.

3.2 Methods

The literature search was carried out using the following electronic databases: Cumulative Index to Nursing and Allied Health Literature (CINAHL), PubMED, Applied Social Sciences Index and Abstracts (ASSIA), The Cochrane Database of Systematic Reviews (CDSR), and PsycINFO. Key words combined on these database searches were: quality of life, Health-Related Quality of life, colorectal cancer, survivors, long-term or post-treatment, qualitative research, focus group, interviews. These terms were applied to searches in both headings and in the abstract text. The search was kept both as consistent and as wide as possible together with manual searching in order to ensure a maximum number of relevant articles. Each search was set over the time period, 1990-2007.

3.3 Research Purposes of Evaluation of Quality of Life in Colorectal Cancer Patients

Evaluation of the HRQOL in colorectal oncology has been achieved by a range of research approaches.

Firstly, HRQOL studies have described the nature and the extent of disease problems with physical and psychosocial symptoms (Sprangers, 1999) and others have compared the cancer-related symptoms and treatment-related symptoms (Sprangers, 1999).

Secondly, the HRQOL of colorectal cancer patients has been compared with the HRQOL of other patients with cancer or benign diseases or a healthy population, to focus on the impact of colorectal cancer and the long-term effects of cancer treatment on survivors (Dunn et al., 2003; Sprangers,

1999). Moreover, the evaluation of effectiveness of different treatments, using clinical randomized trials, has been established with cost-effectiveness studies in which the cost of survival gain is weighed against the quality of that gain (Sprangers, 1999). Also, quality of life information is essential in palliative care setting in order to enlighten patients' important concerns (Sprangers, 1999).

Finally, some research suggests that the evaluation of baseline HRQOL may is a predictor of survival (Efficace et al., 2006; Dunn et al., 2003; Maisey et al., 2002; Sprangers, 1999).

3.4 Predictors of Health-Related Quality of Life in Colorectal Cancer Survivors

Research suggests a number of factors associated with the perceived HRQOL of colorectal cancer patients. These factors refer to certain disease or treatment characteristics such as the stage of the disease, the type of surgery or disease recurrence and certain demographic characteristics such as age, gender, educational level or income. Also, the time since diagnosis and support received have been confirmed as factors that modified the perceived HRQOL of colorectal cancer survivors (Dunn et al., 2003). According to one author: *"better understanding of how these factors combine to determine long-term HRQOL would assist with clinical decision-making, especially in a situation in which maximization of HRQOL is the goal of medical intervention"* (Anthony et al., 2003 p.119-120).

3.4.1 Long-term Effect of Surgery on Health-Related Quality of Life

Since the different surgical techniques (anterior resection with preservation of the sphincter function or abdominoperineal excision that results in a colostomy) involved in the treatment of the cancer of the colon or rectum lead to similar mortality and morbidity rates, an important issue for consideration is how these different surgical techniques affect the patients' quality of life (Sprangers et al., 1995).

There is a body of literature which suggests that the quality of life of people with a colostomy was considerably inferior to those without a colostomy (Engel et al., 2003; Kuzu et al., 2002; Camilleri-Brennan & Steele, 1998; Sprangers et al., 1995; MacDonald & Anderson, 1985; Mac Donald & Anderson, 1984; Williams & Johnston, 1983; Delvin et al., 1971). Sprangers et al. (1995) reviewed 17 studies which focused on those that directly compared patients' reported quality of life after having stoma and non-stoma interventions. The results of all of these studies refer to the long-term effect of surgery on HRQOL. The time elapsed since surgery varied widely within these studies between 1 and 10 years or more than 10 years. The results also showed that stoma and non-stoma patients both report limitations in several domains of quality of life including physical functioning, psychological well-being as well as social and sexual functioning. In addition, stoma patients were generally found to have a greater degree of impairment in all of the above quality of life domains.

Although Sprangers et al.'s (1995) findings were confirmed by Camilleri-Brennan & Steeles' 1998 review, more recently a number of researchers have failed to agree with these findings and have questioned the conclusions (e.g. Pachler & Wille-Jorgensen, 2005; Grumann et al., 2001; Allal et al., 2000; Koller & Lorenz, 1998). However, similar findings are reflected in a prospective research study by Bekkers et al. (1997) that indicated stoma patients do not encounter more problems in daily life than non-stoma patient four years after surgery.

Several researchers have noted the need to consider carefully the possible methodological limitations of research in this area which may be responsible for the variance in findings (Pachler & Wille-Jorgensen, 2005; Camilleri-Brennan & Steele, 1998; Sprangers et al., 1995). This will be discussed in further detail at a later stage.

In a recent study by Grumann et al. (2001) twenty-three patients underwent abdominoperineal resection resulting in permanent colostomy compared with fifty patients who underwent anterior resection which did not result in a colostomy. Quality of life was measured before surgery (baseline assessment) and then 6 to 9 months and 12 to 15 months post-surgery. Surprisingly, patients with a permanent colostomy tended to have better quality of life across several quality of life domains as it is measured by the EORTC QLQ-30 and CR38 colorectal cancer specific instrument than patients without a colostomy. Although these findings were not statistically significant Grumann et al. (2001) suggest further investigation and explanation of such results given that the small sample size and the missing items constitute some limitations of the study. Grumman et al also evaluated

if the level of anastomosis –from both low and high anterior resections - affected patients' quality of life. Interestingly the results showed that low anterior resection patients experienced significantly poorer QOL than patients with high anterior resection anastomosis. Despite the fact that these findings contradict most of the findings of "traditional" studies, similar findings have been reported elsewhere.

For example, more recently The Cochrane Collaboration reviewed relevant published studies in order to compare the quality of life in rectal cancer patients with or without permanent colostomy (Pachler & Wille-Jorgensen, 2005). In this review study thirty potential researches were identified. Eleven met the inclusion criteria that identified studies which used self-reported, validated multidimensional quality of life questionnaires and were filled in by the individual or a relative. Among the included studies six found no significant difference in overall quality of life between patients with a colostomy and without a colostomy appliance (Harisi et al., 2004; Rauch et al., 2004; Camilleri-Brennan, 2002; Hamashima, 2002; Grumann et al., 2001; Allal et al., 2000). A study by Jess et al. (2002) also suggested that "a stoma only slightly affected the patients QOL" (Pachler & Wille-Jorgensen, 2005, p.g 7). Four studies suggested that stoma patients were affected significantly by their disease in all QOL dimensions. As the findings in this review study vary significantly, the authors highlighted the lack of a definitive conclusion about whether QOL is more impaired in patients with a permanent stoma compared to those patients without a stoma due to a lack of evidence to support the assumption that stoma patients fare less well than non-stoma patients. The authors also suggested that well designed and executed prospective studies with baseline data and

preoperative values for QOL are required in order to address the long-term impact on Heath-Related Quality of Life in the future (Pachler & Wille-Jorgensen, 2005).

Physical Functioning

Despite improvements in surgical techniques used for therapy of colorectal cancer, a number of physical side-effects may negatively impact patients' quality of life over time. Cancer patients with or without a stoma were troubled by frequent or irregular bowel movements, diarrhoea and faecal leakage (Lewis et al., 1995; Sprangers et al., 1995; Williams & Johnston, 1983). Although bowel function usually improves during the first year post surgery (Frigell et al., 1990), in some cases bowel problems can remain beyond this (Engel et al., 2003; Lewis et al., 1995). Irregular or unpredictable bowel habits often prevent patients from leaving their home, or doing certain activities, due to a fear of having an accident leading them to social isolation and further impairment to their quality of life (Sprangers et al., 1995).

Other physical symptoms commonly experienced by colorectal cancer patients include flatulence, urinary problems such as micturition, retention and dysuria, constipation problems or sleeplessness due to irregular bowel movement (Camilleri-Brennan, 1998; Sprangers et al., 1995). Studies suggest that the degree to which these problems are experienced by colorectal cancer patients depends on some independent factors such as age - Camilleri-Brennan (1998) concluded that urinary problems generally increase with age -or the level of anastomosis (high or low anterior resection) (Engel et al., 2003; Grumann et al., 2001; Camilleri-Brennan,

1998). Engel et al. (2003) in a four-year prospective study showed that in the first three years patients with low anterior resection had significantly worse defecation scores than those patients with high anterior resection.

Sprangers et al. (1995) also report that the degree to which all these symptoms are experienced in stoma and non-stoma patients varies. For example, research has showed that stoma patients may report more problems with gas and urinary function (Engel et al., 2003; Sprangers et al., 1995) while non-stoma patients report more constipation and gastrointestinal tract problems (Rauch et al., 2004; Engel et al., 2003; Allal et al., 2000; Sprangers et al., 1995). Ramsey et al. (2002) also reports that, although long-term survivors may experience a relatively high QOL, diarrhoea in non-stoma patients remains a problem. Sixteen percent report two or more bowel movements a day and 49% report chronic recurrent diarrhoea. Grumann et al. (2001), however, also reported that patients who had a permanent stoma reported less fatigue, gastrointestinal symptoms, sleeplessness, and significantly better scores for constipation and diarrhea compared to patients who had undergone sphincter-conserving surgery.

Despite advances in stoma surgery and in stoma care, complications with stomas are an important potential source of ongoing problems. Studies exploring the long-term complications of colostomy have found that approximately 30% of patients develop problems related with their stoma and 10% of patients required at least one further surgical procedure to correct a complication (Fielding & Padmanabhan, 1994). Anthony et al. (2003) in a longitudinal prospective study indicated that surgical

complications can influence, both negatively and significantly, HRQOL one year after surgery.

Social Functioning

Some time ago Delvin et al. (1971) compared patients who had undergone surgery resulting in a stoma with those who underwent sphincter-preserving surgery and found that a high proportion of stoma patients experienced considerable social problems which related to employment and social isolation. These results were replicated by Williams & Johnston (1983) who reported that stoma patients returning to work often faced difficulties with the stomas which caused them to leave work in contrast with non-stoma patients who were more likely to return to work and remain in their job.

Sprangers et al. (1995) in the literature review study point out that the operational definition of social functioning used across studies varies considerably. It may include a variety of dimensions such as employment, frequency of social contacts, quality of relationships and restrictions in social activities due to the effect of illness or treatment. This impairment is sometimes common between stoma and non-stoma patients. In particular, stoma patients were more restricted in visiting cinemas and leisure pursuits. Such findings suggest that restriction from outside activities may be related to the fear of being a nuisance to others or to general embarrassment of having a stoma (Sprangers et al., 1995). Sprangers et al. review (1995) drew attention to the fact that several of the studies included, which purported to measure social functioning, used non-standardised study specific questionnaires.

Qualitative studies on describing quality of life in colorectal cancer patients are very limited. A literature search by Dunn et al. (2005) identifies only seven qualitative articles relevant to quality of life experienced by people with colorectal cancer. Dunn et al. (2005) using interviews (15 interviews-six males, nine females) and focus group data tried to gain an understanding of what was important to participants in terms of their own experience with colorectal cancer and their quality of life within the past 18 months.
Concerning social life some participants reported that it had not been adversely affected by the diagnosis and treatment; however they felt less comfortable in engaging activities where they may not be able to access toilet facilities with ease. Some other participants reported "reduced socialization, primarily due to tiredness, but a couple of participants said that they deliberately avoided friends because they were now treated differently to what they had been before getting ill". Given that most participants had retired, employment problems and vocational matters were not raised. Only one woman, who was suffering from an advanced stage of the disease, reported that she could not return to full time work after the cancer diagnosis.

Similarly, in another qualitative study (39 interviews contacted short and long-term colorectal cancer survivors) the loss of ability to socialize was an important theme to emerge (Rozmovits & Ziebland, 2004). Changes in the control of bowel habits, inconvenience of chronic constipation or changes in dietery habits were identified by a great number of the interviewees as persistent problems. They impact considerably on people's abilities to travel,

socialize, eat away from home, or engage in leisure pursuits (Rozmovits & Ziebland, 2004).

Also, many authors emphasise the relevance of age to the level of social activity and social network, especially given that colorectal cancer patients are often elderly and may be restricted in their activities and ability to perform roles due to a general decline in physical health and the normal ageing process (Trentham-Dietz et al., 2003; Ferrell & Ferrell, 1998).

Sexual Functioning

An important area of consideration relevant to quality of life is that of sexual functioning. Several authors have reported on the potential negative impact of cancer treatment on sexual expression (Dunn et al., 2005; Brown & Randle, 2005; Rozmovits & Ziebtand, 2004; Engel et al., 2003; Grumann et al., 2001; Allal et al., 2000; Camilleri-Brennan & Steel, 1998; Havenga et al., 1996; Sprangers et al., 1995). Problems in sexual functioning may be the result of medical treatment, psychological factors or a combination of both. However, there is considerable variance in the prevalence estimates of sexual problems among colorectal cancer patients within different studies (Sprangers et al., 1995).

There are a number of reports that the surgical procedures used to treat colorectal cancer, either abdominoperineal resection or low anterior resection, may result in damage to pelvic nerves which supply the genitals, resulting in sexual dysfunction. The types of sexual problems most commonly found in patients following these operations include erectile and

ejaculatory dysfunction in men - although other symptoms such as a loss of desire, diminished sexual activity and anorgasmia may also occur (Sprangers et al., 1995). For women, given that their sexual dysfunction after surgery has been relatively ignored in the literature, the main problems are cessation of intercourse, anorgasmia and pain during sexual intercourse, known as dyspareunia – however, these are more prevalent among stoma patients (Camilleri-Brennan, 1998; Shcover, 1998; Bambrick et al., 1996). In male patients loss of erectile capacity may be accompanied by a loss of fertility (Schover, 1998).

Several authors have concluded that the prevalence of sexual dysfunction is high among stoma patients compared to patients whose surgical treatment did not involve the formation of a stoma (Engel et al., 2003; Sprangers et al., 1995; Koukouras et al., 1991). Allal et al. (2000) reported that sexual functioning was low for both groups -stoma and non-stoma- included in their study while there were notably high scores in relation to sexual dysfunction in males although statistical significance was not achieved.

In a very recent study by Hendren et al. (2005) highly sensitive male and female sexual functioning instruments (Female Sexual Function Index or International Index of Erectile Function) were administered to eighty one women and ninety nine men to evaluate levels of sexual activities before surgery, after surgery and during "the last 4 weeks" in patients following surgery for rectal cancer. A percentage 29% of women and 45% of men reported that "surgery made their sexual life worse". Specific sexual problems in women included lowered libido 41%, arousal 29%, lubrication 56%, orgasm 35%, and dyspareunia 46%. In men lowered libido 47%,

impotence 32% and partial impotence 52%, orgasm 41%, and ejaculation 43% were recorded. Both genders reported a more negative body image. 80% of women reported that the ostomy caused a negative change to their sexual life. They stated that they were afraid their appliance may leak, or the ostomy make noise, causing them to feel embarrassed, and so they were less spontaneous. In men, the ostomy caused a negative change in sexual life for 85.7% while 92% of them reported one or more specific sexual problems after surgery.

Surgery may also cause sexual dysfunction indirectly through related side-effects. For example, post-operative pain is related to the problems of relaxing and enjoying physical intimacy. On the other hand, negative body image and bowel problems are likely to affect both sexual desire and confidence (Hendren et al., 2005; Moyer & Salovey, 1997; Schag et al., 1994).

Radiotherapy also has been reported to increase the likelihood of damage being caused to the urogenital nerves and organs also resulting in impairment of sexual functioning (Hendren et al., 2005; Mannaerts et al., 2001). It also contributes to fatigue and loss of libido which may indirectly disrupt sexual functioning in the first year or so following surgery (Schover et al., 1993).

Sexual dysfunction may occur for reasons other than surgical treatment or radiation therapy. For instance, sometimes they may also be related to difficulties with psychological adjustment (Schover et al., 1993), with

depression and anxiety being known to have a negative impact on sexual functioning (Teusch, 1995).

Sexual functioning is also determined by a range of other variables and Hendren et al., (2005) suggest that sexual function is multifactorial. Preoperative sexually inactivity and older age were significant independent predictors of current sexual inactivity (Hendren et al., 2005). It is important to consider the relevance of age when exploring the impact of treatment on sexual functioning among colorectal cancer patients. Given that the majority is likely to be aged between sixty and seventy years of age their level of sexual interest and sexual capacity may already have declined independent of the effect of treatment.

Psychological Functioning

In a review of papers investigating psychological functioning in colorectal cancer, Sprangers et al. (1995) showed that general psychological dysfunction may include depression, loneliness, suicidal thoughts, feelings of stigma and low self-esteem. Also, they concluded that these findings were significantly more prevalent in stoma patients (from 10 percent to 54 percent) than in non-stoma patients (from 3 percent to 43 percent). Williams and Johnston (1983) also reported a 32 percent prevalence of depression following an abdominoperineal resection, compared with 10 percent prevalence after anterior resection. However, the definition of psychological functioning employed in these studies varied considerably. In some cases unstandardised measures with unknown reliability and validity were used (Sprangers et al,, 1995). Tsunoda et al. (2005), when examining the

psychological distress and its relationship with quality of life dimensions in colorectal cancer patients, concluded that the emotional functioning dimension, as measured by a generic quality of life instrument such as the EORTC QLQ-C30, predominantly assess anxiety but the use of additional instruments is also necessary for the assessment of depression in outpatients with colorectal cancer (Tsunoda et al., 2005).

An early study by McDonald and Anderson (1984) assessed the stigma of having rectal cancer. Half of the patients reported signs of feeling stigmatized as reflected in decreased attractiveness, avoidance of other people and feeling different. More symptoms were seen in younger patients and in those with colostomy while stigma was particularly prevalent in women.

It is well known that patients with a diagnosis of cancer are at increased risk of depression; particularly those patients who suffer from pain and physical disability (Hopwood & Stephens, 2000; Massie & Holland, 1992). While some data indicates that depression behaviours affect a number of aspects in patients' life, such as health status, quality of life, or working role (Pasquini & Biondi, 2007), other studies have also linked depressive disorders with survival or cancer progression (Onitilo et al., 2006; Prieto et al., 2005; Faller et al., 1999). On the other hand, even if cancer patients' psychological distress decreases over time, a substantial number may continue to experience anxiety and depression during follow-up (Watson et al., 2005; Howard & Harvey, 1998). A study by Schag et al. (1994) concluded that patients who survived lung, colon and prostate cancer have experienced psychological distress during the disease-free phase of their illness.

Furthermore, Ramsey et al. (2002), using a depression rating scale, concluded that people who had survived beyond 5 years after colorectal cancer had higher rates of depression in comparison with age-matched populations. Depression was also reported as being highest among younger, and female, stoma patients (MacDonald & Anderson, 1984).

Careful consideration needs to be given to the methodological issues involved in these studies. The assessment of depression in cancer patients is difficult because symptoms of depression are often similar to those of the physical illness or its treatments. Many scales used to measure depressive symptomatology include items relating to tiredness, loss of appetite and sleep disturbance - all of which may be symptoms of the cancer itself or side-effects of treatment (Trask, 2004). Such findings, therefore, need to be treated with some caution.

3.4.2 Stage of the Disease at Diagnosis

Although the stage at diagnosis is strongly related to the length of survival of colorectal cancer patients - when diagnosed in an early stage, the disease has a 5-year survival rate of 90% (American Cancer Society, 2000) - this factor may have an association with QOL of long-term survivors. Both the stage and site of colorectal cancer at diagnosis are associated with symptoms and treatment modalities used and, subsequently, with alteration in quality of life.

Ramsey et al. (2000) found that people with colorectal cancer with TNM Stage I and Stage IV disease experienced relatively uniform increases and

decreases respectively in quality of life from the time of the diagnosis. Patients with Stage II and III disease experienced an initial decline in their quality of life, which then improved over time. Also, a survey of female long-term colorectal cancer survivors by Trentham-Dietz et al. (2003) concluded that the stage of the disease at diagnosis was not significantly associated with current heath status. They reported that most patients who were diagnosed at an earlier stage may resume their regular lifestyle after treatment.

3.4.3 Time since Diagnosis

Studies have showed that the time since diagnosis may also be associated with quality of life in colorectal cancer patients. As the time from diagnosis lengthens quality of life appears to improve for these patients (Ramsey et al., 2002; Ramsey et al., 2000; Schag et al., 1994).

A study of 27 long-term, 33 intermediate-term and 57 short-term survivors of colon cancer concluded that quality of life, and particularly its psychosocial domains, tend to improve as length of survival increased (Schag et al., 1994).

Ramsey and colleagues (2000) carried out a community-based sample of 173 survivors who participated in the study and completed the Functional Assessment of Cancer Therapy Scales for Colorectal Cancer (FACT-C) and the Health Utilities Index (HUI) Mark III questionnaires to examine how HRQOL varied as a function of stage at diagnosis and time since diagnosis. They suggested that for all TNM stages of the disease, the impact of colorectal carcinoma on HRQOL was greatest in the first 2-3 years from initial diagnosis. After this time, HRQOL was relatively uniform and

remained relatively high in all stages of the disease except stage IV. The subscale scores of FACT-C suggested that emotional components of HRQOL improved significantly over time, however, functional and social well being were impacted most and improved little across all stages as the time from diagnosis lengthened. Pain also remained a substantial problem and did not improve with time. HRQOL also declined for patients during their last year of life and for patients who had recently experienced surgery for their disease. However, this survey had some limitations as respondents had been healthier than non-respondents and advanced age was the only factor significantly associated with the non-respondents. The researchers suggest that re-sampling would be necessary to include patients with advanced stage disease and a more distant history of colorectal cancer.

3.4.4. Disease Recurrence

Unfortunately, recurrence of rectal cancer after potentially curative surgery is also a major problem as recurrence may be local or distant, and commonly arises in the liver. The incidence of tumour recurrence varies from centre to centre. Local recurrence occurs in up to one third of patients after surgery and most tumours recur within the first two years post-operatively (Esnaola et al., 2002; Camilleri-Brennan & Steele, 2001). It is suggested that the experience of recurrence in cancer patients is likely to be more distressing than the initial diagnosis (Mahon, Cella & Donovan, 1990). The presence of recurrence in rectal cancer patients is likely to lead to a poorer HRQOL but few studies are available that can confirm this hypothesis. It is not known which quality of life dimensions are affected and to what extent the patients' quality of life is impaired. Camilleri-Brennan and Steele (2001) showed that

most dimensions of HRQOL of patients with recurrent disease were significantly lower than those in remission.

3.4.5 Demographic Characteristics

Age, Comorbidities and Gender

As previously discussed, the physical component of QOL in colorectal cancer is strongly associated with age. For example, many urinary problems or problems concerning sexual function increase with age. In addition, younger or female stoma patients may experience more initial depression, stigmatization and feelings of being different than males and older patients (Mc Donald & Anderson, 1984). The age variable is also suggested in Devlin's early study (1971) reporting that 50 percent of stoma patients who felt socially isolated were over 65 years old. Gender differences were also found by Northhouse et al. (2000) in a prospective study of the adjustment of patients and their spouses to colon cancer. Women were found to report more distress, more role problems and less marital satisfaction.

On the other hand, a major methodological issue in many long-term QOL studies is the distinction between the effect of the disease itself on QOL and the effect of age or other comorbidities, since the probability of having a chronic disease or functional limitation also increases with age. This distinction for long-term colorectal cancer studies is very important since the incidence rates of the disease rise with age and over 40% of cases occur in subjects over the age of 74 years (Gotay & Muraoka, 1998).

Trentham-Dietz et al. (2003) in a sample of 307 women, with a mean age of 72 years and an average survival time of 9 years, showed that the physical component of HRQOL, as it is measured by Short-Form 36 Health Status Survey, was significantly lower for participants of greater age. The degree to which cancer survivors were able to participate in physical activities (such as walking, routine self-care) and the extent to which activities or time involved in their social "role" (of, e.g., employee or spouse) are limited is associated strongly with age. However, the factor most strongly associated with QOL in long –term colorectal survivors is the existence of other diseases experienced together with cancer: *"Spearman correlation coefficients were significant ($p<0.001$) between the number of co-morbid conditions and all SF-36 domain and summary scales"* (Trentham-Dietz et al., 2003, p.345).

These co-morbid conditions included arthritis or rheumatism (57%), hypertension (46%), depression or anxiety (19%), and bone break or osteoporosis (18%). However, this study used statistical techniques that do not enable us to conclude a causal relationship between depression or other comorbidities and HRQOL.

The largest study assessing HRQOL in long–term colorectal survivors by Mosconi et al. (2002), suggested that comorbidity and age had a larger impact on HRQOL. Females had a poorer overall HRQOL than males with more evidence in the physical component of HRQOL.

In agreement with previous studies Ramsey et al. (2002), with a population of 227 colorectal cancer survivors and an average age 74 years, reported that a substantial number of non-cancer comorbidities (overall 77,5% reported at

least one comorbid condition) were strongly and negatively associated with all measures of HRQOL using multivariate regression analysis.

Educational level and Income.

Little evidence emerges from the literature describing the effect of household income and educational level upon the quality of life in colorectal cancer patients.

One study by Trentham-Dietz et al. (2003) showed that the overall mental health status of female survivors were lower in those patients with a lower level of education. Moreover, lower income status may be associated with poorer outcomes for pain, social and emotional well-being dimensions of quality of life scale according to Ramsey et al. (2000).

In addition, Ramsey et al. (2002) also reported that lower socioeconomic status was a risk factor for depression; while higher levels of income were significantly associated with more favorable scores for depression.

3.4.6 Social Support Received

Studies have shown that social support for cancer patients seems to be associated with better quality of life (Sultan et al., 2004; Sapp et al., 2003). Social support encompasses many different and varing forms including emotional or instrumental support. Emotional support refers to individuals who are available to listen, sympathize, and make the individual feel valued. Instrumental support refers to the assistance to the activities of daily life or with household chores. Emotional support may be considered the most helpful and the type that patients needs more (Sultan et al., 2004).

While information is available on the association between social support and quality of life for some cancer sites (Michael et al., 2002; Courtens et al., 1996) there is limited information on the association between social support and quality of life in colorectal cancer patients. A study by Sapp et al. (2003), which included 259 female colorectal cancer survivors, evaluated the correlation between social network and HRQOL of study population. Findings demonstrated that social network was associated significantly with HRQOL and in particular with mental health. Similarly, Sultan et al. (2004) showed that the emotional and instrumental support was associated with higher mental component scores with the Medical Outcomes Study Short-Form instrument.

However, information is very limited on how the support that patients receive from a partner influences their quality of life.

Qualitative studies have shown that the main source of support for colorectal cancer patients includes family and friends - in particular for emotional and instrumental support (Sahay et al., 2000; Forsberg et al., 1996; Forsberg & Cedermark, 1996). The support that colorectal cancer patients received from their family or friends seem to influence their quality of life. In particular, the relationship between colorectal cancer patients and their spouse is related to peoples' quality of life scores (Forsberg et al., 1996; Forsberg & Cedermark, 1996). Patients who live with a family express higher perceived well-being than those who live alone (Forsberg et al., 1996; Forsberg and Cedermark, 1996). Northhouse et al. (2000), when examining the factors that affect adjustment to the disease, showed that role adjustment problems were strongly predicted by similar problems in spouses.

Understanding how social support, especially emotional support, influences peoples' quality of life is important because the social environment can change and appropriate psychological interventions can improve patients' quality of life.

3.5 Overall Effect of Colorectal Cancer Disease and Treatment on Survivors' Quality of Life

Studies have compared colorectal survivors' Health-Related Quality of Life with that of similar aged/sex-matched people in the general population (Arndt et al., 2004; Kopp et al., 2004; Rauch et al., 2004; Trentham-Dietz et al., 2003; Mosconi et al., 2002). Surprisingly, these studies have showed that the impact of colorectal cancer on patients' quality of life over a period of time is not necessarily negative. Colorectal survivors report a more satisfied HRQOL, very often comparable with those of general population in most HRQOL domains (Arndt et al., 2004; Rauch et al., 2004; Trentham-Dietz et al., 2003; Mosconi et al., 2002). Arndt et al. (2004) tried to identify how, 1 year after diagnosis of colorectal cancer, survivors cope with the awareness of living with a chronic and potentially life-threatening disease in comparison with men and women of the general population. HRQOL scores of a population–based cohort of 309 patients were compared with published reference data of the EORTC-QLC30 questionnaire from the general population. The results showed that overall HRQOL and physical functioning of patients is comparable to population norms even if deficits in emotional and social functioning continue to exist. Similarly, Mosconi et al.

