UTILITY ASSESSMENT OF HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN COLORECTAL CANCER PATIENTS: A MIXED METHODOLOGY STUDY

by

Sarah E. Costa

Master of Science (MSc) Thesis
A thesis submitted in conformity with the requirements for the degree of
MSc, Health Services Research

Graduate Department of Health Policy, Management and Evaluation

University of Toronto

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Abstract

**Background:** Variation exists in quality of life (i.e., utility) estimates depending on the utility elicitation method utilized. Using the EQ-5D, VAS, and HUI-III, the aim of this thesis was to determine whether these measures adequately capture HRQOL in a CRC population and assess the relationship between utility estimates generated. **Methods:** A mixed methods study design was employed to collect health status scores and interview data from a sample of 50 CRC patients in Toronto, Ontario. **Results:** Mean utility scores between the EQ-5D and HUI-III were identical at 0.76 (95% CI), with an overall VAS score of 0.72 (95% CI). **Conclusion:** The fact that the EQ-5D and HUI-III resulted in identical mean utility scores provides assurance for future studies using these tools in CRC. However, many factors that CRC patients identify as important to their HRQOL are not captured by these instruments. These findings have implications for informing economic evaluations.
Acknowledgements

This thesis would not have been possible without an enormous amount of support and guidance from my supervisor, Jeffrey Hoch, PhD; my sincerest gratitude is extended to you Jeffrey. I am also extremely grateful to my committee member, Mark Dobrow, PhD, for his mentorship and feedback on this thesis. Appreciation is also extended to the members of my defense committee, Dr. Craig Earle and Audrey Laporte, PhD, for taking the time to review this thesis and their offering of critiques on how to improve it’s quality.

I would also like to thank the two supervising oncologists at the Odette Cancer Centre and Princess Margaret Hospital who, without their willingness to assist me with my research, this research study would not have been possible. Thanks is also extended to the patients who took the time to participate in my study. I am very grateful as well to my colleagues at Cancer Care Ontario, as well as my friends and family for their tremendous support and encouragement along my journey.

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<th>Description</th>
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<tbody>
<tr>
<td>EQ-5D</td>
<td>EuroQol 5-Dimension Survey on Health Status</td>
</tr>
<tr>
<td>CBA</td>
<td>Cost-Benefit Analysis</td>
</tr>
<tr>
<td>CEA</td>
<td>Cost-Effectiveness Analysis</td>
</tr>
<tr>
<td>CED</td>
<td>Committee to Evaluate Drugs</td>
</tr>
<tr>
<td>CDN</td>
<td>Canadian Dollars</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>CRC</td>
<td>Colorectal Cancer</td>
</tr>
<tr>
<td>CUA</td>
<td>Cost-Utility Analysis</td>
</tr>
<tr>
<td>FACT-C</td>
<td>Functional Assessment of Chronic Illness – Colorectal</td>
</tr>
<tr>
<td>FOBT</td>
<td>Fecal Occult Blood Test</td>
</tr>
<tr>
<td>HRQOL</td>
<td>Health-related Quality of Life</td>
</tr>
<tr>
<td>HUI-III</td>
<td>Health Utility Index, version 3</td>
</tr>
<tr>
<td>ICER</td>
<td>Incremental Cost-Effectiveness Ratio</td>
</tr>
<tr>
<td>MoHLTC</td>
<td>Ministry of Health and Long-Term Care</td>
</tr>
<tr>
<td>NDFP</td>
<td>New Drug Funding Program</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Health and Clinical Excellence</td>
</tr>
<tr>
<td>OCC</td>
<td>Odette Cancer Centre</td>
</tr>
<tr>
<td>OS</td>
<td>Overall Survival</td>
</tr>
<tr>
<td>PMH</td>
<td>Princess Margaret Hospital</td>
</tr>
<tr>
<td>QALY</td>
<td>Quality Adjusted Life Year</td>
</tr>
<tr>
<td>SG</td>
<td>Standard Gamble</td>
</tr>
<tr>
<td>TNM</td>
<td>Tumour Nodes Metastases</td>
</tr>
<tr>
<td>TTO</td>
<td>Time Trade-Off</td>
</tr>
<tr>
<td>USD</td>
<td>United States (US) Dollars</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual Analog Scale</td>
</tr>
<tr>
<td>WTP</td>
<td>Willingness-to-Pay</td>
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KEYWORDS

Colorectal Cancer (CRC); Economic Evaluation; EuroQol (EQ-5D); Health-related Quality of Life (HRQOL); Health Services Research; Health Utility Index (HUI-III); Qualitative; Quality Adjusted Life Year (QALY); Utility Weights; Visual Analog Scale (VAS)
CHAPTER 1: INTRODUCTION

The concept of health-related quality of life (HRQOL) is a hotly debated one. The basic premise is that we experience various health states for a specified time period, and that each state is associated with a certain preference or utility. The integration of quantity and quality of life is captured by the concept of the quality-adjusted life year (QALY), which is widely debated in theory and application (Gold et al., 1996); (Fitzpatrick et al., 1992); (Hoffmann et al., 2002); (Nord, Daniels, & Kamlet, 2009); (Hall, 1991); (Greenberg & Pliskin, 2002). Nevertheless, the QALY serves an important purpose in economic evaluation. The QALY offers a way to compare different outcomes in different disease settings, enabling economic evaluations to offer a ‘rational approach’ to healthcare resource allocation decision-making, (Drummond, Sculpher, Torrance, O’Brien, & Stoddart, 2005); (Dolan, 2000); (Kind, Lafata, Matuszewski, & Raisch, 2009).

