

Quality of Life versus Length of Life:  
Are Cancer Patients' Preferences  
Stable Over Time?

Claire Paton

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## Abstract

**Background:** Balancing treatment-related gains and losses with respect to quality of life (QoL) and length of life (LoL) is common in cancer. Little is known about patient preferences for QoL versus LoL and preference stability in the setting of adjuvant therapy. An appropriate assessment tool could inform both patient and clinician.

**Objectives:** *Primary* – to describe the distribution and stability of preferences for QoL versus LoL in early cancer, using scores obtained on the Quality Quantity Questionnaire (QQQ). *Secondary* –to determine concurrent scores on three other questionnaires to inform the interpretation of the QQQ and to test the validity of the QQQ. To examine the association between sociodemographic variables, type of cancer and preferences for QoL versus LoL. To trial the QQQ with non-metastatic cancer patients, and to discuss possible cultural influences in relation to studies from different countries. To further develop the Daily Time Trade Off (TTO) instrument, and to trial it with non-metastatic patients.

**Design:** an observational, prospective, cohort study. Assessment following diagnosis and approximately 4 months later.

**Setting:** Dunedin Hospital, New Zealand.

**Participants:** *Baseline* - 44 adult patients (70% participation rate) receiving either adjuvant chemotherapy for breast (n=15) or bowel (n=14) cancer, or radiotherapy for prostate (n=15) cancer (mean age, 57 [SD, 12.1] years). 21 men, 23 women. *Follow-up* – 39 patients (breast n=13, bowel n=11, prostate n=15) (mean age, 56 [SD, 12.0] years). 20 men, 19 women.

**Measurements:** The QQQ questionnaire, supplemented with the Functional Assessment of Cancer Therapy-General (FACT-G), Daily Time Trade-off (TTO), EuroQol (EQ-5D), and a socio-demographic checklist.

**Results:** *Primary* – at baseline 75% of adjuvant patients did not report a clear preference for QoL versus LoL; 20% preferring LoL (n=9), 5% preferring QoL (n=2). There was a significant association between baseline and follow-up scores ( $r=0.84$ ,  $n=39$ ,  $p<0.001$ ). There was no significant difference in QQQ scores from baseline (mean 15.9, SD 6.3) to follow-up (mean 16.8, SD 5.6),  $p=0.093$ . With an estimated increase of 0.95, clinically significant changes could not be ruled out. Exploratory subgroup analyses showed significant positive changes for women (baseline mean 16.4, SD 5.5; follow-up mean 17.9, SD 5.1;  $p=0.029$ ), and for people with a degree (baseline mean 15.2, SD 6.3; follow-up mean 17.2, SD 6.9;  $p=0.010$ ). *Secondary* –No significant associations between socio-demographic variables, type of cancer, and baseline QQQ score. No significant associations between the QQQ and the FACT-G, TTO or EQ-5D.

**Conclusions:** Most adjuvant patients do not express a clear preference for QoL versus LoL. A small minority do, so assuming an individual's preference is inappropriate. Results indicate good relative and absolute stability of preference using the QQQ, although there may be an increase in preference for QoL for women and people with a degree. Other socio-demographic variables, cancer type and reported QoL may not significantly influence preference. Future studies may favour the Daily TTO over other utility measures, given its acceptability to patients. The reliability and validity of the QQQ have been enhanced by this study.

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This piece of research depended, to a large extent, on the willingness of oncology patients to participate. The men and women who consented to take part in both the pilot and main studies, were all outpatients at Dunedin Hospital, and had been diagnosed with either breast, bowel or prostate cancer. As this was a longitudinal study, it was a privilege to be able to meet with participants on more than one occasion, and to be updated on “where things are at”. Their willingness to contribute to the study is much appreciated and their stories of how they were coping, of how receiving a diagnosis of cancer had altered their values and their view on life, I will long remember. Not only have they made a valued contribution to a study, but they have also given inspiration at the personal level. I wish them all the very best for the future.

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# Chapter One: Introduction

A diagnosis of cancer usually precipitates a journey of decision-making. Each journey is unique. However where treatment is available, some fundamental decisions are typically required following the diagnosis. For example, “Do I wish to pursue conventional medical treatment?”, “Is there an available treatment that I do not want to have?”, “Am I ready to start treatment yet?”.

There are many factors that can impinge on cancer treatment decision-making. These include the anticipated outcome of treatment; the influence of health professionals; opinions or pressure from one’s partner, family members or friends; and the age or stage of life of the person with cancer. Typically there is a weighing up of the relative importance of such factors before any decision to proceed with treatment is made.

Given that cancer may shorten the lifespan of an individual, it is only natural that questions about the likelihood of cure, or the effect of treatment on length of life (LoL), are usually the immediate focus when a person is first diagnosed. Another frequent area of concern is the impact of treatment or disease on quality of life (QoL).

## **1.1 Quality of Life and Cancer**

### **1.1.1 Background**

Although most people in the Western world are familiar with the term QoL, it is a very general concept meaning different things to different people. In health care it is often referred to as health-related quality of life (HRQoL). Despite this attempt to focus attention on those aspects of QoL, which are considered to be important in clinical medicine or health research, the concept remains loosely defined. However most clinicians and researchers will agree that QoL encompasses functioning in physical, psychological, occupational and social domains;

and that it should be evaluated with reference to the patient (Fayers & Machin, 2007; O'Connor, 2004).

Quality of life assessment has become one of the main ways in which the outcomes of health programmes are measured. It is used increasingly to assess the impact of clinical therapies and the effectiveness of health programmes. Underlying all of this is the recognition that patients have their own view of their health, which may not mirror the perceptions of their healthcare professionals, friends and relatives (O'Connor, 2004).

Quality of life assessments fall broadly into two categories: generic and disease-specific. The former allow for standardized QoL assessment across diseases and between interventions. The latter focus on those aspects of QoL that are most affected by a particular illness. Each approach has its own set of advantages and disadvantages (Guyatt, Feeney & Patrick, 1993).

### **1.1.2 Quality of Life Assessment of People with Cancer**

Cancer is one area of medicine that is particularly concerned with QoL issues. Survival time (or LoL) was historically regarded as the benchmark of cancer treatment effectiveness. With the development of QoL questionnaires, it became possible to examine the quality of survival alongside duration. This opened the way for both benefits and negative effects of treatment to be assessed from the perspective of the patient in one-off, short-term evaluations. It has also paved the way for longitudinal assessment of patient responses over time (Cella & Bonomi, 1995).

These days there are many different types of QoL questionnaires used in studies of people with cancer. Global, cancer-specific, and treatment-specific assessments can be made, using well-defined domains. The focus of each piece of research determines which type of assessment(s) are employed (Varricchio, 2006).

## ***1.2 Length of Life and Cancer***

One of the reasons why many people are afraid of cancer is because it is usually regarded as being a life-threatening disease. When cancer cannot be cured, the natural progression of the disease inevitably shortens a person's lifespan, and sometimes very quickly. When cure of cancer is the goal, some patients find themselves in the position of having to decide whether or not to undergo adjuvant chemotherapy or radiotherapy in addition to surgery. The adjuvant therapy further reduces the chance of cancer recurring by eliminating any microscopic, residual cancer cells (i.e. it helps to maximise LoL). However, only a small proportion of patients will benefit. Very little research has been conducted exploring the preferences and attitudes of patients in this situation (Grimison & Stockler, 2007; Knobf, 2006).

## ***1.3 Quality of Life versus Length of Life and Cancer Treatment***

### **1.3.1 Background**

We know that cancer treatments often have unpleasant side effects that can impair quality of life. We also know that appropriate treatment can prolong survival. Therefore when people with cancer are deciding whether or not to have a particular treatment, they often have to weigh up the expected benefits of therapy against the possible side effects. This may involve weighing quality of life against length of life or chance of cure (Stigglebout, de Haes, Kiebert, et al., 1996).

### **1.3.2 Cancer Patients' Preferences for Quality of Life versus Length of Life**

Nowadays oncologists recognise the importance of the patients' perspective regarding the aims of treatment, and in weighing the benefits and side effects of available therapies. Patients vary in their preferences. Some will say they want to maximise quality, while others prefer to prolong survival even if it involves undergoing treatments that severely impair quality of life. However, there is no real assistance given to help patients with the weighing up process. Furthermore, providing this sort of help is not an easy task. Consultants can help by providing information about such areas as the likely side effects of treatments or the

chances of success based on previous clinical findings. Counsellors may help by listening to the expression of patient concerns, but they cannot be prescriptive regarding treatment decision-making. Having an assessment tool (such as a questionnaire) that could help both patient and clinician weigh up the competing factors involved would be of benefit to both parties (Stiggelbout, et al., 1996).

### **1.3.3 Stability of Patient Preferences for Quality versus Quantity**

Very little is known about the stability over time of patients' attitudes towards quality versus quantity (Stiggelbout & de Haes, 2001). Furthermore, very few empirical studies have investigated which factors influence the process of weighing up quality versus quantity. To date, the clearest indication of preference has been the age of the patient, with older people favouring quality of life. Since the 1980's several authors have called for more extensive study of both the stability of patient attitudes over time, and the factors influencing preferences (Stiggelbout, et al., 1996; Voogt, van der Heide, Rietjens, et al., 2005). Descriptive longitudinal research is therefore required not only to lay the foundation for a better understanding of the stability of preferences and the factors influencing attitudes, but also to assist oncologists as they guide their patients through the treatment decision-making process in the clinical setting. It is possible that this type of research may promote changing strategies during the treatment process.

### **1.3.4 Practical Value**

As implied from the discussion above, cancer treatment decision-making typically involves input from a number of sources. Broadly speaking the two main sources of input will be health professionals (notably oncologists and probably also the patient's general practitioner), and friends or family of the person diagnosed with cancer. It is a lay expectation that health professionals will provide their patients with a picture of prognosis and treatment options that is based on medical evidence (i.e. factual information). In contrast, the desire to accommodate the perspectives of family and friends indicates a willingness to take into consideration judgments that may be strongly influenced by values (e.g. familial, cultural or spiritual). One factor that appears to be often overlooked in the decision-making process is how the perceptions of doctors and patients (and indeed society as a whole) may differ regarding the benefit or value of treatment. Oncologists routinely deal with patients who are facing serious

situations where it is not unusual to recommend therapies that offer only modest survival gains (measured in weeks or months rather than years). Most people receiving a first-time diagnosis of cancer have not been exposed to this type of situation, and therefore approach decision-making with a completely different frame of reference or mind-set. As people adjust to living with cancer, their attitudes and preferences may or may not remain the same over time – yet they may be reluctant to suggest change in treatment strategy (Zafar, Alexander, Weinfurt, et al., 2009).

Hence the complexity of factors impinging on cancer treatment decision-making highlights the need for a clinical assessment tool that could be used repeatedly along the cancer trajectory to: 1) give patients some clarity regarding their attitudes toward QoL versus LoL 2) provide doctors with a better understanding of their patients' attitudes and 3) give both parties an indication of changing attitudes over time.

#### **1.4 Aims of the Study**

The current study is a longitudinal, descriptive project involving a sample of New Zealand adult patients with early cancer receiving either adjuvant chemotherapy for bowel or breast cancer, or radiotherapy for prostate cancer at Dunedin Hospital. All treatment is being given with curative intent.

Our primary aims are 1) to describe the distribution of preferences for quality of life versus length of life in patients with recently diagnosed early stage cancer, and 2) to measure the stability of patients' preferences for quality of life versus length of life as a treatment goal in early cancer, using the Quality Quantity Questionnaire (QQQ) (Stiggelbout, et al., 1996).

The secondary aims are 1) to determine concurrent scores on the FACT-G, EQ-5D and Daily TTO scales to inform the interpretation of the QQQ and to test the validity of the QQQ, 2) to examine the association between socio-demographic variables and type of cancer, and attitudes toward treatment goals as measured by the QQQ, 3) to trial the QQQ with patients who have non-metastatic disease, and to discuss cultural influences in relation to existing oncological Dutch studies that have included the QQQ (Stiggelbout, et al., 1996; Voogt, et al., 2005), and 4) to further develop the Daily TTO, and trial it with patients who have non-metastatic disease.

Given the ethnic composition of the sample, this study will predominantly describe the attitudes and preferences of New Zealand Europeans and therefore study findings might not be able to be generalised to other cultures.

## Chapter Two: Review of Literature

*Few words inspire fear like the 'c' word – 'cancer'. No longer considered the death sentence it once was, it's a diagnosis that nevertheless manages to take the breath away and frighten even the most stalwart amongst us (Saavedra-Duff, 2008, p. 44).*

The anxiety that accompanies a diagnosis of cancer often hinders the ability of individuals to fully or to accurately comprehend medical details (Siteman Cancer Center, 2006). Treatment decisions are typically based on quantitative factors and probabilistic concepts, which can be difficult for many people to grasp and internalise, even under conditions of normal health and well-being (Langer, 2001). Nonetheless, it is during this challenging initial phase of the cancer journey that important decisions regarding treatment preferences are usually made.

From the oncologist's perspective, key factors in determining treatment options are stage of disease, the age of the patient, and comorbid illnesses (Zafar, et al., 2009). As far as stage of disease is concerned, whether or not the cancer has metastasised (or spread beyond the primary site) is of particular significance, because cancers at this stage are generally harder to treat and have a worse prognosis than early stage. This study involves only people with early stage cancer. Therefore discussion in the literature review focusses mainly on research involving patients with non-metastatic disease.

From a lay perspective, there are many variables that can influence how people with cancer make decisions regarding treatment. These include their preferences for treatment, quality of life, role responsibilities, and their degree of fear of uncertainty (Zafar, et al., 2009).

Numerous studies have measured patient preferences for adjuvant treatment in cancer. Several of these studies have reported that people with cancer are willing to undergo adjuvant chemotherapy or radiotherapy for very small benefit (Yellen & Cella, 1995; Ravdin, Siminoff & Harvey, 1998) or even no benefit at all (Palda, Llewellyn-Thomas, Mackenzie, et al., 1997; Jansen, Kievit, Nooij, et al., 2001). Given the emphasis nowadays on patient autonomy and shared decision-making, it is important for clinicians to be able to elicit and understand the preferences of patients regarding treatment (Jansen, Otten & Stiggelbout, 2004; Zafar, et al., 2009).

During the complex treatment decision-making process, two key considerations are the effect of therapy on length of life (LoL) and on quality of life (QoL). Sometimes the side effects associated with life-prolonging therapies are such that a weighing up of the relative importance of quality versus quantity is required. It is a common lay perception that the most important consideration in treatment decision-making will be QoL. This assumption may or may not be correct. Although QoL is likely to be a very important consideration, it is only one component of treatment decision-making. Furthermore very little is known about the stability of the weighting attached to QoL and LoL over time, or how preferences evolve as patients experience the realities of therapy. A greater understanding of this is likely to be helpful to clinicians (Zafar, et al., 2009).

‘Treatment’ can be broadly classified into two groups: mainstream medical therapy and alternative (or complementary) therapies. This study focusses on conventional medical treatment. The four main medical therapies are chemotherapy, radiotherapy, biological therapy (hormone therapy and immunotherapy), and surgery. For the purposes of this study the term ‘treatment decision-making’ refers to both the choice of therapy and the expectations surrounding treatment.

Part one and part two of this review describes the significance of QoL and LoL respectively for cancer treatment decision-making. Part three provides an overview of the factors that influence patient preferences in cancer treatment decisions. Part four describes the ways in which QoL is assessed for cancer treatment decision-making. Part five explores in greater depth the significance of QoL and LoL for treatment choices.

## ***2.1 The Significance of QoL for Cancer Treatment Decision-making***

Nowadays, because of increasing improvements in cancer therapy, it is generally recognised that “studying quality of life for any cancer, for any anatomical site and for either [sex] is... highly relevant” (Montazeri, 2008, p. 24). Whilst acknowledging the importance of the QoL literature as it relates to cancer per se, this review focusses on QoL studies involving patients with non-metastatic breast, bowel and prostate cancers. An overview will be provided

describing how therapy for each of these cancers can affect QoL both throughout treatment and in the long-term.

### **2.1.1 QoL and Treatment for Breast Cancer**

Of all QoL studies in patients with cancer, breast cancer has received the most attention. The psychosocial concerns of women with this disease have been the focus of numerous studies since the early-mid 1970s. Three key reasons for this have been identified. Firstly, the number of women being diagnosed with breast cancer worldwide is increasing, with over 1.1 million being diagnosed annually. It is the most common cancer amongst New Zealand women. Secondly, due to medical advances survivors are now living longer. Thirdly, breast cancer can have a very significant impact upon women's identities and self-esteem (Perry, Kowalski & Chang, 2007; Montazeri, 2008).