(2002) report that no significant difference was found for the overall HRQOL of 197 colorectal cancer survivors when compared (according to age and sex) with those of the Italian population as long as no serious co-morbidity or relapse appeared.

These findings could be interpreted as a widespread selection bias or as a result of a positive coping strategy and processes that cancer survivors used for "reframing" their standard of health. For example, a patient with bone metastasis may state a "good" physical functioning that may mean they are happy since the condition does not get worse. Patients may change their personal values in this new reality and obtain a new understanding of what now constitutes an acceptable quality of life. This phenomenon has been described as "response shift" and is used for interpreting unexpected quality of life findings (Sprangers et al., 2002; Sprangers & Schwartz, 1999; Sprangers et al., 1996).

An adaptation process to disease and treatment of colon cancer patients is confirmed by Bernhard et al. (1999) whose findings showed that these patients may reframe their perception in estimating HRQOL substantially after surgical resection, adjuvant chemotherapy or observation. Although an understanding of the response shift phenomenon is very important for patient care and HRQOL research, it has rarely been studied empirically and needs further investigation (Sprangers et al., 1996).

3.6 Summary and Conclusions

The primary purpose of this review was to examine the long-term consequences of colorectal cancer disease and cancer treatment on patients' life. The research to date has paid little attention to the late-effects of colorectal cancer while data from a Greek population are not available. Similarly, there is uncertainty of the variables which apparently contribute to high or low quality of life in patients over time. On the basis of this investigation, it appears that variables, such as stage at diagnosis, time since diagnosis, type of surgery, recurrence, depression, age and comorbidities, gender, educational level, and income may modify the level of patients' HRQOL. Independent of the quality of research that explores these variables, the effect that these variables have on the overall HRQOL is unclear. Particularly, there is ongoing confusion on how HRQOL differs between people with a colostomy appliance and people without a colostomy appliance. It is not obvious that stoma patients experience a low HRQOL while sometimes they appeared to have a quality of life comparable to a healthy population. On the other hand, although depression symptoms are mentioned as one problem that colorectal cancer patients may experience at follow-up, it is rarely discussed in the literature and no specific information was found on the possible effect of depression symptoms on patients' HRQOL.

There is also an issue regarding the limitations of the measures used to assess the impact of colorectal cancer disease and treatment on the lives of people who suffer from it, which needs to be taken into account in researching this area.

CHAPTER 4

QUALITY OF LIFE: CONCEPTS AND METHODS

4.1. Introduction.

During the last 30 years, there has been increasing interest in the concept of quality of life (QOL) and its application in evaluating the outcome of health care. This is particularly evident for chronic and life-limiting diseases, where by definition, cure is unachievable.

As such, there is increasing recognition that assessment of QOL is required to complement traditional outcomes such as survival and treatment toxicity.

The proliferation of interest in quality of life is clear. There is a plethora of publications in the health, psychological and social sciences literature devoted to understanding, assessing and interpreting QOL. In addition, there are an ever-increasing number of professional societies and journals devoted to this research field. The phrase "quality of life" has become commonplace in the vocabulary of health professionals, researchers, and indeed, society in general. Enthusiasm continues despite the inherent difficulties and complexities in trying to understand, assess and interpret approaches to capturing the perspective of patient. One major criticism of previous studies purporting to assess "QOL" is the lack of attention given to understanding its conceptual basis.

This chapter reviews the current understanding and the rationale for consideration of QOL focusing on follow main areas:

1. What is the need and demand for QOL assessment?
2. What constitutes QOL within the context of health, illness and cancer experience?
3. How has the conceptual basis of Health-Related Quality of Life been constructed and debated in the literature?
4. How has Health Related Quality of Life been assessed in the context of the cancer experience?

4.2.0 The conceptual basis of Quality of Life.

4.2.1 The historical basis of Quality of life

In public life, social and human sciences the term QOL derives from the 1960s and was used routinely in order to describe the "liveability"of towns or cities, assess the aims and effects of social policy and generally refer to the social scientific index of well-being of population (Rapley, 2003).

Although the concept became popular during 1960s it has a long history and has its roots can be traced back to the Greek ancient philosopher Socrates, who said that an unexamined life is a life that not worth living (Plato, 1903). In the first half of the twentieth century QOL was correlated with the material level that a country can achieve; the higher that level in a country, the better the life of its citizens. The need to measure the level of quality was born and one of the first tools of QOL measurement came from economists who used the Gross National Product (GNP) as an indicator for QOL (Veenhoven, 1996).

The need for developing broader indicators of QOL beyond economical growth emerged in 1960s, when it started to become clear that the happiness of a society or a population could not be determined only by the quantity of goods consumed. A movement towards "social indicators" of a good life became more popular and objective social conditions such as health, life expectancy, unemployment rate, poverty rate, school attendance and environment began to be measured and used as indicators of social progress (Rapley, 2003). Despite advances in socio-economic conditions, and the fact that the 1960s and 1970s were characterized as a period of prosperity, research findings showed that from 1957 to 1972 the happiness of general population steadily declined (Campbell, 1976).

The need for new indicators for 'a good life' were clear and in the 1980s the interest of QOL as a construct moved from the population to an individual level while issues about culture, personal values, self reports of life satisfaction or dissatisfaction or happiness, health satisfaction and the subjective sense of people about their individual lives began to emerge (Rapley, 2003; Kahn & Juster, 2002; Ware, 1991).

Since then, interest in QOL became a reality and the most sustained efforts in social and human sciences focused on defining, describing and understanding quality of life while a number of conceptual approaches to QOL assessment started to be developed.

In 1990s the QOL literature became an arena for controversy about conceptual issues that related to cultural, religious and personal values which

might influence its influence and perception. Moreover, methods and the meaning of QOL measurement were also debated issues.

Hughes et al. (1995) identify 44 separate QOL definitions between 1970 and 1993. Antaki and Rapley (1996) identify over 2500 journal articles specifying "quality of life" as a keyword in the preceding three years. In Google the "quality of life" term returned about 3,410,000 webpages (Rapley, 2003).
Moreover, the development of professional societies (e.g. the International Society for Quality of Life Research) and the establishment of specialty journals (e.g. Quality of Life Research), offer further evidence of increasing interest in the concept.

Despite the plethora of efforts within literature to define QOL, the concept remains vague while research in the field has been marked by numerous problems in measurement and uncertainties about its changing pattern over the life course.

In order to become more comprehensive, an abstract concept as QOL now has many sub-areas of research. Since health is among *"the most valued states, and among the most important areas of life"* (Bowling, 2001, p. 5), the term Health Related Quality of Life has become a familiar field in medicine and its assessment an important medical goal.
In particular, the interest of medical scientists has moved away from the functional ability of patients towards subjective well-being while the most recent research field requires new approaches beyond the traditional methods used in medicine.

4.2.2 Defining Quality of Life.

As the interest in QOL has moved from populations to individual people, and from objective life conditions to subjective personal values and aspirations, the construct begins to be correlated with terms such as "well-being", "happiness" or "life-satisfaction". But any attempt at describing QOL using these terms includes very broad definitions. For instance, QOL has been defined as *"the extent to which a person's hopes and ambitions are matched and fulfilled by experience"* (Gerson, 1976) or that QOL encompasses qualities such as the degree to which an individual succeeds in accomplishing his desires (Calman, 1984).
Many others similar or broader definitions of QOL are also available in the literature. These heterogenic and abstract descriptions of QOL across the social scientific literature contribute to the complexity of the construct and lead researchers to specify societies' and individuals' quality of life within "domains" or "components" for specific purposes of measurement (Rapley, 2003).

More recently, multidimensional definitions of quality of life have been adopted. The World Health Organization defines QOL as *"individuals' perceptions of their position in life in the context of the cultural and value system in which they live and in relation to their goals, standards, and concerns"* (WHO, 1993, p. 1).

More specifically, at the subjective individual level, quality of life, as defined by Cummins (1997, p. 6) is *"both objective and subjective, each axis being the aggregate of seven domains: material well-being, health,*

productivity, intimacy, safety, community and emotional well-being. Objective domains comprise culturally relevant measures of objective well-being. Subjective domains comprise domain satisfaction weighted by their importance to the individual"

4.2.3 Moving towards a definition of Quality of Life in context to health and illness

In health settings, the multidimensional aspect of these definitions means that the impact of illness on patients' life must be evaluated subjectively within broad cultural, environmental, and social contexts. (Cella et al., 2002).

One of the most debated issues in the literature remains the possibility of such definitions being operationalized into the scientific measurement of quality of life and proving useful in everyday clinical practice.

Koller et al. (2005, p. 186) point out that these definitions are so ideal that they cannot be practical from a clinical point of view. Particularly, they wonder, *"Which doctor would be able to "treat" the cultural context of his/her patients?"*

4.2.4 Health-Related Quality of Life

Concurrently there has been a change in the way health and disease has been viewed within medicine. Traditionally, the effect of the disease and the

outcome in health care has been measured in terms of mortality and morbidity rates. The length of life, or deaths, was the main objective measures of health status outcomes before World War II. Here the emphasis is on the pathogenic abnormalities of diseases, with ill-health described within a negative context (Bowling, 2001).

Some years later, advances in medicine have changed the demographic characteristics as well as the health profile of population, in particularly in industrialized countries. The elderly population has increased together with chronic diseases such as cancer, heart disease or diabetes and degenerative diseases. Few cures are achieved for chronic and degenerative disease while laboratory data is increasingly inadequate to capture important effects of many new interventions on patients' QOL (Fitzpatrick et al., 1998)).

This new reality has also changed the way that health and disease have to be viewed in modern medicine.

Doctors re-consider their goals about the outcomes of medical care as new types of scientific evidence about health begin to be investigated (Sullivan, 2003). There have also been increasing moves to view health as a positive construct.

The World Health Organization (WHO) in 1947 defined health as *"a complete state of physical, mental, and social well-being and not merely absence of disease" (p.29).*

Even if the complete absence of disease can not be a realistic goal in the clinical arena, this definition has been considered the foundation for the concept of HRQOL and its measurement. (Koller et al., 2005; Cella et al., 2002; Aaronson, 1991c).

Health outcomes research, based on this definition for health, wish to highlight holistic evaluation of patients' physical and psychosocial well-being and have settled on the main goal as the importance placed on the patients' point of view in evaluating medical care. Patients give their subjective information about perceived health and quality of life while a number of terms have been adopted into the literature to describe the health related quality of life (HRQOL) from the patients' perspective (Rapley, 2003; Sullivan, 2003; Testa & Nackley, 1994).

Most of these terms are concerned with those aspects (domains or components) of HRQOL that are important to patients and are experienced as a result of illness and medical procedures. (Cella et al., 2002; Aaronson et al., 1996; Cella, 1995; Moinpour, 1994). Table 4.1 demonstrates some different perspectives that describe Health-Related Quality of Life.

The purpose of HRQOL assessment will determine which of the available definitions have to be adopted, as well as the way HRQOL is understood (Rapley, 2003; Cella, 1997). For example, a health economist's interests lie in the economic impact of the disease on patients' lives, whilst a sociologists' perspective might consider HRQOL as the gap between achievement and expectations (Fitzpatrick et al., 1998).

Table 4.1: Descriptions and included dimensions of Heath-Related Quality of Life

Description	Dimensions/Domains	Source
A state of complete physical, mental, and social well-being and not merely the absence of disease and infirmity	Physical well-being Mental well-being Social well-being	World Health Organization, 1947, p.29
An individual's perceptions of well-being that stem from satisfaction or dissatisfaction with dimensions of life that are important to the individual	Health and functioning Psychological/spiritual Family Social and economic	Ferrans & Powers, 1985, p.16
Patients' appraisal of and satisfaction with their current level of functioning compared to what they perceive to be possible or ideal	Physical concerns Functional ability Family well-being Emotional well-being Spirituality Treatment satisfaction Future orientation Sexuality/intimacy Social functioning Occupational functioning	Cella & Tulsky, 1990, pp. 30-31
A personal statement of the positivity or attributes that characterize life	Psychological well-being Physical well-being Symptom control Nutritional concerns Social concerns Affective states	Grant, Padilla, Ferrell & Rhiner, 1990, p. 261
The perception of the impact of the disease is both subjective and culturally bound	Physical functioning Emotional functioning, or psychological functioning Social function Symptom of disease and its treatment	Clinch & Schipper, 1993, pp. 62-63
An individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations values and concerns.	Physical health Psychological state Level of independence Social relationship Personal beliefs Relationship to the environment	WHOQOL group, 1993, p.1
	Physical, Psychological, social and spiritual well-being Economic impact of illness	Taylor, Jones, & Burns, 1995, p.195
Quality of life... is those aspects of an individual's subjective experience that relate both directly and indirectly to health, disease, disability, and impairment...health related quality of life is the gap between our expectations of health and our experience of it.		Carr et al., 2001(b), p. 1240
"QOL encompasses not only disease symptoms and functional consequences (eg, impairment in activities of daily life (ADLs), but also subjective life satisfaction, happiness, and overall value one places on life at any given time".		Cella et al., 2002, p. S10

4.2.5 Conceptualization and measurement of HRQOL

Since there in no a generally accepted definition of HRQOL, within most of the available studies it is impossible to identify a strong theoretical basis for the concept. Many inconsistencies and ambiguities remain in the literature and a number of conceptual and methodological problems arise particularly when the assessment of HRQOL is attempted (Fitzpatrick et al., 1998; Aaronson et al., 1991b).

Even if most experts consider that the concept is complex and vague, they have agreed on basic "conceptualization principles" for the construct that should be included in any HRQOL measurement.

In the cancer field particularly, it is generally agreed that any health-related quality of life measurement used with cancer patients should be multidimensional (Aaronson et al., 1996; Cella, 1994; O'Boyle et al., 1992; Zhan, 1992; Aaronson, 1991b; Katz, 1987) and subjective (Cohen et al., 1996; Bowling, 1995; Cella, 1994; Aaronson et al., 1991c).

Also, the dynamic nature of the quality of life has been identified by a number of researchers such as psychologists, sociologists, and health care providers, even if this aspect is very often is overlooked in the literature (Alison et al., 1997).

People change their perception of their health outcome, or their expectations over time, in terms of existing factors, patients' timing or specific life circumstances (Carr et al., 2001b; Alison et al., 1997; Calman, 1984). Therefore, patients' with an apparently similar health status may have different perceptions of their HRQOL.

HRQOL as a Multi-Dimensional Construct.

Clearly, it would be inappropriate and overwhelming to incorporate all of the potential dimensions relevant to quality of life in one study. The selected domains that constitute patients' quality of life are an important issue that has brought many authors to a debate in the literature about defining the domains and variables that illustrate HRQOL (King et al., 1997). Several researchers have focused on four main domains in their evaluation of HRQOL in cancer patients which include: physical well-being, psychological well-being, social functioning and disease-related and treatment-related symptoms. (King et al., 1997; Aaronson et al., 1996; Cella, 1994; Moinpour, 1994; Ferrans, 1990; Ferrell, 1990). More recently there has also been an increase interest in including spirituality in the core set of HRQOL (Taylor, 2003; Cohen et al., 2000; Ferrell et al., 1992a; Ferrell et al., 1992b).

Table 4.2 demonstrates a variety of important life domains that may contribute to the concept.

The specific purpose of HRQOL assessment will determine the hierarchy of the selective domains and will drive researchers to either include or not include other important perceived quality of life aspects such as occupational functioning, the stigma of cancer, happiness with care, financial satisfaction, expectations of recovery and level of optimism or others (Cella et al., 2002; Higginson & Carr, 2001; Koller et al., 2000). A criticism of previous approaches to HRQOL evaluation in medicine is that they give priority to physical functioning and symptoms while other

important life domains are not considered as important (Fallowfield et al., 1990). A conceptual model by Ferrans in 1990 demonstrated the hierarchical relationship between global HRQOL and the four major domains and specific aspects of the domains in cancer patients. Ferrans' model distinguishes clearly between the domains and provides a strong example of the connection between theory and research (Vallerand & Payne, 2003).

Also, should one wish to assess HRQOL, it is necessary to keep in mind the interrelationship among the constituent domains (Aaronson et al., 1991c) and that the relationship among all of these aspects may vary between individual patients (Bernheim, 1999). For example, the psychological effect of the disease may have an important impact on physical well-being and social functioning but not be a common effect in all patients.

One of the purposes of this study is to evaluate the impact of colorectal cancer disease on the lives of patients; the above four main domains (physical well-being, psychological well-being, social functioning and disease-related and treatment-related symptoms) are considered important.

Table 4.2: Domains of Health-Related Quality of Life

Physical Functioning
Physical mobility
Physical activities
Self-care activities (e.g bathing, dressing)
Ability to perform every- day activities (walking uphill/upstairs, household)
Disease symptoms (e.g pain, appetite, fatigue)
Treatment side-effects
Psychological Functioning
Mood state (depression, anxiety, fear, joy)
Psychological well-being (happy, pleased, life satisfaction)
Self-esteem, self-image
Cognitive status (memory, concentration, perception, confusion)
Social and Role functioning
Interpersonal relationships (visits with friends and relatives, family, work and school relationship)
Sexual functioning
Performance usual role activities (work, school, carry out hobbies and interests)
Satisfaction with care
Information and communication
Support from health providers
General Health Perceptions
Self-rating of health
Self-rating of QOL

HRQOL as a Subjective Construct

The HRQOL perspective that wishes to assess quality of outcomes in medical care, and go beyond objective clinical or biological outcome data, has to reflect the importance of patients' feelings and satisfaction to any health care or medical intervention. Thus the patients' perspective about their perceived health care or their preferences for treatment must be reflected within any HRQOL assessment.

Since most researchers agree on the subjective and individualized nature of QOL they support the view that that answers about HRQOL should be

selected directly by patients (Fitzsimmons et al., 1999; Kassa, 1995; Selbyet al., 1992). Studies have also shown differences among the rating of HRQOL given by patients, family members and health care providers. (King et al., 1995; Osoba, 1994).

In particular the psychosocial aspect of HRQOL may vary significantly between patients and proxy or health professionals and may be biased by these individuals' own standards of desirable QOL (Osoba, 1994).

A recent review of 23 studies by Sneeuw et al. (2002) indicates that judgments that are made by significant others and health care providers concerning various aspects of patients' HRQOL are reasonably accurate while a proxy may often recognize more HRQOL problems than patients themselves. Also, *"proxy ratings tend to be in greater agreement with those of patients for physical HRQOL domains compared to psychosocial domains" (p. 1141).*

It is also important to consider limitations of self-reported data such as missing data, language problems, cultural differences and patients burden (Osoba, 1994).

Approaches to assessment HRQOL

Even if the conceptual "principles" of HRQOL have been accepted by most researchers, the approach taken to assess the concept will differ and mainly be determined by the scope of assessment.

Two main methods have been adapted for gathering multidimensional and patients-based HRQOL data.

First, is the use of standardized structured questionnaires in which important aspects of HRQOL are presented as items or scales (quantitative measurement). The second method is the use of interviews in which the main goal of the measure is to gain the individual's perspective of HRQOL and gather patient-centred QOL data (qualitative measurement). A combination of both methods can also be used for gathering HRQOL data for different research purposes.

The use of standardized measures is intended to produce values (usually numerical) in order to reflect a 'good' or 'bad' HRQOL. Therefore, this method can provide quantifiable data that can be expressed as an aggregate score or dimension score, item score or a global score (Osoba et al., 1991b). The psychometric property of the measurement is very important within any proposed instrument that must be tested in order to ensure adequate validity, reliability, and clinical responsiveness. Some of the advantages of self-assessment questionnaires are that they are easy to administer and complete so that they are applicable to large population of subjects. Also, the establishment norms permit comparisons among different cultural groups and populations – such as cancer survivors (Haberman and Bush, 2003).

The qualitative approach focuses more on the assumption that each individual has their own particular definition of what constitutes quality of life and this definition may vary among individuals, and more subtly may vary further with the individual under specific life circumstances. A number of qualitative approaches have been used to measure individual perspective of quality of life including a case study (Silverman, 2005), grounded theory and phenomenology (Lowe and Rapin, 1994; Benner, 1985).

Types of HRQOL Instruments

A variety of reliable and valid instruments that purport to evaluate HRQOL are available. The plethora of instruments means that there is not a 'gold standard' or a criterion which everyone accepts as being the best measure of HRQOL or the best measure of the impact of all diseases, or cancer, on quality of life (Cella et al., 2002; Osoba et al., 1991b).

In particular for cancer, the variety of treatments, as well as the variety of outcomes and meanings attached to quality of life itself, may explain the lack of a single instrument for use in all situations. To the question, *"which HRQOL measure should be used or which of the available questionnaires is the best?"* there is no a single answer (Cella, 1997). The scope of the assessment should be first determined by the population of interest, the outcome of interest and the characteristics of the instruments available (Haberman & Bush, 2003; Cella et al., 2002; Osoba, 1991b).

If the purpose of interest is, for example, to gain specific information into clinical practice (e.g. in clinical decision making, in predicting survival, improving quality of care), or in managed care settings, or for policy decision making or to evaluate treatments into clinical trials or patients' preferences for one treatment or preference for various health status, then the appropriate instrument has to be selected (Cella et al., 2002; Higginson & Carr, 2001).

The HRQOL measures are divided into two broad categories: health profile (descriptive) questionnaires and utilities questionnaires. Health profile questionnaires are generic or specific (e.g. disease specific -as cancer specific- or dimension specific). Utilities questionnaires are generic and used

for economic evaluation of HRQOL and for assessing the patient preferences.

Advantages and disadvantages of some of them are demonstrated in Table 4. 3.

Generic health profile measures include items that are general enough, or are intended for use not only across a wide range of chronic disease but also the general population. Generic tools often give a score in a number of dimensions and may then be summarized into a single score. This type of instrument is useful in determining whether a patient-population has returned to the same quality of life as the general population. They also permit comparisons across different diseases and conditions or different interventions. Two of the most widely used generic measures are the Medical Outcome Survey (MOS) Short-Form (SF-36) (SF-36 Ware et al., 1993) and the Nottingham Health Profile (NHP) (Hunt et al., 1985).

When the scope of inquiry is to identify every possible symptom and side-effect of a procedure or to identify clinically important changes - particularly in clinical trials - then a disease specific or treatment specific instrument is required. For example, within the field of cancer clinical trials, HRQOL assessment has become increasingly popular as a key endpoint. So, in most interventions against cancer the quality of survival should be taken into account (Bowling, 2001; Fitzsimmons, 2000; Aaronson et al., 1996; Cella, 1994; Slevin, 1992; Department of Health, 1992). This consideration is very important in case there is no potential cure and the palliative care and HRQOL are the primary endpoints (Girling et al., 2003).

Dimension specific instruments have also been designed to assess specific dimensions of HRQOL that are not included in disease specific or generic instruments, The Beck Depression Inventory (Beck et al., 1961) and the McGill Pain Questionnaire (Melzack, 1975) are two examples.

Another strategy for assessing HRQOL combines a generic or "core" instrument with a disease or treatment specific module. Such a combination ensures the advantages of both while minimizing the limitations of each. So, this permits cross-study comparisons and assess clinical changes for a specific condition (Cella et al., 2002).

At present two research programmes, The European Organization for Research and Treatment of Cancer (EORTC) and David Cella in US have developed the EORTC QLQ modular approach to HRQOL and the Functional Assessment of Cancer Therapy (FACT) system of HRQOL assessment accordingly. Both systems are primary designed for cancer diseases and a number of specific cancer modules are now available (including breast, lung, head and neck, colorectal and others). They fulfill methodological, psychometric and other criteria in the development of their scales and subscales which are the most widely used.

Utility approaches derive from health economics and decision theories. They seek to produce a summary score for a particular state of quality of life without reporting symptom severity or functional impairment and are equivalent to a numerical value for decision making (Bowling, 2001; Cella, 1997; Goodwin, 1991; Osoba, 1991b). Patients may be asked to express

their health status with a scale of 0-10 in which 0 is death or worst quality of life and 10 is perfect health or highest quality of life. Utilities are also used with groups of subjects evaluating preferences for policy decisions or allocation of health care resources or to groups of patients for treatment decision (Berzon, 1998).

Within clinical trials the assessment of patients' preferences distinguishes those who are in favour of one treatment over another when both have equivalent survival outcomes. (Bowling, 2001; Cella, 1997; Osoba, 1991b). Furthermore, they allow the evaluation of the effect of treatment on quality-adjusted life year (QALYs) (standard gamble-time trade off techniques) indicating what risk patients could take in order to gain their preferred health standards (Goodwin, 1991; Osoba, 1991b). However, this latter use of assessment of patients' preferences into decision making raises many methodological and ethical issues. For example, all aspects of health cannot be including in a single number (Bowling, 2001; Cella, 1997; Till, 1991). Also, patients vary significantly in understanding of personal risks to their health. These may include, for example, old people or those who may have "unrealistic optimism", patients who are physically handicapped, socially isolated or have lost motivation and may accept the greater risk of a radical treatment over other people with different expectations (Bowling, 2001; Carr & Higginson, 2001; Till, 1991). The Quality-Adjusted Time Without Symptoms and Toxicity (Q-TWIST) is the only utility approach that was developed specifically for cancer patients. Also, the EuroQol, the Visual Analog Scale and the Quality-Adjusted Life Years (QALYs) are some more examples of utility measures.

Individualized measures have also been developed such as the Schedule for the Evaluation of Individualized Quality of Life (SEIQOL) (O'Boyle et al., 1992) and the Patients Generate Index (Ruta et al., 1994). Although these measures have not widely been used, and a number of methodological obstacles have to be overcome, they have been receiving increasing attention lately (Scientific Advisor Committee of the Medical Outcomes Trust, 2002; Carr & Higginson, 2001).

Table 4.3: Advantages and Disadvantages of HRQOL Instruments.

Examples of HRQOL Instrument	Advantages	Disadvantages
Generic (examples). SF-36 (Ware et al. 1993). SIP (Benger et al 1976). NHP (Hunt et al. 1985).	Provide an overall health status. Used in a wide variety of population or conditions. Permit cross-study comparisons. Normative data often available. Widely tested for validity and reliability. Short version often available. Identify unsuspected findings. Sensitivity to comorbid conditions.	Do not detect important clinical changes in QOL. Emphasis on functional status. Lack of specificity.
Disease specific (Cancer specific). RSCL (de Haes et al. 1992). FACT (Cella et al. 1993). EORTC QLQ-C30 (Aaronson et al. 1993). FLIC (Schipper et al. 1984). CARES (Schag et al. 1990)	Describe specific disease problems and benefit due to treatment Allow clinically important changes over time. Relevant to patients. Used in clinical trials. Strong relation to physical disease findings. Some provides a module specific to certain cancer location.	Lack of cross-study comparison between different conditions. Lack of normative data and cultural norms. Rarely captures all aspects of functional status and well-being. Fail to distinguish between treated and untreated patients.
Dimension specific. BDI (Beck et al. 1961). McGill Pain (Melzack 1975). HADS (Zigmond and Snaith 1983. Anxiety and Dipression Scale (Radloff 1997).	Describe in details the domain of interest. Used across range of patients populations Cross-study comparison. Used as screening tools.	Does not capture multidimensional aspect of HRQOL. Not primarily designed as outcome measures.
Individual. SEIQOL (O'Boyle et al.1993).	Capture individual perception. Content validity. Responsive to change in individuals across time.	Trained interviewer for administration. Applicable to limited population. Validity and reliability requires further assessment.
Utility. Q-TWIST (Gelber (1991).	Captures individual perception. Allow cost-benefit analysis. Produce single score.	Does not capture multidimensional aspect of HRQOL. Requires statistical interpretation.

Choosing a HRQOL Instrument

In a systematic review of literature on HRQOL Fitzpatrick et al. (1998) suggested eight requirements that should be directed at an instrument when it is purposed as an outcome measure (Table 2.4). These refer to the general principles of psychometric theory and should be addressed by any researcher who may wish to develop a new scale (Cella et al., 2002).