The availability of a variety of techniques and methods that are used to measure an individual’s preferences (or utilities) for health states has led to inquiry about the various methods and whether they yield different results; other important issues include how much variation are we willing to accept, and what are the implications of such differences on policy and resource allocation decisions (Feeny & Eng, 2004); (Konerding, Moock, & Kohlmann, 2009); (Grutters et al., 2007).

The choice of which utility measure to use is an important one for any disease area, cancer in particular. The various physical, mental, emotional, and psychological implications of the more than 200 diseases referred to as ‘cancer’, and the effects they have on the patient experiencing the disease often negatively and severely impact quality of life. In particular, a diagnosis of CRC can have significant implications on HRQOL. Depending on the stage of cancer (I through IV) and treatment undergone, a diagnosis of CRC can be accompanied by a
series of side effects that can impact patient quality of life in a variety of ways – physically, emotionally, and psychosocially (Wilson, Birks, & Alexander, 2010; Sahay, Gray, & Fitch, 2000).

In 2010, 22,500 new cancer cases of CRC were expected to be diagnosed in Canada with 9,100 deaths from the disease - 3,400 of which would be in Ontario alone. Second to lung cancer, CRC is the second leading cause of death from cancer in Canada (Canadian Cancer Society, 2009a). Costs for treatment of CRC are also very expensive, for instance Avastin, a newly approved chemotherapy regime for certain CRC patients, can cost $35,000 for a 10-month regime (Ontario Ministry of Health and Long Term Care, 2009). In addition to prevalence of CRC, attitudes toward the disease help to contextualize the perceived ‘burden’ on patients. For instance, the results of a recent national survey on the attitudes and awareness of Canadians on CRC screening reported that approximately one-third of people surveyed felt that CRC was the “worst possible cancer to have” (Parsons, 2010).

While a number of research studies have found that different preference-based measures (i.e. EQ-5D) produce different utility scores for the same group of respondents, little consideration has been given to the implications of these findings, specifically in the economic and policy decision-making arenas (Grutters et al., 2007); (Sach et al., 2009); (McDonough & Tosteson, 2007); (McNamee & Seymour, 2005). Of interest to the current research study is whether the observation that different measures yield different outcomes holds true in CRC. To the best of the researcher’s knowledge, this is an area that has not been well studied. Considering these questions, this research study has been designed to explore and better understand HRQOL in CRC and how it is measured and valued by patients with the disease.
1.1 Research Questions

The overall aim of this thesis was to determine how well current health status measures capture HRQOL in a CRC population, as well as offer insights into the level of agreement between the EQ-5D, VAS and HUI-III utility assessments. To this end, the research objectives of this study are threefold: (i) to assess the relationship between health state preference measurements and utility estimates generated from two generic preference-based instruments and one rating scale in a group of colorectal cancer (CRC) patients receiving treatment in Toronto, Ontario; (ii) to better understand the experience of CRC patients and uncover the factors they attribute to being important to their HRQOL; and (iii) to determine whether these HRQOL factors already exist as dimensions on the EQ-5D and HUI-III. This mixed-methods study will address four research questions:

1. Are there differences in utility scores in a sample of CRC patients when using the EQ-5D and the HUI-III?
2. How do various factors impact the utility scores generated using the EQ-5D and the HUI-III?
3. What are the factors of HRQOL that CRC patients describe as important to them?
4. Do the EQ-5D and the HUI-III satisfactorily capture patient-described HRQOL factors in their respective survey dimensions?
CHAPTER 2: BACKGROUND

This chapter provides an overview of CRC, specifically the characteristics of the disease and its prevalence in Ontario. Following this is a discussion of economic evaluation and the various methods for measuring health-related preferences (i.e., utilities), and some of the methodological debates surrounding these methods. Finally a discussion of HRQOL in CRC is explored, providing the reader with a contextual and conceptual framework for the study.

2.1 Colorectal Cancer

In a recent national survey on the behaviours and attitudes of healthy Canadians in relation to CRC, one-third of respondents felt that CRC was the ‘worst’ type of cancer, one that was feared the most (Parsons, 2010). CRC, highly curable if caught early but accompanied by rapidly decreasing prognosis as the disease develops, still stands as the second-leading cause of cancer-related deaths in Ontario for males and the third-leading for women, despite improvements in five-year survival over time (see Figure 1) (Canadian Cancer Society, Public Health Agency of Canada, & Statistics Canada, 2010). Recent provincial initiatives and investments such as the ColonCancerCheck (CCC) program, Canada’s first comprehensive screening program for CRC, have raised interest and brought attention to this disease in an effort to increase patient survivorship. However in light of these efforts, the fact remains that survivors of non-metastatic CRC face an estimated 40% chance of recurrence of the disease, and that many of these survivors face disease-specific lingering issues such as neuropathy, sexual dysfunction, and bowel dysfunction (Faul, Shibata, Townsend, & Jacobsen, 2010).

This chapter begins with an overview of the burden of the disease, including prevalence, treatment and cost, to set the stage for study of this disease. Following this, a broad outline of economic evaluation and its application in the field of healthcare and patient preferences for health status will be provided. Finally, the chapter concludes with an in-depth exploration of
HRQOL as experienced by patients having the disease, providing the rationale for this multi-method research study.