Breast cancer may be treated by surgery, chemotherapy, radiotherapy and hormone therapy. The choice of treatment(s) depends on the type, size and extent of cancer as well as the general health, age and personal choice of the patient. The initial treatment is usually surgery on the breast and, more often than not, on the lymph glands in the armpit. Side effects of surgery may include wound infection, bruising and hematoma, pain, cording (pain like a tight cord running down from the armpit to the back of the hand), reduced sensitivity of the inner side of the upper arm should nerve damage occur, fluid retention and lymphoedema.

In early breast cancer, radiotherapy is frequently administered in conjunction with breast-conserving surgery. Side effects of radiotherapy can include fatigue, reddening of the skin, and small changes in the size or shape of the breast.

Adjuvant chemotherapy is offered to some women with early breast cancer as an additional treatment to surgery and radiotherapy. The side effects of chemotherapy vary considerably. During adjuvant treatment women may experience fatigue, a general sense of 'unwellness', cognitive dysfunction, nausea and vomiting, thinning or loss of hair, and changes in sexual functioning. Menstruation may cease, and may not recommence following treatment if a woman is perimenopausal.

Hormone treatment may also be offered to some women with early stage breast cancer to lower the chances of the cancer recurring (Kayl & Meyers, 2006; Cancer Society of New

Zealand, 2003). The side effects of hormone therapy include “temporary preservation of menses, reversible amenorrhea, irregular menses (perimenopause), or irreversible amenorrhea (ovarian failure – menopause)” (Knobf, 2006). In a review of randomized clinical trials of patients receiving adjuvant chemotherapy and hormonal therapy for early-stage cancer, Grimison and Stockler demonstrated that the long-term effects of chemotherapy-induced menopause and hormonal therapy on QoL were not well recognised. Vasomotor symptoms and altered sexual function were prevalent, distressing, and inadequately treated (Grimison and Stockler, 2007; Montazeri, 2008).

With respect to QoL concerns, it is important to note that the breast cancer experiences of women under the age of 50 differ from those of older women. Studies have shown that younger women have greater psychological distress, higher levels of anxiety, more unmet needs, and greater concern about self-image, work, and finances. A key issue is having to cope with menopause at an unusually early age (Knobf, 2006; Carrizosa & Carey, 2005).

Assessing QoL in women with breast cancer is not straight forward. This is because of the complexity of the disease and the diverse characteristics of the patients involved. No one instrument can adequately measure outcomes across all phases of care. A 2007 review of breast cancer outcomes literature identified 21 QoL instruments as being the most useful. Of these 16 were designed to be used across the spectrum of cancers, with the remainder specific to breast cancer (Perry, et al., 2007).

### **2.1.2 QoL and Treatment for Bowel Cancer**

Relative to breast cancer the impact on QoL of bowel cancer is under-researched, with the earliest studies emerging during the late 1970’s (Sharma, Walker, Sharp, et al., 2007). The most common treatment for all stages of rectal cancer is surgery. After the cancer is removed, the surgeon will either do an anastomosis (whereby healthy remaining tissue is sewn together for restored bowel continuity), or make a stoma (i.e. an opening) from the rectum to the outside of the body. A bag is then placed around the stoma to collect waste. This latter procedure, called a colostomy, is sometimes only needed until the rectum has healed and it can then be reversed. Neo-adjuvant chemotherapy or radiotherapy is sometimes given before surgery to shrink the tumour, make surgery easier, or decrease problems with bowel control. Adjuvant chemotherapy or radiotherapy may be administered after surgery to increase the chances of cure (National Cancer Institute, 2008).

The side effects of surgery for bowel cancer can include anastomotic leakage and genitourinary impairment (which may be permanent). Chemotherapy side effects may include those described above for breast cancer and may, depending on the specific drugs used, cause reddening and soreness of the hands and feet; skin rashes and sensitivity of skin to sunlight; sweating; abdominal pain and diarrhoea; and numbness and tingling of the hands, feet, or lips. Radiotherapy for bowel cancer may cause diarrhoea, nausea, tiredness, sore skin, the need to pass urine more often, loss of fertility (for both men and women), leaking of urine, early menopause and sexual difficulties. Most side effects disappear over time, although some (e.g. incontinence, diarrhoea, narrowing of the vagina) may be long-term or permanent. (Fisher & Daniels, 2006; Cancer Research UK, 2008).

Clearly the above-described side effects will impair QoL in varying degrees. It is important to note that patients having sphincter-preserving surgery may experience different side effects from stoma patients. Traditionally it was thought that QoL was poorer for stoma patients. However a 2005 systematic review by the Cochrane Cancer Collaborative concluded that no apparent differences in QoL could be established when stoma patients were compared with non-stoma patients (Pachler & Wille-Jorgensen, 2005. Updated 2007). “Good function from a permanent stoma may be better than bad function from a poorly functioning coloanal pouch” (Fisher & Daniels, 2006, p. 40).

### **2.1.3 QoL and Treatment for Prostate Cancer**

Of the three cancers included in this study, prostate cancer has the most limited QoL literature with assessments of patients only beginning in the early 1990s (Penson, 2007). Over the past decade there has been a dramatic increase in prostate-specific antigen (PSA) testing and prostate biopsies, which has resulted in an increase in the incidence of prostate cancer diagnosis, an increasing diagnosis-to-mortality ratio, and the detection of large numbers of small lesions. Current intensive therapies are not always appropriate for small or indolent tumours, and some treatments can have significant adverse effects on QoL (Talcott & Clark, 2005; Penson, Rossignol, Sartor, et al., 2008).

To make an informed treatment decision, men with prostate cancer” need to understand the unusually prolonged natural history of prostate cancer compared with other common tumours, make judgements about the efficacy of competing treatment alternatives in the absence of

rigorous data, appreciate the potential toxicity of treatments and estimate how it might affect them over a time period of a decade or more” (Talcott & Clark, 2005).

Common treatments include watchful waiting, surgery to remove the prostate gland (radical prostatectomy), interstitial radiotherapy (brachytherapy) and external-beam radiotherapy (EBRT), and hormonal therapy (androgen deprivation therapy, ADT). The first three treatments all cause urinary, bowel or sexual dysfunction. ADT does not cause urinary or bowel problems. The duration, frequency and severity varies among therapies, with the most frequent treatment-related dysfunction being erectile dysfunction (notably in the majority of men receiving ADT) (Talcott & Clark, 2005; Wilt, MacDonald, Rutks, et al., 2008).

Unfortunately there is a paucity of high quality evidence to guide patients and health care providers on the comparative benefits and harms of treatments for clinically localized prostate cancer, especially in men with PSA-detected disease (Wilt, et al., 2008). Furthermore it is well documented in the literature that treatment decisions are “strongly influenced by physicians’ treatment preferences that in turn pivot on the physician’s oncology specialty” (Talcott & Clark, 2005, p. 923).

As with breast and bowel cancers, QoL associated with prostate cancer has been measured using generic, cancer-specific, and prostate-cancer-specific instruments (Talcott & Clark, 2005; Dandapani & Sanda, 2008). More recent developments in the measurement of prostate cancer-specific QoL have moved beyond focussing on urinary, bowel, and sexual dysfunction to include additional psychosocial domains. For example, several studies have examined behavioural, interpersonal, and emotional adjustments associated with the side effects of treatment. There has also been the realisation that there may be long-term psychosocial effects of being involved in making decisions about treatment in the face of ambiguous data and conflicting physician recommendations (Talcott & Clark, 2005; Roth, Weinberger, & Nelson, 2008).

## ***2.2 The Significance of LoL for Cancer Treatment Decision-making***

Alongside QoL, LoL is a primary consideration during the process of treatment decision-making. As in the preceding review of the significance of QoL for cancer treatment decisions,

this section describes the implications for LoL of adjuvant therapies for people with early stage breast, bowel and prostate cancers.

Surgery for early stage breast cancer can remove all detected cancer. However undetected malignant tissue remaining in the breast and lymph nodes (or distant sites) may develop into a life-threatening recurrence if it is not treated. Adjuvant chemotherapy aims to control any remaining deposits of disease, lower the rate of recurrence, and improve long-term survival (Early Breast Cancer Trialists' Collaborative Group [EBCTCCG], 2005). A 2005 Cochrane overview of 194 randomised trials in early breast cancer concluded that adjuvant therapies which were being tested in the 1980s, and which significantly reduced 5-year recurrence rates, were subsequently associated with substantial reductions in 15-year mortality rates (EBCTG, 2005). Similarly, with operable early stage bowel cancer, fluorouracil-based adjuvant chemotherapy offers significant disease-free survival benefit, mainly by lowering the recurrence rate (Sargent, Sobrero, Grothey, et al., 2009; Gunderson, Sargent, Tepper, et al., 2004). As a general rule the adjuvant chemotherapy treatments for both types of cancer achieve an extra five to fifteen percent cure rate on top of the post-surgical chance of cure of fifty to seventy percent (D.J. Perez, personal communication, 11 April 2009).

In contrast, the situation for men with localized prostate cancer differs on several fronts. Cancer of the prostate typically occurs in older men, and it is a slow growing cancer. Therefore most men with this cancer will not die from it. Furthermore, radiotherapy for early prostate cancer improves the cure rate by approximately five percent from a baseline probability of eighty-five percent (Walsh, DeWeese & Eisenberger, 2007).

A high proportion of people with breast, bowel and prostate cancers do not achieve curative benefit from adjuvant therapies, and patients who do not benefit will have experienced an impaired QoL for no ultimate benefit. However the treatments may delay relapse. As a rule of thumb the risk of death from complications of adjuvant therapies is about 0.5 percent. Although, on a patient by patient basis, there is no way of knowing who really requires adjuvant treatment for undetectable residual cancer, oncologists generally know which categories of patients have the greatest risk and those are the groups recommended for this type of treatment. Similarly once adjuvant therapy is completed, no one really knows whether or not it has been successful – the passage of time alone yields the answer (D.J. Perez, personal communication, 11 April 2009).

## **2.3 Overview of Determinants of Patients' Preferences in Cancer Treatment Decision-making**

Many factors may influence the preferences that patients have for cancer treatment. In their 2004 review of determinants of patients' preferences for adjuvant therapy in cancer Jansen, Otten and Stigglebout evaluated 23 papers examining the relationships between determinants and preferences. Forty determinants were classified into seven categories. The categories were: treatment-related determinants, socioemographic characteristics and current QoL, clinical characteristics, time-related determinants, cognitive/affective determinants, and specialist-related determinants. They provide a useful framework for presenting the literature.

This overview of determinants summarises the findings of Jansen, et al., (2004) and additional recent research is also presented. (As our purpose is to provide background material for the current study, the reader is referred to the 2004 review for details of earlier published studies).

### **2.3.1 Treatment-Related Determinants**

Within this category, the first important determinant of patients' preferences identified by Jansen, et al., (2004) was the extent to which the treatment is beneficial (i.e. in terms of increased disease-free survival, decreased probability of recurrence, or added life-years). Studies (Simes & Coates, 2001; Kiebert, Stigglebout, Leer, et al., 1993; Zimmerman, Baldo & Molino, 2000; Palda, et al., 1997; Solomon, Pagar, Keshava, et al., 2003; Yellen & Cella, 1995; Slevin, Stubbs, Plant, et al., 1990) showed that patients were more willing to accept treatments that offered greater benefit.

A second important determinant was the degree of toxicity of treatment. In four of five studies (Yellen & Cella, 1995; Killbridge, Weeks, Sober, et al., 2001; Yellen, Cella & Leslie, 1994; Slevin, et al., 1990) patients were more accepting of adjuvant therapy when the associated toxicity was smaller. In a fifth study, (Irwin, Arnold, Whelan, et al., 1999) side effects (rather than duration of treatment) were significantly more important for patients choosing a milder chemotherapy regimen than for those opting for a more toxic (but shorter) regimen. However, while patients reported that the perceived impact of side effects on QoL

was very important, it did not distinguish between those choosing milder versus more toxic treatment regimens. This suggests that QoL is a subjective phenomenon, and is defined by what the individual patient perceives as being of greatest significance for their personal well-being (Irwin, et al., 1999).

Findings were mixed regarding the effect of having experience with side effects. Treatment scheduling and treatment efficacy were not related to treatment preference (Jansen, et al., 2004).

Studies showed that patients did not significantly alter their preferences from before to during treatment (Slevin, et al., 1990; O'Connor, Boyd, Warde, et al., 1987). Jansen, et al., (2001) reported that women undergoing chemotherapy for early stage breast cancer rated the median benefit of treatment at 1% before, during and one month after chemotherapy. However several studies reported that when the preferences of patients with treatment experience were compared with patients with no experience, the latter group was more negative in attitude (Jansen, et al., 2001; Cullen, Billingham, Cook, et al., 1996; Lindley, Vasa, Sawyer, et al., 1998; Yellen, et al., 1994). This finding is in keeping with results obtained in utility studies (Stiggelbout & de Haes, 2001).

A 2008 report by Jansen, Otten, Baas-Thijssen, et al., investigated the impact of treatment decision, experience, and the passing of time on stability of preferences with regard to adjuvant chemotherapy for early-stage breast and colorectal cancer. The authors concluded that the above-described discrepancy in treatment preferences between experienced and inexperienced patients was an effect of having made a decision to undergo therapy and was not attributable to experiencing the treatment.

### **2.3.2 Socio-demographic Characteristics and QoL as Determinants**

In the Jansen, et al., (2004) review, 7 of 10 studies (Ravdin, et al., 1998; Palda, et al., 1997; Cullen, et al., 1996; Kiebert, et al., 1993; Lindley, et al., 1998; Simes & Coates, 2001; Irwin, et al., 1999) found no evidence of a relationship between age and patients' preferences. An age effect was reported for specific patient groups in two studies (Jansen, et al., 2001; Bremnes, Anderson & Wist, 1995) and specific methods (Yellen, et al., 1994) in one study.

Furthermore neither ethnicity, sex, place of residence, income, menopausal status, having a relative with cancer, nor current quality of life were statistically significant determinants of patients' preferences. Regarding employment status, Simes and Coates (2001) and Irwin, et al., (1999) found no evidence of a relationship between employment status and preferences for adjuvant chemotherapy in women with breast cancer. Palda, et al., (1997) reported that patients in employment were more likely to forego radiotherapy.

No clear trend emerged between patients' acceptance of chemotherapy and marital status, family concerns, being a parent or the availability of childcare. Similarly, findings were mixed regarding a possible effect of living with others. Overall, with regard to family situation the most notable finding was that parents may be more accepting of adjuvant treatment when children or other dependents are living at home (Jansen, et al., 2004).

A 2004 stand-alone study investigated the effects of media information on cancer patients' opinions and feelings, and the factors influencing the decision-making process and doctor-patient communication. The authors concluded that while the media did exert a strong influence on patients' opinions and feelings, the doctor-patient relationship and the decision-making process were not subject to media influence but were related most strongly to level of education of the patient. Sex of the patient and place of residence also influenced decision-making, but to a lesser degree (Passalacqua, Caminiti, Salvagni, et al., 2004).

In the earlier 2001 review Stiggelbout and de Haes reported that when utility assessments are used to determine cancer patient preferences for treatment, the method of assessment and the framing of the questions appear to be more strongly associated with variation in preference than are clinical or socio-demographic variables (for example age, socioeconomic status and sex) (Froberg & Kane, 1989). Stiggelbout and de Haes (2001) defined utility as "the level of desirability that people associate with a particular outcome" (p. 222).

In contrast, probability trade-off scores have been significantly associated with age, with older patients being less accepting of aggressive cancer therapies than younger patients (Bremnes, et al., 1995; McQuellon, Muss, Hoffman, et al., 1995; Ludwig, Fritz, Neuda, et al., 1997; Silvestri, Pritchard & Welch, 1998; Stiggelbout & de Haes, 2001). In hypothetical scenarios, both social well-being and having children living at home was associated with higher willingness to undergo aggressive treatment (Bremnes, et al., 1995; Yellen & Cella, 1995; Stiggelbout & de Haes, 2001).

### **2.3.3 Clinical Characteristics as Determinants**

Jansen, et al., (2004) reported that patient preferences were not generally associated with type of cancer, stage of disease, lymph node status, or recurrence of cancer. One study (Palda, et al., 1997) reported that amongst women with breast cancer, those with smaller tumours were more willing to forego postlumpectomy radiotherapy. In most of these studies the preferences were typically based on hypothetical scenarios, and not the patient's current medical condition. Jansen, et al., (2004) concluded that this may explain why expressed preferences were not generally associated with clinical characteristics.

### **2.3.4 Time-related Determinants**

Similarly no effect was found for time between diagnosis and interview, time between treatment and interview, and waiting time for treatments (Jansen, et al., 2004). Two studies (Jansen, et al., 2001; Zimmerman, et al., 2000) reported no change over time in patients' preferences for adjuvant therapy. Simes and Coates (2001) investigated patient preferences for adjuvant chemotherapy in early breast cancer. They found that at second interviews (approximately 3 to 6 months after the initial interview), a larger increment in survival rate (an extra 1 to 2 percent) was required for a preference for adjuvant therapy ( $p \leq .003$ ).