Table 4.4. Eight questions That Need to be addressed in Relation to a Patient-Based Outcome Measure Being Considering for a Clinical Trial (Fitzpatrick et al. 1998)

1. Is the content of the instrument appropriate to the questions that the clinical trial is intended to address? (Appropriateness).
2. Does the instrument produce results that are reproducible and internally consistent? (Reliability).
3. Does the instrument measure what it claims to measure? (Validity).
4. Does the instrument detect changes over time that matter to patients? (Responsiveness).
5. How precise are the scores of the instrument? (Precision).
6. How interpretable are the scores of the instrument? (Interpretability).
7. Is the instrument acceptable to patients? (Acceptability).
8. Is the instrument easy to administer and process? (Feasibility).

Instruments that have been developed throughout this process and meet all these standards could be used with more confidence by researchers. A brief synopsis of these questions is demonstrated next.

The first consideration should be to ensure that the instrument is suitable for the intended purpose. The generic or the disease-specific measures, for example, purported to capture the most important and relevant aspects of quality of life to a specific patients group (Cella et al., 2002).

Reliability of the instrument refers to the existence of error-random or systematic after a measurement. In fact, reliability is synonymous with repeatability and consistency. A question that could be addressed and may express the reliability of a measure would be: "does the test measure produce the same results (consistent results) when repeated in the same population?" Reliability can be determined using a variety of methods. The test-retest method assesses the reliability (stability) of a measure and determines whether similar results are obtained (at two separate time points in time), when the test measure is administered to the same population. Similarly the inter-rater method assesses whether similar scores are obtained by different observers. However, a number of biases can occur, for example, the time between two administrations should be chosen with care. If the disease progression changes rapidly or patients undergo treatment, the quality of life measure can be expected to remain stable for a short time. On the other hand, when the time of measuring is too short the respondents may remember their last responses (Streiner and Norman, 2003).

The internal consistency is also a method for assessing the reliability of a measure and is an important concept particularly for multi scales. The term refers to the homogeneity of the items of a scale, to the degree that items correlated with one another and with the overall scale score. High correlation among items is the evidence that a measure is internally

consistent. The more comprehensive statistical test for the internal consistency is Cronbach's alpha coefficient (values range from 0 to 1 but a correlation coefficient above 0.70 is important). But, a high value of Cronbach alpha (0.9-0.999) may mean that the same question is asked more than once. Finally, one should have in mind the reliability of a measure is not a fixed property in any one measure, but is instead a property that may be used with certain people under certain conditions (Streiner and Norman, 1995; Hays et al., 1998). Thus, it may not produce generalizable results and should be reevaluated in new applications (Cella, 1997).

The validity of an instrument refers to its ability to measure what it claims to measure, for instance, quality of life. In many fields of measurement, the validity of an instrument is established by comparing it with a "gold standard" or to a superior measure and the new tool provides evidence of criterion validity. In psychometrics there are no gold standards, so other techniques have developed in which the validity of an instrument is examined indirectly (Streiner and Norman, 2003).

So, the face validity examines the degree to which a measure appears clinically important and sufficiently appropriate to the setting being measured - including patients with cancer. Does the tool contain questions that are appropriate to the area that is measured, and is this area covered completely? (Streiner and Norman, 2003).

Criterion validity is usually established by correlating the scale data results with a pre-existing standardized measure of the same construct (convergent

validity) - since the gold standard does not exist - or with the results of other parallel measure (concurrent validity) (Streiner and Norman, 2003).

Construct validity refers to the ability of a measure to produce results that confirm the theory or the hypotheses. If, for example, a theoretical model supports that weakness correlated with the stage of patients' disease or with muscle strength etc. and a measure confirms the above theory having high scores (indicating weakness) for people with advanced disease or muscle debility, then the measure presents some construct validity. Factor analysis is an approach that contributes to construct validity confirming the multidimensional nature of HRQOL measures (Hays et al., 1998).

Responsiveness to change or sensitivity is also an important requirement of a measure, particularly in clinical trials. Clinically meaningful changes refer to those that are expected to occur with time; for example, improving or worsening health status or changes correlating to the proposed treatment and side-effects. Many criticisms exist about the sensitivity of available standardized measures given that they may capture only something of the overall HRQOL of individual patients. They may capture the clinical changes in patients' functional level but they are unlikely to reflect changes in other important aspects of HRQOL such as family support, sexuality, spirituality or other important components of care or other outcomes of treatment. Such criticism leads some authors to find difficulties in interpreting the scores of many of these measures (Carr & Higginson, 2001; Bowling, 1995). However, as discussed previously, although such aspects might not be useful as outcome measures, they might serve as explanatory variables. As with reliability and validity, the sensitivity of an instrument

can be also established by a number of statistical approaches. These include correlation of changes in QOL with patients' clinical status or calculation of effect-size (Streiner and Norman, 2003).

The precision of a measurement is very important since they wish to express subjective responses as numerical values. This is assessed through the response categories used in the instrument (Likert scales or Visual Analogue scales) (Osoba, 1991).

Interpretability of instruments is a relatively new area that has now begun to be explored in the clinical arena. This is concerned with the ability of an instrument to interpret what changes in HRQOL are clinically significant (Lydick and Yawn, 1998). Small numerical changes, for example, in HRQOL may have a high level of statistical significance in a large population. Many authors agree that the level of statistical significance may fail to reflect the clinical relevance from a patient perspective of changes in HRQOL scores (Efficace et al., 2004; Osoba, 1999; Cella, 1997; Osoba, 1991b). The assessment of subjective significance information, or the examination of the differences in mean scores between studies of patients, are two approaches used in assessing the interpretability of instruments (Osoba, 1999). Other approaches are the establishment cut-off points for clinical intervention (e.g. depression scale) that derive from normal population or from other disease populations (Weissman et al, 1997) or the use of clinical anchors or distribution-based techniques (Funk et al., 2004).

During the last two decades a new approach has been taken in the construction and scoring of instruments. It is based on the "item response

theory" (IRT) that provides a number of methodological advantages and contributes to the development of Item Banks and computerized adaptive assessment (Ware, 2003a; Cella, 2002; Hays, 1998). The acceptability of a measure, either by patients or by staff, is a very important property for any measure. The length of a questionnaire and time taken to complete are important aspects. Questionnaires that take less than 10 or 15 minutes to answer are considered brief and may be more preferable to patients with cancer than long questionnaires (Osoba, 1991). Missing data is a problem, particularly for long-term follow-up measures, leading to serious problems in the analysis and interpretation of the results. Patients may miss out items for many reasons (including not understanding the item) or they may be unsure about the most appropriate response options, or feel that some items are not relevant to them (Conroy, 2003).

The feasibility of using the HRQOL assessment is also an important issue and barriers have been described in carrying out assessment. Some of them related to the time that is demanded for the assessment, the financial support needed, the perceived lack of an appropriate instrument and the belief that HRQOL assessment is unrealistic (Osoba, 1991a). Also, any HRQOL assessment demands ethical consideration with respect to informed consent and confidentiality of data. This may require an in-depth knowledge by research staff on collecting HRQOL data.

4.3 Summary and conclusions

The assessment of QOL within health care has become an interesting area of research in recent years. Although there is debate with regard to the conceptualization of QOL, there has been a proliferation of interest in the assessment of Health-Related Quality of Life (HRQOL) as an outcome of disease and treatment. Assessment of quality of life has changed the interest of quantity of life to quality of life.

This has resulted in a wealth of instruments that purport to assess aspects of HRQOL. Consideration of the type of instruments and their properties is fundamental in choosing an instrument for any HRQOL measure. One of the main issues of concern is whether an instrument is appropriate for use in a particular patient group. A disease specific instrument promises to be if it covers important issues for a particular disease and is responsive to changes over time. Therefore, a consideration of an appropriate assessment of HRQOL in survivors of cancer of the colon and rectum as well as an appropriate method of approaching HRQOL assessments is required.

CHAPTER 5

METHODS

5.1 Introduction

This study utilized a cross-sectional survey designed to assess the current state of the quality of life of long-term Greek colorectal cancer survivors. It focused on the disease-related factors and factors regarding patients' characteristics that might modify the level of HRQOL.

For these research purposes, a self-administered generic and cancer specific multidimensional HRQOL instrument was used as well as dimension specific instruments.

Presented in this section are the research questions, the objectives and hypotheses as well as the procedures and design of the study. Included are: description of the criteria instruments, procedures for translation of the research instruments, estimated sample size of the research and data analysis.

5.2 Research questions

The research questions of this study are:

1. How do Greek colorectal cancer patients perceive their HRQOL during the post-treatment/survivorship phase?
2. What factors (clinical, demographic) may influence Greek colorectal cancer patients HRQOL?
3. How do HRQOL measures change for patients with colorectal cancer of different stages at diagnosis, and at different times since diagnosis?

5.3 Objectives

To address the research questions, specific objectives were set:

1. To assess specific dimensions of HRQOL such as the physical functioning, the emotional/mental functioning, the social/family functioning and the functional well-being in Greek colorectal cancer survivors following treatment as measured by FACT-C and MOS Short-form 36 instruments.
2. To determine the overall HRQOL of Greek colorectal cancer survivors as measured by the FACT-C instrument.
3. To identify specific factors that might contribute to patients' HRQOL. The independent variables were: stage of the disease at diagnosis, time since diagnosis, colostomy appliance, disease recurrence, depression as comorbidity, relationship with the partner and certain demographic characteristics such as age, gender, marital status, educational lever and income.

5.4 Hypotheses

Hypothesis 1: The overall HRQOL would be higher for those patients further from diagnosis and with early disease stage.

Hypothesis 2: The HRQOL of patients with a colostomy appliance would be lower than those without a colostomy appliance.

Hypothesis 3: The HRQOL of patients who experienced remission of the disease would be better than that of patients with recurrent disease.

Hypothesis 4: Increased age, depression, poor communication with partner and lower income status would be associated significantly with poorer outcomes on the HRQOL of cancer survivors.

5.5 Plan of investigation

A survey design was decided for the present study because the main purpose of the study was to describe the overall and dimension specific HRQOL (physical well-being, emotional well-being, social functioning, disease specific dimension) of a patient's population, and to compare HRQOL between groups (stoma patients with non stoma patients or patients with recurrence or metastasis with patients without recurrence or metastasis). Furthermore, a cross-sectional survey design permits of making comparisons over time among HRQOL of patients at different times since diagnosis and different disease stages that was one of the objectives of this study.

A range of measures were required in order to address the objectives of the study. For investigating the impact of disease and treatment on HRQOL domains and overall HRQOL, the primary objective of the study, required a quality of life measure specific to colorectal cancer patients. The "core" Functional Assessment of Cancer Therapy-General (FACT-G) was used (a generic, cancer-specific HRQOL instrument) together with its colorectal cancer "module" (FACT-C) (Appendix 9). One of the advantages of this measure, in addition to its responsiveness to disease-related changes in HRQOL, is that it provides scores for the overall QOL of the research population.

It was decided to use the mental component of the generic quality of life instrument Medical Outcome Study Short Form Health Survey (SF-36) (Appendix 11).

In order to explore independent variables that may influence or determine patients' HRQOL demographic data were gathered directly from the patients (age, gender, marital status, income, educational level) (Appendix 7). In addition, disease and treatment data were gathered from medical notes (stage at diagnosis, time since diagnosis, treatment choice, recurrence) in order to allow HRQOL comparisons between gender, age groups, income categories, educational levels, stoma patients with non- stoma and correlations among HRQOL variables e.g. how disease characteristics such as disease stage, time since diagnosis or patients' characteristics are related to one another.

The relationship between depression and HRQOL was also explored by the use of the depression measure The Center for Epidemiology Studies Depression Scale (CES-D) (Appendix 13).

The support that patients perceived by their partner as well as how it was related with their quality of life was investigated by the psychological scale The Enriching and Nurturing Relationship Issues, Communication and Happiness (ENRICH) which measures the level of communication between couples (Appendix 15).

All instruments except ENRICH had officially been adapted and translated into Modern Greek language. The official Greek translated version of FACT-C (version 4) scale was obtained by the official body the Functional

Assessment of Chronic Illness Therapy (FACIT) Measurement System, Center on Outcomes, Research, and Education (CORE) together with permission for its use.

The SF-36 and the CES-D scales have been officially translated and validated into Greek by Pappa et al. (2005) and by Foundoulakis et al. (2001).

For the ENRICH instrument a translation process was required by the researcher that is described at the section below.

The Consent Form was translated into Greek from the original form by this author. The letter that invited patients to participate, the information sheet, as well as the demographic data questionnaire were originally written in Modern Greek and were translated in English and then were checked by the academic supervisor.

A pilot study was carried out in which a small number of colorectal cancer survivors were interviewed in order to assess the clarity and acceptability of the research instruments that also is described at the section below.

Sample size calculation was made by STATISTICA, a software programme details of which are described in the section below.

5.5.1 Translation of the ENRICH research instrument.

The Greek version of the 10-items communication scale of the ENRICH instrument (Appendix 15) was obtained by following standard translation procedures. The first step of the translation process involved forward

translations of the original English questionnaire into Greek by two translators who were native speakers of Greek. Each translator produced one translation of the ENRICH items and established a list of translations of the response choices. Translators were to place emphasis on conceptual and culturally-sensitive rather than literal equivalence. Differences in translations were discussed, alternatives were documented and a target translation of ENRICH was produced. The forward translation was given to two translators who were native speakers of English and spoke Greek, who translated the questionnaire back into English. The translations were discussed for equivalence, and modifications were made to some translations.

There were differences between forward and backward translation regarding the phrase "silent treatment" of item 2 of the instrument. During the forward translation the above phrase was translated into Greek as (adiaforia) and during backward translation process the word (adiaforia) translated back to English as "indifference". It was decided to translate the phrase "silent treatment" as (adiaforia) since in Greek this word means the lack of interest or attention.

Finally, the modified forward translated instrument was pilot tested with a small group of colorectal cancer patients (N=10). Respondents completed the questionnaire and were asked if they found any items difficult to understand or the answer, confusing or upsetting. Generally all items were well accepted by patients without any problems in understanding. The only problem that emerged by pilot testing was about the group of patients who were divorced or was widow/widower since the communication scale of the ENRICH questionnaire investigates the relationship between partners. As one of the purposes of this study was to investigate the independent variables that contribute to patients' quality of life it was decided that anyone person who

was close to patients and could be a support, or not, to them would be accepted as the person who contributes to his/her quality of life. The communication scale of the ENRICH instrument was, however, administered to those patients who lived without a partner asking them to reply to the questions in case an important person did support them. In this case the phrase "my partner" that used in some items of the instrument modified to "this person" for this category of patient.

5.5.2 Pilot testing

The research questionnaires were administered to colorectal cancer survivors for pilot testing before administering to the research population.

Methods

Identification of Patients

Ten colorectal cancer patients coming to the clinic for follow-up examination were approached by the researcher and interviewed with their physician's permission. Patients who took part in the pilot study were identified as being suitable according to the same eligibility criteria set for the research study. Purposeful sampling allowed a cross section of subjects to be identified. So, patients were recruited who represented different Duke's stages, treatment choices, different times from diagnosis (early-term, middle and long term survival), and a variety of socio-demographic characteristics. The table 5.I below shows the socio-demographic and clinical features of the pilot patients.

Table 5.1 Socio-demographic and clinical features of the Patients (n=10)

AGE (mean)	62.5 years (27-76)
SEX	6 male, 4 female
MARITAL STATUS	9 married, 1 widow
OCCUPATION	4 retired 2 housewives 4 full-time workers
TIME SINCE DIAGNOSIS	Long-term: 5 Mid-term: 2 Earl-term: 3
STAGE	3 Stage B, 7 stage C
TREATMENT INTERVENTION	Surgical resection,: 10 Colostomy:2 Chemotherapy: 1 Radiation therapy: 2
RECURRENCE/METASTASIS	Liver:2 Liver and Lung:2

Recruitment and data collection

The researcher was introduced to patients identified as being eligible and discussed the study with them in a private room. They were informed of the aim of pilot testing, conduct of the study and were asked to participate.

Patients who opted to take part in the testing were asked to examine and "think aloud" as they completed the questionnaires in order to gather their perceptions of the instrument's completion taking into account the following:

1. Whether they had difficulties in replying to the questions
2. Whether there were items that they found confusing
3. Whether difficult words were used

4. How they would have rephrased a confusing question
5. Whether they had problems distinguishing between the points within the answer scale.
6. Whether they felt that any questions were irrelevant to their current health situation.
7. Whether there were too many questions or whether some of them should not have been included, thus avoiding overload.
8. They were also asked if they found some questions a distressing reminder of their period of illness.

The researcher kept notes for each patient's comments according to the above.

Results

Fourteen patients were initially identified as being suitable for the pilot study. Two patients immediately declined to take part because they not had time to be interviewed and two others were withdrawn due to illness. Therefore, ten patients eventually participated in the pilot testing.

In general, the patients were positive about the questionnaires. Most found the questionnaires clearly worded without facing any serious problems in replying to the items.

Although most patients found psychological issues very relevant and important to be asked they felt that questions about physical health tended to repeat often. Taking into account this comment it was decided to take out the

physical component of SF-36 questionnaire in order to minimize patients' burden. SF-36 physical component was selected to be excluded because the SF-36 questionnaire does not produce a score for overall QOL. In order to address a primary purpose of the study the FACT-C questionnaire was preserved as it produces a summary score for overall QOL. So, only the mental component of SF-36 questionnaire included in the study.

Two patients suggested that the list of occupations /jobs that were included in the demographic data questionnaire was limited. According to this comment, in the Employment Status list was added the option "other job".

One man found the wording of items C8 and C9 of FACT-C instrument (ostomia) and (orthostomia) (stoma area) not very clear and suggested to rephrase them into (colostomia). Since this would have not changed the overall meaning of the items as well as the fact that the word (colostomia) is a colloquial word and widely used in Greek language for expressing this meaning, it was decided to adapt these items according to patient's suggestion.

Two patients faced problems in the understanding of the word (naftia) (nausea) in FACT-C instrument GP2 item. It was decided to keep the word (naftia) and to add the translation of the word into Greek for those people who may face any problem about its meaning. So, the GP2 item became (eho naftia e tassi gia emeto) (I feel nauseated).

One woman found the GP3 item of FACT-C instrument confusing. When she was asked what made it so she answered that she faced difficulty in understanding the phrase (fissikis mou katastasis) (my physical condition). When the phrase changed to (somatikis mou katastasis) (my bodily

condition) she did not face any problem. So, this phrase was changed to the above suggestion taking into account that it is a phrase that focuses on problems that related to physical well-being. Thus it is familiar to everyone and did not change the meaning of the phrase.

Two patients mentioned that SF-36 and CED-S instruments should have used a bigger font and larger spacing between the lines. According to them, and given that the research population would be older people, changes were made to the font and spaces in all instruments.

Changes made by pilot study results concerning the ENRICH instrument were described in detail in a previous section.

5.5.3 Sample size

Concerning sample size, the Power and Sample size calculation subroutine of the statistical software programme <STATISTICA> was employed to establish the parameters for analyzing sample size for multiple regression. The question to be answered was the following: How big a sample size would we need to have a power of 0.80 and Type I Error (Alpha)= 0.05, in a situation where there are 9 predictor variables (age, sex, stage at diagnosis, time since diagnosis, economical status, educational level, colostomy, metastasis, depression)?

In a study of HRQOL evaluation for long-term survivors, Ramsey et al. (2002) used multiple regression with HRQOL measures as dependent variables (health utility index, SF-36, FACT-C self evaluation). Time since

diagnosis, income, co-morbidity, and chronic diarrhea were included as predictor variables. The proportion of variation explained (R^2) was modest and ranged from 12.5% (for HUI) to 22.8% (for self-evaluation). Thus, a value of sample R^2=18% can be considered realistic.

For these figures, a sample size (N) equal to 137 is estimated to be sufficient for 9 predictor variables in order to achieve a power of 0.80, assuming that the population coefficient of determination (P^2) is equal to 0.35, thus rejecting the null hypothesis that $P^2<R^2$. The value of P^2 (=0.35) can be considered satisfactory, since it explains one third of the variance in QOL accounted for by the regression.

5.5.4 Participants

Since the population of interest of the present study was colorectal cancer survivors, colorectal cancer patients from the archives of two Athenian institutions were identified. The institutions were one public oncology hospital and one private oncology clinic. This was done in order to obtain socioeconomic heterogeneity among patients. The public hospital most commonly provided its services to a population of low socioeconomic level whereas the private clinic cared for patients of middle and upper-middle socioeconomic level. Also, the archives from which the data were collected involve patients from all over Greece and of both sexes, who satisfy the inclusion criteria. Therefore, it was a sample that except of the socio-demographic heterogeneity among people (different income categories and educational levels) it involved patients with various medical conditions. So,

patients from all disease stages as well as from all periods of time since diagnosis were included into the study.
So, 145 Greek patients of both sexes, diagnosed with cancer of the colon and rectum who had survived at least 1 year from initial diagnosis were investigated.

Survival from colorectal cancer was determined in time periods from the date of initial diagnosis: "Early-term" (1 year post treatment), "Middle-term" (2-4 years post treatment) and "Long-term" (>5 years post treatment).

The demographic characteristics of the study sample (age, gender, marital status, educational level, employment status, income) as well as and the medical characteristics (disease stage, diagnosis, time since initial diagnosis, type of therapy, stoma, non-stoma patients, reccurence, metastasis) are presented below in table 5.2. and in table 5.3.

Table: 5.2 Demographic characteristics of colorectal cancer survivors (N=145)

	No	%
Gender		
Male	87	60
Female	58	40
Age (yrs)		
≤60	67	46.2
61-70	45	31.0
>70	33	22.8
Marital Status		
Single	9	6.2
Married	114	78.6
Divorced	9	6.2
Widowed	13	9.0
Education		
Primary school	30	20.7
Secondary School	53	36.6
College/University	62	42.7
Employment Status		
Unemployed	2	1.4
Household	15	10.3
Retired	73	50.3
Clerk Officer	23	15.9
Skilled workman	1	0.7
Farmer	1	0.7
Work in their own job	17	11.7
Other	6	4.1
Not working due to disease	7	4.8
Family Income (euros per month)		
<440	14	10.8
440-880	27	20.8
881-1,467	28	21.5
1,467-2,347	33	25.4
>2,347	28	21.5
Missing	15	
Residence		
Athens	109	75.2
Province	36	24.8

Table 5.3: Disease-related characteristics of the sample (N=145)

	No	%
Diagnosis		
Colon cancer	100	69.0
Rectum cancer	45	31.0
Disease stage at diagnosis		
Stage B		
Stage C	55	37.9
Stage D	79	54.5
	11	7.6
Years since diagnosis		
1-2	36	24.8
2-4	75	51.7
≥5	34	23.5
Type of therapy		
Colectomy	142	97.9
Adjuvant Chemotherapy	139	95.8
Adjuvant Radiation Therapy	42	29.0
Ostomy	22	15.2
Metastasis	38	26.2
Recurrence	8	5.5

Eligibility was determined by the inclusion and exclusion criteria below.

Inclusion criteria

a. Cancer of colon and rectum was a confirmed diagnosis and the primary malignancy.

b. Patients had survived at least 1 year since the time of diagnosis.

c. They were over the age of 18 at time of diagnosis.

d. Dukes B, C, or D tumor stage were confirmed.

e. They had not received any treatment (surgery, chemotherapy, radiation therapy) for their disease in the past month. Since the main purpose of the study was to capture the late effects of the disease and its treatment on patients' quality of life since any treatment had been completed, the short term side-effects of any treatment would contribute to the difficulty in capturing the late effects of the disease on cancer survivors. It was supposed that a time of one month would be sufficient for any short side-effects to have ceased.

Exclusion criteria

a. Difficulties in reading or understanding Greek.
b. A second non-colorectal carcinoma-related malignancy.
c. Patients with known evidence of cognitive impairment or severe mental illness.

5.5.5 Recruitment and data collection strategy

The survey was conducted between March 2003 and July 2006. The eligible patients were identified from the period of the last 12 years; that is between 1993 and the end of 2005.

Permission for having access to the public hospital archive was obtained from the director of the institutions and information relating to general health status, type of disease, disease stage, type of surgery, and other adjuvant therapy (chemotherapy or radiation therapy that follow surgery) received was obtained from medical case notes. Permission was also obtained from

subjects' physicians before the individuals were contacted and consent gained. The consent form was also obtained from the patients.

From the first archive those patients who met all eligibility criteria were selected. All selected patients were contacted by phone in order to monitor the population that had died or changed address. Because the response rate was low, particularly due to those subjects with advanced disease and those who might were moved, re-sampling through the use of the second archive was necessary.

During telephone communication, the investigator had the opportunity to screen patients' ability to speak and understand Greek. The telephone respondents were informed about the research purposes as well as the fact that permission to contact them and use of their personal data (name, telephone number, address) had been obtained from their physicians. Those patients who accepted to learn more about the study were sent by mail a letter marked "Private and Confidential" with a letter, a detailed information sheet with a reply slip. In the patient's letter, direct contact details were given for the researcher, including a 24 answer phone if patients had any queries or concerns (APENDIX 1, 2). The information sheet included details about the aim of the research the significance of their participation as well as instructions on how to complete the questionnaires (APENDIX 3, 4). One week after sending the letter and the information sheet a telephone contact would confirm that patients had received it. During telephone communication the investigator had the opportunity to discuss any aspect of the study in a further detail. For people who did not receive the letter a new one was sent.

Participants who accepted to participate in the study and finally returned the reply slip were sent a Research package by mail.

After two weeks, non-respondents were sent a second research package and reminder to complete. Four patients declined to complete the survey at this time and were not contacted again.

5.5.6 Response rate

Through the archive survey, 362 eligible patients were identified and contacted by phone. Of the patients contacted, 196 answered the phone call (54.1%). Five of them had difficulties in communication due to low educational level or because of advanced age. So, the information sheet and the reply slip were sent to 191 eligible patients. One hundred and forty nine patients accepted the invitation to participate in the study by sending the reply slip and so they received the Research Questionnaires. Nineteen patients needed a reminder to complete. In total, from those patients who had been sent the letter, the information sheet and the reply slip one hundred and forty five (145) patients returned the completed questionnaires (response rate 75.9 %).

5.5.7 HRQOL assessment administration

Patients were asked to complete the Research Package that included:

a. A consent form (APPENDIX 5, 6)

b. A Demographic data questionnaire (APPENDIX 7, 8).

c. A copy of the research questionnaires (FACT-C, SF-36, CES-D, ENRICH) (APPENDIX 9-16). (Detailed description of these questionnaires and the rationale for their use is discussed in the section below).

d. Two stamped addressed envelopes: one for returning the completed questionnaires and the other for returning the signed consent form. The signed consent form was returned separately for ensuring the anonymity of the completed participants' questionnaires.

5.6 Description and validation of the instruments

The Demographic data questionnaire included questions about: age, gender, marital status, educational level, employment status and income-factors that may influence patients' QOL.

The Functional Assessment of Cancer Therapy (FACT) system is one of the most widely used QOL assessment system and its development commenced in 1987 by David Cella in the USA. The system has already been used by international research organizations. One of the important advantages has been the emphasis on cross-cultural development in a range of languages and cultures. The system contains the core generic instrument (FACT-G) that assesses health status of cancer patients in terms of 4 HRQOL dimensions: physical well-being (PWB, 7 items), emotional well-being (EWB, 6 items), social well-being (SWB, 7 items), and functional well-being (FWB, 7 items) (Cella et al., 1993). Disease-specific subscales have been developed to complement the FACT-G. Each subscale addresses concerns associated with the specific cancer. Colorectal Cancer Subscale (CCS) contains 9 items that assess issues related to the QOL of all disease stages in colorectal cancer

patients, covering a variety of areas such as stoma related issues, emotional status, social effect of illness and functional changes. Each item is rated on a 5-point Likert type scale. The FACT-C instrument is a measure which combines the FACT-G with the 9-item colorectal cancer subscale (CCS). Scoring of FACT-C allows for the calculation of individuals' subscale scores which are then added to produce an overall QOL score; higher scores reflect better QOL. The summary scores range from 0 (worst possible) to 144 (best possible) (Ward et al., 1999).

In the original study (Cella et al., 1993) internal consistency of three out of five scales (PWB, FWB, and EWB) and total QOL score of FACT-C instrument was >0.70 (Cronbach's Alpha coefficient). The SWB was below this, with an Alpha coefficient of 0.69. Test-retest reliability on 70 patients was undertaken and the response rate was high at 86% and correlation coefficients ranged from 0.82-0.92 for all scales. In the validation of the colorectal cancer specific instrument, (FACT-C) (Ward et al., 1999) for both the English and Spanish versions, internal consistency was above 0.85 (Cronbach's alpha coefficients) for the FACT-C total score and above 0.84 for the FACT-G total score. So, the FACT-C evidenced good internal consistency reliability.