**Figure 1 - Age-standardized 5-year survival for 14 common cancers in Ontario including CRC**

![Figure 1](image_url)

(Cancer Quality Council of Ontario, 2010)

### 2.1.1 Epidemiology

Colon and rectal cancers arise from the same cell type, and hence are often referred to collectively as CRC. When the cells lining both the colon and rectum become abnormal and divide, they can develop benign growths called polyps (Boyle & Langman, 2000). Although not all polyps are cancerous, over a period of time (i.e., generally 8 to 12 years), some polyps can become malignant (Chu, 2010). Due to the relatively long precancerous phase between exposure to a risk factor and development of cancerous polyps, as well as better prognosis and chance at cure the earlier the disease is caught, CRC is an ideal candidate for screening programs (Marshall et al., 2007). So far in Canada, four provinces (Ontario, British Columbia [in selected regions],
Alberta and Manitoba) have implemented province-wide CRC screening programs based on the fecal occult blood test (FOBT), a non-invasive type of screening procedure for the disease.

As earlier stage at diagnosis is correlated with increased overall survival (OS) rates, some consideration must be given to the process of staging the cancer. Staging is based on how far the cancer has progressed into the surrounding colon and rectal walls, and whether the cancer has spread to the lymph nodes and surrounding organs and tissues (O'Connell, Maggard, & Ko, 2004; Boyle & Langman, 2000).

In CRC, the most precise and most frequently used staging system is the Tumour Nodes Metastases (TNM) system, a disease grading system that describes the extent to which the cancer has spread beyond its initial point of diagnosis (Colorectal Cancer Association of Canada, 2010). Prognosis of CRC can be measured according to its expected five-year OS, which ranges dramatically depending on the stage classified at diagnosis. For instance, for patients diagnosed with stage I CRC, five-year OS is high, at 93%, compared to 72-85% for stage II, 44-83% for stage III and just 8% for stage IV (O'Connell et al., 2004). Despite the advances in five-year OS, survival rates for CRC are in fact lower than for many other cancers (Kurtz, Kurtz, Stommel, Given, & Given, 2002).

2.1.2 Disease Burden

Disease burden includes prevalence of the disease, treatment protocols and costs associated with treatment and long-term care.

(i) Prevalence: CRC is highly prevalent in Canada, primarily in adults aged 50 years and over, with Ontario having one of the highest rates of CRC in the world (Canadian Cancer Society, 2008). According to the Canadian Cancer Society, one in 14 men and one in 16 women will develop CRC during their lifetime (Canadian Cancer Society, 2009a), with one in 27 men and one in 31 women at risk of dying of CRC (Canadian Cancer Society 2009). In 2009 alone, an estimated 171,000 new cancer cases are expected to be diagnosed in Canada, with an expected
8,100 of those cases diagnosed in Ontario alone. CRC is the third most common cancer in Canada and the most common cause of cancer deaths among non-smokers in Ontario (Schultz et al. 2004).

There are many risk factors associated with CRC, including family history, diet, low levels of physical activity and age (Boyle & Langman, 2000). Increasing age can lead to greater prevalence of and mortality from CRC (Canadian Cancer Society et al. 2008). Figure 2 illustrates the distribution of the 21,500 new cases of CRC in 2008 by age and sex combined (Canadian Cancer Society et al. 2008), and Figure 3 depicts the changing demographics from 2008 (Statistics Canada, 2008). Growth projections for the next 23 years show a larger percentage of the population will be aged 50 years or older, thereby increasing the number of individuals at risk of CRC.

(ii) Treatment Protocols: Treatment protocols for CRC vary depending on the severity of the disease (i.e. stage of cancer), general health of the patient including the patient’s age, and whether the cancer is a newly diagnosed or recurrent (National Cancer Institute, 2011). In Canada, surgery and chemotherapy are the most common types of treatment modalities for CRC, with radiation therapy also used for the treatment of rectal cancer (Canadian Cancer Society, 2009b).
Table 1 outlines the characteristics of each stage of CRC and the most common treatment options for each. Chemotherapy is appropriate as a treatment modality in particular for stage III
and IV CRC. Most patients with stage I to III diagnosis of CRC undergo surgery, followed up with adjuvant chemotherapy for stage II and III patients (Maroun et al., 2003). Cancer Care Ontario’s Program in Evidence-Based Care has developed a series of evidence-based clinical practice guidelines that advise on treatment protocols for specific disease sites, including CRC. The guideline recommendations for adjuvant chemotherapy for CRC support the use of FOLFOX, a type of chemotherapy that combines fluoropyrimide, leucovorin, and oxaliplatin drugs, as the preferred chemotherapy treatment regimen in stage III cancer, with capecitabine being considered the next most appropriate treatment option (Program in Evidence-Based Care, 2009). Capecitabine is delivered orally, while FOLFOX is delivered intravenously, a more traditional format for delivery of chemotherapy. Although preferred, there are challenges associated with delivering chemotherapy intravenously, including side effects that can be troublesome for patients and more burdensome in terms of time required by the healthcare team to deliver the treatment. These side effects, which can impact quality of life significantly, will be discussed further in this section.

(iii) Cost - The economic impact of treatment for CRC in Ontario is substantial. From 2005 to 2008, the provincial government, the MoHLTC, had invested $53 million in CRC drugs alone, committing another $30 million until 2011 to fund Bevacizumab (Avastin), the controversial and hailed ‘groundbreaking drug’ for advanced CRC (Ontario Ministry of Health and Long Term Care, 2008).