### **2.3.5 Cognitive/affective Determinants**

Very few quantitative results were available regarding the influence of cognitive or affective determinants on preference. Jansen, et al., (2004) argued that until more research is conducted in these arenas, we remain unsure as to whether preferences "truly represent the patient's well-considered point of view, or whether they are the result of undesirable cognitive and emotional processes... or a tendency to follow the specialist's recommendation" (p. 3189).

### **2.3.6 Specialist-related Determinants**

In the 2004 review, several studies suggested that the specialist's recommendation for treatment was an important determinant of patients' preference for therapy. However the authors concluded that more quantitative research was needed to assess this domain.

A subsequent 2007 study by Stiggelbout, Jansen, Otten, et al., examined the importance of the opinion of significant others to adjuvant chemotherapy decision-making. In this investigation of 123 breast and colorectal cancer patients, the opinion of the treating specialist ranked as most important, with that of their partner, children, other family, friends and colleagues following. The implication of these findings was that knowledge of the opinions of significant others could assist clinicians during the treatment decision-making process.

Sommers, Beard, D'Amico, et al., (2008) examined determinants of patients' preferences for health states associated with prostate cancer, and assessed whether treatment choice is predicted by preferences or other factors. The actual treatment choices of 167 men bore little relation to their expressed preferences, but were strongly associated with clinician speciality (radiation oncology versus urology) at the time of the survey. The authors concluded that paying more attention to the variation in patients' treatment preferences and using decision-support aids may help clinicians to facilitate more individualised treatment choices for men with prostate cancer.

### **2.3.7 Summary of Determinants of Patients' Preferences**

In summary, patients are more willing to accept adjuvant treatment when it is associated with greater benefit, less toxicity, personal experience with the treatment, and having dependents (notably children) living at home. More quantitative studies are needed to assess the impact of cognitive/affective and specialist-related determinants, and larger studies are required assessing the relationships between preferences and determinants within the context of a "cognitive cost-benefit model" (Jansen, et al., 2004, p. 3181).

## **2.4 Approaches to Assessing QoL for Cancer Treatment Decision-making**

### **2.4.1 Background**

Two main approaches are used for assessing QoL in the general medical literature. These have been described as descriptive health-status measures, and valualational measures (Bosch & Hunink, 1996).

Descriptive health-status measures typically ask the respondent to provide information on the presence, intensity and frequency of physical symptoms, as well as emotional, social or functional well-being. The items are coded, and aggregated to form subscales or a global score, which reflects the characteristics of a health state. The questionnaire thereby captures a snapshot of HRQoL as perceived by the patient across a number of different domains (Bosch & Hunink, 1995; Fallowfield, 1990).

In contrast, the valualational approach requires that the respondent assign utilities or numerical values to a health state. The terms ‘preferences’, ‘utilities’, and ‘values’ are commonly used interchangeably in the literature, although some authors regard the terms as having different meanings: preference being an ‘umbrella term’ (Drummond, Sculpher, Torrance, et al., 2005), values being cardinal preferences for particular health outcomes measured under certainty, and utilities being preferences measured under uncertainty (Bosch & Hunink, 1996; Drummond, et al., 2005). Health economists have developed several scaling techniques that assign a single numerical value to a health state. The three most commonly used methods for measuring individual preferences for health outcomes are the rating scale (RS) and its variants, the time trade-off (TTO), and the standard gamble (SG) (Drummond, et al., 2005). Of these, the TTO has been shown to be more reliable and valid than the SG (Bowling, 1995).

When compared with descriptive QoL measures, an often-cited advantage of the utility approach is that because it combines morbidity, mortality and treatment side effects into a single score, concurrent consideration is given to both quality and length of life. This is usually measured in quality-adjusted life years (QALYs), which are a combination of utility measures and time (Feeny & Torrance, 1989; Weeks, 1995).

A small number of clinical studies have included both descriptive and valuations assessments, and have reported on the relationship between the two approaches. In general these studies have shown poor to moderate correlations. In a review article on the relationship between psychometric and utility-based approaches to measuring QoL, Revicki and Kaplan (1993) reported a correlation range of 0.01 to 0.6.

#### **2.4.2 Descriptive and Valuations QoL Measures in Cancer**

Descriptive QoL measures have been used in psycho-oncological studies of people with cancer since the late 1970's to describe the impact of disease and treatment. Now days such assessments have become standard practice in cancer research. They are commonly used as an endpoint for clinical trials of new therapies and have also been used increasingly as an evaluation tool for clinical decision-making (Holland, 1998; Holzner, Kemmler, Cella, et al., 2004). There is limited evidence to suggest that performing QoL assessments in the clinic improves patient satisfaction with the interview experience (Ramage & Davies, 2003). However, when clear guidelines or normative data are unavailable, clinicians and health care providers can find it difficult to interpret global QoL scores – beyond rough guidelines such as, “higher scores are preferable to lower scores” (Bosch & Hunink, 1996; Fallowfield, 1990; Gulbrandsen, Hjerstad & Wisloff, 2004; Holzner, et al., 2004; Weeks, 1995).

One of the most commonly used cancer-specific descriptive QoL instruments is the Functional Assessment of Cancer Therapy-General (FACT-G) questionnaire, which was developed by Cella, Tulsky, Gray, et al., (1993). It is the core questionnaire of the Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System and has been used extensively in North American, European and worldwide studies (Kemmler, Holzner, Kopp, et al., 1999).

Valuations QoL measures have been less widely used in oncology than descriptive measures. They have received more attention from researchers in recent years (Perez, Williams, Christensen, et al., 2001), but some authors take the view that health utilities are “underutilized” (Kramer, Bennett, Pickard, et al., 2005, p. 15).

At the level of individual patient decision-making utility assessment does have several limitations. These include the cognitive complexity of the questions asked, the reality that

patients often do not behave in accordance with expected utility theory (Stiggelbout & de Haes, 2001; Nunally & Burnstein, 1994).

## ***2.5 QoL versus LoL in Treatment Decision-making***

So far this review has sought to demonstrate that a balancing of treatment-related gains and losses with respect to QoL and LoL is very common in decision-making in oncology, and that over the last thirty years patient participation in the decision-making process has assumed increasing importance. It would seem that preferences cannot be explained solely in terms of treatment-related determinants, or clinical and patient characteristics. Furthermore the measurement of preferences, using methods such as TTO, is neither an explicit measure of the balance between QoL and LoL nor an indicator of the stability of such weightings over the course of the cancer trajectory.

Given the weaknesses of existing methods of assessing patient treatment preferences, Stiggelbout, et al., (1996) suggested that it would be useful to have an assessment tool that could be used in the research setting to measure general attitudes of patients toward the weighing up of quality of life versus length of life. A questionnaire of this nature “might provide more insight into this deliberation process and into the assignment of utilities” (p. 185). Furthermore, it could potentially be used to explore variations in attitudes between patient groups, the factors that influence the weighing up process, and to evaluate the stability of treatment preferences over time.

Accordingly they developed the Quality Quantity Questionnaire (QQQ), aimed at addressing “the attitudes of respondents toward the weighing of benefits and side effects of cancer treatment” (Stiggelbout, et al., 1996, p. 185). The QQQ is a short instrument comprising only eight questions, and is based on comments made by patients with cancer during interviews for utility assessment (Stiggelbout, Kiebert, Kievit, et al., 1994). The psychometric properties of the scale will be outlined in the methods chapter of this thesis. The QQQ has proven feasibility for use with patients with cancer in two published Dutch studies (Stiggelbout, et al., 1996; Voogt, et al., 2005) and in a recent New Zealand study (Buckingham, Perez, & Gray, 2006). Because the more recent Dutch study (Voogt, et al., 2005) examines the stability of preferences over time, it will be discussed in section 5.2 below.

### **2.5.1 Studies on Preferences of Patients with Cancer for QoL versus LoL**

The earliest Dutch study (Stiggelbout, et al., 1996) was a feasibility study for using the QQQ. It surveyed four groups of patients with cancer. The first group comprised 59 consecutive testicular cancer patients who were either currently receiving treatment or who had been treated within the previous two years. The second group consisted of 73 consecutive colorectal cancer patients who either had been diagnosed as having “incurable recurrences” (p. 186) and who were receiving treatment or were being referred for therapy, or who were in post-treatment follow-up phase. Twenty-nine women participating in a randomised controlled study of chemotherapy for breast cancer comprised the third group. The fourth group consisted of 63 outpatients in their second or third week of radiotherapy (mixed cancers).

Associations were found between age and both Q and L scores, with the association being stronger for the Q scale. The older the respondent, the more QoL appeared to be the aim of treatment. Patients who were younger, and patients who had children viewed striving for LoL as more important than pursuing QoL. The authors concluded that their results demonstrated the feasibility of using the QQQ with cancer populations, and reported that the next step in the development of the questionnaire would be to assess the test-retest reliability. Given the general nature of the questions in the QQQ, the authors suggested that it could be a useful supplement to existing preference and utility instruments.

Accordingly a New Zealand study by Buckingham, et al., (2006), examining the use of a daily version of TTO in patients with metastatic disease, incorporated the QQQ to derive attitudes toward life expectancy versus attitudes to QoL. When the data were analysed using the same methodology employed by Stiggelbout, et al., their results replicated those of the Dutch study. However, an interesting finding of the New Zealand study was that when data analysis techniques were altered (from the original principal components extraction to a principal factors extraction) the New Zealand data confirmed the Dutch authors original (but unconfirmed) hypothesis that a single factor existed, “in which preferences for quality of life and length of life are seen as extreme ends of a single continuum” (p. 7). The Dutch study had yielded two factors.

The primary aim of the New Zealand study was however, to test a new daily TTO measurement instrument. Conventional TTO measures ask patients to consider trading reduced life expectancy for improved health. This may be insensitive and potentially

threatening for patients with reduced life experiences, such as patients with metastatic or advanced cancers. The daily version instead asks patients to consider how much time they would give up each day (via extra sleep hours) for improvements in health. The main conclusion of this study was that as compared with the conventional TTO, the daily version appeared to be significantly more acceptable, and possibly also more sensitive in measuring the value attached to health states.

Given the promising results of these initial findings, further trialling of the daily TTO in studies of people with cancer was now required and thus forms a secondary goal of the current study (see section 2.6).

An adaptation of the QQQ has also been used beyond the context of cancer to assess attitudes of the Dutch general public toward striving for quality or length at the end-of-life (Rietjens, van der Heide, Voogt, et al., 2005). Statements were reworded to imply serious illness per se, rather than being cancer specific. In this study a preference for LoL was associated with people who were younger, male, had children, held religious beliefs, and who did not have a history of serious illness.

### **2.5.2 The Stability of Patients' Preferences for QoL versus LoL**

Although the value of health states stemming from treatment are well documented in the literature, less is known about the stability of patients' expectations of medical treatment across the cancer trajectory. We know that patients vary in their aims. We do not know much about the extent to which patients either maintain a preference for either QoL or LoL as a treatment goal, or fluctuate in their preferences over time. Little is known about the processes involved because few prospective longitudinal studies have been conducted. In developing the QQQ, Stiggelbout, et al., (1996) suggested that their questionnaire could be used in prospective studies "to learn whether and how patients change their attitudes when faced with the actual decisions".

Only one study has applied the QQQ in a prospective manner to address the issue of stability of patients' preferences for QoL and LoL over time. The Dutch study conducted by Voogt, et al., (2005) tracked the development of attitudes over time in a group of 128 outpatients with incurable breast, colorectal, ovarian, lung or prostate cancers. Participants were recruited within two months of being told that their cancer was "in principle, incurable" (p. 191). A

baseline assessment was followed by a 6-month and 12-month follow-up session. Patients were interviewed and completed written questionnaires that included the QQQ, along with questionnaires addressing socio-demographic variables and psychological status.

At baseline approximately one third of participants had relatively high Q scores and low L scores. The opposite was true for about another one third of the patients. The remaining one third of the participants did not indicate a clear preference for either QoL or LoL. In other words, these patients did not seem able or willing to state a preference concerning the aim of cancer therapy. Furthermore, 12 percent of the people who remained in the study for at least six months had refused a life-prolonging therapy during the initial six months of follow-up. This group was more inclined to strive for QoL than others (mean Q-score, 18.3 v 15.2 respectively;  $P \leq .01$ )

Regarding stability of preferences of treatment aims, no significant change in attitude was found 6 or 12 months after inclusion, except with patients who had a history of cancer of less than 6 months at inclusion. For this group LoL scores decreased over time (mean L-score, 14.2 at baseline v 12.9 at 6 months;  $n=36$ ;  $P=.02$ ), whereas Q-scores were stable over time (mean Q-score, 14.8 at baseline v 14.5 at 6 months;  $n=35$ ;  $P=.75$ ). The authors concluded that patients seem to prefer life-prolonging therapy shortly after diagnosis, but QoL assumes greater importance as death becomes imminent.

When associations between personal or disease characteristics of patients and their attitude toward treatment were examined, patients who were “older, more tired, or had less positive feelings and patients who had more often taken initiatives to engage in advance care planning were more inclined to strive for quality of life than others” (p. 2012).

No studies have been found applying the QQQ in a research setting with a sample comprising only patients with early stage cancer. There is also value in using the questionnaire to assess patient attitudes in cultures other than Holland. For example, given the greater acceptance of euthanasia in Holland than in New Zealand, Dutch studies may demonstrate a stronger preference for QoL than do studies with New Zealand patients. The current study is an attempt to fill such gaps existing in the research.

## **Chapter Three: Methods**

### **3.1 Aims of the Study**

The current study aims to fill gaps in the literature that were identified in the preceding discussion. Primary aims are:

- To describe the distribution of preferences for quality of life versus length of life in patients with recently diagnosed early stage cancer.
- To measure the stability of patients' preferences for quality of life versus length of life as a treatment goal.

Secondary aims are:

- To determine concurrent scores on the FACT-G, EQ-5D and Daily TTO scales to inform the interpretation of the QQQ scores and to test the validity of the QQQ instrument.
- To examine the association between socio-demographic variables (age, sex, education, employment status, smoking status, and ethnicity), type of cancer, and attitudes toward treatment goals as measured by the QQQ.
- To trial the QQQ with patients who have non-metastatic cancer, and to discuss cultural influences in relation to the Dutch studies.
- To further develop the Daily TTO, and to trial it with patients who have non-metastatic cancer.

### **3.2 Study Design**

In his discussion of the dimensions of research, Neuman (2000) stated that social research can be broadly classified into three groups, depending on whether the main purpose of the study is to explore a new topic (exploratory research), describe a phenomenon (descriptive research),

or to explain why something is occurring (explanatory research). He noted that while studies may have several purposes, one is typically dominant.

While this study is primarily exploratory, it is also descriptive. It would appear to be the first study using the QQQ longitudinally with early stage cancer patients receiving adjuvant therapy. Also, the project aims to describe the distribution of preferences, and to document the stability of those preferences over time. We are therefore focusing on “what”, “who”, and “how” questions. This distinguishes the study from explanatory research, which aims to unravel the reasons behind what has been observed in previous studies (Neuman, 2000).

The overall design can be described as an observational, prospective, cohort study; as it is non-experimental, and follows a group of patients who have all been diagnosed as having early stage cancer (Greenhalgh, 1997; Fowkes & Fulton, 1991).

### **3.3 Setting and Sample**

This study was carried out in the Hematology/Oncology Outpatient Department of Dunedin Hospital in New Zealand. The geographical area served by Dunedin Hospital encompasses the regions of Otago, Central Otago, and North Otago for breast and bowel cancer patients requiring chemotherapy, and extends to include Southland for men receiving radiotherapy for prostate cancer.

The approximate number of patients eligible for adjuvant chemotherapy at Dunedin per annum is 60 for breast cancer, and 80 for bowel cancer. The number of prostate cancer patients per annum suitable for radical radiation therapy is about 40 to 50 across Otago and Southland (D.J. Perez, personal communication, 11 April 2009; J. North, personal communication, 11 April 2009).

The eligibility criteria for participation in the study were:

1. Patients with recently diagnosed early (curable) breast, bowel, or prostate cancers who are receiving chemotherapy or radiotherapy as outpatients at Dunedin Hospital.
2. Aged 18 to 79 years of age.
3. Able to understand written English.
4. Provision of written consent.