As far as construct validity is concerned, the FACT-C was compared to other psychosocial measures. Correlational analyses showed a significant positive association with positive mood indicators and significant negative correlations with negative mood indicators. Therefore FACT-C has evidenced good concurrent validity (convergent). The FACT-C was able to distinguish between groups based on functional status and extent of disease. The FACT-C has also been found to be sensitive to change in functional status. The FACT-C (both English and Spanish versions) appears to be

sufficiently reliable and valid measure of HRQOL for use in research with colorectal cancer patients (Ward et al., 1999). The official Greek translated version of FACT-C (version 4) scale was obtained by the official body the Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System, Center on Outcomes, Research, and Education (CORE) together with permission for its use.

Medical Outcome Study Short-Form 36 Health Status Survey (MOS SF-36), version 1. The MOS SF-36 is a generic well-established instrument measuring HRQOL that measures physical, psychosocial functioning and morbidity due to health condition through eight health concepts: physical functioning, limitation in role functioning due to physical health problems, bodily pain, general mental health capturing feelings of nervousness, unhappiness and sadness, limitations in role functioning due to emotional problems, vitality, social functioning and general health perceptions (Ware et al., 2003b). The SF-36 instrument has been validated in many European countries such as France, Italy, Germany, Spain, U.K., Sweden, Denmark (Gandek &Ware, 1998). It has been validated in Greece and normative data from a Greek general population have been provided by Pappa et al. (2005). The SF-36 subscales have been reported to have satisfactory alpha reliability coefficients ranging from 0.73 to 0.94. (Ware et al., 2003b).
In the Greek version, internal consistency, measured by Cronbach's alpha, ranged from 0.79 to 0.95. Item discriminant validity showed that items discriminated well across scales while the Greek version provides evidence of a distinction between sub-groups of respondents in terms of known socio-demographic or clinical differences (Pappa et al., 2005). With regard to construct validity, Anagnostopoulos et al. (2005), using a structural equation

modeling method, confirmed the multidimensional structure of the SF-36 observed in the U.S and many European countries, and underscored the feasibility of multinational comparisons of health status using this instrument.

According to the pilot testing results of the present study only the mental component of SF-36 was administered that included a four-item vitality scale, a two item social functioning scale, a three-item scale measuring role limitations due to emotional problems and a five-item scale measuring mental health. For each item, responses were coded, summed and transformed into a scale ranging from 0 (worst possible health status) to 100 (best possible health status) (Ware et al., 2003b). The physical component of SF-36 was not administered since it overlapped with the FACT-C questionnaire.

The Enriching and Nurturing Relationship Issues, Communication and Happiness (ENRICH) is a self-administered 115-item instrument that describes marital dynamics for research (Olson et al., 1982). It contains twelve content categories which are as follows: Idealistic Distortion, Marital Satisfaction, Personality Issues, Communication, Conflict Resolution, Financial Management, Leisure Activities, Sexual Relationship, Children and Marriage Family and Friends, Equalitarian Roles and Religious Orientation. The communication scale of ENRICH was used for studying the impact of colorectal cancer on the relationship between colorectal cancer patients and their partner. It is a brief 10-item scale that measures individual's feelings, beliefs, and attitudes related to communication with her/his partner. Items focus on the level of comfort felt by both partners in being able to share important emotions and beliefs with each other, the perception of the

partner's way of giving and receiving information, and the respondent's perception of how adequately she/he communicates with their partner. Each item is rated on a 5-point Likert type scale. (Olson et al., 1982). According to the author "high scores reflect the couple's awareness and satisfaction with the level and type of communication in their relationship. Low scores reflect a deficiency in the level of communication essential to satisfactorily maintain a relationship and focus on the need to work on improving their communication skills" (Olson, 1982, p.47). Since for seven items 2, 3, 4, 5, 6, 7, 9, a high score indicated poor communication, these items were reverse-scored in order to reflect good communication. The alpha reliabilities for all the ENRICH scales averaged 0.74 while test-retest reliability was assessed over a week period and the average reliability was 0.87 with a range from 0.77 to 0.92 across all the categories. Because ENRICH instrument had not officially been translated into Modern Greek language a translation process was required by the researcher that is described in the section 5.5.1.

The Center for Epidemiology Studies Depression Scale (CES-D) is a unidimensional self-reported instrument, consisting of 20 items designed to measure depression symptomatology in patients with emphasis on the affective component of depressed mood (Radloff 1977). It is commonly used to measure depressive symptomatology in cancer patients. It has been officially translated and validated in Greece (Foundoulakis et al., 2001) and its alpha reliability coefficient is quite satisfactory (a=0.95). The score is the sum of the 20 item weights. Each item is rated on a 4-point Likert type scale. CES-D values ranged from 0 to 60, with higher values indicating more depression symptoms. In screening studies, a cut-off-score of >16 has been validated as identifying individual at high risk for depression in older adults

(Weissman et al., 1997) while for Greek population the cut off level is 23/24 (Foundoulakis et al, 2001).

5.7 Methods of data analysis

The cross-sectional profile of patients included descriptive statistics and exploratory analysis. These included descriptive statistics of demographic and disease-related characteristics of the sample and description of mean values of HRQOL variables.

Histograms related to scale variables (FACT-C, SF-36, CES-D, ENRICH) were performed for evaluating the normality of variables. Because histograms showed skewed HRQOL data, the non-parametric Kruskal-Wallis H test was used for comparing differences in HRQOL across colorectal cancer Dukes's stages and times since diagnosis. Differences in HRQOL between two group categories such as stoma patients and non-stoma patients or patients with metastasis and patients without metastasis were tested using the non-parametric Mann-Whitney U test.

The method of data analysis utilized in this study for evaluating the effect of predictor variables on global HRQOL was the logistic regression analysis.
The statistical programme utilized for the analysis of the data was the Statistical Package for the Social Sciences (SPSS) version 11.

5.8 Ethical considerations

There are practical and ethical difficulties when doing research involving people with cancer and it is important to protect the rights of all study participants. One important factor that must be considered is fatigue, both mental and physical. For this reason, the researcher aimed to diminish respondent burden by focusing data collection on specific issues (i.e. the relevant domains of HRQOL).

Patients' medical records were reviewed and the researcher liaised with the relevant physicians before approaching suitable patients. Detailed records of the recruitment process were kept and identified patients were approached and informed of the study and written information was given. Sufficient time of two weeks was given to allow patients to consider participation before informed consent was obtained.

Patients were provided with a detailed information sheet about the purpose of study and a signed consent form was obtained. A copy of their signed consent form was sent to all participants. All patients were informed that they would be able to withdraw from the research at any time and without giving reasons and without detriment to their care. Also, patients were informed about the possible effects that may be caused by their participation and what the potential risks might be. The possibility patients to find some of the questions upsetting or face difficulty in answering some of the questions or they may becoming tired was set. These potential issues were minimized by providing clear instructions on how to complete the questionnaires, and by providing a contact telephone number if patients had any queries or

concerns about the questionnaires. They were assured that all data from this project would be confidential and would be used only for research purposes. The anonymity of the collected data would be also presented. So, a unique code number was be placed on each questionnaire and corresponded to a private medical record that the researcher kept for each patient. This code was only be accessible to the researcher and kept in a locked storage file, separate from the research data. Also, the anonymity of each patient was ensured by asking the patients to return the consent form separately from the questionnaires using the stamped addressed envelope that was enclosed in the research package.

Participants were also informed that the investigator was a research student and permission to contact them and use their personal data (name, telephone number, address) had been obtained from their physicians. They were also informed that the data may be used in written and oral presentations (Appendix 3, 4).

Permission from the relevant and necessary authorities had been granted to undertake the research, including ethical protection of participants, in the chosen study sites (Appendix 17, 18). Formal ethical approval process is not required to undertake research in Greece and Ethics Committee has not been established in the Greek hospitals in which the research took place.

Also, ethical approval was not obtained from the University of Wales Swansea Research Ethics Committee because at the time that the research was undertaken the School of Health Sciences Research Ethics Committee

had not been established. Subsequently, approval was sought and obtained from the Ethics Committee of Middlesex University.

CHAPTER 6

RESULTS

6.1 Introduction

This chapter is directed toward providing answers to the research questions addressed in the Methods chapter. The data collected were analysed using the Statistical Package for the Social Sciences (SPSS) version 11. Statistical analysis was carried out using descriptive statistics. Appropriate non parametric tests such as Kruskal-Wallis H test and Mann-Whitney U tests were used for evaluating differences between group categories and continuous data. Furthermore, hierarchical logistic regression analysis was carried out for evaluating the effect of independent variables on a selected dependent variable.

The present study was designed to answer the following questions:

1. How do Greek colorectal cancer patients perceive their HRQOL during the post-treatment /survivorship phase?
2. What factors (demographic or clinical) influence colorectal cancer patients HRQOL?
3. How do HRQOL measures change for patients with colorectal cancer of different stages at diagnosis, and at different time since diagnosis?

6.2 Demographic and disease-related characteristics of the respondents

Table 6.1 summarizes the demographic characteristics of the respondents.

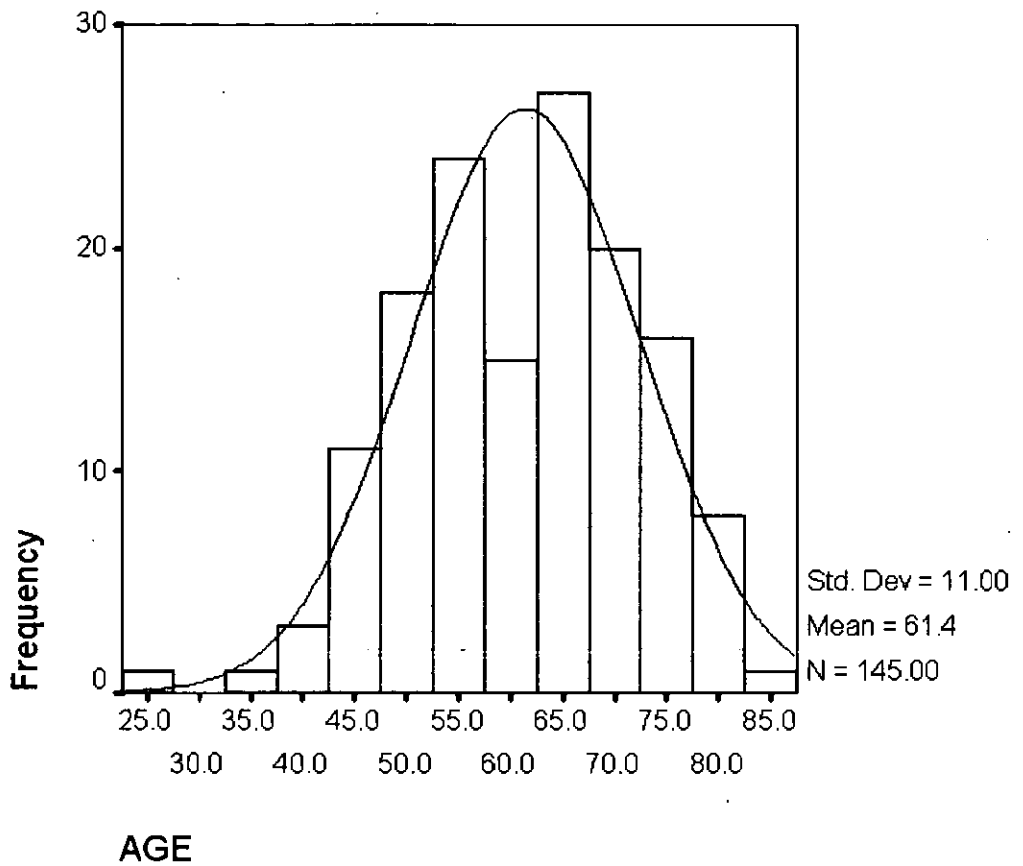
Table 6.1: Demographic characteristics of colorectal cancer survivors (N=145)

	No	%
Gender		
Male	87	60
Female	58	40
Age (yrs)		
≤60	67	46.2
61-70	45	31.0
>70	33	22.8
Marital Status		
Single	9	6.2
Married	114	78.6
Divorced	9	6.2
Widowed	13	9.0
Education		
Primary school	30	20.7
Secondary School	53	36.6
College/University	62	42.7
Employment Status		
Unemployed	2	1.4
Household	15	10.3
Retired	73	50.3
Clerk Officer	23	15.9
Skilled workman	1	0.7
Farmer	1	0.7
Work in their own job	17	11.7
Other	6	4.1
Not working due to disease	7	4.8
Family Income (euros per month)		
<440	14	10.8
440-880	27	20.8
881-1,467	28	21.5
1,467-2,347	33	25.4
>2,347	28	21.5
Missing	15	
Residence		
Athens	109	75.2
Province	36	24.8

Reflecting the fact that the incidence of colorectal cancer increases with age, more than half (53.8%) of the respondents were older than 60 years (range= 27- 83 yrs, mean= 61.40, SD= 11.00) while 60% of them were male. In epidemiological studies the estimated ratio for men and women is 1.3:1 for colon cancer and 1.5:1 for rectal cancer respectively. In this case, the estimated ratio was 1.5:1. The distribution of the ages is presented in figure 6.1.

The majority of the respondents were married (78.6%) and well educated, with 36.6% reporting secondary education and 42.7 % reporting college/ university education. Half of the participants (50.3%) were retired and only 4.8% reported unemployed due to the disease. Also, a minority of the respondents reported a low income status (10.8%) and the majority of the participants were (75.2%) living in the capital city of Athens.

Figure 6.1: Distribution of ages



The ages of the participants were relatively normaly distributed while the majority of the respondents were older than 60 years.

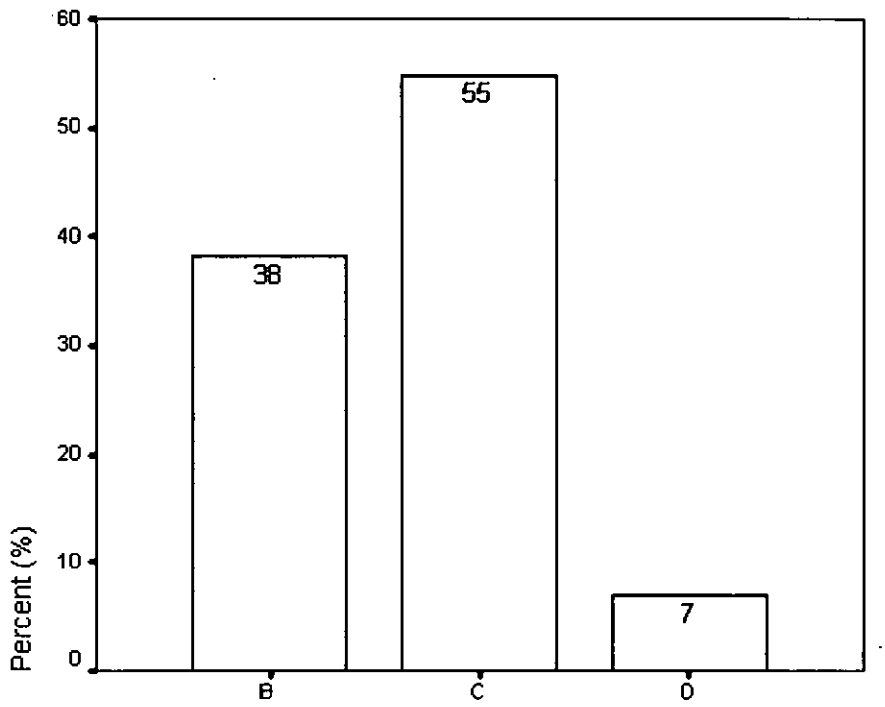
The disease-related characteristics of the study sample are presented in Table 6.2.

Table 6.2: Disease-related characteristics of the sample (N= 145)

	N	%
Diagnosis		
Colon cancer	100	69.0
Rectum cancer	45	31.0
Disease stage at diagnosis		
Stage B	55	37.9
Stage C	79	54.5
Stage D	11	7.6
Years since diagnosis		
1- 2	36	24.8
2- 4	75	51.7
≥5	34	23.5
Type of therapy		
Colectomy	142	97.9
Adjuvant Chemotherapy	139	95.8
Adjuvant Radiation therapy	42	29.0
Ostomy	22	15.2
Metastasis	38	26.2
Recurrence	8	5.5

Most of the respondents were diagnosed with stage C (54.5%) and stage B (37.9%) of the disease (Figure 6.2). The time elapsed since the initial diagnosis was on average 3.2 ± 2.2 years (Figure 6.3) and the majority of patients had received both surgery (97.9%) and chemotherapy (95.8%). Metastases are recorded for 38 patients (26.2%). Less than one third of the sample had received radiation therapy while twenty two respondents (15.2 %) had received a colostomy appliance.

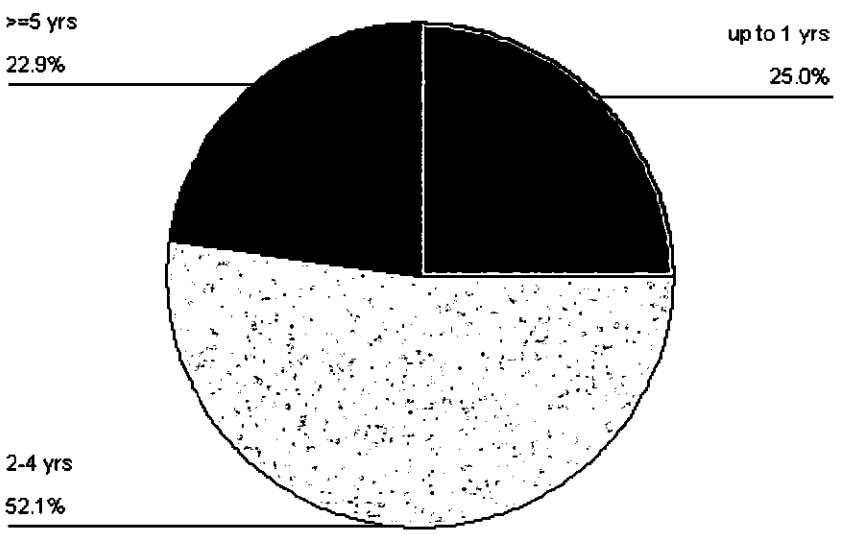
Figure: 6.2: Disease stages at time of initial diagnosis



Stage at cancer diagnosis

The propotion of colorectal cancer stages (B, C and D) at time of initial diagnosis was prevalent for stages C (55%) and B (38%).

Figure 6.3: Pie chart showing proportion of participants by time since diagnosis

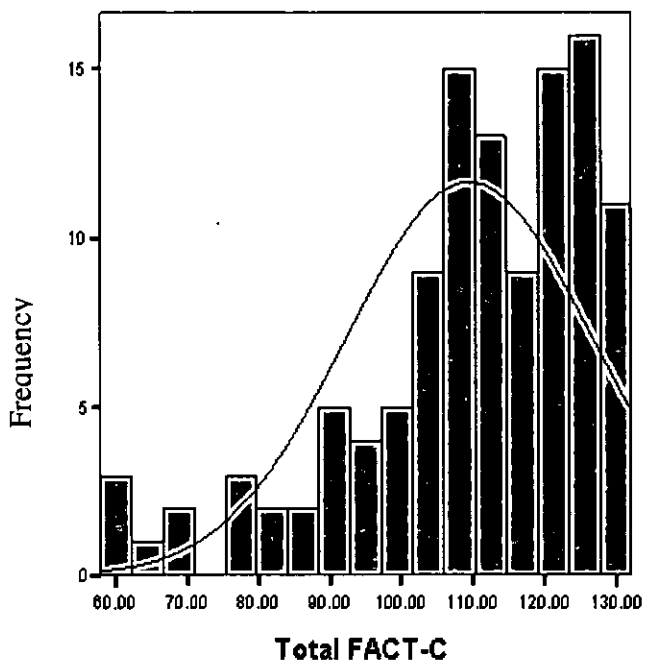


More than half of the patients survived 2-4 yrs from the time of the initial diagnosis while the proportion of patient who survived 5 yrs and beyond was 22.9% and a propotion 25% survived up to 1 year.

6.3 Choice of statistical tests

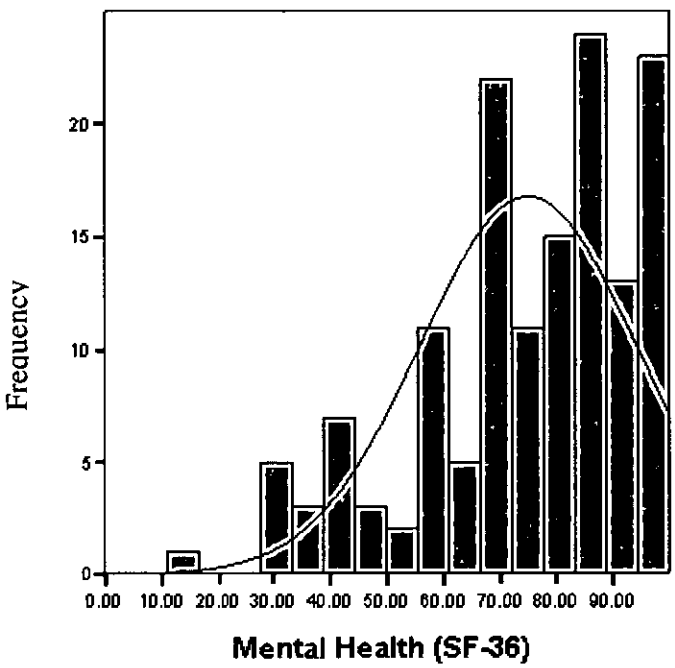
Histograms related to scale variables (FACT-C, SF-36, CES-D, ENRICH) were performed for evaluating the normality of distributions (Figure 6.4, Figure 6.5, Figure 6.6, Figure 6.7). Because the distributions were skewed non-parametric tests were performed to evaluate the unadjusted, stratified data. So, differences in HRQOL across colorectal cancer stages and times periods from diagnosis were compared using the Kruskal-Wallis H test. HRQOL differences between stoma and non stoma patients as well as between patients with recurrence or metastases and patients without recurrence or metastases were tested using the Mann-Whitney U test. Also, since the study data was skewed a non parametric logistic hierarchical regression analysis was carried out for evaluating the effect of predictor variables on global HRQOL.

Figure 6.4: Frequency histogram for total FACT-C scale scores



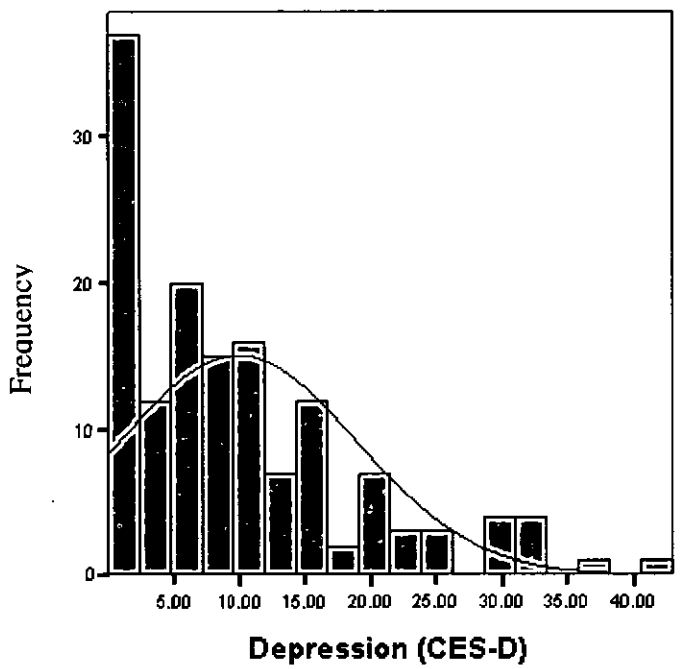
This figure showed that the distribution of FACT-C total scores was negatively skewed. Therefore, the data was not normally distributed.

Figure 6.5: Frequency histogram for SF-36 mental health scale scores



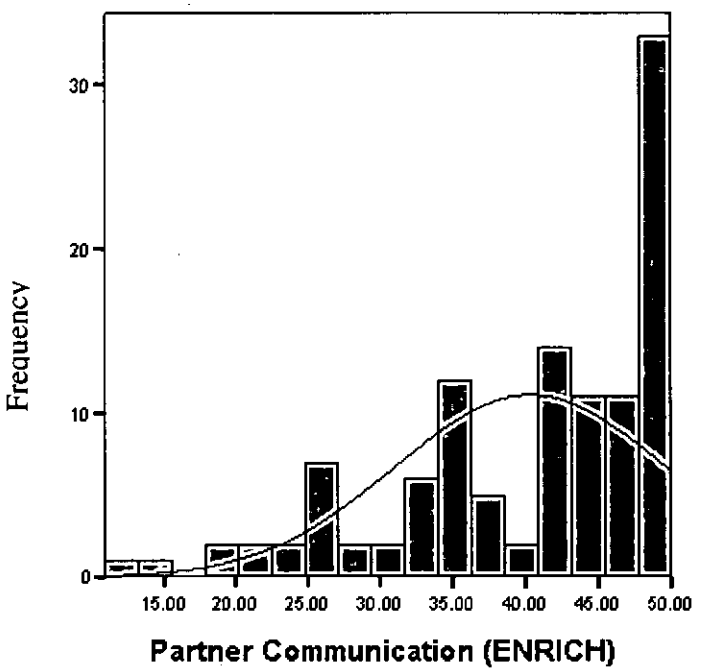
The distribution of SF-36 scores was negatively skewed. Therefore, the data was not normally distributed.

Figure 6.6: Frequency histogram for CES-D scale scores



The distribution of CES-D scores was positively skewed. Therefore, the data was not normally distributed.

Figure 6.7: Frequency histogram for ENRICH scale scores



The distribution of ENRICH scores was negatively skewed. Therefore, the data was not normally distributed.

6.4 Summary measures of research questionnaires

Overall health related quality of life as measured by FACT-C questionnaire averaged 109.46 (SD=17.15, range= 58-132). In general, respondents rated a summary measure of HRQOL as relatively high (possible range 0-144, mean=72). Depressive symptomatology, as measured by CES-D, averaged 9.85 (SD=9.10, range= 0-43) which is a low score given that the cut-off score for depressive symptoms is 23/24. Communication scale of ENRICH instrument averaged 40.31 (SD=9.31, range= 11-50). The mental component of SF-36 does not produce a summary score.

6.5 HRQOL by stage and time since diagnosis

Tables 6.3, 6.4 and 6.5 list mean (SD) values and median (ranges) values of the overall FACT-C HRQOL and FACT-C subscales by stage at diagnosis and time since diagnosis.

Table 6.3: Average Overall FACT-C Score by Stage and Time since Diagnosis

Stage	Time since diagnosis		
	1- 2 year	2-4 years	≥5 years
	Mean (SD) Median (range)	Mean (SD) Median (range)	Mean (SD) Median (range)
B	116.44 (11.52) 114.0 (100-132)	108.19 (15.53) 113.0 (60-127)	108.50 (17.89) 113.0 (67-127)
C	109.60 (21.17) 116.0 (58-128)	108.00 (1877) 111.0 (58-132)	110.08 (11.56) 107.0 (91-126)
D	103.80 (22.17) 112.0 (66-121)	117.00 (18.38) 117.0 (104-130)	124.00 124.0
χ^2	1.249	0.458	1.784

Overall FACT-C scores (Table 6.3) did not differ substantially by stage at diagnosis and different times since diagnosis. A Kruskal-Wallis test indicated that patients with different disease stages at diagnosis did not differ significantly 1-2 years after diagnosis (p=0.536), 2-4 years after diagnosis (p=0.795) or more than 5 years after diagnosis (p=0.410). Also, there is not a significant trend toward declining HRQOL for more advanced stages of colorectal cancer.