Table 1 - Characteristics of CRC Disease Stage and Suggested Protocols

<table>
<thead>
<tr>
<th>Stage of Cancer</th>
<th>Characteristics of Stage</th>
<th>Suggested Treatment Protocol</th>
</tr>
</thead>
</table>
| 0 (in Situ)     | • Abnormal cell formation in innermost lining of colon  
                   • Risk of cells becoming cancerous and spreading to normal tissue areas | • Surgery: local excision or polypectomy  
                                                                                   • Possible resection and anastomosis |
<table>
<thead>
<tr>
<th>Stage of Cancer</th>
<th>Characteristics of Stage</th>
<th>Suggested Treatment Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (Duke’s A)</td>
<td>▪ Cancerous cells have spread to inner wall of colon or rectum</td>
<td>▪ Surgery: resection</td>
</tr>
</tbody>
</table>
| II (Duke’s B)   | ▪ Tumour extends more deeply into the wall of the colon or rectum  
|                 | ▪ Cancerous cells have not spread to lymph nodes | Can include either:  
|                 |                                                       | ▪ Surgery: resection and anastomosis  
|                 |                                                       | ▪ Chemotherapy post-surgery |
| III (Duke’s C)  | ▪ Cancer has spread to nearby lymph nodes but not to other parts of the body | Combination of  
|                 |                                                       | ▪ Surgery: resection and anastomosis  
|                 |                                                       | ▪ Chemotherapy post-surgery |
| IV (Duke’s D)   | ▪ Cancer has spread to other parts of the body, i.e. liver or lungs | Combination of  
|                 |                                                       | ▪ Surgery: resection with or without anastomosis  
|                 |                                                       | ▪ Surgery to remove parts of other organs (liver, lungs)  
|                 |                                                       | ▪ Chemotherapy |
| Recurrence      | ▪ Cancer that has returned after treatment, either in the colon or other parts of the body (lungs, liver) | |

(National Cancer Institute, 2011)

With cost estimates of this drug stated to be as high as $35,000 per patient for one 10-month treatment course or between $1,500 and $2,000 per treatment, it comes as little surprise that significant controversy surrounded the decision made by the MoHLTC Executive Officer to fund this drug, despite the recommendation made by the Committee to Evaluate Drugs (CED), an independent advisory group that makes recommendations to the MoHLTC regarding the inclusion of certain drugs, not to fund Avastin through Cancer Care Ontario’s New Drug Funding Program (NDFP) (Ontario Ministry of Health and Long Term Care, 2009). Despite this however, the provincial government announced in 2008 its decision to fund the drug for first line chemotherapy for the first six months of treatment (Ontario Ministry of Health and Long Term Care, 2009); (Ontario Ministry of Health and Long Term Care, 2008). At least one additional cost-effectiveness analyses also concluded that Avastin was not a cost-effective investment ((Tappenden et al., 2007b; Tappenden et al., 2007a). The Ombudsman Report, *A Vast Injustice*
Sarah E. Costa (September 2009), was a strong influence in the decision of the Ontario government to continue to fund the drug for patients who otherwise would be forced to pay out-of-pocket for the cost of Avastin once their 16-cycle treatment term had expired (Marin, 2009). As the Ombudsman André Marin states in the report:

I do not believe that Ontarians, for the sake of cost containment, should be left to pay for treatment with Avastin out of their own pockets or abandon a treatment that is working and that specialists consistently agree should be continued until disease progression…(Marin, 2009).

In one study conducted by Maroun et al., it was found that the average lifetime cost of managing CRC patients ranged from $20,319 (CDN) for a TNM stage I colon cancer patient, to $39,182 (CDN) for a more advantaged stage III rectal cancer patient, with the majority of these costs attributable to periods of hospitalization (NB: cost estimates for colon and rectal cancers combined were not available); (Maroun et al., 2003). Similarly in another Canadian cost-of-illness study conducted in Nova Scotia, it was estimated that the three-year hospital cost for 593 patients with invasive CRC was $9.8 million (O’Brien, Brown, & Kephart, 2001). Other more recent estimates report the estimated lifetime cost for treatment and care in North America for a patient with CRC as closer to $100,000 USD (approximately $105,000 CDN) (Paramore, Thomas, Knopf, Cragin, & Fraeman, 2006).

2.1.3 Impact of age, sex, and time since diagnosis on side-effects

As the five-year survival rate of CRC has improved over time thanks in part to technological advances, a shift in focus on survivorship programs and outreach to CRC survivors is gaining more emphasis both in Canada and in the United States (Donovan, Thompson, & Hoffe, 2010). There is evidence that patients of different age groups have different attitudes toward the disease, specifically, that younger patients express concern over their own mortality and their families, with some studies having found that levels of emotional distress and ‘post-traumatic stress disorder’ are higher among younger patients than older (Sharma et al., 2007;
Zebrack, Yi, Petersen, & Ganz, 2008). Older patients on the other hand, are found to experience relatively more depression and anxiety than their younger counterparts; one likely reason for this is the presence of co-morbidities in older patients, which may contribute to the feelings of distress (Kurtz et al., 2002; Ramsey, Berry, Moinpour, Giedzinska, & Andersen, 2002).

In Wilson et al.’s research where quality of life survey results for patients younger than 65 years were compared to those older than 75 years, it was found that the survey scores of the younger patients were significantly worse compared to the older group of patients (Wilson, Alexander, & Kind, 2006). Regardless of age however, physical issues such as bowel problems, diarrhea and constipation were not found to vary significantly in terms of severity or frequency by age (Phipps, Braitman, Stites, & Leighton, 2008). Overall, age is an independent predictor of quality of life in CRC (Sharma et al., 2007).

Important differences in quality of life findings have also been noted between males and females in how they approach the disease and the impact of the disease on them. For instance, female patients more frequently presented in a clinical setting with depressive symptoms as compared to males, while also reporting greater limitations with respect to problems with feeling energized and ‘performance of daily activities’ (Kurtz et al., 2002; Phipps et al., 2008). Women generally express feelings of depression and anxiety more frequently than men do; as one researcher stated, feelings of ‘hopelessness’ and ‘fatalistic’ feelings were higher among women (Nordin & Glimelius, 1997). Not surprisingly, males were found to report significantly higher quality of life scores than females in a study conducted by Zebrack et al., although females were more likely to report a more ‘positive’ experience with the cancer (Zebrack et al., 2008). Significant differences between sexes in how they perceive their bodies is not evident in the literature, as both males and females report feeling to some degree that a diagnosis of CRC has contributed to body image issues (Nordin & Glimelius, 1997). In more recent research, body
image issues have been found to be linked more significantly to younger, female patients as opposed to their male counterparts (Ramsey et al., 2000).