At the planning stage of the study, it was estimated that approximately 100 patients would be eligible for inclusion. Based on past experience with clinical studies in the Hematology/Oncology Outpatient Department at Dunedin Hospital a participation rate of 65 percent was considered reasonable, and the dropout rate was not expected to exceed 10 percent, yielding approximately 60 participants at four-month follow-up. This would allow for baseline and follow-up scores to be estimated to within approximately 0.2 standard deviations using 95% confidence intervals. The study would have 80% power to detect a change of approximately 0.5 standard deviations from baseline using a two-sided alpha of 0.05 and without making any assumptions about the correlation between baseline and follow-up measurements.

### ***3.4 Ethical and Regulatory Procedures***

Approval for the study was given by the University of Otago Board of Graduate Studies (Health Sciences), the Lower South Regional Ethics Committee, and the Ngai Tahu Research Consultation Committee.

#### **3.4.1 Minimisation of Harm**

Whilst there were no physical risks to participants or third parties, it was acknowledged that being asked to directly consider their mortality (in the QQQ) could be a potential psychological risk for some patients. It was however considered unlikely that patients who were uncomfortable with discussing such issues would accept an invitation to participate in the project. Furthermore, a previous study (Buckingham, et al., 2006) carried out at Dunedin Hospital with patients with advanced cancer indicated that the assessment instruments were acceptable to participants, and did not cause any recognisable distress.

As an added precaution several additional measures were implemented. Firstly, the wording of the Study Information Sheet had the phrase “or improved chances of cure” added alongside the phrase “length of life”, and the phrase was also used in verbal presentation of materials to participants. Secondly, the QQQ was introduced with an explanation that whilst all statements in the questionnaire had been made by people with cancer, some of them may appear

hypothetical and not reflect the participant's clinical circumstances or treatment scenario. Thirdly, at the outset of both baseline and follow-up assessments, the participants were reminded that should they not wish to answer a particular question they could choose to leave it out. Fourthly, patients were told that should they have any questions or concerns about the study they could discuss these with their doctor or the investigator. Fifthly, before the pilot or main studies began, the investigator had discussions with the oncology research nurses at Dunedin Hospital who were experienced with the administration of four of the five questionnaires.

To monitor and detect adverse reactions to the study material, questions about the acceptability of the questionnaires were included for patient comment. The Study Information Sheet also stated that participants were free to withdraw at any time without having to give a reason (and without implications for their treatment), that they did not have to answer all the questions, and that they may stop the interview.

### **3.4.2 Privacy and Confidentiality**

To ensure privacy and confidentiality, each participant was assigned a code number that was not their NHI number. Code numbers were stored independently from data files. Only the investigator and statistical supervisor had access to raw data, and the medical supervisor had sole access to clinical records. The participant's Oncologist(s) and General Practitioner were not given access to data, but the proviso was made that this could occur should a participant request it.

### **3.4.3 Informed Consent**

The eligibility criteria for the study included the provision of written consent. A copy of the Consent Form and Study Information Sheet are provided in Appendices A and B respectively. These were given to prospective participants at recruitment. Further details of how the study was explained to patients is outlined in section 3.7.

### **3.4.4 Cultural and Social Responsibility**

It was envisaged that the study could potentially involve all ethnic groups in New Zealand conditional upon the participant being able to understand written English. However, given the ethnic composition of regions served by the Otago District Health Board, it was expected that by far the majority of study participants would be European New Zealanders.

The study was consistent with Articles One, Two and Three of the Treaty of Waitangi (i.e. partnership in governance, self-determined protection, and participation by equity). Prior to the project's development, the investigator had participated in a workshop on Collaboration with Maori in Health Research.

The consent form included a clause asking whether the participants would like to receive a written report of the findings of the project following its completion.

## **3.5 Questionnaires Used to Assess Patients**

### **3.5.1 Functional Assessment of Cancer Therapy-General (FACT-G)**

The FACT-G (version 4) has 27 items that are general questions. Subjects answer the questions by choosing one number on a five-point scale ranging from 0 (not at all) to 4 (very much). The questions are grouped into four subscales measuring four primary QoL domains: physical well-being, social/family well-being, emotional well-being, and functional well-being. FACT-G is suitable for use with patients having any type of cancer and it has been used extensively internationally (Webster, Cella & Yost 2003).

The latest version of FACT-G (Version 4) is used in the current study. Whilst retaining the established reliability and validity of Version 3, it was designed to improve the clarity and precision of measurement of its predecessor (Webster, et al., 2003). The reliability of the scale is satisfactory. Reported test-retest reliability coefficients range from 0.82 – 0.92. Cronbach's alpha coefficients of the subscales range from 0.60 – 0.89 (Cella, et al., 1993; Dapuetto, Francolino, Gotta, et al., 2001; Holzner, et al., 2004).

The FACT-G was chosen as the cancer-specific QoL measure in this study because of its well-established and published psychometric properties, as well as its extensive interpretive information (including the minimum important difference analysis). It is presented in Appendix C.

### **3.5.2 Quality Quantity Questionnaire (QQQ)**

The QQQ was developed by Stiggelbout, et al., (1996). It is a short questionnaire designed to assess a patient's preferences for QoL and LoL.

The QQQ has eight items, which are statements about preferences for QoL versus LoL, preferences for QoL and chance of survival, and attitude toward the discontinuation of treatment. The statements were based on comments made by 30 disease free testicular cancer patients during semi-structured interviews (Stiggelbout, et al., 1994). Four of the eight items stress QoL, four stress either chances of survival or duration of survival (Appendix D). Each statement is followed by a five-point Likert scale which rates the strength of the respondent's agreement, ranging from 1 (completely disagree) to 5 (completely agree).

During test development, Stiggelbout and colleagues (1996) found the QQQ to be feasible for use with patients with varying types of cancers. In factor analysis the questionnaire was shown to have two factors rather than the expected single factor: a Quality factor (Q) and a Length factor (L). Cronbach's alpha values for the Q and L scales were 0.68 and 0.79 respectively. The authors suggested that assessment of the reliability of the QQQ be undertaken in future studies. As was previously discussed in the review of literature, a subsequent New Zealand study (Buckingham, et al., 2006) replicated the original findings using the same methodology (a principal components extraction), but found a single factor solution when using principal factors extraction (a technique deemed to be more suitable by the authors). This study assumes a single factor.

Unlike the FACT-G, the QQQ does not yet have well-established psychometric properties, especially with respect to reliability. However, it directly addresses the main question of this research project. Furthermore, with only eight questions, the QQQ is not burdensome, and is therefore suitable to be administered to people who are unwell.

### 3.5.3 Daily Time Trade-Off (TTO)

Buckingham has developed the daily TTO as a variation on the conventional TTO method of health valuation. The standard approach asks respondents to consider giving up time via a reduced life expectancy in exchange for an improvement in their health. In contrast, the daily TTO uses the metaphor of sleep as the means of giving up time (see Appendix E).

Buckingham et al (1996) initially tested the daily TTO with a random sample of the population of Scotland. It was compared with two other formulations of the TTO: one that asked people to consider giving up time during a 12-month interval; the other over a period of 20 years (i.e. the more conventional TTO). Buckingham, et al., found that the daily TTO correlated more strongly with self-reported descriptors of health than did the versions using longer time horizons. Furthermore, the proportion of respondents refusing to trade time was much smaller using the daily TTO (17%) compared with the conventional TTO (40%). The authors suggested that the daily TTO could be tested with terminally ill patients as presenting a less 'threatening' way of obtaining values than the conventional TTO, because it does not ask people to consider their mortality.

Buckingham, et al., (2006) went on to examine whether the daily TTO was acceptable to patients with metastatic cancer. Most respondents found the question acceptable, with only one of eighty-eight people refusing to answer the question. Seventy-three respondents said they would give up time for improvements in health. For males only, the amount of time they would be willing to give up was related to their physical well-being as recorded by the FACT-G questionnaire. For men, an increase of 1 on the FACT-G would result in a willingness to trade an extra 2.97 hours of sleep per day. Furthermore, performance on the daily TTO did not appear to be affected by attitudes toward length of life (as measured by the QQQ).

The authors concluded that the daily TTO appeared to be far more acceptable than the conventional TTO, and possibly more sensitive in discovering the value that is attached to health states.

The current study was seen as providing an opportunity to explore the acceptability of the daily TTO for patients with non-metastatic cancer, and to test again whether attitudes toward LoL influence performance on the TTO.

### **3.5.4 EuroQol Questionnaire (EQ-5D)**

The EQ-5D was developed by an international research group, the EuroQol Group (which was established in 1987). The main aim of the group was to develop a standardized, generic instrument that would describe and value weighted health-related QoL, and which would complement other health-related QoL measures. The instrument was designed to 1) be an easy ‘add-on’ to studies using a battery of tests, 2) be suitable for self completion, 3) take only a few minutes to complete, 4) be relevant to healthy or severely ill people of all ages, 5) capable of yielding a single index value, 6) and be consistent with health states “worse than dead” (Rabin & de Charro, 2001, p. 337).

The EQ-5D (Appendix F) consists of a two-page questionnaire, comprising the EQ-5D descriptive system and a visual analogue scale (VAS) – the EQ VAS. For the descriptive system, the respondent is asked to record the level of problem they encounter on each of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension contains three levels: no problems, some problems, and extreme problems. By choosing one level for each dimension, the five digits obtained can be combined into a 5-digit number describing the respondent’s health state. This is called an EQ-5D profile.

The EQ VAS records the respondent’s self-rated health state on a vertical, 20 cm visual analogue scale, the endpoints of which are labelled ‘Best imaginable health state’ and ‘Worst imaginable health state’.

Data from the EQ-5D can be presented in a number of ways. Results from the descriptive system may be presented as a health profile. Alternatively, a profile may be converted to a weighted index (EuroQol Group, 2009). Devlin and Parkin (2007) recommend that when summarising a profile for statistical analysis, it may be more appropriate to focus on the EQ VAS data provided by the patients themselves, rather than by applying social value sets to the EQ-5D profiles. This depends on the purpose of the research: “In principle, social value sets are used in any context where a single number is required to summarise or represent the social value of an EQ-5D state” (pp. 41). The results of the EQ VAS are presented as a quantitative measure of self-rated health outcome (Devlin & Parkin, 2007; EuroQol Group, 2009).

The time taken to complete the EQ- 5D questionnaire is about 1 minute, varying with age, health status, and setting. There is also an optional page of standard demographic questions (Rabin & de Charro, 2001).

The EQ-5D was chosen as an additional QoL measure for the current study because the VAS scale adds a component of value measurement to the instrument, so that it is not purely descriptive as is the FACT-G. There is data suggesting that the FACT-G (cancer-specific) and the EQ-5D (non-disease specific) measure some common concepts with patients. In a 2005 study, Thompson et al found moderate correlations between the FACT-G Physical Well-being Scale and the Usual Activities ( $r=0.60$ ) and Pain/Discomfort ( $r=0.70$ ) dimensions of the EQ-5D. Similarly, the Emotional Well-being Scale of the FACT-G was moderately correlated with the Anxiety/Depression dimension of the EQ-5D ( $r=0.66$ ).

### **3.5.5 Demographics**

The socio-demographic checklist used in the current study (“Questions About Yourself”, Appendix G) comprised the optional page of standard demographic questions in the EQ-5D. One extra question was added to ensure that the ethnicity of the respondent was recorded. This was a question used by Buckingham et al (2006) in their study of patients with metastatic cancer at Dunedin Hospital.

## ***3.6 Pilot Study and Development of the Daily TTO***

### **3.6.1 Pilot Study**

A pilot study was conducted at Dunedin Hospital from January to March 2008. The goals of the study were 1) to determine whether the estimated duration of assessment was accurate and feasible, 2) to determine the acceptability of the battery of tests for the respondents (Are the questions distressing or embarrassing? Are the questions easy to understand?), and 3) to provide the researcher with experience in administering the questionnaires with people being treated for cancer.

Outpatients were identified by a senior Medical Oncologist at Dunedin Hospital (the Primary Supervisor of the current project). They were to be assessed alongside an outpatient appointment or treatment session. The patients were approached by their own Consultant who explained the purpose of the study, and introduced them to the researcher. Written consent was obtained for each participant and they were provided with a Study Information Sheet.

### **3.6.2 Development of the Daily TTO**

Given that the daily TTO was still under development, the researcher was trained by Buckingham in the administration and understanding of the question prior to the pilot study. After the pilot study she worked under the supervision of Buckingham to make minor changes to the wording and formatting of the TTO question.

## **3.7 Recruitment**

Recruitment for the main study took place over a period of eight months, from mid-April 2008 to late December 2008. Patients meeting eligibility criteria were identified by the Clinical Supervisor of the project through clinical lists. From this point on, the recruitment process varied slightly, depending on whether the patient was receiving adjuvant chemotherapy or radiotherapy.

For chemotherapy patients, the initial approach was made by their Consultant at the end of an outpatient appointment. If the patient was keen to find out more about the study, they were then introduced to the researcher, given a Study Information Sheet and Consent Form, and had the opportunity to ask questions about the project. For radiotherapy patients, recruitment took place through a Nurse clinic using the same introductory process.

While some patients were happy to consent on the day, most appreciated the opportunity to have a few days to think about whether or not they would participate. The researcher then typically phoned the patient to confirm whether or not they wished to take part. The first assessment took place at the patients' earliest convenience and was booked alongside an existing outpatient appointment. For prostate patients, this occurred on the day of a radiotherapy treatment. For chemotherapy patients, this took place either during a

chemotherapy session in the Medical Day Unit or during the week prior to receiving chemotherapy when the patient met with their clinician.

The researcher again met with each participant for the follow-up assessment approximately four calendar months (from 16 to 20 weeks) after baseline assessment. In most cases this would coincide with an existing outpatient appointment at Dunedin Hospital.

### **3.8 Procedure for Data Screening and Cleaning**

Guidelines for handling missing data on the FACT-G and the EQ-5D are provided by the respective questionnaire developers (FACIT Organisation, 2009; EuroQol Group, 2009). As there are no published guidelines for handling missing data with the QQQ and the TTO, it was planned that missing data would result in the respondent being excluded for the questionnaire under consideration. Screening and cleaning of data followed guidelines provided by Pallant (2007).

### **3.9 Statistical Analysis**

Statistical analyses were performed using SPSS, Version 16.0 (SPSS Inc, 2008). For interpretation of results, two-sided  $p < 0.05$  was deemed to be statistically significant.

#### **3.9.1 Primary Analyses**

Descriptive statistics were used to describe the distribution of patient preferences for QoL versus LoL at baseline (mean, standard deviation, and 95 percent confidence interval). Cronbach's alpha coefficient was used to assess internal consistency.

To examine the relative stability of preferences for QoL versus LoL, correlational analyses were performed between QQQ scores at baseline and follow-up. A paired samples t-test was conducted to assess the absolute stability of QQQ scores over time. Exploratory t-test analyses were conducted to examine whether statistically significant changes in QQQ scores occurred within subgroups, over the duration of the study.

### **3.9.2 Secondary Analyses**

Associations of independent variables and preference for QoL versus LoL at baseline were explored using Pearson product-moment correlation for age, t-tests for sex, employment status, education after the minimum school leaving age, university degree (or equivalent), and smoking status. A one-way ANOVA was conducted to explore the impact of cancer type on baseline QQQ scores.

Correlational analyses were performed to examine whether statistically significant associations existed between the QQQ and the FACT-G, TTO, and EQ-5D questionnaires.

## **Chapter Four: Results**

### ***4.1 Pilot Study***

Nine outpatients of Dunedin Hospital (2 male, 7 female) took part in the pilot study. One participant had just completed adjuvant therapy for bowel cancer. The others were part way through therapy for either early or advanced breast or bowel cancers. The age range was from 42 to 79 years (median age=53 years).

The assessment typically took between 50 to 60 minutes, which was acceptable to the respondents. All participants reported that the questionnaires did not cause embarrassment or distress. However, four of the nine respondents (1 male, 3 female) reported that they found answering the QQQ difficult. Of these one breast cancer patient explained that she found the wording of some of the questions ambiguous.

### ***4.2 Main Study***

#### **4.2.1 Participation**

A total of 67 patients were invited to take part in the study. Twenty people declined participation and 47 agreed to take part, giving an acceptance rate of 70 percent.

Ten men with prostate cancer, seven women with breast cancer, and three patients with bowel cancer declined to take part in the study. The reasons for refusal are presented in Figure 4.1.