Table 6.4: FACT-C Subscale Scores by Stage at Diagnosis

	Colorectal cancer module	Physical well-being	Social well-being	Functional well-being	Emotional well-being
Duke's Stages	**Mean (SD)** [1] **Median (Ranges)**	**Mean (SD) Median (Ranges)**	**Mean (SD) Median (Ranges)**	**Mean (SD) Median (Ranges)**	**Mean (SD) Median (Ranges)**
B	4.92 (3.62) 4.5 (0-16)	2.80 (3.85) 2.0 (0-16)	20.75 (5.00) 22 (0-24)	21.94 (6.20) 24 (0-28)	4.35 (3.97) 4.0 (0-16)
C	5.11 (4.14) 4.0 (0-19)	3.59 (4.38) 2.0 (0-20)	20.73 (3.56) 21.5 (16-24)	21.71 (5.32) 22.5 (9-28)	4.71 (4.84) 5.5 (0-13)
D	5.55 (4.82) 4.0 (0-13)	4.00 (5.43) 2.0 (0-17)	21.50 (2.72) 21.5 (16-24)	21.50 (6.54) 22.5 (9-28)	5.40 (5.08) 5.5 (0-13)
χ^2	0.013	0.730	0.787	0.368	0.178

Examining all subscales of the FACT-C across all stages at diagnosis (Table 6.4) a kruskal-Wallis test indicated that none of the HRQOL aspects of FACT-C were associated significantly with Duke's stages at diagnosis. For physical well-being p=0.69, social well-being p=0.67, emotional well-being p=0.91; functional well-being p=0.83 and for colorectal cancer module p=0.99.

Table 6.5: FACT-C Subscale Scores by Time Since Diagnosis

	Colorectal cancer module	Physical well-being	Social well-being	Functional well-being	Emotional well-being
TSD*	**Mean (SD)** **Median (Ranges)**	**Mean (SD)** **Median (Ranges)**	**Mean (SD)** **Median (ranges)**	**Mean (SD)** **Median (Ranges)**	**Mean (SD)** **Median (Ranges)**
1 year	4.91 (3.96) 4.0 (0-16)	3.23 (4.00) 2.0 (0-17)	21.85 (2.62) 23 (14-24)	22.21 (5.53) 24 (8-28)	4.61 (4.67) 3.0 (0-14)
2-4 yrs	5.20 (4.05) 4.0 (0-19)	3.57 (4.74) 1.0 (0-20)	20.73 (4.41) 22 (0-24)	21.15 (6.20) 23 (0-28)	4.73 (4.88) 4.0 (0-19)
> 5 yrs	5.03 (3.93) 4.5 (0-15)	2.87 (3.34) 2.0 (0-16)	19.72 (4.47) 21 (8-24)	22.72 (4.65) 24 (7-28)	4.43 (3.58) 4.0 (0-14)
χ^2	0.162	0.561	4.432	1.453	0.160

Examining all subscales of the FACT-C across all times since diagnosis (Table 6.5) a Kruskal-Wallis test indicated that none of the HRQOL aspects of FACT-C were associated significantly with different times from the initial diagnosis. So, for physical well-being p=0.75, social well-being p=0.10, emotional well-being p=0.92, functional well-being p=0.48 and for colorectal cancer module p=0.92.

Table 6.6 list summary values of SF-36 HRQOL dimensions, Depression and ENRICH scales by stage at diagnosis.

Table 6.6: Mean (SD) SF-36 HRQOL Scores, Depression Scores and ENRICH Scores by Stage at Diagnosis

Stage at diagnosis	VT	SF	RE	MH	CES-D	ENRICH
B	74.91 (18.94)	85.45 (18.94)	78.79 (32.94)	74.05 (19.66)	9.36 (8.39)	40.97 (8.69)
C	73.12 (22.52)	80.38 (25.61)	70.99 (37.60)	75.16 (18.87)	10.27 (9.46)	40.41 (8.99)
D	70.00 (30.18)	80.00 (25.14)	80.00 (35.83)	75.60 (20.26)	10.10 (10.52)	36.50 (13.52)
χ^2	0.012	1.818	1.788	0.100	0.167	0.751

There is little variation in SF-36 HRQOL mean scores, CES-D, and ENRICH mean scores after stratification by stage at diagnosis (Table 6.4). Kruskal-Wallis test showed that this variation is not statistically significant at the 5% level in the vitality scale (VT) (p=0.99), social functioning scale (SF) (p=0.40), role emotional scale (RE) (p= 0.40), mental health scale (MH) (p=0.10), CES-D scale (p=0.92) and ENRICH scale (p=0.68) in stages at diagnosis.

Table 6.7 list summary values of SF-36 HRQOL dimensions, Depression and Communication scales by time since diagnosis.

Table 6.7: SF-36 HRQOL Scores, Depression Scores and Communication Scores by Time Since Diagnosis

Time since diagnosis	VT	SF	RE	MH	CES-D	ENRICH
1- 2 years	72.36 (25.20)	86.11 (20.87)	73.15 (37.22)	75.39 (19.48)	9.90 (10.17)	40.56 (10.31)
2-4 Years	72.80 (21.94)	79.67 (26.70)	77.48 (36.22)	74.31 (19.55)	9.27 (8.35)	40.42 (8.89)
≥ 5 years	76.72 (18.88)	84.09 (19.08)	69.79 (33.18)	75.15 (15.38)	11.38 (9.57)	39.50 (9.71)
χ^2	0.214	0.592	2.381	0.080	1.891	0.377

There is also little variation in SF-36 HRQOL mean scores, CES-D, and ENRICH scores after stratification by different times from the initial diagnosis (Table 6.7). Kruskal-Wallis test showed that this variation is not statistically significant at the 5% level in the vitality scale (VT) (p=0.89), social functioning scale (SF) (p=0.74), role emotional scale (RE) (p=0.30), mental health scale (MH) (0.96), CES-D scale (p=0.38) and ENRICH scale (p=0.82) in times since diagnosis.

6. 6 Socio-demographic variables and FACT-C HRQOL

The FACT-C dimension scores and overall QOL score according to a selected list of socio-demographic variables are reported in Table 6.8.

Table 6.8: FACT-C mean values (SD), median values and (ranges) according to a selected list of socio-demographic variables

Variable	Physical well-being	Social/family well-being	Emotional well-being	Functional well-being	Colorectal module	Overall QOL
Gender						
Male	2.73(3.55)	20.99(4.14)	4.24(4.23)	21.92(5.77)	5.05(4.01)	111.37 15.15)
	1.0 (0-14)	22.0 (0-24)	3.0 (0-16)	23.0 (0-28)	4.0 (0-19)	113 (58-132)
Female	4.04(5.02)	20.51(3,97)	5.12(4.92)	21.68(5.68)	5.10(3.93)	106.14(19.92)
	2.0 (0-20)	22.0 (8-24)	4.0 (0-19)	23.5 (7-28)	4.0(0-15)	110 (58-131)
Age						
≤60	2.47(3.39)	20.62(4.30)	4.334.20)	22.24(5.68)	5.13(3.87)	111.32(14.08)
	1.0 (0-14)	22.0 (0-24)	4.0 (0-19)	24.0 (0-28)	4.0 (0-16)	113 (60-131)
61-70	4.42 (5.03)	21.00(3.69)	4.59(4.73)	21.39(5.46)	5.49(4.43)	106.81(19.79)
	3.0 (0-20)	23.0 (10-24)	3.0 (0-13)	23.0 (8-28)	4.0 (0-19)	111 (58-132)
>70	3.46 (4.39)	20.96(4.17)	5.16(5.00)	21.58(6.25)	5.41(3.55)	109.18(19.61)
	2.0 (0-16)	22.0 (8-24)	4.0 (0-16)	24.0 (7-28)	4.0 (0-13)	113 (67-132)
Income						
< 440	31(6.43)	10.08(5.23)	6.21(6.04)	20.00(6.38)	5.21(4.77)	101.25(22.70)
	3.0 (0-20)	20.0 (8-24)	4.5 (0-19)	21.0 (7-28)	4.5 (0-15)	104.5 (58-131)
440-880	4.52(5.05)	19.58(4.66)	6.18(5.54)	19.77(6.18)	6.42(4.06)	100.00(20.50)
	3.0 (0-16)	20.5 (6-24)	4.0 (0-16)	20.0 (8-28)	6.5 (1-16)	104 (58-130)
881-1,467	2.78(4.10)	21.11(3.68)	4.56(4.17)	21.72(6.86)	4.93(3.32)	110.72(16.09)
	1.0 (0-17)	22.0 (10-24)	4.0 (0-15)	24.0 (0-28)	4.0 (0-13)	113 (66-128)
1,468-2,347	2.19(2.37)	22.03(1.85)	4.03(4.05)	23.67(3.64)	4.61(2.94)	115.71(9.75)
	2.0 (0-10)	22.0 (18-24)	3.0 (0-14)	24.0 (12-28)	5.0 (0-13)	115 (95-132)
> 2,347	3.38(4.05	20.87(5.11)	3.85(3.01)	22.04(6.33)	5.37(4.95)	110.36(16.36)
	1.5 (0-13))	22.0 (0-24)	4.0 (0-11)	23.0 (0-28)	4.0 (0-19)	110 (60-130)
Marital status						
Single	2.56(3.54)	20.25(5.25)	5.11(4.40)	19.78(9.73)	4.00(4.42)	107.50
	1.0 (0-11)	22.5 (8-24)	4.0 (0-12)	22.0 (0-28)	3.0 (0-15)	109.5 (67-132)
Married	3.31(4.29)	21.38(3.46)	.4.35(4.31)	22.19(5.20)	5.14(3.86)	110.32
	2.0 (0-20)	22.0 (0-24)	4.0 (0-16)	24.0 (0-28)	4.0 (0-19)	113.5 (58-132)
Divorced	4.57(5.88)	14.33(6.25)	5.44(6.10)	20.75(6.84)	7.37(5.45)	102.40
	2.0 (0-14)	14.0(6-24)	2.0 (0-15)	22.5 (8-28)	4.5 (2-16)	110 (58-127)
Widowed	2.90(3.21)	18.12(4.05	5.69(5.45)	20.92(5.88)	3.54(2.940	104.17(14.44)
	2.0(0-10)	19.0 (10-24)	5.0 (0-19)	22.0 (9-28)	3.0 (0-9)	106.5 (88-127)

In colorectal cancer patients, among the socio-demographic variables significant differences were observed between income and marital status grouped categories. In the income categories the median difference between patients with low income (*Mdn*=104) and patients with upper (*Mdn*=115) were significant at the 5% level for their overall QOL; Kruskal-Wallis $\chi^2(4)=9.44$, $p=0.04<0.05$. Also, a significant higher difference was found in social functioning aspect of HRQOL of married people compared also with divorced people; Kruskal-Wallis $\chi^2(4)=13.751$, $p=0.003<0.05$. No evident difference in any HRQOL aspects and overall QOL was observed for variables describing age and gender options.

6.7 The association between treatment and HRQOL: Stoma and non stoma patients

Participants were grouped by type of surgery: sphincter-saving resection and sphincter sacrificing. Median values and ranges were then obtained on the FACT-C sub-scales and overall FACT-C HRQOL for patients whose sphincter was conserved and for those patients whose sphincter was sacrificed. The results of Mann-Whitney U test are shown below in Table 6.9.

Table 6.9: FACT-C sub-scales and overall FACT-C mean, median values and ranges and Mann-Whitney U Tests

Subscales	Type of surgery[1]	Median (Ranges)	U	Z	Sig. (2-tailed)
Physical Functioning	SC SS	1.5 (0-17) 4.0 (0-20)	837	-1.92	0.05 *
Social well-being	SC SS	22 (0-24) 22 (16-24)	110	-452	0.65
Emotional well-being	SC SS	4.0 (0-19) 4.0 (0-16)	914.	-1.61	0.10
Functional Well-being	SC SS	24 (0-28) 21 (11-28)	100	-1.23	0.21
Colorectal module	SC SS	4.0 (0-16) 5.0 (0-19)	921	-1.09	0.27
Overall	SC SS	113 (58-132) 102.5 (5-130)	645	-2.05	0.04 *

*$p \leq 0.05$

[1] **SC=sphincter conserving (Non-stoma patients), SS=sphincter sacrificing (Stoma patients)**

Overall HRQOL

The overall QOL of patients with a colostomy appliance was statistically significantly lower in comparison with those without a colostomy appliance U=645, $p \leq 0.05$, (Table 6.9).

Physical functioning

This subscale included questions relating to the side-effects of the treatment such as nausea, fatigue, pain or the degree to which a patient feels ill. There was a significant difference between stoma and non-stoma patients in reported level of physical functioning, U=837, p=0.05, (Table 6.9).

Social/family well-being

This subscale included questions related to the extent to which an individual received support by friends/family about his/her illness. Also, it included an item related with patients' satisfaction about their sexual life. No significant difference was found in the level of total social functioning of FACT-C instrument between stoma and non-stoma groups U=110, p>0.05, (Table 6.9). Also, no significant difference was found between the two groups concerning the social functioning of SF-36 subscale.

Regarding the sexual life of participants, responses to the sexual enjoyment item were available for 9 out of 22 (40.9%) stoma patients and for 81 out of 121 (66.9%) non-stoma patients. The proportion of stoma patients who did not respond about sexual functioning was significantly greater than the proportion of non stoma patients who did not respond to this item, $x^2(1)$= 5.41; p=0.020.

Among those with a colostomy appliance who did not respond to the sexual life item, 69.2% were female, 15.4% were widowed (the proportion of

widowed participants in the total sample was 9%), while their mean age was 64.6 years.

Emotional well-being

Mean scores and the results of independent samples t-test for the emotional well-being subscale of the FACT-C are showed in Table 6.9. This subscale consisted of items relating to worries about the outcome of patients' illness such as death or worry that the health condition may get worse.

There were no significant differences between the stoma and non-stoma group on the FACT-C emotional well-being subscale U=914, $p>0.05$, or on the subscales of mental component of SF-36 instrument and CES-D scale.

In emotional sub-scale of FACT-C instrument a statistically significant difference was found among stoma patients in the item related to the worry associated with death, U=915, $p\leq 0.05$.

Functional well-being

The role functioning sub-scale of the FACT-C is based on ratings about the extent to which the individual is limited in doing work or in enjoying sleep, his/ her life, hobbies and leisure time activities. No significant difference was found between the two groups (stoma and non-stoma) on the role functioning sub-scale U=100, $p>0.05$ (Table 6.9).

Colorectal cancer module

The colorectal cancer sub-scale includes items related to colorectal cancer symptoms such as gastrointestinal problems (appetite, constipation, bowel movements, diarrhoea, and weight loss). Also, one item relates to the satisfaction with body appearance and two items relate to problems that are faced by patients with a colostomy appliance. These two items were only completed by patients with a stoma.

No significant difference was found between stoma and non-stoma patients on the colorectal cancer sub-scale of the FACT -C, U=921, $p>0.05$, (Table 6.9).

Among those patients who completed the colostomy related items a proportion of 27.3% was embarrassed by ostomy appliance and a proportion of 18.2% faced problems in caring for the stoma.

A significant difference was identified between the two groups on the body image item U=937, $p\leq 0.05$. This result indicated that the group of stoma patients was significantly more dissatisfied with their body image than patients without a stoma.

6.8 The effect of metastasis on HRQOL

FACT-C dimensions median values and ranges as well as overall FACT-C median values and ranges of patients with metastatic and no metastatic disease were also obtained. The results of Mann-Whitney U test are shown in Table 6.10.

Table 6.10: FACT-C and SF-36 sub-scales, overall FACT-C and CES-D median values and ranges and results of Mann-Whitney U test.

FACT-C dimensions*	Metastasis /No metastasis	Median (Ranges)	U	Z	Sig. (2-tailed)
Physical functioning	M NM	4.0 (0-20) 1.0 (0-14)	134	-2.17	0.03 *
Social-well being	M NM	22 (10-24) 22 (0-24)	169	-0.25	0.80
Emotional well-being	M NM	5.0 (0-19) 3.0 (0-16)	147	-1.93	0.04 *
Functional well-being	M NM	21 (0-28) 24 (0-28)	124	-2.85	0.004 *
Colorectal Module	M NM	6.0 (0-19) 4.0 (0-16)	125	-2.41	0.01 *
Overall QOL	M NM	104.5(58-130) 114(60-132)	894	-2.63	0.008 *
SF-36 Vitality	M NM	75 (15-100) 80 (15-100)	176	-1.14	0.25
SF-36 Social Functioning	M NM	87.5(12-100) 100 (0-100)	152	-2.34	0.01 *
SF-36 Mental Health	M NM	76 (32-100) 80 (16-100)	181	-0.89	0.37
CES-D	M NM	10 (0-32) 8.0 (0-43)	157	-1.78	0.07

*$p \leq 0.05$

M: Metastatic Disease, NM: No Metastasis

The quality of life of patients with metastases was significantly lower for overall quality of life and for most dimensions of quality of life, than those of the matched sample of patients who were considered to be free of cancer. There were statistically significant differences in median values in overall HRQOL, physical functioning, emotional well-being, functional well-being, SF-36 social functioning and colorectal module in patients with metastasis: Overall HRQOL U=894, $p \leq 0.05$; physical functioning U=134, $p \leq 0.05$; emotional well-being U=147, $p \leq 0.05$; functional well-being U=124, $p \leq 0.05$; social functioning U=152, $p \leq 0.05$; colorectal cancer module U=125, $p \leq 0.05$.

6.9 Effect of predictor variables on Overall QOL

The main effect of a number of variables on overall HRQOL was examined by a multivariate regression analyses (Table 6.11). Overall HRQOL was used as a dichotomized categorical variable in the analyses (low overall HRQOL scores vs high overall HRQOL scores). Thus logistic regression models were used to estimate the odds ratio (OR) for each variable in the equation. In order to identify cases and outliers, Cook's distances (>1.0) and standardized residuals (>3.0 or <-3.0) were respectively computed and examined. Multicollinearity was detected by examined the standard errors (>2.0) for the estimeded coefficients (B). The results are shown as ORs with 95% confidence intervals (CIs) for ORs. The fit of the models was judged by Hosmer-Lemeshow goodness-of- fit statistic. The models were considered acceptable if $p>.05$ for model chi-square, given that a better model fit was

indicated by a smaller difference in the observed and predicted values of the dependent variable, and a nonsignificant chi-square value.

Hierarchcal logistic regression analyses was conducted to find out the significant predictors of overall HRQOL by controlling for demographic, disease-related variables as well as variables that related to the communication with partner and depression. Five steps were taken: the demographic variables (age, gender, residence, income, education) were entered first as independent variables, the disease-related variables (stage at diagnosis, time since diagnosis) were included in the second step, the variables stomia and metastases were included in the third step, while the ENRICH scale scores were included in the fourth step and in the last step the CES-D scale scores were introduced. There were no cases with large standardized residuals and there was one Cook's distances that was considered outlier. Multicollinearity or numerical problems were not detected, as none of the independent variables had a large standard error. The model chi-square value indicated that there was a statistically significant overall relationship between the dependent variable and the set of independent variables, $\chi^2(11)=37.951$, $p<0.001$. The chi-square value associated with the Hosmer-Lemeshow test was $\chi^2(8)=9.264$, $p=.321$, indicating a good overall model fit. The Negelkerke R square was equal to 0.464.

Table 6.11 Logistic regression on overall HRQOL; estimated regression coefficients, standard errors and related statistics odds and 95% confidence intervals (CI)

Explanatory variables	*B*	*SE*	Wald	*p*-value	*OR*	95% CI
Block 1						
Age	0.375	0.423	0.785	0.376	1.455	0.635, 3.335
Gender	-0.161	0.593	0.074	0.786	0.851	0.266, 2.719
Residence	0.087	0.720	0.014	0.904	1.091	0.266, 4.473
Income	0.318	0.316	1.012	0.314	1.374	0.740, 2.552
Education	-0.346	0.350	0.976	0.323	0.708	0.356, 1.406
Block 2						
Stage	0.036	0.552	0.004	0.948	1.037	0.351, 3.061
Time sinse diagnosis	-0.089	0.405	0.048	0.827	0.915	0.414, 2.024
Block 3						
Stomia	0.740	0.879	0.710	0.399	2.097	0.375, 11.735
Metastases	-1.040	0.741	1.971	0.160	0.353	0.083, 1.510
Block 4						
Communication with partner	0.014	0.029	0.0.233	0.629	1.014	0.957, 1.075
Block 5						
Depression	-0.248	0.062	16.314	0.000	0.780	0.691, 0.880

Table 6.11 shows that, according to tha Wald criterio, the coefficient for depression (B=-0.248) appeared to be significantly different from zero in predicting depression, Wald=16.314, $p< .001$. The negative coefficient for

depression implies that those patients who have high overall HRQOL values (coded 1) have lower scores on that variable relative to those who have low HRQOL scores (coded 0). By increasing the value of depression by one unit, the odds of the participant having high HRQOL values decrease by a factor of 0.780, controlling for other variables in the model. The odds of having high HRQOL for participants with high depression are 22% (=1-0.780). The classification accuracy rate was equal to 77.5% which is quite greater than the propotional by chance accuracy rate (50.3%), supporting the ytility of the logistic model.

CHAPTER 7

DISCUSSION

7.1 Introduction

The experience of colorectal cancer involves a complex mix of physical and psychosocial changes that is still poorly understood particularly for those patients who enter the "after treatment phase" of their disease. Interest in evaluating aspects of health that are related to Quality of Life (QOL) has increased in recent years in Greece as in other European countries. However, little is known about the way that Greek colorectal cancer patients perceive their quality of life years following diagnosis.

Reviewing the relevant literature for this thesis it soon becomes apparent that there was need of a thorough investigation of the impact of colorectal cancer and treatment on specific dimensions of quality of life. This includes physical health, emotional or social functioning and overall HRQOL of Greek survivors of colon and rectum cancer, one and up to ten years after the diagnosis of their disease. This investigation should take into account the most common aspects of colorectal cancer experience and be based on patients' point of view about the current state of their quality of life. The study design that was developed should also include those factors that might influence the level of patients' quality of life. So, disease related factors as well as factors that are related to patients' characteristics may contribute to Greek colorectal cancer survivors' quality of life several years after diagnosis. The primary hypothesis was that time since diagnosis and early

disease stage at diagnosis were factors that could positively influence the level of patients' quality of life. Also, patients with an ostomy and patients who experienced a metastasis of their disease might experience a lower quality of life in comparison with those without a colostomy appliance or those patients who experienced life free of their illness respectively. Patients who experienced depression, poor communication with their partner or those older patients or with a low income might also be expected to experience poorer quality of life.

In order to test the research hypotheses and research questions, 145 Greek outpatients were recruited into the study and data were gathered on their quality of life through the use of self-assessment questionnaires.
Advances have been made in methods that describe patients' subjective well-being using standardized instruments. Several valid and reliable self-assessment measures are available in the clinical oncology research setting such as generic or disease specific instruments. The FACT-C and the SF-36 quality of life instruments were selected for exploring the quality of life in this research population. The FACT-C and the SF-36 instruments are popular in U.S as well as in Europe when quality of life is assessed. However, few applications of them are available for assessing health related quality of life in colorectal cancer survivors and neither used for assessing Greek's colorectal cancer survivor's quality of life.

In this section is an overview of the significant findings of the study, a consideration of them in the light of existing research together with an examination of those findings that fail to support the hypotheses as well as limitations of the study. The implications of the study for practice as well as

recommendations for further research are explored further in the concluded section.

7.2 Summary of main findings

In this study no statistically significant differences were identified in the level of overall quality of life or among quality of life domains for colorectal cancer survivors at different stages at diagnosis and different times since diagnosis. This means that patients at all disease stages experienced a high quality of life years after diagnosis.

Among disease-related and patients-related factors that would have an effect on patients' quality of life over time, vitality, social functioning and depression were most prevalent. Also, patients with low income had a significantly lower overall quality of life than those patients with upper income. Divorced patients experienced a poorer social functioning compared to that of married, single or widowed patients.

Regarding the quality of life of patients following sphincter-conserving versus sphincter-sacrificing surgery, the results of this study confirmed the hypothesis that the overall quality of life of patients with a colostomy appliance would be significantly inferior to that of patients without a colostomy. Even thought no statistically significant differences were identified between the quality of life domains between the two groups significant differences were found between the two groups in terms of body image, and worry about death.

The study findings confirmed the hypothesis that patients with metastases would experience a lower quality of life compared to patients who had experienced a remission of the disease.

The findings most relevant to this study are discussed below and are compared with those previously reported in the literature.

7.3 Discussion of main findings

7.3.1 The effect of stage of colorectal cancer at diagnosis and the effect of time since diagnosis on long-term patients' HRQOL

The results of this study did not confirm the hypothesis that the overall quality of life of colorectal cancer survivors would be higher for those patients at a longer time since diagnosis or early disease stage. The results of the current study showed that colorectal cancer patients who had survived at least 1 year from the time of diagnosis experienced relatively high health status independently of the stage at diagnosis. In the first two years after diagnosis, patients with Duke's B stage reported a relatively high level of quality of life that was found to be better than that of C or D stages. However, this difference was not statistically significant. The overall HRQOL after two years from diagnosis did not vary substantially between disease stages. As time after diagnosis increased from 1year to 2-4 years and more than 5 years patients seemed to experience deficits in social

functioning, but this finding was not statistically significant. Generally speaking, quality of life remained uniformly high among all disease stages as well as time since diagnosis. These results were confirmed by using both HRQOL survey tools such as FACT-C, and SF-36 and applying both univariate and multiple regression analyses. The number of studies that have evaluated the effect that stage of disease at diagnoses, and time since diagnosis, have on the overall colorectal cancer survivors quality of life, are very limited (Trentham-Dietz et al., 2003; Ramsey et al., 2002; Ramsey et al., 2000). Ramsey et al. (2002; 2000) researches were the only identified studies that used the FACT-C instrument for evaluating quality of life in survivors.

Ramsey et al. (2000) who considered health-related quality of life through the FACT-C instrument, in line with the results of this study, showed little variation over time after stratification by stage at diagnosis. Similar results were found with multivariate regression analyses during which they did not find that health-related quality of life was significantly different in relation to disease at diagnosis, or for time since diagnosis. Also, in line with these findings, Ramsey et al. (2000) FACT C summary scores showed a non-significant trend toward declining HRQOL for more advanced stages of colorectal cancer. Also, small sample sizes and the possibility that there was a response bias favoring healthier people were considered limitations by these authors.

Similarly with the current study Ramsey et al. (2002), when exploring quality of life of U.S patients with cancer of colon and rectum who had survived at least 5 years after diagnosis, no differences were found among

patients at different disease stages either in multivariate regression analyses or in univariate analyses. Patients at or beyond 5 years since diagnosis appeared to have a relatively high health-related quality of life regardless of their initial stage at diagnosis.

The findings of the current study were also confirmed by those presented by Trentham-Dietz et al. (2003) in a US female population. They concluded that over the long term, the initial stage at diagnosis did not play a dominant role in determining physical and mental health of patients, as measured by the SF-36 questionnaire, while other factors such as concurrent chronic medical conditions or body weight might play a more important role.

Although the stage of colorectal cancer at diagnosis is related to the length of survival, this factor did not have a strong association with quality of life among Greek long-term colorectal cancer survivors in the present thesis. This showed that long-term cancer survivors had a substantially satisfied health-related quality of life with factors such as depression, vitality and social functioning playing a dominant role in determining patients' physical and emotional health.

The results of the present study suggest that the impact of colorectal cancer and treatment on quality of life is not so devastating in those who survive longer. This finding is not so surprising since a number of authors have described quality of life as a dynamic process that changes over time as patients change their perceptions about their health status, or change their expectations in terms of specific life circumstances (Addington-Hall, 2001; Carr et al., 2001b; Alison et al., 1997; Calman, 1984).

Several studies have presented well documented evidence that in self-reported quality of life assessments individuals may use a number of psychological mechanisms, such as social comparisons, or reframing of their expectations about the negative impact that the disease has on their health status or their well-being (Hagedoorn et al., 2002; Carr et al., 2001; Sprangers and Schwartz 1999; Gotay & Muraoka, 1998). Such an adaptation process has been termed a "response shift" (Sprangers and Schwartz, 1999). Response shift reflects changes in internal standards, in values and life goals, or changes in conceptualization of quality of life over time (Sprangers & Schwartz, 1999). Although this phenomenon has received little attention until now, it may explain a number of unexpected quality of life findings regarding cancer survivors or patients with other chronic and life threatening illnesses. For example, the largest study conducted to date by Mosconi et al. (2000) in Italy showed that people's quality of life was comparable with that of a healthy population several years after diagnosis.