Limited information is available on quality of life since time of diagnosis with respect to CRC; however, Ramsey et al. did find in their study on quality of life in survivors of CRC that HRQOL was highest during the first two to three years after diagnosis (Ramsey et al., 2000).

A diagnosis of cancer is a life-altering change in anyone’s life, and to some extent, the cancer type, stage, treatment, and ensuing side effects may all play a role in shaping one’s experience with the cancer diagnosis. This may include changes in levels of distress or anxiety, the presence of strained relationships and other emotional issues (Zebrack et al., 2008). It may seem a challenging, if not near impossible task to measure or quantify such experiences.

In the next section, we explore the concept of the quality adjusted life year (QALY), a measure used in cost-utility analyses (a type of economic evaluation) that incorporates not just the quantity of one’s life, but also the multiple and varying states of health, or quality of life, that exist in our lives.

2.2 Economic Evaluation and the QALY

Factors mentioned in the preceding section - the combination of the relatively high incidence and prevalence of CRC among Ontarians, the high cost of treating CRC including dedicated funding for expensive drugs, and the impact on quality of life of the disease - are all important motivations for conducting economic evaluation of cancer treatments and programs. As part of the evidence base used to make healthcare decisions, economic evaluations combine cost information, as well as information on the effect of the intervention in question on the quality of life of its targeted audience (i.e. decision-makers), to model these comparisons. As final decision-making often involves the findings from comparative economic evaluations,
consideration must be given to the quality of the inputs, including the quality of life estimates - the accuracy, relevancy, validity, and completeness of this information.

In the coming sections, we move towards applying what is known about CRC including the high cost of treatment drugs and their side effects, and provide an overview of economic evaluation and the various methods which are used to measure HRQOL for these evaluations.

2.2.1 Economic Evaluation

Resources are scarce and finite in most environments, including the healthcare market (Hall, 1991). An opportunity cost exists for everything that is manufactured, delivered, and serviced (Folland, Goodman, & Stano, 2004). Hence, a tradeoff between competing choices is inevitable, and a decision must be made regarding which healthcare intervention to invest in given the amount and type of resources consumed by the intervention (costs), and the health improvement (output) generated by the intervention (Torrance, 1987).

Economic evaluations have increasingly been used in the healthcare field to aid decision making when faced with various options for investment. In an economic appraisal, competing options are analyzed based on their costs, which are usually monetary, and consequences, that is, the impact on health outcomes (Drummond et al., 2005); (Raftery, 1998). The change in cost and health outcome from using a certain (i.e. newer) technology or intervention is compared to the competing intervention, and a decision is made about whether the intervention in question is “cost-effective” by comparing the outcome to an accepted threshold. In Canada, a cost-effectiveness threshold does not exist per se, although some state the range is between $20,000 to $100,000 per QALY, a concept explored later in this chapter (Laupacis, Feeny, Detsky, & Tugwell, 1992). In the United Kingdom, the National Institute of Clinical Excellence (NICE) uses a threshold range of £20,000 to £30,000 per QALY gained (Cameron & Bennett, 2009). Variation does exist however in the quality of such evaluations due in part to a lack of
methodological rigor, thereby limiting the usefulness of them in informing decision makers (Hoffmann et al., 2002). In other cases, the role of political influence and pressure can strongly influence decision-making behaviors beyond what the evidence in an economic evaluation provides. An example of such turmoil in a healthcare decision-making context can be seen in the recently publicized case of Avastin, a drug which provides only minimal advantage in terms of improved health outcomes and survival time compared to conventional treatment for the CRC patient population (Deber, 2008).

There are three main types of economic evaluations: cost-effectiveness (CEA), cost-benefit (CBA), and cost-utility analyses (CUA) (Raftery, 1998). Although each type of evaluation serves a similar purpose, each has been adapted to take account of various shortcomings that limit their applicability, differing in their approach to measuring health outcomes (Tan et al., 2006). For instance, a CUA focuses particularly on the quality of life in the health outcomes produced. In a CUA, health outcomes are measured in terms of QALYs gained, a measure of health that combines duration of life and health-related quality of life (Drummond et al., 2005). The primary outcome of a CUA is the incremental cost-effectiveness ratio (ICER), or cost per QALY. ICERs are calculated as the difference in the cost of two interventions, divided by the difference in the QALYs produced by the two interventions (McCabe, 2009).

A CUA is intended to address four areas that conventional CEAs do not: i) limited comparability across interventions, ii) explicitly stating the opportunity cost of selecting one intervention over another (although, a CEA may also do this), iii) addressing multiple health outcomes of interest, and finally, iv) assigning weights (utilities) to different outcomes (Drummond et al., 2005). The number of published CUAs has steadily increased over the last twenty years (see Figure 4).
2.2.2 Utilities and the QALY

Quality of life assessment is growing in popularity in health research studies as a means of capturing people’s preferences, or utilities (Torrance, Furlong, & Feeny, 2002); (Ko, Maggard, & Livingston, 2003). While there are other methods available that capture quality of life, in economic evaluation, the QALY is the most popular.