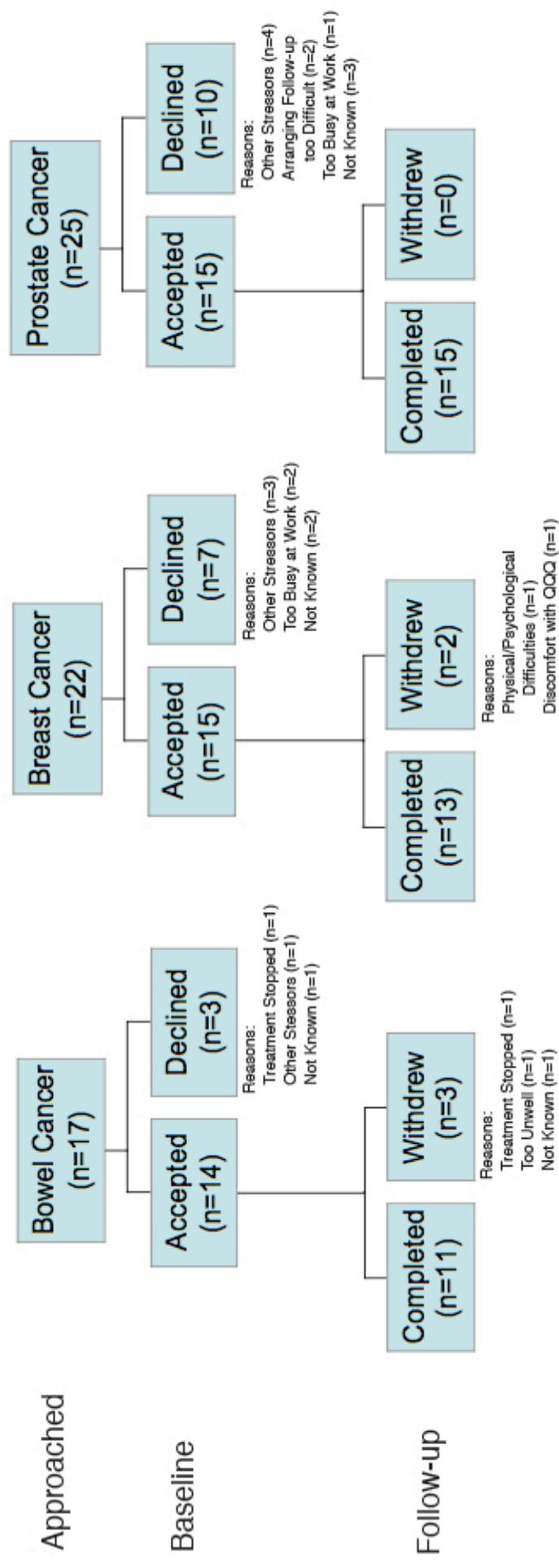


Figure 4.1 Participation Chart

Of the people who agreed to take part, three were subsequently withdrawn from the study prior to their first assessment. One patient developed a liver metastasis; a second person developed a spinal abscess and was transferred to another hospital for treatment, with radiotherapy put on hold; and a third patient became unavailable for his first assessment within the required timeframe due to an extended holiday away from the South Island of New Zealand.

Five patients withdrew after their baseline assessment. One elderly patient with bowel cancer developed complications after a stoma reversal resulting in multiple hospital admissions that left her in a weakened physical state. A male with bowel cancer decided to stop having chemotherapy part way through his course of treatment, and therefore said he did not wish to continue in the study. One woman with bowel cancer was withdrawn from the study because she failed to show for two booked follow-up appointments. A woman with breast cancer withdrew because she was “going through a difficult time”. A fifth patient asked to be withdrawn from the study because she did not wish to fill out the QQQ again. She explained that the questionnaire had presented her with hypothetical scenarios that she had not previously thought about, and which she found to be “not upsetting, but unsettling”. During a subsequent stay on the Oncology Ward at Dunedin Hospital the patient found herself thinking around some of the issues raised by the QQQ, and did not want to “go there” again in a follow-up assessment.

Statistical analyses were carried out to determine whether the personal characteristics of patients who dropped out of the study differed systematically from those who completed follow-up. The results of an independent samples t-test showed that there was no statistically significant difference in age between completers (mean 56.0, SD 12.0) and drop-outs (mean 64.0, SD 11.4),  $p=0.165$ . Fisher’s exact tests carried out on a further seven patient characteristics also indicated that attrition bias was not a concern for this study (see Table 4.1) with all  $p \geq 0.065$ .

**Table 4.1 Characteristics of people invited to participate in the study**

	<b>Approached at recruitment (n=64)</b>	<b>Completed baseline assessment (n=44)</b>	<b>Completed follow-up assessment (n=39)</b>	<b>Drop-outs (n=5) versus Competers (n=39)</b>
<b>Mean age ± SD, years</b>	59.5 ±11.8	56.9 ± 12.0	56.0 ± 12.0	64.0 ± 11.4 (n=5) 56.0 ± 12.0 (n=39)
<b>Sex</b>				
<b>Male</b>	34 (50.7%)	21 (47.7%)	20 (51.3%)	p = 0.348
<b>Female</b>	33 (49.3%)	23 (52.3%)	19 (48.7%)	
<b>Cancer</b>				
<b>Breast</b>	21 (31.3%)	15 (34.1%)	13 (33.3%)	p = 0.178
<b>Bowel</b>	20 (29.9%)	14 (31.8%)	11 (28.2%)	
<b>Prostate</b>	26 (38.8%)	15 (34.1%)	15 (38.5%)	
<b>Smoking status</b>				
<b>Current</b>	NA	3 ( 6.8%)	2 ( 5.1%)	p = 0.314
<b>Ex-smoker</b>	NA	19 (43.2%)	18 (46.2%)	
<b>Never</b>	NA	22 (50.0%)	19 (48.7%)	
<b>Employment Status</b>				
<b>Employed</b>	NA	27 (61.4%)	26 (66.7%)	p= 0.065
<b>Not employed</b>	NA	17 (38.6%)	13 (33.3%)	
<b>Education after min school leaving age</b>				
<b>Yes</b>	NA	34 (77.3%)	31 (79.5%)	p = 0.317
<b>No</b>	NA	10 (22.7%)	8 (20.5%)	
<b>Degree or equivalent</b>				
<b>Yes</b>	NA	19 (43.2%)	18 (46.2%)	p = 0.370
<b>No</b>	NA	25 (56.8%)	21 (53.8%)	
<b>Ethnicity</b>				
<b>NZ European</b>	65 (97.0%)	42 (95.5%)	37 (94.9%)	p = 1.000
<b>Other</b>	2 ( 3.0%)	2 ( 4.5%)	2 ( 5.1%)	

NA = not applicable (information was not available)

#### **4.2.2 Characteristics of Participants**

The characteristics of patients invited to take part in the study are reported in Table 4.1. A one-way analysis of variance (ANOVA) showed that the cancer groups differed in age ( $p < 0.001$ ). Post-hoc comparisons using the Tukey HSD test showed that the mean ages differed statistically significantly between all three cancer groups (all  $p \leq 0.009$ ), with the breast cancer group being the youngest (mean 46.5 years), followed by the bowel cancer

group (mean 57.1 years), and the prostate cancer group (mean 67.1 years) (see Table 4.2). The bowel cancer group was the only group with both male and female participants.

**Table 4.2 Mean age descriptors for breast, bowel and prostate participants (n=44)**

	<b>N</b>	<b>Mean</b>	<b>Std. Deviation</b>
<b>Breast</b>	<b>15</b>	<b>46.5</b>	<b>7.2</b>
<b>Bowel</b>	<b>14</b>	<b>57.1</b>	<b>11.1</b>
<b>Prostate</b>	<b>15</b>	<b>67.1</b>	<b>7.0</b>
<b>Total</b>	<b>44</b>	<b>56.9</b>	<b>12.1</b>

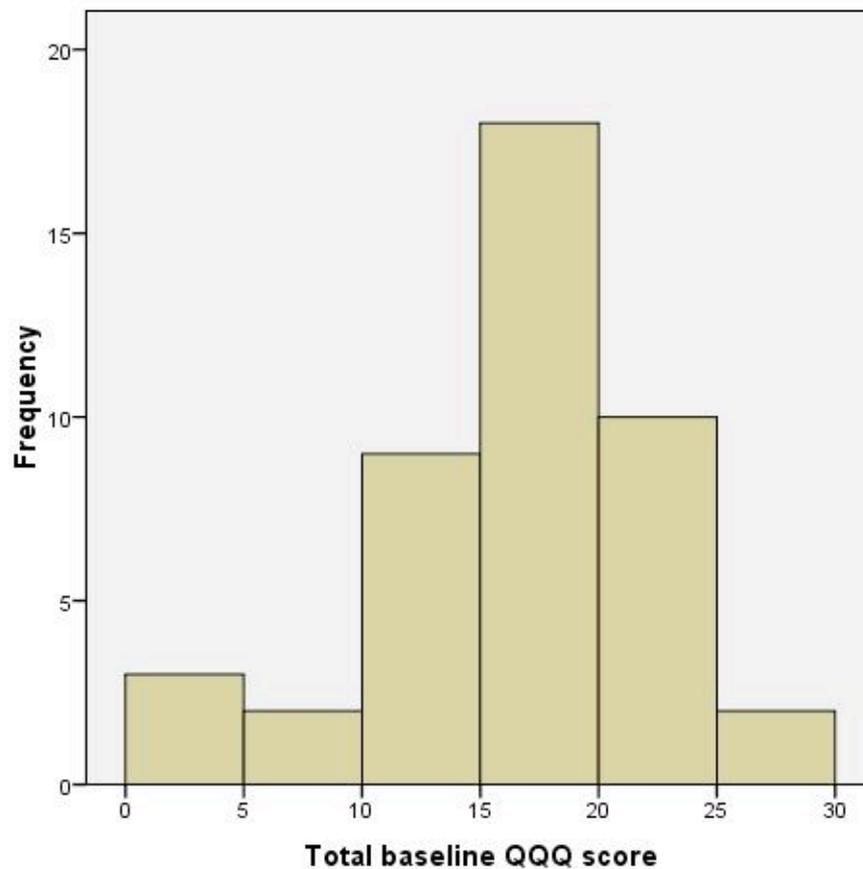
### **4.2.3 Procedure for Data Screening and Cleaning**

Procedures for data screening and cleaning were described in Chapter 3. There was very little missing data, details of which are provided in Appendix H.

## **4.3 Primary Results**

### **4.3.1 Baseline Distribution of Preferences for QoL versus LoL**

The QQQ scores were recoded so that a higher score indicated a stronger preference for QoL. Cronbach's alpha coefficient was .88, indicating good internal consistency. The majority of respondents did not report a clear preference for either QoL or LoL at baseline. A histogram of the baseline total QQQ score is presented in Figure 4.2. In the absence of guidelines from the test developer regarding cut-off scores for assigning preference categories, cut-off was chosen from visual inspection of the histogram shown in Figure 4.2. From this inspection, scores were divided into categories as follows: (0–10) more inclined toward QoL, (11–24) no clear indication, (25–32) more inclined toward LoL. On this basis 20 percent of the respondents were more inclined toward LoL (n=9), 75 percent did not have a clear quality/quality preference (n=33), and 5 percent were more inclined toward QoL (n=2).

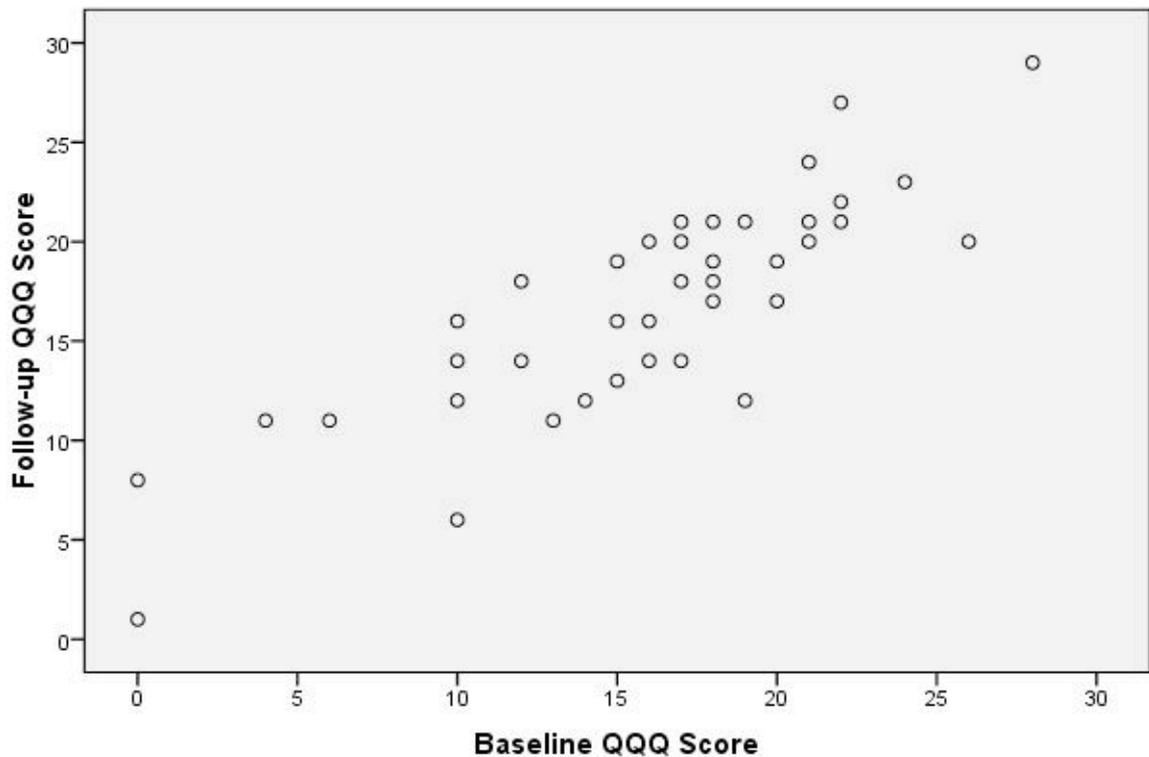


**Figure 4.2 Histogram of Baseline QQQ Scores (n=44)**

### **4.3.2 Stability of Preferences**

#### *a) Relative Stability of Preferences for QoL versus LoL*

Scatterplot (Figure 4.3) and correlational analyses were carried out to assess the relative stability of QQQ scores. There was a significant association between baseline and follow-up scores ( $r=0.84$ ,  $n=39$ ,  $p< 0.001$ ). These results indicate that the scores have remained in much the same linear order over time.



**Figure 4.3 Scatterplot of QQQ Scores at Baseline and Follow-up**

*b) Absolute Stability of Preferences for QoL versus LoL*

A paired samples t-test was conducted to examine the absolute stability of scores over time. There was no statistically significant difference in QQQ scores from baseline (mean 15.9, SD 6.3) to follow-up (mean 16.8, SD 5.6),  $p=0.093$ . This result indicates that there was no evidence for an overall change in preferences across the study population. However, given an estimated increase of 0.95 (95% CI -0.2, 2.1),  $p=0.093$  clinically significant changes cannot be ruled out.

Exploratory subgroup analyses using t-tests showed that over the duration of the study, statistically significant positive changes in QQQ scores occurred for women (mean at baseline 16.4, SD 5.5; mean at follow-up 17.9, SD 5.1;  $p=0.029$ ), and for people with a degree (or equivalent qualification) (mean at baseline 15.2, SD 6.3; mean at follow-up 17.2, SD 6.9;  $p=0.010$ ). There were no statistically significant changes in QQQ scores over the duration of the study for the other subgroups (cancer type, education beyond the minimum school leaving age, employment status, and smoking status). This is an exploratory study, and these findings remain to be confirmed in future studies.

## 4.4 Secondary Results

### 4.4.1 Associations of Socio-demographics and Cancer Type with Preference for QoL versus LoL at Baseline

#### a) Age

The relationship between age and QoL score was examined using Pearson product-moment correlation coefficient. There was no evidence for a correlation between the two variables,  $r=0.04$ ,  $n=44$ ,  $p=0.796$ .

#### b) Sex, Employment Status, Education After School Minimum Leaving Age, University Degree (or equivalent) and Smoking Status.

As Table 4.3 shows, none of these variables were statistically significantly associated with QoL preference. Given the small number of current smokers ( $n=3$ ), this subgroup was excluded from the analysis comparing never with ex-smokers.

**Table 4.3 Univariate models of preference for QoL versus LoL at baseline**

Variable*	N	Mean score	Difference (95% CI)	P
Sex				
Male	21	15.2	1.1 (-4.9 – 2.7)	0.556
Female	23	16.3		
Employment Status				
Employed	27	16.1	0.9 (-3.0 – 4.8)	0.652
Not employed	17	15.2		
Education after min school leaving age				
Yes	34	15.9	0.6 (-3.9 – 5.1)	0.787
No	10	15.3		
Degree or equivalent				
Yes	19	15.2	1.0 (-4.8 – 2.8)	0.604
No	25	16.2		
Smoking status				
Ex-smoker	19	16.9	1.0 (-2.6 – 4.7)	0.567
Never smoker	22	15.9		

\* T-tests used for each variable.

#### c) Ethnicity

Given that 42 of 44 respondents described themselves as being NZ European and 2 of 44 identified themselves as “other”, no analyses were performed on mean scores for the two categories of ethnicity.