Changes in the internal standards of colorectal cancer patients have also been explored by Bernhard et al. (2001; 1999). These studies showed that people with newly diagnosed colon cancer gradually changed their internal standards on which they based their health status and their quality of life estimation, either under radical resection or under adjuvant chemotherapy.

However, before trying to interpret changes in patients' quality of life by adopting a response shift approach, some methodological issues should be taken into account. As Carr et al. (2001) noted, existing measures did not always take into account the expectations of people and may not distinguish between changes in the experience of disease, or changes in expectations of health.

7.3.2 Depression as a predictor variable of colorectal cancer patients' HRQOL

In this study, among those factors that would predict patients' quality of life years after diagnosis, depressive symptoms were more prevalent even if the psychological distress appeared to have been decreased.

From the literature, it is well known that the diagnosis of cancer is a risk factor for depression during the diagnostic, treatment or palliative care phase of the disease; particularly among patients who suffer by pain and physical disability (Hopwood & Stephens, 2000; Grassi & Rosti 1999; Grassi et al., 1996; Massie & Holland, 1992). Pasquini and Biondi (2007), in a review study, examined the effect of depression on cancer patients and concluded that depression affected several aspects of life such as health status, quality of life, or working role.

Even if numerous studies have evaluated depression during the treatment phase of cancer, some evidence has been found for the prevalence of depressive symptoms during cancer follow-up. A previous study on early breast cancer survivors showed that the prevalence of depression and anxiety was 15% one year after diagnosis and 45% after the diagnosis of recurrence (Burgess et al. 2005).

To our knowledge, only two studies to date have investigated depressive symptoms in colorectal cancer survivors, using a standardized specific depression scale (Tsunoda et al., 2005; Ramsey et al., 2002).

In Ramsey's et al. (2002) study cancer patients had higher rates of depression in comparison with a healthy population. Also, lower

socioeconomic status and the presence of multiple comorbid conditions were identified as risk factors for depression. Although Ramsey et al. (2002) did not present data at two or three years post diagnosis their study might indicate a need to identify patients who might be at greater risk of depression and to consider including this into their follow-up schedule.

In a long-term Japanese colorectal cancer population, Tsunoda et al. (2005) concluded that depression - as measured by Hospital Anxiety and Depression Scale - had a strong impact on overall HRQOL dimensions for patients who had survived for at least 1 year since operation. Despite the cross-cultural differences between Western countries and Asian countries, Tsunoda et al. (2005) study highlighted the need for identifying depressive symptoms in the screening process of colorectal cancer outpatients. They also concluded that depression was not sufficiently evaluated by the emotional functioning subscale of the EORTC QLQ-C30 instrument and that the use of a depression specific scale was required. Even if the detection of depressive symptoms in Greek colorectal cancer outpatients was not the main aim of this study, the results showed that depressive symptoms, as measured by CES-D, were the strongest predictor of patients' quality of life.

7.3.3 The overall effect of surgery on HRQOL: Stoma and non stoma patients

A main result of this study is that colorectal cancer patients who undergo sphincter-sacrificing surgery resulting in a stoma have a poorer health-related quality of life than those without a stoma. This is consistent with the results of a vast body of "traditional" research studies (Engel et al., 2003;

Kuzu et al., 2002; Camilleri-Brennan & Stele, 1998; Sprangers et al., 1995; Mac Donald & Anderson, 1984; Williams & Johnston, 1983; Delvin et al., 1971). In contrast with the current study in which an overall quality of life score was obtained for stoma and non stoma participants, very few studies have produced a global health-related quality of life score and used well researched questionnaires. In Camilleri-Brennan and Steele's (1998) review from a total of 54 papers "in only three studies was global quality of life formally measured using a well researched questionnaire" (p. 1036). Most previous researchers have concluded that stoma patients had reduced well-being in most quality of life domains and therefore an assumption was made that this reduction would reflect a total quality of life reduction (Camilleri-Brennan & Steel, 1998; Sprangers et al., 1995) In the current study stoma patients had reduced well-being in all quality of life domains, except social functioning, compared to that of non-stoma patients, however, this reduction was not statistically significant. Even though the differences among quality of life domains were not statistically significant, when all these domains were combined to produce an overall quality of life effect, the difference between the two groups was statistically significant and stoma patients experienced an overall worse quality of life than non-stoma patients. Such a finding highlights the importance of obtaining overall scores for any quality of life measurement, since small impairments in specific domains cannot always show up the overall cumulative, impairment.

Studies that provide a summary health-related quality of life score for patients with and without a stoma are very scarce and none have used the FACT-C instrument. So, a comparison between the overall quality of life scores of the present study and the total HRQOL scores of other studies

cannot be made. One identified study conducted by Ramsey et al. (2000) who explored the health-related quality of life of colorectal cancer survivors in the USA, and had used the FACT-C questionnaire, suggests that a colostomy does not significantly affect overall health-related quality of life. Since this study was not designed to explore differences between two groups (stoma and non-stoma) certain information about stoma patients such as age, gender or time since surgery was not available for making valid comparisons. The EORTC QLQ-C30/CR38 questionnaire, the one most commonly used in European countries unfortunately has not been designed to provide a total health-related quality of life score, consisting of the summation of individual sub-scale scores. On the contrary, it includes a visual analogue scale in which patient are asked to evaluate global health and quality of life in a scale from "very poor" to "excellent". In a recent review by Pachler and Wille-Jorgensen (2005) the findings of the included studies that had used the disease specific EORTC QLQ-C30/CR38 health-related quality of life instrument on global HRQOL scores of stoma and non-stoma patients contradict and a firm conclusion on this issue could not be drawn. For example, a number of included studies concluded that non stoma patients experienced similar or poorer global HRQOL than stoma patients (Rauch et al., 2004; Grumann et al., 2001; Allal et al., 2000) while others supported that the formation of a colostomy impaired a patients' quality of life severely (Engel et al., 2003; Kuzu et al., 2002)

Therefore, the literature to date has failed to show consistently that there is a difference in the overall health-related quality of life between stoma and non-stoma patient's life and that this is affected by the disease and treatment several years after diagnosis. In the present study specific health-related quality of life domains in stoma patients were not significantly affected even

several years after surgery but they remained in lower levels than that of the non stoma group. Improvements that may have occurred in many aspects of quality of life of stoma patients do not suggest that these patients experience had an overall higher quality of life. One interpretation of this finding is that stoma patients are likely to expect preoperatively that a colostomy will change negatively many aspects of their life. It may be that negative lay perceptions about colostomy appliance worried patients extremely about the consequences of the stoma on their future quality of life. However, after surgery, many stoma patients might realize that a colostomy did not affect their life as much as they had anticipated and so certain quality of life aspects was experienced as better and less traumatic.

It is necessary to consider in detail all the other health-related quality of life domains which may also impact on patients' life.

Physical functioning

The fact that there was no statistically significant difference between stoma and non-stoma patients in relation to physical functioning is perhaps not surprising given the high rating of health status of the sample. Patients who had undergone curative surgery would not be expected to be significantly physically incapacitated as a result of their treatment at one year, or more than one year post surgery. In a prospective study Grumann et al. (2001) indicated that levels of physical functioning improved between 6 to 9 months and 12 to 15 months post surgery, although no significant difference between stoma and non-stoma patients was found. As might be expected

Allal et al. (1999) found that although there were no significant differences between the two age groups in terms of physical functioning, older patients tended to report lower scores indicating poorer physical functioning. This emphasizes the need to consider the possible effect of age in reporting on this sub-scale. Grumann's et al. (2001) as well as Allal's et al. (1999) research findings evaluated the physical functioning of patients using the EORTC QLQ-C38 instrument which included one sub-scale that was completed by patients with a stoma, and one sub-scale which was completed by patients without a stoma. As these scales were not completed by both groups it was not possible to compare their mean scores using independent samples t-tests.

Moreover, the FACT-C instrument used in the present study includes two items more relevant to patients who experience the side-effects of chemotherapy or radiation therapy such as nausea or vomiting and one item relevant to patients who suffer from pain. Patients included in the present study were selected to have completed any curative treatment at least one month before completing the questionnaires. So, it was expected that patients would not experience side-effects, of chemotherapy or radiation therapy during the survey. Taking this into account one would expect that the physical component of FACT-C questionnaire would not be completely relevant to survivors. However, it was decided initially to include in the study these "irrelevant" items because any changes made to the number of items would potentially alter the original psychometric properties of the instrument. Also, any change made to this component would have an effect on the total FACT-C quality of life score, since the total score was produced by adding the score of each component.

Social/family well-being

A vast amount of research literature has reported that stoma patients often experienced reduced social functioning as a result of embarrassment, stigma and worry in relation to their stoma (Engel et al., 2003; Sprangers et al., 1995; Williams & Johnston, 1983; Delvin et al., 1971). However, in a review Sprangers et al. (1995) noted that studies which had reported differences between stoma and non-stoma patients had tended to use a range of different indicators of social function such as employment, frequency of social contacts and quality of relationships. The variance of operational definition of social functioning used across studies might yield divergent results (Sprangers et al., 1995).

The current study included a variety of social indicator variables for assessing the social activity of the participants. For instance, the social/family subscale of FACT-C instrument provides information on the support that patients receive by friends or their family as well as the sexual functioning of patients. In addition, the SF-36 instrument provides information about the extent of social inactivity that patients experience because of specific physical or psychological problems.

No significant difference was found between the two groups (stoma vs non-stoma) in terms of their reported level of social functioning as measured by FACT-C and SF-36 instruments even if patients with a colostomy appliance had higher FACT-C mean score than patients without a stoma. The social functioning of stoma patients may not be influenced by the consequences of surgery because this may alter their social behavior. For example they may

reduce the time spent in social activities or may take care about the amount and kind of the food they consume during social events, thus preventing bowel disfunction (e.g. gas, faecal leakage). Furthermore, given that half of the patients of the current sample had retired (50.3%), employment problems or vocational matters were not raised.

Before coming to conclusions it is important to consider a person's pre-morbid social functioning in relation to quality within this life domain. Three recent studies have also reported no significant differences between stoma and non-stoma patients in terms of social functioning (Rauch et al., 2004; Grumman et al., 2001; Allal et al., 2000).

Sexual functioning

Regarding sexual functioning of patients with and without a stoma, in the present study we could not have a clear scenario because there were a high proportion of stoma patients who declined to respond to the relevant question and so a formal statistical analysis was difficult to apply. Only nine stoma patients out of twenty-two responded to this item. It should be noted that this question was optional. Examining carefully the characteristics of stoma patients who did not respond to the sexual activity item it was apparent that non-respondents were mostly female and widowed. Also, their mean age was 64.6 years. The non-respondents' characteristics perhaps highlight the importance of taking into consideration a person's relationship status as well as age when interpreting any results regarding sexual functioning in the context of close relationships.

An assumption that one can make is that Greek women with a stoma and widowed patients may face difficulties about their sexual activity and may not be willing to discuss this issue. It is well known that a negative body image may negatively affect people's sexual functioning. In the current study the women with stoma who not respond to the sexual activity item, had a negative body image. Therefore, a negative body image that women with stoma experience may negatively affect their sexual life.

Engel et al. (2003) suggested that it is difficult to evaluate the magnitude of sexual functioning without making a comparison to healthy population scores. Peoples' sexual capacity may decline because of age or due to other reasons. For instance, Greek women may differ in sexual satisfaction from men. Also, the questionnaire item related to sexual capacity included in the current study asked about the extent to which the patient was satisfied with sexual activity. The item did not refer to the effect the illness and treatment had on patients' sexual functioning. Pre-treatment scores among stoma and non-stoma patients, as well as information about the damage caused to the nerve responsible for sexual functioning, would be essential for a clearer scenario about the effect that treatment or other factors have on stoma and non-stoma patients' sexual life. For instance, Engel et al. (2003) showed that high-anterior resection patients and low-anterior resection patients had better sexual functioning scores at 2 and three years than patients with abdominoperineal resection.

Emotional well-being

In this study, no statistically significant differences were found between patients who had undergone either sphincter-conserving or sphincter-sacrificing surgery in relation to the psychological functioning domain as measured by the FACT-C instrument. Even though the difference in psychological well-being between the two groups was not statistically significant, stoma patients had lower mean scores than non-stoma patients. Also, when psychological functioning was assessed by the SF-36 questionnaire, no statistically significant differences were observed between the two groups. Furthermore, no difference was found between the two groups in relation to the depression scale. When examining the subscale items of FACT-C, was found that stoma patients were statistically more worried about death than the non stoma patients.

The above data contradict the findings of previous studies which report that patients with a stoma are more anxious and depressed than patients who do not have a stoma (Sprangers et al., 1995; McDonald & Anderson, 1984; Williams & Johnston, 1983). On the other hand, recent studies have also reported no significant differences between the stoma and non-stoma groups in terms of emotional functioning (Grumann et al., 2001; Allal et al., 2000).

Functional well-being

The role functioning sub-scale may be regarded as a more appropriate index of quality of life for patients who are at least one year post surgery. Role functioning encompasses the extent to which patients are limited in doing

work, or daily activities, hobbies and leisure time activities. Consistent with the current study, other researchers have found no significant differences between sphincter-conserving and sphincter-sacrificing patients in terms of role functioning (Rauch et al., 2004; Grumann et al., 2001; Allal et al., 2000).

In the current study, the difference in the functional level between the two groups was not statistically significant, but again stoma patients experienced lower functional level than non-stoma patients. Bekkers et al. (1997) showed that stoma patients did not encounter more problems in daily life than non-stoma patients four years after surgery. In the current study, 52% of patients had survived between 2 and 4 years and 23% of patients had survived beyond 5 years since diagnosis and only seven patients reported an inability to fully return to their work due to the disease.

In addition, before drawing safe conclusions about the capacity of people to undertake everyday roles, it is important to consider the effect of age on the level of activities and ability to perform roles, taking into account the generally older adult age of colorectal cancer patients. Many older adults gradually become less active and have fewer roles as a result of their life stage, independently of the limitations related with their disease. In this sample more than half of patients were older than the age of 60 years and had retired. However, it is important to treat with caution the explanation that patients in this sample avoid undertaking some roles or stop their hobbies and leisure time activities due to their age; especially as many adults a similar age very often have important and demanding roles.

Colorectal cancer module (symptom sub-scale)

Previous research has documented that many patients suffer from symptoms such as diarrhoea related to bowel functioning after surgical treatment (Engel et al., 2003; Lewis et al., 1995; Sprangers et al. 1995; Williams & Johnston, 1983). The research literature suggests that stoma patients tend to report more problems with gas and urinary function while non-stoma patients report more constipation (Engel et al., 2003).

In contrast with these findings, no statistically significant differences were found between stoma and non-stoma groups on this subscale relating to any of these symptoms experienced by colorectal cancer patients; even though stoma patients' mean scores were indicative of low levels of colorectal cancer symptoms than non-stoma patients' mean scores. It should be noted that the symptom sub-scale of the FACT-C instrument includes items that related only to bowel functioning, and no item is concerned with urinary problems that may also be experienced by colorectal cancer patients. So, we cannot conclude about urinary problems experienced by patients in this sample.

One explanation for these findings relates to the research literature that suggests that bowel function often improves within the first year post surgery (Frigell et al., 1990). The time interval of at least one year post surgery used in this study might mean that for many patients relief from such symptoms had already occurred by the time they completed the survey.

An alternative explanation is that improvements which have occurred in recent years in surgical techniques, as well as improvements in care of colorectal cancer patients are reflected in the current study. Such improvements might not be reflected in previous studies in which different, less optimal techniques might have been used. Such an explanation is supported by the findings of more recent studies conducted by Rauch et al., (2004), Grumann et al., (2001); Allal et al., (2000). Regarding non-stoma patients' symptoms, the level that the tumour is located is essential for obtaining a clear picture of symptoms experienced because it affects patients' bowel function (Engel et al., 2003; Kuzu et al., 2002). For example, in a four year prospective study (Engel et al., 2003) showed that in the first 3 years, low-anterior resection patients had significantly worse defecation scores and less frequent or painful bowel movements than high-anterior resection patients. Similar results have also been supported by other researchers such as Kuzu et al. (2002) who showed that high-anterior resection patients had significantly better scores in other aspects of quality of life such as in mental health and vitality, compared with those with low-anterior resection. In line with the current study, the number of other studies that have evaluated stoma and non-stoma patients' health-related quality of life, and have taken into account the level of anastomosis in patients with anterior resection, are very limited. Therefore, in non-stoma patients there are many differences in symptoms that patients experience and so comparison between stoma and non-stoma groups is difficult to make. For instance, if our sample had included more patients with high-anterior resection, defecation problems experienced due to low-anterior resection would not have been detected.

Satisfaction with body appearance

In this study, patients who had undergone sphincter-sacrificing surgery resulting in a stoma, reported statistically significant more dissatisfaction with their body appearance compared to non-stoma patients. This is consistent with the findings of several research studies (Engel et al., 2003; Persson & Hellstrom 2002; Grumann et al., 2001; MacDonald & Anderson, 1984; Williams & Johnston, 1983). Also, in this study, women with a stoma were found to experience more dissatisfaction with their body appearance compared to men. This body dissatisfaction may result in a difficulty that stoma women experienced with their sexual life. It has to be noted that the FACT-C instrument included only one item related to the satisfaction that colorectal cancer patients had with their body appearance. However, this item does not lead to a safe conclusion about body image perception.

Research evidence regarding body image differences between sexes in colorectal cancer patients is scarce. Fallowfield et al. (1990) has suggested that patients who were given a choice of treatment appeared to do better psychologically, independently of the type of treatment chosen. Even if choice of treatment is not possible for all patients, it may be important to consider the potential effect of patients being prepared for the possibility of having a colostomy on subsequent body image satisfaction.

7.3.4 The effect of metastasis on HRQOL

Local or distant recurrence of colorectal cancer had a profound effect on Greek patients' quality of life. This finding is consistent with a study by

Camilleri-Brennan and Steel (2001) as well as a recently published population based study by Arndt et al. (2006). Indeed, in the current study, patients with recurrent disease faced not only physical limitations in their every day life, but also psychological and social well-being deterioration. The use of both health-related quality of life instruments, FACT-C and SF-36 confirmed this finding.

The interrelationship among HRQOL domains is an important issue. In this study, the physical effect of the disease evidently had an important impact on social, psychological or overall functioning of patients' life and should be noted as a key finding.

7.4 Limitations of the present study.

Some methodological limitations of the present study have to be noted. These limitations are related with the study design, the sample, as well as the study instruments.

The study design

There are a number of limitations of the cross-sectional design used in this study. This type of design does not provide a baseline measure from which to evaluate subsequent assessments. This made it difficult to accurately assess the extent to which impairments to quality of life had resulted from patients' cancer disease or cancer treatment rather than from other extraneous factors such as another illness or life event. For instance, if a patient suffered heart disease, it would not be possible to detect the extent to

which this might have affected his/her quality of life independently of his/her cancer or cancer treatment. Since other comorbidities might exist, the most appropriate approach might be to decide about the appropriateness of patients' inclusion to the study, based on an individual basis and carefully weighing up the impact of the relevant factors on quality of life. Apart from other comorbidities which might occur together with cancer, the effect of age on patients' quality of life is major issue. Particularly in patients with colon and rectal cancer, which is a disease of the elderly, the effect of age should be explored with caution. Furthermore, when assessing health-related quality of life of stoma and non-stoma patients, a retrospective design cannot give information on quality of life of patients before surgery, thus making comparison impossible. Thus, the advantage of a prospective study design which involves repeated measures at different times is that confounding variables may be more easily monitored and controlled for.

Despite certain weaknesses that are inherent in the retrospective design of the present study, significant results were found.

Representativeness of sample

The majority of patients (60%) were Greek men while the mean age of patients in this sample was 61.40 years of age which are consistent with the average age range and sex reported for incidence of colorectal cancer in Greece. Although these characteristics make the sample more representative of the whole colorectal cancer population, the sampling was limited by consisting mainly of Greek patients. Therefore, the results found here may not be generalized to patients from other ethnic origins. No data were gathered on other ethnicities. Albanian immigrant patients for instance, who

consist of the majority of people from foreign counties who live in Greece, were not found in any archive used in this study, either the archives of the public hospital or those of the private oncology clinic. However, Albanians who immigrate to Greece are often of a younger age. Since colorectal cancer is a disease of the elderly it would be unlikely that colorectal cancer patients from Albania would included in this study. Extrapolation of the current findings to patients of other ethnicities should be made, therefore, only with caution.

Also, the sample used in this study consisted of patients who had been treated for colorectal cancer at two Greek hospitals –one public and one private oncology clinic- for a period of the last 12 years. All patients who met the inclusion criteria were asked to participate. Although it was decided to recruit patients from two different hospitals in order to achieve socioeconomic heterogeneity among patients, the sample consisted mainly of patients who were well educated and their family income was above average. This may have occurred because the majority of participants-100 out of 145-were recruited from the private oncology clinic. It is known that patients of middle and upper-middle socioeconomic level receive their care in the private health sector and may not necessarily represent the wider population of patients.

One important issue is the potential for selection bias among patients who decided to participate in the study. A number of patients -46 out of 191-had refused to participate. Therefore, the response rate for this study was 75.9%. Although comparison between respondents and non-respondents indicated that the latter did not differ in demographic or disease related characteristics

from the former, it is possible that non-respondents experience different levels of quality of life, such as lower HRQOL, and this may have influenced the results of the present study.

Moreover, one of the problems common in any investigation of quality of life in cancer patients, is the inherent sampling bias, in that only patients who have survived their treatment and who are well enough to participate are included in such studies. This may result in conclusions being made on the basis of unrepresentative samples.

In addition to this, because this study has focused on long term survivors, few patients with advanced colorectal cancer or at a longer time since diagnosis have been included. So, there is the possibility that the respondents were in better health status in order to be able to respond to the survey.

The study instruments

The primary requirement of FACIT QOL instrument is that it should be suitable for use in an international setting, that is, the translated instrument should measure the same aspect of quality of life regardless of language version. Although the translation of the FACT-C instrument into Greek was obtained by the official FACIT organization body, there is not enough evidence that this translated version meets all the requirements of cross-cultural equivalence. This translation may support the content (each item is relevant to the culture being studied) and semantic (each item has the same meaning after translation) equivalence of the instrument, but there is not sufficient evidence that conceptual equivalence (measurement of the same

theoretical construct) has been met. Also, little account has been made in considering the social, ethnic, religious or cultural background of the patients. The cross-cultural equivalence of HRQOL instruments has been largely overlooked to date.

The purpose of using the FACT-C instrument was to gain an overall and dimension specific score of the quality of life for patients who have survived colorectal cancer, and of the impact that the disease and treatment have on their lives. However, the FACT-C instrument, like all the available instruments on quality of life today, has been designed primarily for clinical trials and may able to capture the most important and relevant changes after treatment or the long-term impact of the disease (Carr et al., 2001; Alison, 1997; Calman, 1984;). Although it includes sections on social, emotional and functional well-being, the questions were all focused on the cancer diagnosis. The study sample of patients did not have active disease and believed themselves free of cancer. Specifically, the dimension of physical functioning of the FACT-C instrument included questions that focused on a range of symptoms appropriate to cancer and cancer treatments. Therefore, these questions might not directly apply to the study sample. However, it was initially decided to include the "irrelevant" items into the study, because any changes made could potentially alter the original psychometric properties of the instrument. Also, any change made would have an effect on the total FACT-C quality of life score, since it was produced by the adding the score of each component.

Furthermore, the communication scale of the Enrich instrument had been adapted and translated from English into modern Greek by this researcher

and evidence for its cultural sensitivity is not still available. Despite these limitations the study provides evidence of HRQOL and associated changes in a Greek context.

7.5 Summary

The patients in this study experienced a relatively high overall and dimension specific health-related quality of life years after diagnosis of the disease. This was characterized by depressive symptoms affecting patients' quality of life. This is not surprising since patients might interpret their conditions through the sense of a "response shift" leading to adaptation to their chronic disease.

Whether the lower levels of overall quality of life in stoma patients is due to treatment side-effects, difficulties in psychological adjustment or both, the fact that these difficulties may exist long after initial diagnosis, requires further attention.

Despite the limitations imposed by the cross-sectional design, the specific characteristics of the sample and the specific study instruments, important practical implications, arise from this study further discussed in the concluded chapter.

CHAPTER 8

CONCLUSIONS AND RECOMMENDATIONS

8.1 Summary of key findings

In this study, an investigation of the experience of Greek colorectal cancer patients following treatment, with specific focus on health-related quality of life (HRQOL), was undertaken. With evidence suggesting that culture may be a major determinant of the experience of cancer, the present study gained an insight into the perspective of HRQOL in Greek patients who are surviving a diagnosis and treatment for cancer of colon and rectum. The main outcomes of this study are: Greek colorectal cancer survivors experience a high overall and dimension specific HRQOL, independently of the disease stage at diagnosis; depression and social activity constitute the strong predictors of patients' HRQOL over time; stoma patients experience an overall lower HRQOL than non stoma patients; metastasis has a negative effect on Greek patients quality of life.

This study has contributed to the body of knowledge surrounding the HRQOL of Greek patients who had experienced cancer of colon and rectum in a number of ways. Therefore, it provides implications for practice into a Greek cultural context as well as recommendations for the assessment of HRQOL in colorectal cancer survivors.

8.2 Implication for practice

In this study it has been found that depression is a predictor that could modify patients' quality of life over years. The timely identification and treatment of depressive symptoms in colorectal cancer patients would be very important for developing a strategy to prevent mental functioning in these patients. It could also provide an ongoing follow-up care on a more individualized basis for improving their overall quality of life.

Also, physicians should not underestimate the cost of the sphincter sacrificing technique on patients' quality of life years after surgery. Furthermore, the existence of specialist stoma care nurses for caring patients suffering from colorectal cancer, with a permanent colostomy, are important, since stoma therapy nursing has not yet been established in Greece. Specialist stoma care nurses can assist rehabilitation starting from the preoperative stage, or as soon as possible after stoma surgery, in order to prevent late adverse effects of stoma surgery on patients' quality of life. Rehabilitation is an ongoing process that encompasses many aspects of life such as physical, emotional, cognitive or social functioning. Through this process, an adaptation strategy must be developed especially for supporting Greek women with a stoma and a poorer body image.

Finally, one priority for nurses who care patients with recurrent disease would be to set goals for supporting both physical needs of the patients (e.g. pain relief) as well as the psychosocial aspects of their quality of life.

Table 8.1 summarizes the statistically significant, the important but not significant and insignificant key findings of the present study as well as the suggested implications.

Table 8.1: Key findings and implications

Statistically significant findings	**Implications**
•Depressive symptoms are significant predictors of the overall HRQOL of colorectal cancer patients.	•Timely identification and treatment of depressive symptoms and strategies to assess negative psychosocial impact on patients post-operatively.
•Patients with a low income experience an overall lower HRQOL.	•Development a policy that would support patients of low income status.
•The overall HRQOL of patients with a colostomy appliance is inferior to that of patients without a colostomy.	•Establishment specialist stoma care nurses in Greece for setting goals in pre-operative, post-operative and rehabilitation stages. The specialist practitioner should adopt a patient-centred approach to care, ensuring that important aspects of care, such as the early teaching to stoma management skills, are not neglected.
•Stoma patients have more dissatisfaction with their body appearance compared to non-stoma and this dissatisfaction is more prevalent to women.	•Preoperative support of women with a stoma and development an adaptation strategy to a new body appearance by helping them to counteract the threats presented by the effects of surgery.
•Stoma patients experience more worry associated with death than non-stoma patients.	•A patient-centred psychological care of stoma patients throughout the treatment process.
•Patients with a metastatic disease experience a lower overall as well as dimension-specific HRQOL than those who considered to be free of cancer.	•Establishment goals for supporting both physical needs of patients as well as psychosocial aspects of quality of life.
Important but statistically insignificant findings	**Implications**
•Stoma patients have a reduced physical functioning, emotional well-being and functional well-being	Preoperative, and post-operative holistic assessment of patients' needs, (physical, emotional, functional),

compared to non-stoma patients. •Women with a stoma and low body image may face difficulties in their sexual activity.	as well effective communication between medical colleagues and stoma care nurses in order to optimize the process of rehabilitation. •Adaptation to a changed body image for preventing the indirect effects of stoma to sexual functioning.
Statistically insignificant findings	**Implications**
•Colorectal cancer patients of different disease stages and at different time since diagnosis do not experience statistically significant differences at the level of their HRQOL. •Gender, and age as well as the level of communication between couples do not associated with outcomes on the HRQOL of survivors.	Publishing the findings of the present study in Greek nursing journals or international nursing journals.