Figure 4 - Growth of the cost–utility literature over time

(Greenberg, Earle, Fang, Eldar-Lissai, & Neumann, 2010)

Quality Adjusted Life Year (QALY)

The QALY represents the best known (and some would argue, the best available) preference-based outcome measure, combining length of life and subjective feelings of well-being (National Information Center on Health Services Research and Health Care Technology (NICHSR), 2009); (Smith, Drummond, & Brixner, 2009). Although there is some controversy over the use of the
QALY as an outcome measure, it is difficult to find another method that compares different health outcomes so effectively and is ‘universally meaningful, valid, reliable and relevant’ (McGregor, 2003). In a review by Richardson et al. (2004) on preference-based health status data, 20 of the 23 published CUAs used QALYs, revealing also that the majority of studies used the EQ-5D and HUI to determine QALYs, with 80% of the studies having used the EQ-5D (Richardson & Manca, 2004).

QALYs are measured on a preference-based scale with 1 representing perfect (or best imaginable) health, and 0 representing the worst imaginable health (or a health state equivalent to death). Utilities that represent HRQOL are used to calculate the QALY, in combination with an estimate of the amount of time a person remains in that health state (Torrance et al., 2002; Horsman, Furlong, Feeny, & Torrance, 2003). When comparing two interventions, and assuming the two groups start with the same baseline utility, the area between the two curves represents the QALYs gained as a result of the intervention or treatment (see Figure 5). A review of utility theory as well as an overview of the two main approaches to measuring utilities will be explored next.

**Figure 5 - Quality-Adjusted Life Year (QALY)**

(Drummond et al., 2005)
Utility Theory

Utility theory is the underlying theoretical framework behind individual decision-making for preferences, developed by von Neumann-Morgenstern over half a century ago (Torrance et al., 2002); (Drummond et al., 2005). This theory is based on the principle of individual ‘rational behaviour’, specifically under uncertain conditions, and provides a model to guide how individuals should make decisions if they follow the assumed principle (Drummond et al., 2005). The robustness of this theory comes from the two main ‘mathematical axioms’ as follows (for a more detailed and complete description, see (Torrance et al., 2002):

i) *preferences exist and are transitive* – this axiom states if there exists two risky prospects ($y_1$ and $y_2$), either $y_2$ must be preferred to $y_1$, $y_1$ to $y_2$, or the individual is indifferent to both; and

ii) *continuity of preferences* – this axiom states that if there are three outcomes of interest, and that outcome A is preferred to B which is preferred to C, there is a certain probability that the individual is indifferent between encountering B (with certainty), encountering A (with probability p), and C (with probability 1-p).

2.2.3 Methods of Measuring Utilities

There are various methods for measuring utility: direct, multi-attribute or indirect (Torrance et al., 2002). This is important because decision-makers who rely on these assessments to inform decisions, should be confident that their decision rests on sound utility elicitation theory. However, research has shown that contrary to this, a number of methods exist to capture this information, subjecting CUAs to a range of utility estimates that when combined with cost information, can yield vastly different cost-per-QALY estimates (Grutters et al., 2007; Bell, Chapman, Stone, Sandberg, & Neumann, 2001); (Drummond et al., 2005). Not all instruments are created equally, and attention needs to be given to the selection of instrument that is best
suited to the research question (Feeny & Eng, 2004; Konerding et al., 2009); (Fryback, Palta, Cherepanov, Bolt, & Kim, 2010); (Morimoto, Fukui, Morimoto, & Fukui, 2002). In a recent review by McDonough and Tosteson, the researchers found no research that directly investigated the impact of choice of method on policy decisions, although the implications are assuming significant if the various methods yield differences in utility scores between them (McDonough & Tosteson, 2007). While the impact of instrument selection is an important one that can affect policy decisions, the focus of this thesis is limited to the presentation and analysis of the results provided on the EQ-5D, VAS and HUI-III health status surveys and does not attempt to make inferences about the implications on policy decision-making. However, if the choice of instrument affects QALY measurement, the implications on policy recommendations seem straightforward.

When reviewing utilities in the literature of CRC patients by stage of cancer, the variation in utilities is evident, depending on the type of instrument used to collect this information. In fact, in a study by Konerding et al., not only was it found that the EQ-5D and the HUI-III produce different utility weights for the same health state, but it was also determined that the values could not be ‘transformed’ into the other using any sort of mathematical algorithm (Konerding et al., 2009). Such variation is commonplace to a variety of cancers and diseases studied – for instance, Ramsey et al. noted a difference in utility scores that occurs when using different utility elicitation methods (i.e. disease-specific and generic instruments) among long-term survivors of CRC; Hornberger et al. found that in the case of kidney dialysis, economic evaluation results using different direct preference-based health status instruments (including standard gamble and time trade-off) can vary by a factor of almost $10,000 per QALY; and other researchers such as Gabriel et al., found an almost four-fold increase in cost-per-QALY estimates for osteoporosis interventions depending on whether utilities were generated from the
Thus, the three main points are: (1) there are various methods that can be used to elicit preference-based scores for an intervention or program of interest; (2) the various methods are known to yield different results, and (3) different results have the potential to change the outcome of the cost-per-QALY estimate, or ICER, which can affect healthcare policy (e.g., the decision of whether to fund a drug).

**Utility Elicitation Instruments (Direct)**

There are a number of instruments that can be used to collect utilities based on direct preference elicitation, but three of the most well-established and commonly used instruments in healthcare are the standard gamble (SG), time trade-off (TTO) and visual analog scale (VAS). In addition to the fact that direct utility elicitation is a very time-consuming task, each of the instruments has its own set of weaknesses and strengths which will be discussed later in this chapter. There is no unanimous agreement regarding an established ‘gold standard’ for a utility elicitation instrument. However, it is agreed upon that the SG direct utility elicitation instrument is taken to be comparatively closer to a ‘gold standard’ than the others (Ness et al., 1999).