#### *d) Cancer Type*

A one-way ANOVA was conducted to explore the impact of cancer type on QQQ scores. There was no significant difference in mean QQQ scores between breast, bowel and prostate patients ( $p=0.558$ ). The average score for each cancer type was as follows: breast patients (mean 17.1, SD 4.1), bowel patients (mean 15.6, SD 6.3), and prostate patients (mean 14.6, SD 7.8).

### **4.4.2 Associations of FACT-G, TTO and EQ-5D with Preference for QoL versus LoL at Baseline**

#### *a) Description of Measures*

This section explores the relationship between QQQ scores and the three other questionnaires administered in this study. As described in detail in Chapter Three, the FACT-G questionnaire is a cancer-specific QoL instrument, comprised of four subscales each measuring a specific domain of well-being. These are summed to obtain a total FACT-G score. The alpha coefficient obtained in this study for the FACT-G was 0.53, suggesting a lower internal consistency than has been reported in earlier studies (Cella, et al., 1993; Dapuelto, et al., 2001; Holzner, et al., 2004).

The daily TTO uses the metaphor of sleep (instead of reduced life expectancy) as the means of giving up time. The respondent indicates the number of extra sleep hours per day they would be willing to accept, in order to feel completely well.

The EQ5-D is a generic instrument measuring QoL at a more general level than the FACT-G. It consists of five questions each measuring one of five dimensions of QoL, and the respondent also rates their overall health on a 0-100 visual analogue scale (VAS).

Descriptive data obtained for each of the four questionnaires is presented in Appendix J. This includes results obtained for each cancer type.

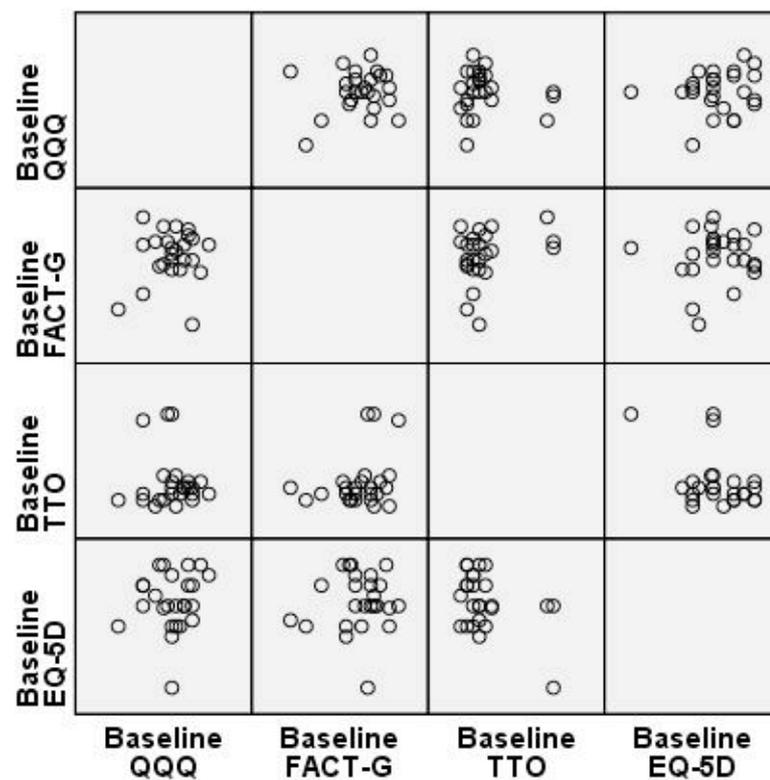
#### *b) Results*

The results of the EQ-5D descriptive system are presented in Appendix J. (Given the subjective nature of the QQQ, converting the EQ-5D descriptive system to a weighted index was considered inappropriate.) No statistically significant associations were found between QQQ scores and those obtained for the FACT-G and EQ VAS questionnaires, nor between

QQQ scores and the total number of sleep hours reported in the daily TTO. The results of secondary analyses are shown in Table 4.4, and matrix scatterplots of baseline and follow-up scores are presented in Figures 4.4 and 4.5 respectively.

**Table 4.4 Correlations between other scales and the QQQ**

	Baseline QQQ n=44		Follow-up QQQ n=39	
	<i>r</i>	P	<i>r</i>	P
<b>FACT-G</b>				
total well-being	-.23	0.131	-.14	0.407
physical well-being	-.18	0.253	-.20	0.231
social/family well-being	-.14	0.367	-.08	0.618
emotional well-being	.02	0.888	.07	0.653
functional well-being	-.23	0.130	-.25	0.122
<b>TTO</b>				
extra hours sleep per day	-.09	0.636	.06	0.740
<b>EQ-5D</b>				
VAS	-.10	0.507	.11	0.535



**Figure 4.4 Matrix Scatterplot of Baseline Scores**

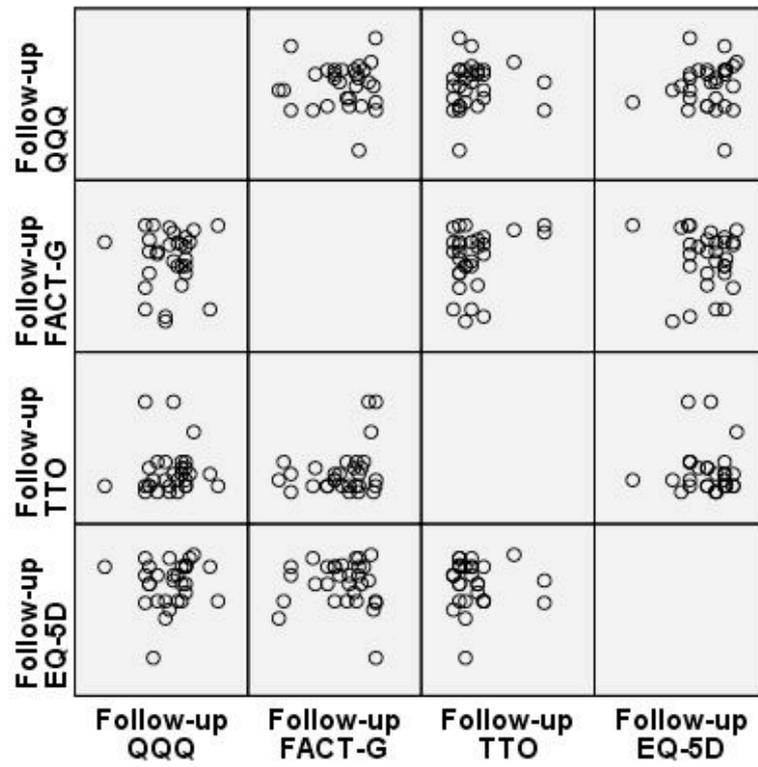


Figure 4.5 Matrix Scatterplot of Follow-up Scores

## **Chapter Five: Discussion**

This chapter aims to interpret the results of the study, to integrate the findings with published literature, and to consider ways in which the study may contribute to future research and to clinical practice.

The discussion is structured as follows: 1) a restatement of the study aims, 2) a brief statement of key findings, 3) a consideration of possible explanations of findings, 4) comparison with other published research, 5) strengths and limitations of the study, and 6) implications for future research and for clinical practice.

### ***5.1 Restatement of the Study Aims***

The primary aims of the study were to describe the distribution of preferences for QoL versus LoL in patients with recently diagnosed early stage cancer, and to measure the stability of patients' preferences for QoL versus LoL as a treatment goal.

There were four secondary aims: 1) to determine concurrent scores on the FACT-G, EQ-5D and Daily TTO scales to inform the interpretation of the QQQ scores and to test the validity of the QQQ instrument, 2) to examine the association between sociodemographic variables (age, sex, education, employment status, smoking status, and ethnicity), type of cancer, and attitudes toward treatment goals as measured by the QQQ, 3) to trial the QQQ with patients who have non-metastatic cancer, and to discuss cultural influences in relation to the Dutch studies, and 4) to further develop the daily TTO, trial it with patients who have non-metastatic cancer, and to test for an association with the QQQ.

## **5.2 Statement of Key Findings**

### **5.2.1 Primary Results**

At baseline 75 percent of adjuvant patients did not seem to have a clear preference for either quality of life or length of life, as measured by the QQQ. With the possible range of scores being 0 to 32, the mean score was 15.8 with a standard deviation of 6.2. However it is important to remember that some patients did have a preference for QoL or LoL, so it is inappropriate to automatically assume what the preference might be.

When the assessment was repeated approximately four months later, 1) a moderately strong association was obtained between baseline and follow-up QQQ scores, (indicating good relative stability of preference), and 2) no significant difference was found between baseline and follow-up scores (implying good absolute stability of preference), although there was a tendency toward change. Exploratory subgroup analyses showed that over the duration of the study, statistically significant positive changes in QQQ scores occurred for women and for participants having a degree (or equivalent qualification).

### **5.2.2 Secondary Results**

No statistically significant association was found between QQQ scores, and sociodemographic variables or type of cancer at baseline. No statistically significant associations were found between QQQ scores and those obtained on the FACT-G and EQ-5D questionnaires, nor between QQQ scores and the daily TTO.

## **5.3 Explanation of Study Findings**

### **5.3.1 Explanation of Primary Analyses**

#### *a) Explanation of baseline distribution of preferences for QoL versus LoL*

We do not know why the majority of patients receiving adjuvant treatment for early stage cancers did not report a clear preference for either QoL or LoL at baseline. However, the

written feedback provided by patients immediately after completing the QQQ may provide us with some clues. Their feedback provides a degree of insight into the thought processes underlying decisions made when answering the questionnaire.

After completing the QQQ, participants were asked to provide written answers to three questions: 1) did they find the questionnaire difficult to answer (Yes/No); 2) did they feel that completing the QQQ caused embarrassment or distress (Yes/No); and 3) would they like to make any comments about the questionnaire. Details of the feedback received for questions one and three are provided in Appendix J. Responses for question two are not listed, because only one person felt that completing the QQQ caused embarrassment or distress, and this occurred at baseline only (and she chose to complete the questionnaire).

For question one, 23 of 44 people (52 percent) reported finding the QQQ difficult to answer at baseline, compared with 13 of 39 (33 percent) at follow-up. (There was no missing data for question one). For question three, 16 of 44 participants (36 percent) wrote comments about the QQQ at baseline, and 10 of 39 (26 percent) did so at follow-up. All comments are reported in Appendix K.

Given the amount of missing data for question 3, it clearly cannot be assumed that the comments provided are necessarily representative of the entire study sample. Nonetheless, there are two common themes readily apparent among the respondents' comments, and these may help to explain why the majority of people did not express a clear preference for either QoL or LoL.

Firstly, six participants reported that some of the questions were difficult to answer given the lack of detail in the statements. Seemingly, this made some of the questions appear ambiguous, and therefore harder to answer. For example, some respondents felt that more information was needed about the severity of side effects, or about the range of therapies available before they could make an accurate decision. We need to remember, however, that the questionnaire developers deliberately set out to develop an instrument that could be used by researchers to "assess patients' general attitudes towards the tradeoff between quality of life and length of life" (Stiggelbout, et al., 1996, p. 185).

Secondly, seven patients wrote that they found it hard to answer the QQQ because the scenarios they were being asked to consider were hypothetical, and were not representative of

their treatment situation. These responses suggest that the QQQ may not have face validity in the adjuvant treatment setting. While some of the vignettes presented in the QQQ do require the respondent to consider quality-quantity weightings that are more typically associated with end stage (as compared with early stage) cancer (notably items 7 and 8), this is not the case for all of the 8 scenarios. Furthermore, several survival studies involving adjuvant patients have reported rates of recurrence of cancer and death from cancer for up to 15 years following treatment. For example, a 2005 Cochrane review of 194 randomised trials in early breast cancer reported that for women diagnosed under the age of 50, 41.1 percent had experienced a recurrence and 32.4 percent had died, within 15 years of receiving adjuvant therapy (Early Breast Cancer Trialists' Cochrane Collaborative Group, 2005). Similarly, a pooled analysis of bowel cancer trials reported 69 percent 5-year disease free survival, and 74 percent 5-year overall survival, for men and women under the age of 60 who had been treated with surgery and adjuvant chemotherapy (Gill, Loprinzi, Sargent, et al., 2004). In the face of such evidence, it would seem that possible explanations for the hypothetical stance taken by some patients are, either that the patient is in denial regarding their situation, or they have not been provoked to think about it, or that they have not been made fully aware of their prognosis. Given the climate of open communication between oncologists and patients these days in New Zealand, the latter explanation would seem to be the least plausible.

Taking into account the themes that were apparent in comments from a subset of adjuvant patients, three possible explanations are offered as to why most participants did not report having a strong preference for either QoL or LoL: Firstly, a small number of patients did not appear to have previously thought about the quality quantity weighting to any great extent. For example, one patient indicated that this was the first time he had “considered some of these possibilities”. The sole participant who found the QQQ upsetting wrote, “Having to consider the concept of dying was hard”. In the interview she said “it is not in my nature to”. It is not unreasonable to expect these patients to hold back from expressing a clear preference. Secondly, it may be that some respondents had thought a lot about the quality quantity dilemma, and had already made a decision not to opt for either extreme (D.J. Perez, personal communication, 8 June 2010). Thirdly, and as discussed in the review of literature, decisions about treatment are usually not made in isolation. Most people take into account the opinions of health professionals, close friends and family. The process of decision-making typically involves discussion, and arguably, the more difficult the decision, the more discussion is generated. One of the prostate cancer patients hints at this, albeit in an indirect way, with his

comment: “I base a lot of my answers on what I consider my worth to those around me especially my close family”.

*b) Explanation of Stability of QQQ Scores between Baseline and Follow-up*

The moderately high positive linear correlation between QQQ scores obtained at baseline and follow-up, indicates good relative stability of preferences throughout the study period, (for approximately four months). Similarly, the absolute stability of preferences remained over time. If the QQQ is a reliable and valid measure of preference, there was no evidence to suggest that participants significantly altered their preferences between commencement and completion (or near completion) of adjuvant therapy.

In attempting to explain this finding, it helps to bear in mind that the people in this study have all chosen to undergo treatments that they know will impair QoL in the short- to medium-term, (and for some there is the likelihood of permanent side-effects), but they doing so in the hope of being cured. Given this context, it is not unreasonable to ask, “what would have to happen in a patient’s world during the study period, to significantly change their attitude regarding the relative value of QoL versus LoL”? Perhaps the most obvious answer is that an extremely unpleasant experience with treatment side effects could increase a patient’s preference for maintaining QoL. However, such a shift in attitude would seem to be more plausible in a palliative care setting, or where cancer is advanced and the benefits of therapy are known to be limited. It is understandable that people in those situations may wish to “make the most of the time that is left”, without the added challenge of coping with unpleasant side effects. It is more difficult to rationalise a preference shift of the same degree amongst people who are receiving treatment with curative intent – especially, for example, with chemotherapy regimens, where drug combinations can be altered should they prove to be too difficult to tolerate.

Exploratory subgroup analyses showed statistically significant positive change in QQQ scores between baseline and follow-up for women and for participants with a degree (or equivalent qualification). There was no evidence of significant change for any of the other subgroups. The statistically significant results may be chance findings and further research is needed to confirm the results. There is limited evidence in the literature that male patients are less likely to admit impaired quality of life than are women (Holzner, et al., 2004; Schwarz & Hinz, 2001; Unruh, Ritchie, Merskey, et al., 1999). It follows from this that men may be less willing to express an increasing preference for quality of life over time than women. Regarding

educational level, the results of several cancer studies have implicated an association between education and quality of life, in particular a poorer quality of life has been reported for patients with lower levels of education (Dapueto, et al., 2001; Janz, Mujahid, Lantz, et al., 2005). If highly educated people are accustomed to a better quality of life, it may be that over time they are less accepting of the ongoing negative impact of treatment on QoL, than are people with lower levels of education. If so, the reduced acceptance may be reflected in an increased preference for maintaining quality of life.

### **5.3.2 Explanation of Secondary Analyses**

#### *a) Explanation of Associations of Sociodemographics and Cancer Type with Preference for QoL versus LoL at Baseline*

The low positive linear correlation achieved between age and QQQ baseline scores indicates a very weak relationship between a preference for QoL with increasing age in this sample of patients with early stage cancer. Given the weakness of the correlation, the statistic needs to be interpreted with caution. However, the direction of relationship is in keeping with the findings of published studies (Stiggelbout, et al., 1996; Rietjens, et al., 2005).

There was no evidence of a difference in baseline QQQ scores between men and women, being employed or not employed, having attended or not attended school beyond the minimum leaving age, having or not having a university degree, and being a smoker or a non-smoker. Similarly there was no evidence of a difference in QQQ scores between the three cancer groups.