8.3 Recommendations for further research

Further research in this area should be conducted within a multidisciplinary context.

The present study has provided a high overall and dimension specific health-related quality of life score for Greek colorectal cancer survivors. Since the number of studies that have investigated the overall health-related quality of life of colorectal cancer survivors is very limited, more longitudinal studies measuring total and dimension specific quality of life have to be designed, particularly for patients who have survived beyond one year after diagnosis. Factors that could influence patients' quality of life such as the existence of other comorbidities or a low income also have to be examined. Also, more patients with advanced stage disease and long history of colorectal cancer as well as of other ethnicities should be necessary to be included.

This study has provided evidence that depressive symptoms predict Greek colorectal cancer survivors' quality of life. Lately, some researchers have tried to link the role of mood in survival. Onitilo et al. (2006) in a 8-year follow-up study demonstrated that the coexistence of cancer and depression is associated with an increased risk of death. Similar findings have been confirmed by Faller et al. (1999) in a lung cancer patients' study. These authors reported that emotional distress and depressive coping style predicted short survival. Although the impact of depression on mortality has not been definitely confirmed by Spiegel & Giese-Davis (2003) review study, the latter concluded that untreated depressive disorders might be a risk factor for cancer progression.

On the basis of the preceding evidence, the results of the present study highlight the need to evaluate the prevalence of depressive disorders in Greek colorectal cancer patients several years after the diagnosis, using specific standardized scales. Also, further work should focus on the risk factors for depressive symptoms in patients at follow-up. The exploration of the relationship between low income, comorbid conditions and depressive symptoms should be an aim of future studies.

The cross-sectional nature of this study did not allow the evaluation of causal associations between depression and quality of life. For a further exploration of the causal effects of depression on quality of life, the use of prospective, longitudinal study designs would be required.

The results of this study highlight the need for obtaining more information on the overall and dimension specific effects of stoma surgery on Greek patients' quality of life. Further work is needed for evaluating the sexual functioning as well as the body image of Greek women with a colostomy appliance through specific scales. Constructs such as body image or sexual activity should be taken into account in such an evaluation.

Generally speaking, for obtaining a clear perception about the differences in quality of life between stoma and non-stoma patients, more work is needed that would include large prospective studies in which patients' quality of life should be evaluated before and after surgery. Also, there may be a difference in certain aspects of quality of life in patients who have undergone a low anterior resection compared to those who were given a high anterior resection. The investigation of the method of surgery (high versus low resection) would be an important addition to future research.

Another area for further research is related to the health-related quality of life instruments. As previously discussed, the available HRQOL instruments, even though provide evidence for validity or reliability, they have been designed for clinical trials. Therefore, they are of limited applicability to long-term survivors. Patients may feel that issues related to hope and fears about the future, worries about recurrence or adaptation to cancer, are problems of equal importance to the physical symptoms produced by cancer and its treatment at follow-up. The development of instruments that would cover issues more relevant to cancer survivors would be an important area for future research. Recent work conducted by Zebrack et al. (2005) reports on the development and the evaluation of a new instrument that measures aspects of long-term survivorship. However, further work is needed to confirm the psychometric properties of this instrument.

Also, it has been agreed that HRQOL instruments may only capture aspects of subjective health status. A fundamental limitation is that whilst they capture issues that the developers of them consider as important, their importance to patients' concepts has been overlooked (Dijkers, 2003; Carr et al., 2001). In order to ensure that the quality of life approach used in this study reflect the health-related quality of life issues of most concern and relevance to a Greek cultural context, an in-depth insight into the experience of Greek patients surviving colorectal cancer would be another area for further work.

Detailed information about Greek patients' quality of life can be obtained by structured and unstructured interview procedures in which a holistic point of view of patients' subjective well being is achieved. The combination of both qualitative and quantitative approaches would provide an in-depth

understanding on patients' perspective, giving at the same time the possibility to generalize and predict.

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APPENDIX 1

PATIENTS' LETTER

Study Title: Evaluation of quality of life of long-term survivors of bowel disease patients

Dear (patient's full name)

I am currently carrying out research into the quality of life in people who have had bowel disease. It is hope that by exploring this area we will better informed of patients' needs and will be able to improve the care offered in the future. I would like to invite you to take part in this study. Your participation is entirely voluntary. Your physicians are already aware of this research being carried out and permission was also obtained from them before I use your personal data.

Before you decide whether you would like to participate, it is important that you understand why this study is being carried out and what it will involve. This letter and enclosed details will give you information which you may wish to discuss with your family, friends and hospital staff. Please take time to decide whether or not you whish to participate. Please ask if anything is not clear or if you have any additional questions or queries about this study. You can contact me directly on 6945-463990.

Thank you for taking the time to read this and for considering taking part in this study.

Yours sincerely

Doga Georgia (Mrs)
Tel: 6945-4639990.

APPENDIX 2
MODERN GREEK TRANSLATION PATIENT'S LETTER

ΠΡΟΣ ΤΟΝ ΑΣΘΕΝΗ

Τίτλος μελέτης Αξιολόγηση της ποιότητας ζωής ασθενών που έχουν επιβιώσει από την νόσο του παχέος εντέρου.

Αγαπητή Κυρία/Κύριε

Πρόσφατα διεξάγω μία έρευνα πάνω στην ποιότητα ζωής των ανθρώπων οι οποίοι νόσησαν και έλαβαν θεραπεία για την νόσο του πεχέος εντέρου. Ελπίζουμε ότι μέσα από μια τέτοια διερεύνηση θα επιτύχουμε καλύτερη πληροφόρηση γύρω από τις ανάγκες των ασθενών και έτσι θα είμαστε σε θέση να βελτιώσουμε την παρεχόμενη φροντίδα για τους μελλοντικούς ασθενείς. Θα ήθελα να σας προσκαλέσω να λάβετε μέρος σε αυτή την μελέτη. Η συμμετοχή σας είναι εντελώς εθελοντική. Ο γιατρός που σας παρακολουθεί έχει ήδη ενημερωθεί για την παρούσα έρευνα. Από τον γιατρός σας επίσης έχω πάρει την άδεια για να επικοινωνήσω μαζί σας και να χρησιμοποιήσω τα προσωπικά σας δεδομένα.

Προτού αποφασίσετε εάν θα επιθυμούσατε να συμμετάσχετε κρίνεται σημαντικό να γνωρίζετε το σκοπό αυτής της μελέτης και τι αυτή περιλαμβάνει.

Αυτό το γράμμα καθώς επίσης και οι επισυναπτόμενες λεπτομέρειες θα σας δώσουν κάθε πληροφόρηση την οποία μπορείτε να συζητήσετε με το οικογενειακό σας περιβάλλον, τους φίλους σας ή με το προσωπικό του νοσοκομείου σας.

Παρακαλώ σκεφτείτε με άνεση χρόνου εάν επιθυμείτε να συμμετέχετε ή όχι. Εάν υπάρχει κάτι που δεν κατανοείτε ή έχετε οποιεσδήποτε απορίες σχετικά με αυτή τη μελέτη μπορείτε να επικοινωνήσετε μαζί μου οποιαδήποτε ώρα της μέρας στο 6945-463990.

Σας ευχαριστώ για το χρόνο που διαθέσατε για να διαβάσετε αυτό το γράμμα και να σκεφτείτε να συμμετέχετε σ΄αυτή τη μελέτη.

Με εκτίμηση

Δόγα Γεωργία
Τηλ. 6945-463990.

APPENDIX 3

INFORMATION SHEET

TITLE: Evaluation of quality of life of long-term survivors of bowel disease patients

Background to this study

When we evaluate a new treatment (e.g. new drugs), one of the most important areas to consider is the impact on people' health and quality of life. Although much work has been undertaken investigating peoples' experience of disease during the diagnostic or treatment phase, we do not know many about the needs of patients as they enter the post-treatment of their journey as well as the late impact of disease and its treatment on their quality of life.

The purpose of this study

Knowledge of the experience of the patient with bowel disease would be useful to health care professional to prevent possible late effect of the disease during follow-up evaluation, or to policy makers to plan specific health care programs to improve quality of life.

Why have I been chosen?

The researcher wishes to explore the quality of life of patients who had survived their disease from one to several years ago. Patients were chosen to reflect a broad range of treatment received for bowel disease.

What will the study involved?

If you decide to take part in the study you will be asked to complete a research pack which contains four questionnaires together with a demographic data sheet. This pack should take approximately 30 minutes to complete.

Do I have to take part?

No, taking part in this study is entirely voluntary. If you decide to take part, I will ask you to complete and sign a consent form giving permission. Even if you decide to take part, you will free to withdraw at any time and without giving reason. Your decision will not affect the medical care or treatment that you receive at any time.

What are the potential risks for me becoming involved in this study?

This study involves competing questionnaires which will ask you about your health and quality of life, and you may find this upsetting. You may also becoming tired or find difficulty in answering some of the questions. The researcher will try and minimize these potential issues by providing clear instructions on how to complete the questionnaires, and by providing a contact telephone number if you have any queries or concerns about the questionnaires.

What are the potential benefits for me becoming involved in this study?

You may find that completing the questionnaires provides a chance to reflect upon your experience. This study will provide other health professionals and

patients with a better understanding of the impact of your illness and treatment once treatment has been completed, and assist in providing treatment and care which improves patients' health and quality of life.

What happens next?

Since you carefully read this information and if you decide to take part you have to return the enclosed reply slip within a couple of weeks. This will allow you time to study the information and give you the opportunity to discuss the study with relatives or friends. A week from the day of sending you this letter I will contact you by telephone in order to ensure that you have received it. If you already have received it we will have the opportunity to discuss any aspects of the study in further detail.

If you agree to complete the questionnaires, I will send you the research pack and a second copy of the letter, information sheet as well as and a consent form. You will be asked to return the pack in a stamped addressed enveloped provided. You will also be asked to send the signed consent form to me in a separate stamped addressed envelope. This is to ensure that your anonymity is maintained.

What if I change my mind about participating?

You can change you mind about participating at any time. You can do this by contacting me directly on the contact number below or asking a relative, friend or health care professional to contact me on your behalf. Messages can be left at any time (including evenings, nights and weekends) on a voice-mail facility. You do not have to give any reason for withdrawing from the study.

Will my details be kept confidential?

All information that is collected about you during the course of this research study will be kept strictly confidential. All data will be anonymous and your data will be given a unique identification number. In addition, any information about you which leaves the hospital will have your name and address removed so that you can not be recognized from it. It will not be possible to identify you in any report or publication of this study.

Who has reviewed this study?

I am MPhil (research) student based at the School of Health Sciences, University of Wales Swansea, Singleton Park, Swansea, SA2, 8PP, United Kingdom. This study has been reviewed by my academic supervisor, Mrs Faye Kinsella, Lecture at the School of Health Science.

If you have any questions or would like any further information please contact:

Georgia Doga (Mrs)
MPhil candidate
Tel: 6945 463990

If you decide to take part in the study you will be sent a copy of your signed consent form.

Thank you for taking the time to read this information.

APPENDIX 4

MODERN GREEK TRANSLATION OF INFORMATION SHEET

ΕΝΗΜΕΡΩΤΙΚΟ ΦΥΛΛΑΔΙΟ

ΤΙΤΛΟΣ Αξιολόγηση της ποιότητας ζωής των ασθενών που έχουν επιβιώσει από την νόσο του παχέος εντέρου.

Αντικείμενο αυτής της μελέτης

Όταν αξιολογούμε μία νέα θεραπεία (π.χ νέα φάρμακα), θα πρέπει να λάβουμε υπ' όψιν μας τον αντίκτυπο που μπορεί αυτή να έχει στην υγεία των ανθρώπων και στην ποιότητα της ζωής τους. Αν και πολλές έρευνες μέχρι σήμερα έχουν εστιάσει στο να μελετήσουν την εμπειρία των ασθενών κατά την διαγνωστική και θεραπευτική φάση της ασθένειάς τους, δεν είμαστε σε θέση να γνωρίζουμε αρκετά για τις ανάγκες των ασθενών καθώς αυτοί μπαίνουν στην μετά θεραπεία φάση αυτού του ταξιδιού καθώς επίσης και τον αντίκτυπο που μπορεί να έχει η ίδια η ασθένεια και η θεραπεία της στην ποιότητα της ζωής τους.

Σκοπός αυτής της μελέτης

Η γνώση της εμπειρίας των ασθενών με τη νόσο του παχέος εντέρου θα ήταν χρήσιμη στους επαγγελματίες υγείας στο να προλάβουνε πιθανές μακροπρόθεσμες παρενέργειες της ασθένειας κατά το χρόνο της επαναξιολόγησής τους ή στους πολιτικούς σχεδιαστές στο να σχεδιάσουν

ειδικά προγράμματα φροντίδας υγείας για την βελτίωση της ποιότητας ζωής τους.

Γιατί έχω επιλεγεί;

Μέσα από την παρούσα έρευνα η ερευνήτρια σκοπεύει να διερευνήσει την ποιότητα ζωής των ασθενών που έχουν επιζήσει μετά από ένα έως και αρκετά χρόνια από τη διάγνωση της ασθένειας τους. Οι ασθενείς έχουν επιλεγεί ώστε να αντιπροσωπεύουν μία ευρεία κατηγορία θεραπειών που έχουν λάβει.

Τι θα περιλαμβάνει αυτή η μελέτη;

Εάν αποφασίσετε να λάβετε μέρος σε αυτή την έρευνα θα σας ζητηθεί να συμπληρώσετε ένα ερευνητικό πακέτο το οποίο θα περιέχει τέσσερα ερωτηματολόγια και ένα φυλλάδιο με τα δημογραφικά σας χαρακτηριστικά. Ο χρόνος που θα απαιτηθεί για να συμπληρώσετε αυτό το πακέτο θα είναι περίπου 30 λεπτά.

Είμαι υποχρεωμένος/η να λάβω μέρος;

Μπορείτε να επιλέξετε εάν επιθυμείτε ή όχι να συμμετέχετε στην έρευνα. Εάν αποφασίσετε να συμμετέχετε θα σας ζητηθεί να συμπληρώσετε και να υπογράψετε το σχετικό έντυπο το οποίο θα επιβεβαιώνει την συγκατάθεσή σας. Σε περίπτωση που αποφασίσετε να λάβετε μέρος θα είστε ελεύθερος/η να αναιρέσετε αυτή σας την απόφαση οποιαδήποτε στιγμή το επιθυμήσετε και χωρίς να είστε υποχρεωμένος/η να δώσετε εξηγήσεις. Η απόφασή σας αυτή δεν θα επηρεάσει σε καμία περίπτωση την φροντίδα υγείας ή την θεραπεία που ίσως λάβετε σε οποιαδήποτε χρονική στιγμή.

Σε ποιους πιθανούς κινδύνους ενδέχεται να υποβληθώ συμμετέχοντας σε αυτή τη μελέτη;

Η παρούσα μελέτη περιλαμβάνει την συμπλήρωση ερωτηματολογίων μέσα από τα οποία καλείστε να απαντήσετε σε θέματα που αφορούν την υγεία σας και την ποιότητα ζωής σας και ενδεχομένως κάτι τέτοιο σας κάνει να αισθανθείτε αναστατωμένος/η. Ίσως νιώσετε κουρασμένος/η ή αντιμετωπίσετε δυσκολίες στο να απαντήσετε σε κάποιες ερωτήσεις. Η ερευνήτρια θα προσπαθήσει να ελαχιστοποιήσει τις πιθανότητες να συμβεί κάτι από τα παραπάνω δίνοντάς σας ξεκάθαρες οδηγίες για το πώς πρέπει να συμπληρώσετε τα ερωτηματολόγια και δίνοντάς σας τη δυνατότητα να επικοινωνήσετε τηλεφωνικώς μαζί της σε περίπτωση που έχετε κάποια απορία ή θέλετε να ρωτήσετε οτιδήποτε σχετίζεται με τα ερωτηματολόγια.

Ποια πιθανά οφέλη θα λάβω συμμετέχοντας σε αυτή τη μελέτη;

Ίσως βρείτε ότι μέσα από τη συμπλήρωση των ερωτηματολογίων σας δίνεται η ευκαιρία να εκφράσετε την εμπειρία σας. Επιπλέον αυτή η μελέτη θα δώσει τη δυνατότητα σε επαγγελματίες υγείας και ασθενείς να κατανοήσουν καλύτερα τον αντίκτυπο της ασθένειά σας όταν κάθε θεραπεία έχει ολοκληρωθεί και να βοηθήσει σε εναλλακτική θεραπεία και φροντίδα η οποία θα βελτιώνει την υγεία των ασθενών και την ποιότητα ζωής.

Ποιο είναι το επόμενο βήμα;

Εφόσον με προσοχή διαβάσετε αυτές τις πληροφορίες και εάν αποφασίσετε να λάβετε μέρος θα πρέπει να επιστρέψετε το απαντητικό δελτάριο μέσα σε δύο εβδομάδες. Κάτι τέτοιο θα σας δώσει το χρόνο που εσείς χρειάζεστε για να μελετήσετε αυτές τις πληροφορίες ή να τις συζητήσετε με συγγενείς ή φίλους. Μία εβδομάδα μετά την αποστολή της παρούσας

επιστολής θα επικοινωνήσω μαζί σας τηλεφωνικώς για να επιβεβαιώσω ότι την έχετε λάβει. Έτσι θα έχουμε την ευκαιρία να συζητήσουμε τηλεφωνικώς και με κάθε λεπτομέρεια οτιδήποτε σχετίζεται με αυτή την μελέτη. Εάν συμφωνείτε να συμπληρώσετε τα ερωτηματολόγια θα σας στείλω ταχυδρομικώς το πακέτο με την έρευνα, ένα αντίγραφο αυτής της επιστολής και το έντυπο της συγκατάθεσής σας. Αφού συμπληρώσετε την έρευνα θα πρέπει να επιστρέψετε το πακέτο ταχυδρομικώς χρησιμοποιώντας τον κενό φάκελο που θα παραλάβετε μέσα στο πακέτο. Δεν χρειάζεται να κολλήσετε γραμματόσημα ούτε να γράψετε στον κενό φάκελο την διεύθυνση του παραλήπτη αφού η διεύθυνση που θα σταλεί ο φάκελος θα υπάρχει ήδη γραμμένη επάνω του.

Μπορώ να αλλάξω γνώμη σχετικά με την συμμετοχή μου στην έρευνα ναι ή όχι;

Έχετε την δυνατότητα να αλλάξετε γνώμη και να μη συμμετέχετε στην έρευνα οποιαδήποτε στιγμή το επιθυμήσετε. Μπορείτε να μου τηλεφωνήσετε στο νούμερο τηλεφώνου που θα βρείτε στο τέλος αυτής της επιστολής ή να ζητήσετε από φίλους, συγγενείς ή από το γιατρό σας να το κάνει εκ μέρους σας. Επίσης μπορείτε να αφήσετε μήνυμα στον αυτόματο τηλεφωνητή οποιαδήποτε ώρα (συμπεριλαμβανομένου βράδια και Σαββατοκύριακα). Δεν είστε σε καμία περίπτωση υποχρεωμένος/η να δώσετε εξηγήσεις για το λόγο για τον οποίο αποφασίσατε να μη συμμετέχετε.

Οι πληροφορίες που θα δώσω θα είναι εμπιστευτικές;

Όλα τα στοιχεία που θα συγκεντρωθούν από αυτή την μελέτη θα είναι απόλυτα εμπιστευτικά. Όλα τα δεδομένα θα παραμείνουν ανώνυμα και θα

αναγνωρίζονται μέσα από ένα κωδικό νούμερο. Επιπλέον, στοιχεία που σχετίζονται με εσάς και που θα περιέχουν το όνομα σας ή τη διεύθυνσή σας από την στιγμή που θα φύγουν από το χώρο του νοσοκομείου δεν θα υπάρχει η δυνατότητα να μπορεί να αναγνωριστούν ότι σας ανήκουν. Τέλος σε καμία αναφορά ή δημοσίευση αυτής της μελέτης δεν θα εμπεριέχετε το όνομά σας.

Ποιος έχει την εποπτεία αυτής της μελέτης;

Είμαι μεταπτυχιακή ερευνητική φοιτήτρια στην Σχολή Επιστημών Υγείας στο Πανεπιστήμιο της Ουαλίας Σουόνζι (University of Wales Swansea), Singleton Park, Swansea, SA2, 8PP, UK. Την Εποπτεία αυτής της έρευνας έχει η ακαδημαική μου επόπτρια Mrs Fay Kinsella, Λέκτορας της σχολής.

Εάν έχετε οποιαδήποτε ερώτηση ή επιθυμείτε επιπλέον ενημέρωση παρακαλώ επικοινωνήστε:

Γεωργία Δόγα
Μεταπτυχιακή φοιτήτρια
Τηλ. 6945 463990

Εάν αποφασίσετε να συμμετέχετε στην έρευνα θα σας σταλεί ένα υπογεγραμμένο αντίγραφο της έντυπης συγκατάθεσής σας.

Ευχαριστώ για το χρόνο που διαθέσατε να διαβάσετε αυτή την επιστολή.

APPENDIX 5

CONSENT FORM

TITLE OF PROJECT:

NAME OF LEAD RESEARCHER:

PLEASE INITIAL YOUR CONSENT IN THE BOXES

1 I confirm that I have read and understand the information sheet for the above study and have had the opportunity to ask questions. I confirm I have received information on how to contact the researcher. ☐

2 I understand that my participation is voluntary and that I am free to withdraw at any time, without giving reason, and without my medical care or legal rights being affected. ☐

3 I understand that sections of my medical notes may be looked at by the researcher. I give permission for the researcher to have access to my records. ☐

4 I understand that all data will remain confidential and used for research purposes only. ☐

5. I wish to receive a summary of the study on completion ☐

6. I agree to take part in this study. ☐

Name of Patient .....

Signature of patient .....

Date .....

Name of Researcher .....

Signature of researcher .....

Date .....

APPENDIX 6

MODERN GREEK TRANSLATION OF THE CONSENT FORM

ΕΝΤΥΠΟ ΣΥΓΚΑΤΑΘΕΣΗΣ

ΤΙΤΛΟΣ ΜΕΛΕΤΗΣ:

ΟΝΟΜΑΤΕΠΩΝΥΜΟ ΕΡΕΥΝΗΤΡΙΑΣ:

ΠΑΡΑΚΑΛΩ ΥΠΟΓΡΑΨΤΕ ΜΕ ΤΑ ΑΡΧΙΚΑ ΣΑΣ ΚΑΘΕ ΕΝΑ ΑΠΟ ΤΑ ΤΕΤΡΑΓΩΝΑΚΙΑ

1	Επιβεβαιώνω ότι έχω διαβάσει και πλήρως κατανοήσει το ενημερωτικό φυλλάδιο που αφορά την παραπάνω έρευνα και ότι μου δόθηκε η δυνατότητα να υποβάλλω διευκρινιστικές ερωτήσεις. Επιβεβαιώνω ότι έχω ενημερωθεί για τον τρόπο με τον οποίο μπορώ να έρθω σε επαφή με την ερευνήτρια.	
2	Έχω πλήρως κατανοήσει ότι η συμμετοχή μου στην έρευνα είναι εθελοντική και ότι είμαι ελεύθερος/η να αποσύρω την συμμετοχή μου σε οποιοδήποτε χρόνο χωρίς να δώσω εξηγήσεις για το λόγο που το κάνω και χωρίς να επηρεαστεί η παροχή της ιατρικής μου φροντίδας ή άλλα δικαιώματα που έχω.	
3	Κατανοώ ότι η ερευνήτρια θα χρειαστεί να γνωρίζει ιατρικές πληροφορίες που με αφορούν. Δίνω την άδεια στην ερευνήτρια να έχει πρόσβαση στο ιατρικό μου αρχείο.	
4	Έχω καταλάβει ότι όλα τα δεδομένα μου θα παραμείνουν εμπιστευτικά και θα χρησιμοποιηθούν μόνο για ερευνητικούς σκοπούς.	
5	Θα επιθυμούσα να ενημερωθώ για τα αποτελέσματα της έρευνας.	
6	Συμφωνώ να συμμετάσχω στην παρούσα έρευνα.	

Ονοματεπώνυμο Ασθενούς:

Υπογραφή ασθενούς:

Ημερομηνία:

Ονοματεπώνυμο ερευνήτριας:

Υπογραφή ερευνήτριας:

Ημερομηνία:

APPENDIX 7

DEMOGRAPHIC DATA QUESTIONNAIRE

This questionnaire asks you to provide some general information related to your demographic or other characteristics.

Please reply to the questions below putting a mark (X) to the relevant box.

Code Number: (it is completed by the researcher).

Gender ☐ Male ☐ Female

Marital status

☐ Single

☐ Married

☐ Divorced

☐ Widowed

Educational level

☐ Primary School

☐ Secondary School

☐ College /University graduate

Employment Status

☐ Unemployed

☐ Household

☐ Retired

☐ Clerk officer

☐ Skilled workman

☐ Farmer

☐ Work on their own job

☐ Other

☐ Not work due to the disease.

Income (per month)

☐ Less than Euro 440

☐ Euro 440-880 Euro

☐ Euro 880-1467 Euro

☐ Euro 1467-2347 Euro

☐ Over Euro 2347

Date of Birth:

APPENDIX 8

MODERN GREEK TRANSLATION OF THE DEMOGRAPHICAL DATA QUESTIONNAIRE

ΕΡΩΤΗΜΑΤΟΛΟΓΙΟ ΔΗΜΟΓΡΑΦΙΚΩΝ ΧΑΡΑΚΤΗΡΙΣΤΙΚΩΝ

Το παρακάτω ερωτηματολόγιο σας ζητά να απαντήσετε σε γενικές ερωτήσεις που σχετίζονται με δημογραφικά ή άλλα χαρακτηριστικά σας.
Παρακαλώ απαντήστε στις παρακάτω ερωτήσεις σημειώνοντας με ένα Χ το αντίστοιχο κουτάκι.

Αύξων αριθμός:

Φύλο Άνδρας ☐ Γυναίκα ☐

Οικογενειακή κατάσταση

☐ Άγαμος/η
☐ Έγγαμος/η
☐ Χωρισμένος/η
☐ Χήρος/α

Εκπαιδευτικό επίπεδο

☐ Δημοτικό
☐ Γυμνάσιο
☐ Λύκειο
☐ ΤΕΙ/ΑΕΙ

Επάγγελμα

☐ Άνεργος
☐ Οικιακά
☐ Συνταξιούχος
☐ Υπάλληλος γραφείου

☐ Εργατοτεχνίτης
☐ Αγρότης
☐ Ελεύθερος επαγγελματίας
☐ Άλλο
☐ Απώλεια εργασίας λόγω ασθένειας

Οικογενειακό μηνιαίο εισόδημα
☐ Έως 440 Ευρώ (150.000δρχ)
☐ Από 440-880 Ευρώ (151.000-3000.000 δρχ)
☐ Από 880-1467 Ευρώ (301.000-500,000 δρχ)
☐ Από 1467-2347 Ευρώ (501.000-800.000 δρχ)
☐ Από 2347 Ευρώ (800.000 δρχ) και άνω

Χρονολογία Γεννήσεως:...