The SG is based directly on the von Neumann-Morgenstern axioms described above (Drummond et al., 2005). With the SG, the individual is presented with two alternatives, where ‘alternative 1’ is a treatment that, if taken, can have two possible outcomes with two different probabilities associated with them. ‘Alternative 2’, on the other hand, is associated with a certain fixed probability for a chronic health state. Participants indicate on a scale, usually from 1 to 10, the number of years in full health they feel is of equal value to a pre-determined number of years in their current health state. The participant’s score is calculated by dividing the number
corresponding to where they indicated on the scale by a factor of 10. This number is then usually used to calculate the QALY.

The TTO is a direct utility elicitation instrument developed specifically for use in healthcare (Morimoto et al., 2002). The TTO is considered to be a viable alternative to the SG method; however, the theoretical underpinnings of this instrument have not been explored as in-depth as they have been with the other methods such as the SG (Torrance et al., 2002); (Drummond et al., 2005). With the TTO, the participant is asked how many years in ‘optimal’ health \(y\) is equivalent to a state that is worse than optimal \(x\) (Van Den Hout et al., 2002). Time is varied until respondents show that they are indifferent between these two possible outcomes. The individual is being asked what their trade-off point is between being in a better health state with fewer years of life compared to their current living state with more years of life (Drummond et al., 2005). The utility value \(U\) is then calculated using the following formula: \(U = y/x\).

Finally, the visual analog scale (VAS) is a rank-based method whereby participants are asked to rate a set of health outcomes from most to least preferred, and then to scale these outcomes (Drummond et al., 2005). Although not a direct method to be used to elicit utilities, the VAS is used to measure health status. This tool is particularly subject to measurement bias, in part because participants will usually avoid placing outcomes at the far ends of the scale. Nevertheless, there are some who advocate for its use (Parkin & Devlin, 2006). Refer to Appendix A for a visual description of the standard gamble and time trade-off tools.

Utility Elicitation Instruments (Indirect)

Preference-based measures capture the effectiveness of a particular intervention and combined with changes in cost, represent the incremental cost-effectiveness ratio, or ICER. ICERs are compared between various interventions to determine their relative economic
attractiveness, enabling payers to make informed decisions about the economic consequences of investing in competing alternatives. There are also many different types of indirect, multi-attribute systems that can be used to directly measure the HRQOL of patients. The EQ-5D has been in existence since 1987 and has since become well-known as a standardized instrument for measuring health outcomes (see Appendix C) (EuroQol Group, 2009). The EQ-5D includes five dimensions against which HRQOL is assessed: i) Mobility; ii) Self-care; iii) Usual Activity; iv) Pain/Discomfort; and v) Anxiety/Depression (Brooks, Rabin, & de Charro, 2003). Validation of the EQ-5D has occurred in a variety of settings, including cancer (McDowell, 2006). Since 2001, the number of published cancer-related studies using the EQ-5D has increased significantly, likely due to the publication of a “catalogue” of utility weights in oncology from Earle et al. in 2000 (Pickard, Wilke, Lin H., & Lloyd, 2007).

The HUI is a set of generic health profiles for measuring health status and health-related quality of life. The HUI-III, one of such generic health profiles, has a descriptive system that is more detailed than that of the EQ-5D, with eight dimensions including: i) vision, ii) hearing, iii) speech, iv) ambulation, v) dexterity, vi) emotion, vii) cognition, and viii) pain. The dimensions are structurally independent of one another and generic enough that they can be applied to people of all ages in clinical and general population settings (Horsman et al., 2003). With between five and six levels to choose from for each attribute, the instrument is sensitive to changes in health status. There is much evidence to support the reliability and validity of the tool worldwide (Horsman & Hors, 2010). Both the EQ-5D and the HUI-III have been used to assess HRQOL in people with CRC although have not been used together (Ness et al., 1999); (Ramsey et al., 2000); (Ramsey et al., 2002).
2.3 Health-related Quality of Life in CRC

2.3.1 Definition and overview of HRQOL

Incorporating a HRQOL component into analyses of healthcare interventions is becoming more commonplace in healthcare research studies (Fitzpatrick et al., 1992; Wilson et al., 2010; Sharma et al., 2007; Gall et al., 2007). Chronic diseases for which there is no cure, can often affect an individual’s overall health and wellness, including physical, psychosocial, mental and other dimensions of health. Simply assessing the impact of a treatment or intervention using patient survival as the only metric is not particularly informative as an outcome measure; rather, the goal should be to influence and improve quality of life (Rosenbloom, Victorson, Hahn, Peterman, & Cella, 2007).

Some researchers have advocated for inclusion of the methodology as part of mainstream clinical practice, in part because of the potential use of these instruments to increase communication between patients and their providers (Buchanan et al., 2007). HRQOL, as a distinct concept from overall quality of life, recognizes aspects of daily functioning and living that are impacted by one’s health status, including physical, biological, and emotional areas of life. Overall quality of life however, involves a broader consideration of factors such as social, economic, cultural and even spiritual facets to life that extend beyond the concept of health-related quality of life, as well as beyond the scope of this research study. As Torrance (1987) states in his seminal paper on measuring HRQOL:

“…overall quality of life is an all-inclusive concept incorporating all factors that impact upon an individual’s life. Health-related quality of life includes only those factors that are part of an individual’s health…for health studies, health-related quality of life is the appropriate concept to use” (Torrance, 1987).