#### *b) Explanation of Associations of FACT-G, TTO and EQ-5D with Preference for QoL versus LoL*

The non-statistically significant correlations obtained between QQQ scores and both FACT-G and EQ-5D scores indicates no evidence was found for an association between participants expressed preference for QoL, and their reported current QoL. The situation is the same for TTO scores and the QQQ. There is no evidence to suggest that the amount of extra hours a patient is willing to spend in sleep per day, so that they can feel completely well, is associated with their preference for QoL versus LoL.

The general picture that emerges from these analyses is that as a group, people undergoing adjuvant therapy for early stage cancers typically report enjoying a good quality of life, and

most of them are fairly undecided as to whether they have a preference for maintaining QoL or prolonging survival. Furthermore, the value that they place on feeling well (as measured by the extra sleep hours) does not appear to be related to their preferences for QoL versus LoL.

In attempting to explain these findings, we need to remember that the FACT-G and EQ-5D quality of life questionnaires are well validated, whereas neither the QQQ nor the daily TTO are. The poor correlations between the QQQ, FACT-G and EQ-5D would seem to suggest that the instruments are measuring different constructs or domains, and therefore the QQQ may have discriminant ability (a component of construct validity) (Murphy & Davidshofer, 2001). This may mean that the patient's actual quality of life does not have a great influence on their expressed preference for QoL versus LoL on the QQQ. Clearly there has been no convergent effect.

Regarding the TTO, given that most people reported having a good quality of life, it is reasonable to assume that they would not feel the need to give up significant amounts of awake time each day, via extra sleep, in order to feel completely well – especially if the treatment causing sleep does not improve their chances of survival. The exceptions here could be patients who reported having sleeping difficulties, or who (for psychological reasons) would prefer to blot out the treatment phase. We might therefore expect a correlation or a convergence between extra sleep hours and a quality preference on the QQQ. The fact that there is no convergence may question the validity of the QQQ, or alternatively the validity of the TTO.

## ***5.4 Comparison of Study Findings With Other Published Research***

### **5.4.1 Comparison with Other Research on the Preferences of Patients with Cancer for QoL versus LoL**

When developing the QQQ, Stiggelbout and colleagues (1996) reported a moderately strong correlation between age and both Q and L scores, with the association being stronger for the Q scale. Spearman correlation coefficients being 0.44 and -0.23 for the Q and L scales respectively ( $p \leq 0.001$  for both). The association in this study was much weaker (Pearson

correlation coefficient being 0.04,  $p=0.796$ ), and with scores recoded to reflect preference for QoL.

The Dutch research involved patients whose prognoses were both good and poor, and when these two groups were compared, no association was found between prognosis and responses given on the QQQ. The authors conceded, however, that this was not surprising, given their “very crude” (p. 190) classification for prognosis. They also questioned “whether the patients were themselves aware of, and did not deny, their poor prognoses” (p. 190). Similarity between the current study sample and the Dutch sample is therefore limited - with the Dunedin sample being more homogeneous with respect to type and stage of cancer, and because participants were drawn from just one treatment centre. The differences in sample composition make it difficult to directly compare the Dutch and New Zealand findings. However the greater spread of preference in the Dutch results may again support discriminant validity of the QQQ, given that the two studies were sampling different disease stages.

#### **5.4.2 Comparison with Other Research on the Stability of Cancer Patients’ Preferences for QoL versus LoL**

Only one other study has made use of the QQQ to track the stability of patient preferences over time. This was another Dutch study, carried out by Voogt et al (2005), involving 128 people with terminal cancer. Recruitment occurred within two months of being told that the cancer had become incurable. At baseline assessment 29% of their sample were unable, or unwilling, to express a clear preference for QoL or LoL. Seventy-five percent of participants in the Dunedin study did not indicate a clear preference. It must be noted, however, that for the purposes of analysis, the Dutch study involved division of the QQQ into two scales (one Q, the other L). This was based on earlier work by Stiggelbout, et al., (1996), which identified two factors using principal components extraction analysis (as discussed previously in section 2.5.1). The 29% of respondents whom they identified as not providing a clear preference for QoL or LoL, were those who had higher than median scores on both scales (14%) and lower than median scores on both scales (15%). In contrast, the current study follows on from work done by Buckingham, et al. (2006), in which a single factor was identified (via principal factors extraction analysis), thus identifying preferences for QoL and LoL as being two extreme ends of a single continuum. It is therefore suggested that future research on the preferences of patients receiving adjuvant treatment for early stage cancer incorporate factor analysis of the QQQ, with a larger sample.

Three possible explanations for the difference in proportions may be firstly, the stage of cancer (terminal versus early stage and hoping for a cure). Secondly, cultural differences regarding end of life decision-making may also be a contributing factor. For example, whereas voluntary euthanasia is legal in Holland, it remains illegal and highly controversial within New Zealand. This may predispose, or at the very least permit Dutch people to be more open than New Zealanders in expressing their views regarding end-of-life decisions. Hence it may be easier to report a preference for maintaining QoL over prolonging survival in Holland, simply because it is culturally permissible to take a strong stance on end of life issues. Thirdly, it may be that oncologists in New Zealand provide more information pertinent to the quality/quantity trade-off, thereby enabling their patients to consider more fully the options available before making a decision regarding treatment. However, it must be noted that preference proportions have been calculated in completely different ways in the Dutch and Dunedin studies.

The Dutch researchers also reported that, at baseline patients with a short history of cancer were more likely to have a preference for LoL over QoL. Again this does not fit with data in the Dunedin sample, where all participants had a short history of cancer, but very few expressed a strong preference for prolonging survival at the expense of maintaining QoL. Similarly, Voogt and co-workers found that older people with incurable cancer were more likely to prefer QoL over LoL (a finding also reported by Stiggelbout, et al., 1996).

Regarding stability of preferences, the assessments carried out by Voogt and colleagues at six- and twelve-month follow-up, found no change in attitude toward treatment, except for the patients with a short history of advanced cancer. For these patients the desire to prolong survival decreased. Given the poor prognosis for participants, only a small group were able to be assessed over time and the authors noted the need for further longitudinal studies to confirm their results. The Dutch finding of a change in the preferences of patients with a short history of cancer after four months, (beyond the timing of the follow-up assessment in the Dunedin study), raises the question of whether a change in preference would be found were a second follow-up assessment to be carried out with the Dunedin sample. However, the more pronounced deterioration in health over time that would inevitably characterise participants in the Dutch study, may have accounted for some of the shift in preference.

## **5.5 Evaluation of the Study**

This evaluation of the study draws on recommended criteria for evaluating QoL studies in people with cancer (Jacobsen, Davis & Cella, 2002; Joly, Vardy, Pintilie & Tannock, 2007; Mandelblatt & Eisenberg, 1995), as well as guidelines for appraising cohort studies per se (Crombie, 1996; Fowkes & Fulton, 1991; Greenhalgh, 1997; Vandembroucke, von Elm, Altman, et al., 2007).

The overall study design is appropriate for the specified objectives of the research. A key strength of the study is that it is prospective, capturing patient preferences for QoL versus LoL at baseline, and several months later at follow-up. This minimises the risk of recall error, which can be a major source of inaccuracy in retrospective data (Tourangeau, 2000). The baseline assessment facilitates the identification of changes in preference over time that may be attributable to the treatment (Jacobsen, et al., 2002; Mandelblatt & Eisenberg, 1995; Osaba, 1991). Ideally, a second follow-up at approximately 18 months would provide a clearer picture of the stability of preferences over time. Furthermore, a qualitative component to the project could have helped to cast more light on the rationale underlying patient preferences.

The sample was well defined, with pre-specified inclusion and exclusion criteria. Although the sample size was smaller than initially anticipated, the baseline participation rate of 70 percent was above the pre-specified target rate (65 percent). This is especially commendable given the considerable time and effort required from both hospital staff and the researcher in order to recruit and maintain patients for research in busy outpatients clinics, and radiotherapy and chemotherapy treatment units. While having participants from only one treatment centre made the sample more homogeneous, the extent to which the final sample is representative of all patients receiving adjuvant therapy for breast, bowel, and prostate cancers at Dunedin remains unknown. However, the reasons why patients declined to participate were provided in most instances, and the details given in Figure 4.1. It is hoped that this information may be useful for future studies involving oncology patients at Dunedin Hospital (A. Gray, personal communication, 3 March 2009). Due to the predominance of European New Zealand participants, the findings cannot be generalised to other ethnic groups without caution.

Regarding drop-out, five patients did not attend for follow-up assessment. The reasons for this were stated in Chapter Four. In four cases we understood that patients withdrew on the grounds of physical and/or psychological discomfort. However, this cannot be compared with the more intense physical and/or psychological suffering that can sometimes explain withdrawal from studies involving patients with advanced cancer, and no patients were withdrawn due to death (Jacobsen, et al., 2002). Fisher's exact test and t-test analyses showed that there were no statistically significant differences between completers and drop-outs regarding age, type of cancer, smoking status, employment status, educational variables and ethnicity. However, the people who withdrew after baseline were mostly female (4 of 5, 80%), were mostly over the age of 60 (4 of 5, 80%), and were mostly not employed (4 of 5, 80%).

With regard to the quality of measurements and findings, three factors are especially pertinent: validity, reproducibility, and quality control (Fowkes & Fulton, 1991). The two QoL questionnaires (FACT-G and EQ-5D) are both validated, with published psychometric properties and interpretive guidelines. In contrast, the QQQ and the daily TTO are less well established. Greater care therefore needs to be taken when interpreting the results obtained with the latter two tests. The study should be readily reproducible. Methods have been outlined in detail, and the questionnaires are straight-forward to administer. Quality control is often easiest to implement in a laboratory-based study, and clinical researchers do receive criticism for not paying adequate attention to this area (Fowkes & Fulton, 1991). However, this project was closely monitored at all stages by three supervisors. Furthermore, with only one interviewer administering the questionnaires, between interviewer bias was eliminated.

In summary, the major limitations of the study design are a small sample size comprising mostly European New Zealanders, and the uncertainty surrounding the reliability and validity of the main testing instrument (QQQ). In contrast, the strengths of the study are its prospective design, the homogeneous sample (with respect to clinical variables), the use of questionnaires that are easy to administer, the small amount of missing data, and the absence of between interviewer bias. The reliability of the QQQ has been enhanced by this study, and the validity of the questionnaire has been slightly enhanced.

## **5.6 Implications for Future Research and for Clinical Practice**

### **5.6.1 Implications for Future Research**

As a piece of descriptive exploratory research, it is hoped that the study helps to lay the foundation for a better understanding of the distribution of preferences for QoL versus LoL within a New Zealand context of adjuvant therapy for early stage cancer. Given the ethnic composition of the sample, however, findings cannot be generalised beyond New Zealand Europeans without caution. Further research would ideally include people from other cultures and living in New Zealand. A clearer picture of the stability of preferences over time could also be achieved with research that includes more than one follow-up assessment.

The interrelationships between QoL, socio-demographic and clinical variables, and preferences for QoL versus LoL clearly require clarification. Larger samples would facilitate better understanding of these domains. The acceptability of the daily TTO to patients with early stage cancer replicates the attitudes of patients with metastatic disease (Buckingham, et al., 1996), and future research involving utility assessment in an oncological setting may well favour this instrument over traditional approaches to utility assessment.

### **5.6.2 Implications for Clinical Practice**

In Chapter One it was noted that the complexity of factors impinging on cancer treatment decision-making highlights the need for a clinical assessment tool that can be used repeatedly along the cancer trajectory to: 1) give patients some clarity regarding their attitudes toward QoL versus LoL, 2) provide doctors with a better understanding of their patients' attitudes, and 3) give both parties an indication of changing attitudes over time.

This study found that at baseline (shortly after diagnosis), slightly more than half of the patients reported difficulties in answering the questionnaire. Four months later, only about one third experienced difficulty. According to comments made by some of the respondents, the difficulties appeared to be caused mostly by the hypothetical nature of the questions, and the lack of detail in the questionnaire statements. Given that only one participant reported feeling distressed while completing the questionnaire, presenting end of life vignettes clearly did not pose an ethical problem at baseline. However one patient did not return for follow-up

as she had found the questions unsettling, and they had played on her mind during a subsequent stay on the oncology ward.

Given the lack of clarity surrounding patient preferences for maintaining QoL versus improving their chances of cure, we need to ask two questions: “How may completing the QQQ benefit the patient?”, and “How may making use of the QQQ with patients aid the consultant?”

There are several potential benefits to both parties at the treatment planning stage. As far as doctors are concerned, by presenting a balanced spectrum of preferences for quality versus quantity via the QQQ vignettes, they are ensuring that their patient is provided with all relevant information relative to any pre-existing attitudes or assumptions. For example, if a patient presents with a strong quality focus, the QQQ could be used to facilitate discussion surrounding the survival benefits of treatment (and vice versa). The implication here is that different QQQ profiles could result in slightly different emphases by doctors so as to ensure that the patient is fully informed. Thus the QQQ potentially allows the patient to consider their health predicament more fully, even if this is a difficult task. At the same time, it ensures that doctors acknowledge that some patients do have a strong preference for quality of life, and may allow doctors to individualise their approach to patients. The results could also be of interest to the community at large and the political domain when resource allocation is considered.

As far as stability of preferences is concerned, repeating the QQQ would make doctors reconsider their patient’s attitudes, rather than simply assuming constancy. It could also pave the way for patients to suggest a change in treatment strategy. It is also possible that the QQQ could have health planning implications, because it demonstrates that significant numbers of patients do value the benefits of active treatment that can improve survival.

With only eight questions, the QQQ takes just a few minutes to complete, and a score can be very quickly tallied indicating the patient’s location on the continuum of preference for QoL versus LoL. Given the ease with which the questionnaire can be administered, its potential to inform doctors and patients, to facilitate dialogue between both parties, and given its implications for health planning, the QQQ may well be a valuable tool for both clinicians and researchers working within oncology.

## Chapter Six: Conclusion

Balancing treatment-related gains and losses with respect to quality of life and length of life is common in cancer. Nowadays oncologists recognise the importance of the patient's perspective regarding aims of treatment, and in weighing the benefits and side effects of available therapies. However, there is no real assistance given to patients to help with the weighing up process. It would seem that preferences cannot be explained solely in terms of treatment-related determinants, or clinical and patient characteristics. Furthermore the measurement of preferences, using methods such as TTO, is neither an explicit measure of the balance between quality of life and length of life, nor an indicator of the stability of such weightings over time. Having an assessment tool (such as a questionnaire) that could help both patient and clinician weigh up the competing factors involved would be of benefit to both parties.

The QQQ, designed by Stiggelbout, et al., (1996), was designed to measure patients' general attitudes toward the weighing up of benefits and side effects of treatment. The questionnaire has been used with cancer patients in Dutch studies (Stiggelbout, et al., 1996; Voogt, et al., 2005) and in a New Zealand study (Buckingham, et al., 2006). The current study is the first study using the QQQ with a sample comprising only patients with early stage cancer.

Bearing in mind the limitations of the study, in particular the small sample (n=44) and the predominance of European New Zealand participants (n=42), several conclusions may be drawn from the obtained results as they relate to the study aims. The first two conclusions pertain to the primary aims of the study, and the remaining conclusions relate to secondary aims: Firstly, most patients receiving adjuvant chemotherapy for early stage breast or bowel cancer, or radiotherapy for prostate cancer did not express a clear preference for QoL versus LoL shortly after diagnosis. However a small minority did, and it would be inappropriate in a clinical setting to automatically assume the direction of their preference.

Secondly, at four-month follow-up the results indicated good relative and absolute stability of patient preferences over time, with the possible exception of participants who were female or

who had a degree (or equivalent qualification). Other than within these two subgroups, there was no evidence to suggest that participants significantly altered their preferences between commencement and completion (or near completion) of therapy. These findings remain to be confirmed.

Thirdly, the relationships between socio-demographic variables, cancer type and preference for QoL versus LoL require clarification.

Fourthly, the lack of association between reported QoL (as measured by the FACT-G and the EQ VAS) and preference for QoL versus LoL (QQQ) suggests that the instruments are measuring different constructs or domains, and therefore the QQQ may have discriminant ability. This may mean that the patient's actual QoL does not have a great influence on their expressed preference for QoL versus LoL.

Fifthly, the value patients place on feeling well (measured using the Daily TTO) does not appear to be related to their preferences. However, the acceptability of the TTO to adjuvant patients supports the findings of an earlier Dunedin study (Buckingham, et al., 2006) carried out with patients with advanced cancer. Future oncological studies may therefore prefer to use the TTO instead of more traditional utility measures.

Finally, cultural differences may have contributed to observed discrepancies between Dutch and New Zealand studies regarding the proportions of reported preferences for QoL versus LoL. However, it is suggested that other factors, such as differences in study design, are also likely to have contributed to the observed discrepancies.