APPENDIX 9

FUNCTIONAL ASSESSMENT OF CANCER THERAPY-COLORECTAL (FACT-C) QUALITY OF LIFE INSTRUMENT

Below is a list of statement that other people with your illness have said are important. **By circling one number per line, please indicate how true each statement has been for you during the last 7 days.**

Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**
0	**1**	**2**	**3**	**4**
1. I have a lack of energy	1	2	3	4

Items (using the same format as above):

PHYSICAL WELL-BEING

1. I have a lack of energy
2. I have nausea
3. Because of my physical condition, I have trouble meeting the needs of my family
4. I have pain
5. I am bothered by side effects of treatment
6. I feel sick
7. I am forced to spend time in bed

SOCIAL/FAMILY WELL-BEING

8. I feel distant from my friends

9. I get emotional support from my family

10. I get support from my friends and neighbors

11. My family has accepted my illness

12 Family communication about my illness is poor

13. I feel close to my partner (or the person who is my main support)

14. Have you been sexually activity during the past year?

No— Yes—— If yes: 1 am satisfied with my sex life

EMOTIONAL WELL-BEING

15. I feel sad

16. I am proud of how I'm coping with my illness

17. I am losing hope in the fight against my illness

18. I feel nervous

19. I worry about dying

20. I worry that my condition will get worse

FUNCTIONAL WELL-BEING

21. 1 am able to work (including work in home)

22. My work (including work in home) is fulfilling

23. I am able to enjoy life

24. I have accepted my illness

25. I am sleeping well

26. I am enjoying the things I usually do for fun

27. I am content with the quality of my life right now

ADDITIONAL CANCERNS

28. I have swelling or cramps in my stomach area

29. I am losing weight

30. I have control of my bowels

31. I can digest my food well

32. I have diarrhea

33. I have a good appetite

34. I like the appearance of my body

Do you have an ostomy appliance?

No— Yes— if yes; answer #35 & 36.

35. I am embarrassed by my ostomy appliance

36. Caring for my ostomy appliance is difficult

APPENDIX 10

MODERN GREEK TRANSLATION OF THE FUNCTIONAL ASSESSMENT OF CANCER THERAPY-COLORECTAL (FACT-C) QUALITY OF LIFE INSTRUMENT

Παρακάτω είναι μια λίστα από δηλώσεις που έκαναν άλλοι άνθρωποι που πάσχουν από την ασθένειά σας και είπαν ότι είναι σημαντικοί. **Σημειώνοντας με κύκλο έναν (Ι) αριθμό ανά γραμμή, καθορίστε το κατά πόσο ανταποκρινόταν στην πραγματικότητα κάθε μια από τις δηλώσεις αυτές για σας, κατά τις τελευταίες 7 ημέρες.**

ΦΥΣΙΚΗ ΕΥΕΞΙΑ	**Καθόλου**	**Λίγο**	***Κάπως***	**Αρκετά**	**Πάρα πολύ**
GP1 Αισθάνομαι κόπωση	0	1	2	3	4
GP2 Έχω ναυτία ή τάση για εμετό	0	1	2	3	4
GP3 Εξαιτίας της σωματικής μου κατάστασης έχω πρόβλημα στο να ανταποκριθώ στις ανάγκες της οικογένειάς μου	0	1	2	3	4
GP4 Έχω πόνους	0	1	2	3	4
GP5 Ενοχλούμαι από τις παρενέργειες της θεραπείας μου	0	1	2	3	4
GP6 Νοιώθω άρρωστος	0	1	2	3	4
GP7 Αναγκάζομαι να μένω στο κρεβάτι	0	1	2	3	4

ΚΟΙΝΩΝΙΚΗ / ΟΙΚΟΓΕΝΕΙΑΚΗ ΕΥΕΞΙΑ	**Καθόλου**	**Λίγο**	**Κάπως**	**Αρκετά**	**Πάρα πολύ**
GS1 Νοιώθω κοντά στους φίλους μου	0	1	2	3	4
GS2 Η οικογένειά μου προσφέρει συναισθηματική συμπαράσταση	0	1	2	3	4

GS3 Υποστηρίζομαι από τους φίλους μου 0 1 2 3 4

GS4 Η οικογένειά μου έχει αποδεχτεί την ασθένειά μου..... 0 1 2 3 4

GS5 Είμαι ικανοποιημένος / η με την επικοινωνία που έχω με την οικογένειά μου όσον αφορά την ασθένειά μου..... 0 1 2 3 4

GS6 Αισθάνομαι κοντά στο (στη) σύντροφό μου (ή στο άτομο που κυρίως μου συμπαραστέκεται)..... 0 1 2 3 4

Q1 *Ανεξάρτητα με το επίπεδο της σημερινής σας σεξουαλικής δραστηριότητας, παρακαλούμε να απαντήστε στην ακόλουθη ερώτηση. Εάν προτιμάτε να μην την απαντήσετε, σημειώστε με Χ το κουτάκι αυτό και συνεχίστε στην επόμενη ενότητα.* ☐

GS7 Είμαι ικανοποιημένος (η) με τη σεξουαλική μου ζωή ***0*** 1 2 3 4

Σημειώνοντας με κύκλο έναν (1) αριθμό ανά γραμμή, καθορίστε το κατά πόσο ανταποκρινόταν στην πραγματικότητα κάθε μια από τις δηλώσεις αυτές για σας, κατά τις τελευταίες 7 ημέρες.

ΣΥΝΑΙΣΘΗΜΑΤΙΚΗ ΕΥΕΞΙΑ	**Καθόλου**	**Λίγο**	**Κάπως**	**Αρκετά**	**Πάρα πολύ**
GE1 Αισθάνομαι θλίψη	0	1	2	3	4
GE2 Είμαι ικανοποιημένος / η με τον τρόπο με τον οποίο αντιμετωπίζω την ασθένειά μου	0	1	2	3	4
GE3 Χάνω τις ελπίδες μου στη μάχη με την ασθένειά μου.....	0	1	2	3	4
GE4 Αισθάνομαι ανησυχία.....	0	1	2	3	4
GE5 Αισθάνομαι ανησυχία ότι θα πεθάνω.....	0	1	2	3	4
GE6 Ανησυχώ ότι η κατάστασή μου θα χειροτερεύει.....	0	1	2	3	4

ΛΕΙΤΟΥΡΓΙΚΗ ΕΥΕΞΙΑ	**Καθόλου**	**Λίγο**	**Κάπως**	**Αρκετά**	**Πάρα πολύ**
GF1 Είμαι σε θέση να εργαστώ (συμπεριλάβετε την εργασία στο σπίτι).....	0	1	2	3	4
GF2 Η εργασία μου (συμπεριλάβετε την εργασία στο σπίτι) με ικανοποιεί	0	1	2	3	4
GF3 Μπορώ και χαίρομαι τη ζωή μου	0	1	2	3	4
GF4 Αποδέχομαι την ασθένειά μου	0	1	2	3	4
GF5 Κοιμάμαι καλά	0	1	2	3	4
GF6 Απολαμβάνω αυτά που συνήθως κάνω για διασκέδαση / αναψυχή.....	0	1	2	3	4

GF7

Είμαι ικανοποιημένος (η) με την ποιότητα ζωής μου αυτή τη στιγμή..... 0 1 2 3 4

Σημειώνοντας με κύκλο έναν (1) αριθμό ανά γραμμή, καθορίστε το κατά πόσο ανταποκρινόταν στην πραγματικότητα κάθε μια από τις δηλώσεις αυτές για σας, κατά τις τελευταίες 7 ημέρες.

ΠΡΟΣΘΕΤΕΣ ΑΝΗΣΥΧΙΕΣ	**Καθόλου**	**Λίγο**	**Κάπως**	**Αρκετά**	**Πάρα πολύ**
C1 Έχω φουσκώματα ή κράμπες στην περιοχή του στομάχου	0	1	2	3	4
C2 Χάνω βάρος	0	1	2	3	4
C3 Ελέγχω το πότε ενεργούμαι	0	1	2	3	4
C4 Χωνεύω καλά το φαγητό μου	0	1	2	3	4
C5 Έχω διάρροια	0	1	2	3	4
C6 Η όρεξή μου είναι καλή	0	1	2	3	4
C7 Μου αρέσει η εμφάνιση του σώματός μου	0	1	2	3	4
Q2 Έχετε συσκευή κολοστομίας (Σημειώστε στο αντίστοιχο πλαίσιο)	**Όχι ή** ☐			**Ναι** ☐	
Αν ναι, παρακαλείστε να απαντήστε στα δύο παρακάτω ερωτήματα:					
C8 Με πειράζει που έχω συσκευή κολοστομίας	0	1	2	3	4
C9 Το βρίσκω δύσκολο να να φροντίζω για τη συσκευής κολοστομίας	0	1	2	3	4

APPENDIX 11
SHORT FORM 36 HEALTH SURVEY
(MENTAL HEALTH)

INSTRUCTIONS: This set of questions asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.
Answer every question by making the answer as indicated. If you are unsure about answer a question please give the best answer you can.

1. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

(Please circle one number on each line.)

	YES	**NO**
a. Cut down on the **amount of time** you spent on work or other activities	1	2
b. Accomplished less than you would like	1	2
c. Didn't do work or other activities as **carefully** as usual	1	2

2. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?

(Please circle one number)

Not at all	1
Slightly	2
Moderately	3
Quite a bit	4
Extremely	5

3. These questions are about how you feel and how things have been with you **during the past 4 weeks.** Please give the one answer that is closest to the way you have been feeling for each items.

(Please circle one number on each line.)

	All of the Time	**Most of the Time**	**A Good Bit of the Time**	**Some of the Time**	**A little of the Time**	**None of the Time**
Did you feel full of fe?	1	2	3	4	5	6
have you been a ery nervous person?	1	2	3	4	5	6
Have you felt so	1	2	3	4	5	6

own in the dumps nat nothing could heer you up?						
. Have you felt calm nd peaceful?	1	2	3	4	5	6
. Did you have a lot f energy?	1	2	3	4	5	6
. have you felt ownhearted and blue?	1	2	3	4	5	6
. Did you feel worn ut?	1	2	3	4	5	6
. Have you been a appy person?	1	2	3	4	5	6
Did you feel tired?	1	2	3	4	5	6

4. During the past 4 weeks, how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives etc).

(Please circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
None of the time	5

APPENDIX 12
MODERN GREEK TRANSLATION OF SHORT FORM 36 HEALTH SURVEY (MENTAL HEALTH)

SF -36 ΕΡΕΥΝΑ ΥΓΕΙΑΣ

ΟΔΗΓΙΕΣ: Το ερωτηματολόγιο αυτό ζητά τις δικές σας απόψεις για την υγεία σας. Οι πληροφορίες σας θα μας βοηθήσουν να εξακριβώσουμε πώς αισθάνεστε από πλευράς υγείας και πόσο καλά μπορείτε να ασχοληθείτε με τις συνηθισμένες δραστηριότητές σας.
Απαντήστε στις ερωτήσεις, βαθμολογώντας κάθε απάντηση με τον τρόπο που σας δείχνουμε. Αν δεν είστε απόλυτα βέβαιος/η για την απάντησή σας, παρακαλούμε να δώσετε την απάντηση που νομίζετε ότι ταιριάζει καλύτερα στην περίπτωσή σας.

1. Τις τελευταίες 4 εβδομάδες, σας παρουσιάστηκε –είτε στην δουλειά σας είτε σε κάποια άλλη συνηθισμένη καθημερινή δραστηριότητα – κάποιο από τα παρακάτω προβλήματα **εξαιτίας οποιουδήποτε συναισθηματικού προβλήματος** (λ.χ επειδή νοιώσατε μελαγχολία ή άγχος);

(κυκλώστε έναν αριθμό σε κάθε σειρά)

	ΝΑΙ	**ΟΧΙ**

α. **Μειώσατε το χρόνο** που συνήθως ξοδεύατε στην δουλειά σας ή σε άλλες δραστηριότητες	1	2
β. Επιτελέσατε λιγότερα από όσα θα θέλατε	1	2
Κάνατε τη δουλειά ή και άλλες δραστηριότητες λιγότερο **προσεχτικά** απ' ότι συνήθως	1	2

2. Τις τελευταίες 4 εβδομάδες, σε ποιο βαθμό επηρέασε η κατάσταση της σωματικής σας υγείας ή κάποια συναισθηματικά προβλήματα τις συνηθισμένες κοινωνικές σας δραστηριότητες με την οικογένεια, τους φίλους, ή τους γείτονές σας ή με άλλες κοινωνικές ομάδες;

(βάλτε έναν κύκλο)

Καθόλου	1
Ελάχιστα	2
Μέτρια	3
Αρκετά	4
Πάρα πολύ	5

3. Οι παρακάτω ερωτήσεις αναφέρονται στο πώς αισθάνεστε και στο πώς ήταν γενικά η διάθεσή σας **τις τελευταίες 4 εβδομάδες.** Για κάθε ερώτηση, παρακαλείστε να δώσετε εκείνη την απάντηση που πλησιάζει περισσότερο σε ότι αισθανθήκατε.

Τις τελευταίες 4 εβδομάδες, για πόσο χρονικό διάστημα

(κυκλώστε έναν αριθμό σε κάθε σειρά)

	Συνεχώς	**Το**	**Σημαντικό**	**Για**	**Μικρό**	**Καθόλου**

		μεγαλύτερο διάστημα	**διάστημα**	**κάποιο διάστημα**	**διάστημα**	
. ιισθανόσαστε εμάτος/η ωντάνια	1	2	3	4	5	6
. Είχατε πολύ κνευρισμό	1	2	3	4	5	6
. ιισθανόσαστε όσο πολύ εσμένος/η υχολογικά ου τίποτε δεν πορούσε να ας φτιάξει το έφι	1	2	3	4	5	6
. ιισθανόσαστε ρεμία και αλήνη	1	2	3	4	5	6
. Είχατε πολύ νεργητικότητα	1	2	3	4	5	6
τ. ιισθανόσαστε πογοήτευση	1	2	3	4	5	6

:αι μελαγχολία						
. \ισθανόσαστε ξάντληση	1	2	3	4	5	6
ι. Ήσαστε υτυχισμένος/η	1	2	3	4	5	6
). \ισθανόσαστε :ούραση	1	2	3	4	5	6

4. Τις τελευταίες 4 εβδομάδες, η κατάσταση της σωματικής σας υγείας ή κάποια συναισθηματικά προβλήματα για πόσο χρονικό διάστημα επηρέασαν τις κοινωνικές σας δραστηριότητες (π.χ επισκέψεις σε φίλους, συγγενείς);

	(βάλτε έναν κύκλο)
Συνεχώς	1
Το μεγαλύτερο διάστημα	2
Μάλλον μικρό διάστημα	3
Για μικρό διάστημα	4
Καθόλου	5

APPENDIX 13

Center for Epidemiologic Studies Depression Scale (CES-D)

Below is a list of some of the ways you may have felt or behaved. Please indicate how often you have felt this way during the last week by checking the appropriate box for each question.

	Rarely or none of the time (less than 1 day)	**Some or a little of the time (1-2 days)**	**Occasionally Or a Amount of time (3-4 days)**	**All the time (5-7 days)**
I was bother by things that usually do not bother me				
I did not feel like eating; my appetite was poor				
I felt that I could not shake off the blues even with help from my family				
I felt that I was just as good as other people				
I had trouble keeping my mind on what I was doing				
I felt depressed				
I felt that everything I did was an effort				
I felt hopeful about the future				
I thought my life had been a failure				
I felt fearful				

My sleep was restless				
was happy				
talked less than sual				
felt lonely				
eople were nfriendly				
enjoyed life				
had crying spells				
felt sad				
felt that people isliked me				
could not "get oing"				

APPENDIX14

MODERN GREEK TRANSLATION OF CES-D

CENTER FOR EPIDEMIOLOGICAL STUDIES DEPRESSION SCALE (CES-D)

Παρακαλώ συμπληρώστε ένα Χ στο τετράγωνο που θεωρείτε ότι ανταποκρίνεται στο πώς αισθανόσασταν κατά τη διάρκεια της περασμένης εβδομάδας (και όχι μόνο πώς αισθάνεστε αυτή τη στιγμή).

	Σπάνια ή καθόλου (λιγότερο από 1 ημέρα)	Λίγες φορές (1-2 ημέρες)	Μερικές φορές (3-4 ημέρες)	Συνεχώς (5-7 ημέρες)
1. Με ενοχλούσαν πράγματα που συνήθως δεν με ενοχλούν.				
2. Δεν είχα διάθεση να φάω. Η όρεξή μου ήταν κακή.				
3. Αισθανόμουν ότι δεν θα μπορούσα να ξεφύγω από τις μαύρες μου, ακόμα ούτε και με τη βοήθεια της οικογένειάς μου ή των φίλων μου.				
4. Αισθανόμουν ότι είμαι το ίδιο καλά όπως οι άλλοι άνθρωποι.				
5. Είχα πρόβλημα στο να κρατήσω το μυαλό μου συγκεντρωμένο σ' αυτό που έκανα.				
6. Αισθανόμουν κατάθλιψη.				
7. Αισθανόμουν ότι οτιδήποτε έκανα απαιτούσε μεγάλη προσπάθεια.				
8. Αισθανόμουν γεμάτος/ η ελπίδα για το μέλλον.				
9. Πίστευα ότι η ζωή μου ολόκληρη ήταν μια αποτυχία.				

10. Αισθανόμουν γεμάτος/ η φόβο.				
11 . 0 ύπνος μου ήταν ανήσυχος.				
12. Ήμουν χαρούμενος/ η.				
13. Μιλούσα λιγότερο από το συνηθισμένο.				
14. Αισθανόμουν μοναξιά.				
15. Οι άνθρωποι δεν ήταν φιλικοί μαζί μου.				
16. Απολάμβανα τη ζωή.				
17. Ξεσπούσα σε κλάμα.				
18. Αισθανόμουν λυπημένος/ η.				
19. Ένιωθα ότι οι άλλοι με αντιπαθούσαν.				
20. Δεν μπορούσα να τα καταφέρω, να ξεκινήσω να κάνω πράγματα.				

APPENDIX 15

ENRICH

Enriching & Nurturing Relationship Issues, Communication & Happiness

COMMUNICATION SCALE WITH PARTNER

The questions below related with your relationship with your familiar social environment. Please replay to the next question putting a mark X to the relevant box.

Do you live with a partner?

YES □

NO □

If your answer is YES please circle one number on each line of the questions below. If your answer is NO please continue to the next page.

	Strongly Disagree	**Moderately Disagree**	**Neither Agree Nor Disagree**	**Moderately Agree**	**Strongly Agree**
1. It is very easy for me to express all my true feelings to my partner.	1	2	3	4	5

2. When we have a problem my partner often gives me the silent treatment	1	2	3	4	5
3. My partner sometimes makes comments which put me down	1	2	3	4	5
4. I am sometimes afraid to ask my partner for what I want	1	2	3	4	5
5. I whish my partner was more willing to share his/her feelings with me	1	2	3	4	5
6.Sometimes I have trouble believing everything my partner tells me	1	2	3	4	5
7. Often do not tell my partner	1	2	3	4	5

what I am feeling because he/she should already know					
8. I am very satisfied with how my partner and I talk with each other	1	2	3	4	5
9. I do not always share negative feelings I have about my partner because I am afraid he/ she will get angry	1	2	3	4	5
10. My partner is always a good listner	1	2	3	4	5

COMMUNICATION SCALE WITH AN IMPORTANT PERSON

Is there someone in your life (friend, family membership) with whom you can share your feelings? Please put a mark X to the relevant box.

YES □

NO □

If your answer is YES, please circle one number on each line of the questions below.

If your answer is NO please put a mark X next to the box □

	Strongly Disagree	**Moderately Disagree**	**Neither Agree Nor Disagree**	**Moderately Agree**	**Strongly Agree**
1. It is very easy for me to express all my true feelings to this person.	I	2	3	4	5
2. When we have a problem this person often gives me the silent treatment.	I	2	3	4	5
3. This person sometimes	I	2	3	4	5

makes comments which put me down.					
4. I am sometimes afraid to ask this person for what I want.	1	2	3	4	5
5. I whish this person was more willing to share his/her feelings with me.	1	2	3	4	5
6. Sometimes I have trouble believing everything this person tells me.	1	2	3	4	5
7. I often do not tell to this person what I am feeling because he/she should already know.	1	2	3	4	5
8. I am very satisfied with	1	2	3	4	5

how this person and I talk with each other.					
9. I do not always share negative feelings I have about this person because I am afraid he/ she will get angry.	1	2	3	4	5
10. This person is always a good listner	1	2	3	4	5

APPENDIX 16

MODERN GREEK TRANSLATION OF THE ENRICHING & NURTURING RELATIONSHIP ISSUES, COMMUNICATION & HAPPINESS (ENRICH) COMMUNICATION SCALE WITH PARTNER

ΕΡΩΤΗΜΑΤΟΛΟΓΙΟ ΕΠΙΚΟΙΝΩΝΙΑΣ ΜΕ ΤΟ/ΤΗ ΣΥΝΤΡΟΦΟ

Οι παρακάτω ερωτήσεις αφορούν την σχέση σας με το στενό σας κοινωνικό περιβάλλον. Παρακαλώ απαντήστε την επόμενη ερώτηση σημειώνοντας με Χ το ανάλογο κουτάκι.

Ζείτε με κάποιο σύντροφο;

ΝΑΙ □

ΟΧΙ □

Εάν ΝΑΙ παρακαλώ απαντήστε στις παρακάτω ερωτήσεις βάζοντας σε κύκλο έναν αριθμό σε κάθε σειρά. Εάν ΟΧΙ, συνεχίστε στην επόμενη σελίδα.

	Διαφωνώ απόλυτα	**Διαφωνώ μέτρια**	**Ούτε συμφωνώ ούτε διαφωνώ**	**Συμφωνώ μέτρια**	**Συμφωνώ απόλυτα**
1. Εκφράζω με μεγάλη ευκολία τα αληθινά μου συναισθήματα	1	2	3	4	5

στο/στη σύντροφό μου.					
2. Όταν αντιμετωπίζουμε ένα πρόβλημα ο/η σύντροφός μου συχνά αδιαφορεί.	1	2	3	4	5
3. Τα σχόλια του/της συντρόφου μου μερικές φορές με κάνουν να νοιώθω μειωνεκτικά.	1	2	3	4	5
4. Μερικές φορές φοβάμαι να ζητήσω από τον/την σύντροφό μου κάτι που θέλω.	1	2	3	4	5
5. Θα ευχόμουν ο/η σύντροφός μου να ήταν περισσότερο πρόθυμος/η να μοιραστεί τα συναισθήματά του/της μαζί μου.	1	2	3	4	5
6.Μερικές φορές δυσκολεύομαι να	1	2	3	4	5

πιστέψω πράγματα που ο/η σύντροφός μου λέει.					
7.Συχά δεν λέω στο/στη σύντροφό μου το πώς αισθάνομαι επειδή θεωρώ ότι θα έπρεπε ήδη να γνωρίζει τα συναισθήματά μου.	1	2	3	4	5
8. Είμαι πολύ ικανοποιημένος/η με τον τρόπο με τον οποίο συζητάμε μεταξύ μας.	1	2	3	4	5
9. Δεν μοιράζομαι ποτέ τα αρνητικά συναισθήματα που τρέφω για τον/την σύντροφό μου επειδή φοβάμαι ότι θα θυμώσει.	1	2	3	4	5
10.Ο/Η σύντροφός μου είναι πάντα διαθέσιμος να με ακούσει.	1	2	3	4	5

ΕΡΩΤΗΜΑΤΟΛΟΓΙΟ ΕΠΙΚΟΙΝΩΝΙΑΣ ΜΕ ΣΗΜΑΝΤΙΚΟ ΠΡΟΣΩΠΟ

Οι παρακάτω ερωτήσεις αφορούν την σχέση σας με το στενό σας κοινωνικό περιβάλλον. Παρακαλώ απαντήστε την επόμενη ερώτηση σημειώνοντας με Χ το ανάλογο κουτάκι.

Υπάρχει κάποιος στη ζωή σας (φίλος, φίλη ή μέλος από το οικογενειακό σας περιβάλλον) με τον οποίο μπορείτε να μοιράζεστε μαζί του τα συναισθήματά σας;

ΝΑΙ □

ΟΧΙ □

Εάν ΝΑΙ παρακαλώ απαντήστε στις παρακάτω ερωτήσεις βάζοντας σε κύκλο έναν αριθμό σε κάθε σειρά. Εάν ΟΧΙ, σημειώστε με ένα Χ το διπλανό κουτάκι □

	Διαφωνώ απόλυτα	**Διαφωνώ μέτρια**	**Ούτε συμφωνώ ούτε διαφωνώ**	**Συμφωνώ μέτρια**	**Συμφωνώ απόλυτα**
1. Εκφράζω με μεγάλη ευκολία τα αληθινά μου συναισθήματα στο άτομο αυτό.	1	2	3	4	5
2. Όταν αντιμετωπίζουμε ένα	1	2	3	4	5

πρόβλημα το άτομο αυτό συχνά αδιαφορεί.					
3. Τα σχόλια του ατόμου αυτού μου μερικές φορές με κάνουν να νοιώθω μειονεκτικά.	1	2	3	4	5
4. Μερικές φορές φοβάμαι να ζητήσω από το άτομο αυτό κάτι που θέλω.	1	2	3	4	5
5. Θα ευχόμουν το άτομο αυτό να ήταν περισσότερο πρόθυμος/η να μοιραστεί τα συναισθήματά του/της μαζί μου.	1	2	3	4	5
6.Μερικές φορές δυσκολεύομαι να πιστέψω πράγματα που το άτομο αυτό λέει.	1	2	3	4	5
7.Συχά δεν λέω στο άτομο αυτό το πώς					

αισθάνομαι επειδή θεωρώ ότι θα έπρεπε ήδη να γνωρίζει τα συναισθήματά μου.	1	2	3	4	5
8. Είμαι πολύ ικανοποιημένος/η με τον τρόπο με τον οποίο συζητάμε μεταξύ μας.	1	2	3	4	5
9. Δεν μοιράζομαι ποτέ τα αρνητικά συναισθήματα που τρέφω για το άτομο αυτό επειδή φοβάμαι ότι θα θυμώσει.	1	2	3	4	5
10. Το άτομο αυτό είναι πάντα διαθέσιμος να με ακούσει.	1	2	3	4	5

APPENDIX 17

Granted permission for undertaking the study research from the relevant authority of "Oi Agioi Anargyroi" hospital.

HELLENIC REPUBLIC

B' SANITATION REGION OF ATTIKI

"OI AGIOI ANARGYROI" GENERAL HOSPITAL (G.O.N.K.)

34-36 ELEUTHERIOU VENIZELOU

METAMORFOSI TK 144 52

I September 2007

CERTIFICATE

It is certified that Ms Georgia Doga within the framework of her postgraduate studies at the University of Wales Swansea submitted to our Department a proposal for a research program with the title: "Evaluation of the Quality of Living of the Greek patients suffering from intestinal and rectal Ca".

The proposal was accepted by the Director of the Hospitalization Service of the Hospital in October 2002.

The research program commenced in November 2002 and was completed in February 2004.

The Director of the Hospitalization Service

B. Vrysanthou

Stamp - Hospital Stamp

TRUE TRANSLATION FROM ATTACHED GK ORIGINAL

THE TRANSLATOR M. DEPIAN 18.10.2007

REPUBLIQUE HELLENIQUE
MINISTERE des AFFAIRES ETRANGERES
Vu pour légalisation de la signature ci-dessus
du Traducteur du Ministère des Affaires
Etrangères ayant traduit le texte ci-annexé.

Athènes le, 24 OKT. 2007

PAR DELEGATION DU MINISTRE
Le Directeur p.m.

ELENI ARGYROU
Secrétaire

APPENDIX 18

Granted permission for undertaking the study research from the relevant authority of "Henri Dunant" hospital.

"HENRI DUNANT" HOSPITAL

107 MESOGEION ST.

115 26 ATHENS

TEL: 210 69 72 000

16 January 2003

Ms Georgia Doga within the framework of her postgraduate studies at the University of Wales Swansea submitted to our Department a proposal for a research program with the title: "Evaluation of the Quality of Living of the Greek patients suffering from intestinal and rectal Ca".

The Director of the A' Oncology Department Mr. G. Stathopoulos accepts the proposal and allows Ms Doga to proceed with the research, the use of the files of the Department's patients and communication with them. The written consent by the patients for their participation in the research as well as a detailed explanation given in writing to the patients explaining the objects and the manner in which the research will take place are judged as fully necessary.

George Stathopoulos MD

Director

A' Oncology Pathological Department

Stamp GEORGIOS P. STATHOPOULOS

2a SEMITELOU STREET 115 26 ATHENS

TRUE TRANSLATION FROM ATTACHED GK ORIGINAL

THE TRANSLATOR M. DEPIAN 19.10.2007

LENIQUE
ETRANGERES
Vu pour légalisation de la signature ci-dessus
du Traducteur du Ministère des Affaires
Etrangères ayant traduit le texte ci-annexé,

Athènes, le 24 OCT. 2007

PAR DELEGATION DU MINISTRE
Le Directeur p.m.