Study findings remain to be confirmed by future research, but overall have served to enhance the reliability of the QQQ, and to a lesser degree, the validity of the instrument. Additional benefits of the QQQ, such as its ease of administration, its potential to inform doctors and patients, and its implications for health planning seem to suggest that the QQQ may well be a valuable clinical and research tool within the arena of cancer.

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## **APPENDIX A: Study Consent Form**



## CONSENT FORM

### **Quality of life: Are the preferences of patients with cancer stable over time?**

1. I have read and I understand the information sheet dated 1 June 2007 for volunteers taking part in the study investigating the stability of preferences of patients with cancer for quality of life versus improved chance of cure or length of life. I have had the opportunity to discuss this study. I am satisfied with the answers I have been given.
2. I have had the opportunity to use whanau support or a friend to help me ask questions and understand the study.
3. I understand that taking part in this study is voluntary (my choice) and that I may withdraw myself or any information I have provided before data collection is completed, and this will in no way affect my continuing health care.
4. I understand that my participation in this study is confidential and that no material which could identify me will be used in any reports on this study.
5. I agree to my hospital records being accessed for the purposes of this study.
6. I have had time to consider whether to take part in this study.
7. I wish to receive a copy of the results of the study on the understanding that there may be significant delay between data collection and publication of the results.  
YES/NO
8. I understand that this project has been approved by the University of Otago Board of Graduate Studies (Health Sciences), the Lower South Regional Ethics Committee, the Otago District Health Board Ethics Committee, and the Ngāi Tahu Research Consultation Committee.
9. I understand that I can contact the following persons between 9.00am-5.00pm Monday-Friday with any questions I have about the study: Claire Paton, Postgraduate Student, Department of Medicine, University of Otago (ph: 027 243 7835); Dr David Perez, Associate Professor in Medicine at Dunedin Hospital (ph: 03 474 0999).

10. Request for interpreter:

I wish to have an interpreter. Yes/No

E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero. Ae/Kao

Ka inangaro au i tetahi tangata uri reo. Ae/Kare

Au gadreva me dua e vakadewa vosa vei au. Io/Sega

Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu. E/Nakai

Ou te mana'o ia i ai se fa'amatala upu. Ioe/Leai

Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika. Ioe/Leai

Oku ou fiema'u ha fakatonulea. Io/Ikai

11. I \_\_\_\_\_ hereby consent to take part in this study.  
(Participants full name)

**Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

**Statement by Researcher**

I have discussed the aims and procedures of this study with:

\_\_\_\_\_  
(Participants full name)

Researcher's name: \_\_\_\_\_ Ph: \_\_\_\_\_  
(please print)

Signed: \_\_\_\_\_ Date: \_\_\_\_\_

## **APPENDIX B: Study Information Sheet**



## STUDY INFORMATION SHEET

### **Quality of life: Are the preferences of patients with cancer stable over time?**

**PRINCIPAL INVESTIGATOR:** Claire C Paton  
Postgraduate Student  
Department of Medicine  
University of Otago  
Ph: 027 243 7835

**CLINICAL SUPERVISOR:** Dr David J Perez  
Medical Oncologist  
Oncology Department  
Dunedin Hospital  
Ph: 03 474 0999

### INTRODUCTION

You are invited to take part in a research study conducted by Claire Paton who is completing a Master's Degree. Please take your time to read through this information sheet carefully before deciding whether to participate. If you have any questions or concerns about the study, please feel free to discuss these with your doctor or the investigator. You do not have to participate in this study. Should you choose not to, your health care will not be affected in any way. If you do agree to take part you are free to withdraw at any time without having to give a reason.

### ABOUT THE STUDY

#### **What is the purpose of the study?**

As you know, cancer treatments often have side effects which can affect quality of life. Therefore when people with cancer are deciding whether to have a particular treatment, they often have to weigh the expected benefits against possible side effects. Little is known about the preferences that patients with cancer have regarding maintaining quality of life versus improving chances of cure or living a longer life. We would like to know the preferences of New Zealand patients, and whether their preferences stay the same over time. We would also like to better understand what factors influence such decisions. This information could help doctors as they guide patients through cancer treatment decisions.

#### **How many people will be involved in the study?**

We hope to have about 70 participants.

#### **Who is being asked to participate?**

Patients at Dunedin Hospital who are receiving chemotherapy or radiotherapy for recently diagnosed breast, bowel or prostate cancers will be invited to participate. They must be between 18 and 79 years of age.

**What will happen during the study?**

Being a part of this study involves having two 45-minute appointments with a research nurse or Claire Paton. The appointments will take place approximately 4 months apart. They will be held at the Oncology Building alongside either an outpatient clinic appointment, or a treatment session at Dunedin Hospital. At the first meeting you will be asked to complete five short questionnaires seeking information about your quality of life, your preferences for quality versus quantity of life and a few details about yourself. At the second session you will be asked to repeat four of the questionnaires, and you will be given the opportunity to make any further comments about the issues raised by the questionnaires. Your cancer specialist will be asked to fill in a short form giving details of your cancer type and treatments.

During the appointments you do not have to answer all the questions, and you may stop the interview at any time. The interview will take approximately 45 minutes.

**How will the information that patients provide be kept confidential?**

To ensure confidentiality of data, you will be given a code number that is not the same as your Hospital ID number. The code numbers will be stored away from data files. No data will be collected without your knowledge. Your specialist will not be notified about any questionnaire material. Data will be stored at Dunedin Hospital.

**How do I find out about the results of this study?**

At the end of the study a report will be written. This will describe the results of the study and you may ask for a copy. Please be aware that there will probably be some delay between the completion of the study and the availability of the results. We intend to publish the findings of the study in a peer-reviewed journal, and there may also be a conference presentation of the results. However, no material which could personally identify you will be used in any reports on this study.

**Who do I contact if I have any queries or concerns about my rights as a participant in this study?**

If you have any questions or concerns about your rights you may wish to contact a Health and Disability Services Consumer Advocate (ph: 03 479 0265 or 0800 37 77 66). If there is a specific Maori issue or concern please contact Linda Grennell 0800 37 77 66.

STATEMENT OF APPROVAL

This study has received approval from the University of Otago Board of Graduate Studies (Health Sciences), the Lower South Regional Ethics Committee, the Otago District Health Board Ethics Committee, and the Ngāi Tahu Research Consultation Committee.

**APPENDIX C: Functional Assessment of Cancer  
Therapy–General (FACT-G)**

For this questionnaire please refer to <http://www.facit.org>.

## **APPENDIX D: Quality Quantity Questionnaire (QQQ)**

For this questionnaire please refer to Stiggelbout, A.M. et al., (1996) “Tradeoffs between Quality and Quantity of Life: Development of the QQ Questionnaire for Cancer Patient Attitudes.” *Medical Decision Making*, vol. 16, no.2, pp. 184-92.

## **APPENDIX E: Daily Time Trade-off (Daily TTO)**

For this questionnaire please contact the author of this Thesis

## **APPENDIX F: EuroQol Questionnaire (EQ-5D)**

For this questionnaire please refer to [www.euroqol.org](http://www.euroqol.org).

**APPENDIX G: Socio-demographic Checklist  
(Questions About Yourself)**

For this questionnaire please refer to [www.euroqol.org](http://www.euroqol.org).

## **APPENDIX H: Details of Missing Data**

## Details of Missing Data

### *a) FACT-G*

On the FACT-G questionnaire, all missing data pertained to the Family/Social Well-Being Scale only. At follow-up one patient did not answer one question, and another patient omitted two questions. At both baseline and follow-up one patient commented that two of the questions didn't apply to her situation, and she wrote "n/a" alongside each statement. All three cases were treated as missing data in accordance with guidelines by the FACT-G developers. This meant prorating scores (calculating the mean for completed items of the subscale containing the missing data), and substituting for the missing data (FACIT Organisation, 2009).

### *b) QQQ*

With the QQQ one patient answered Question 4, then scribbled out the response without choosing a substitute answer. The answer was retained as it was her initial choice.

### *c) TTO*

On the TTO one person indicated they would sleep one extra hour per day, would possibly sleep an extra two or three hours per day, but would not sleep four or more extra hours. Her response was taken to be one extra hour of sleep, on the grounds that the nature of the trade-off question engenders uncertainty, and that her only definitive response was for one extra hour.

### *d) EQ-5D*

With the EQ-5D descriptive system, one respondent ticked two boxes for question one. A second person ticked the space between the first two boxes for question two. A third patient drew a box (and ticked it) between two boxes for question four, then proceeded to tick an adjacent box as well. Whilst it is unclear why the first respondent ticked twice for question one, it was obvious from comments made to the interviewer, that the other two patients were not happy with the wording of the EQ-5D questions. The difficulties were encountered with the Mobility, Self-Care, and Pain/Discomfort questions. In accordance with EQ-5D User Guide recommendations (EuroQol Group, 2009), the ambiguous answers were treated as missing data. There were no missing data for the EQ VAS.

## **APPENDIX I: Test Results for each cancer type**

**Table 1: Test means and standard deviations for each cancer type at baseline**

Test instrument		Type of cancer			Overall (n=44)
		Breast (n=15)	Bowel (n=14)	Prostate (n=15)	
FACT-G	Mean	85.6	92.3	89.8	89.2
	SD	8.5	8.5	10.8	9.6
QQQ	Mean	17.1	15.6	14.6	15.8
	SD	4.1	6.3	7.8	6.2
Daily TTO	Mean	5.9	3.7	1.8	3.8
	SD	5.5	4.8	1.7	4.5
EQ VAS	Mean	78.3	84.5	81.7	81.4
	SD	9.6	11.7	15.7	12.5

**Table 2: Test means and standard deviations for each cancer type at follow-up**

Test instrument		Type of cancer			Overall (n=39)
		Breast (n=13)	Bowel (n=11)	Prostate (n=15)	
FACT-G	Mean	85.4	92.4	88.9	88.4
	SD	13.8	8.1	11.9	11.7
QQQ	Mean	17.9	17.1	15.7	16.8
	SD	4.7	6.4	5.8	5.6
Daily TTO	Mean	4.5	3.6	2.7	3.5
	SD	2.8	4.7	4.0	3.8
EQ VAS	Mean	75.9	82.6	83.3	80.7
	SD	16.9	10.3	11.5	13.3

## **APPENDIX J: Results of EQ-5D Descriptive System**

## Results of EQ-5D Descriptive System

Table 1. Frequency of Reported Problems by Dimension on the EQ-5D and Type of Cancer at Baseline

EQ-5D DIMENSION		TYPE OF CANCER			TOTAL (n=44)
		Breast (n=15)	Bowel (n=14)	Prostate (n=15)	
MOBILITY	No problems	15	14	13	42
	Problems	0	0	1	1
	Missing data	0	0	1	1
SELF-CARE	No problems	14	14	15	43
	Problems	0	0	0	0
	Missing data	1	0	0	1
USUAL ACTIVITIES	No problems	7	10	12	29
	Problems	8	4	3	15
	Missing data	0	0	0	0
PAIN/DISCOMFORT	No problems	13	12	11	36
	Problems	2	2	4	8
	Missing data	0	0	0	0
ANXIETY/DEPRESSION	No problems	13	12	13	38
	Problems	2	2	2	6
	Missing data	0	0	0	0

Table 2. Frequency of Reported Problems by Dimension on the EQ-5D and Type of Cancer at Follow-up

EQ-5D DIMENSION		TYPE OF CANCER			TOTAL (n=39)
		Breast (n=13)	Bowel (n=11)	Prostate (n=15)	
MOBILITY	No problems	13	11	12	36
	Problems	0	0	3	3
	Missing data	0	0	0	0
SELF-CARE	No problems	13	11	14	38
	Problems	0	0	1	1
	Missing data	0	0	0	0
USUAL ACTIVITIES	No problems	7	8	10	25
	Problems	6	3	5	14
	Missing data	0	0	0	0
PAIN/DISCOMFORT	No problems	6	10	10	26
	Problems	6	1	5	12
	Missing data	1	0	0	1
ANXIETY/DEPRESSION	No problems	11	11	13	35
	Problems	2	0	2	4
	Missing data	0	0	0	0

## **APPENDIX K: Patient Feedback on the QQQ**

### Appendix K: Patient feedback on the QQQ

id	Ca	Sex	Age	Baseline	QQQ Difficult Follow-up	Comment
01	bowel	F	56	Yes	No	Baseline: "Some are hard to imagine without actually being in the position at this time, but actually will give me something to think about should I ever be in that situation." Follow-up: "Its actually been useful in making me clarify/act on my plans & thoughts"
02	breast	F	56	Yes	Yes	Baseline: "Some questions are hypothetical for me personally, therefore somewhat tricky to respond to" Follow-up: "I felt I'd need more information about possible treatments in order to answer the questions in this section easily"
03	prostate	M	62	Yes	No	Baseline: "Makes one think a bit" Follow-up: nil
04	prostate	M	61	No	No	nil
05	prostate	M	69	Yes	Yes	nil
06	prostate	M	77	Yes	Yes	Baseline: "compounds a lot of ifs" Follow-up: nil
07	bowel	M	70	Yes	Drop out	nil
08	prostate	M	66	Yes	No	Baseline: "At this early stage of treatment some decisions are hard to make. I have been assured my ailment is in the minor category and many of the answers given hopefully will not be necessary to take into account" Follow-up: nil
09	prostate	M	78	Yes	No	nil
10	bowel	M	59	No	No	Baseline: nil Follow-up: "pleased to be able to help"
11	bowel	F	59	No	No	nil
12	bowel	M	41	No	No	nil
13	prostate	M	72	Yes	Yes	nil
14	breast	F	40	Yes	Yes	Baseline: "I would need to know the degree of unpleasantness of side effects etc, to accurately answer this" Follow-up: nil

id	Ca	Sex	Age	QQQ Difficult		Comment
				Baseline	Follow-up	
15	Bowel	M	41	No	No	nil
16	prostate	M	77	Yes	Yes	nil
17	bowel	M	60	Yes	Yes	Baseline: "First time I have considered some of these possibilities" Follow-up: "These questions give the opportunity to think about attitudes to illness" Baseline: "I found it quite pleasant and enjoyed the chance to partake"
18	bowel	F	76	No	Drop out	nil
19	breast	F	44	No	No	nil
20	prostate	M	54	No	Yes	nil
21	breast	F	52	Yes	Yes	nil
22	breast	F	41	Yes	Yes	Baseline: "Difficult to answer given that my position is from aiming to get any rogue cells that may have got elsewhere as opposed to someone who is having treatment to eg shrink a tumour" Follow-up: "Life has been very stressful on several other fronts (i.e. not including dealing with cancer treatment) so it is somewhat difficult to answer questions without allowing that to affect my answers"
23	prostate	M	65	No	No	nil
24	breast	F	38	Yes	No	nil
25	breast	F	48	Yes	No	Baseline: "It is hard to predict how one might deal with events in future that may not happen or that you do not know enough about the side effects or impact on one's enjoyment or life quality"
26	breast	F	46	Yes	Drop out	nil
27	prostate	M	63	Yes	No	Baseline: "I base a lot of my answers on what I consider my worth to those around me especially my close family" Follow-up: nil
28	prostate	M	59	No	No	nil
29	bowel	F	66	See comment	Yes	Baseline: "If 'difficult' relates to emotional difficulties in thinking about such things 'No'. If it relates to the possible ambiguity of some statements 'Yes'. Follow-up: "I found some questions ambiguous and would have liked space for an alternative answer"
30	bowel	M	55	No	No	nil

id	Ca	Sex	Age	QQQ Difficult Baseline	QQQ Difficult Follow-up	Comment
31	breast	F	54	No	No	nil
32	breast	F	44	No	Yes	Baseline: "My answers would depend entirely on the length of survival time therefore I answer neither agree nor disagree" Follow-up: "Difficult to answer unless actually have to make these choices"
33	breast	F	45	Yes	No	nil
34	breast	F	48	No	No	nil
35	breast	F	47	No	No	nil
36	prostate	M	71	Yes	No	Baseline: "My situation is not dire enough to personally be confronted with some of these issues" Follow-up: nil
37	bowel	F	43	Yes	No	Baseline: "Having to consider the concept of dying was hard" Follow-up: nil
38	bowel	F	62	No	No	Baseline: nil Follow-up: "Some questions were difficult to answer as it would depend on how severe the side effects might be"
39	bowel	F	45	Yes	Yes	Baseline: nil Follow-up: "Too many variations in real life. And the 'always' questions don't really make sense as an absolute, not a scale"
40	bowel	F	67	No	Drop out	nil
41	prostate	M	69	Yes	No	nil
42	breast	F	61	No	Drop out	Baseline: "I liked the neither agree nor disagree choice"
43	prostate	M	64	No	No	nil
44	breast	F	33	No	No	Baseline: nil Follow-up: "Answers may change when actually faced with treatment in life"