Improvements in healthcare have led to extending length of life; so too the ways we measure morbidity have also improved over time. Including the aspects that are important to
people when their health is at question has numerous uses and applications. By incorporating HRQOL assessment in research trials, we gain insight into the effects of the intervention to changes in overall health status, including associated side effects (Dolan, 2000; Sharma et al., 2007). In clinical practice, HRQOL assessments can be used as a baseline measure of health status that can be tracked over time, acting as a prompt for underlying secondary symptoms caused by treatments (Buchanan et al., 2007); describing and monitoring population health (Leonardi, McGory, & Ko, 2007); and finally, they can be used to help inform policy decision-making when used to establish QALYs (Santana & Feeny, 2008).

While research on HRQOL has been undertaken in CRC (refer to Table 2), the focus has predominately remained within the realm of CRC patients as a group without much consideration of the impact of factors (such as sex, age, time of diagnosis) on an overall assessment of HRQOL. In addition, while there are disease-specific health status assessment tools available for use in CRC such as the Functional Assessment of Cancer Therapy for Colorectal Cancer, or FACT tool, currently these tools cannot be used to establish utility weights for calculating QALYs. To date, no other research study has assessed HRQOL in a CRC patient population using the EQ-5D, VAS and HUI-III and assessed how well these generic preference-based health status surveys capture the factors of HRQOL that are important to CRC patients.

It should be noted that three articles (Aballea et al., 2007; Cassidy et al., 2006; Eggington et al., 2006) were not included in Table 2 as the utility estimates were based on the estimates provided by Ramsey et al., 2000 as well as Ness et al., 1999.
### Table 2 - Utility Values for CRC Stages from the Literature

<table>
<thead>
<tr>
<th>Type of patients (sample size)</th>
<th>Description</th>
<th>Estimate (mean scores unless otherwise indicated)</th>
<th>Method of elicitation</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRC patients (n=173)</td>
<td>Utility scores were reported for varying stages of cancer and time since diagnosis:</td>
<td></td>
<td>HUI-III FACT-C (disease-specific HRQOL instrument)</td>
<td>(Ramsey et al., 2000)</td>
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<tr>
<td></td>
<td>a) stage I</td>
<td>a) 0.84</td>
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<tr>
<td></td>
<td>b) stage II</td>
<td>b) 0.86</td>
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<td></td>
<td>c) stage III</td>
<td>c) 0.85</td>
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<td></td>
<td>d) stage IV</td>
<td>d) 0.84</td>
<td></td>
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<tr>
<td></td>
<td>e) 1-2 y</td>
<td>e) 0.80</td>
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<tr>
<td></td>
<td>f) 2-3 y</td>
<td>f) 0.88</td>
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<td></td>
<td>g) 3-5 y</td>
<td>g) 0.84</td>
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<td></td>
<td>h) &gt;5 y</td>
<td>h) 0.90</td>
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<td></td>
<td></td>
<td>In general, average HUI scores were 0.85 for survivors versus 0.65 for those who died</td>
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<tr>
<td>Colorectal cancer patients who had survived at least 5 years (n=227)</td>
<td>Utility scores were reported for varying stages of cancer and time since diagnosis:</td>
<td></td>
<td>HUI-III FACT-C SF-36</td>
<td>(Ramsey et al., 2002)</td>
</tr>
<tr>
<td></td>
<td>a) stage I</td>
<td>a) 0.83</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>b) stage II</td>
<td>b) 0.86</td>
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<td></td>
<td>c) stage III</td>
<td>c) 0.87</td>
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<td></td>
<td>d) stage IV</td>
<td>d) 0.81</td>
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<td></td>
<td>e) 5-9 y</td>
<td>e) 0.85</td>
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<td></td>
<td>f) 10-14 y</td>
<td>f) 0.84</td>
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<td></td>
<td>g) 15+ y</td>
<td>g) 0.86</td>
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<tr>
<td>Persons who had previously undergone removal of colorectal adenoma/polyps (n=40 for b, c, f, g; and 81 for a, d, e, h)</td>
<td>Eight outcome states of CRC assessed:</td>
<td></td>
<td>SG</td>
<td>(Ness et al., 1999)</td>
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<tr>
<td></td>
<td>a) stage I rectal or stage I/II colon cancer</td>
<td>a) 0.74</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>b) stage III colon cancer w/out significant side effects</td>
<td>b) 0.70</td>
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<tr>
<td></td>
<td>c) stage III colon cancer with significant side effects</td>
<td>c) 0.63</td>
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<tr>
<td>Type of patients (sample size)</td>
<td>Description</td>
<td>Estimate (mean scores unless otherwise indicated)</td>
<td>Method of elicitation</td>
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<tr>
<td>d) stage II/III rectal cancer w/out ostomy</td>
<td>d) 0.59</td>
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<tr>
<td>e) stage II/III rectal cancer with ostomy</td>
<td>e) 0.50</td>
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<tr>
<td>f) stage IV metastatic w/out ostomy</td>
<td>f) 0.24</td>
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<tr>
<td>g) stage IV metastatic with ostomy</td>
<td>g) 0.84</td>
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<tr>
<td>h) current state of health</td>
<td>h) 0.84</td>
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<tr>
<td>Dukes’ B and C colorectal cancer patients (n=62)</td>
<td>Patients on chemotherapy, with and without experience of relapse</td>
<td>0.83, regardless of treatment modality</td>
<td>EQ-5D</td>
<td>(Norum et al., 1997)</td>
</tr>
<tr>
<td>Dukes’ A-C colorectal cancer patients (n=unclear)</td>
<td>Patients who underwent curative colon cancer resection</td>
<td>0.6 – 0.8, mean of 0.75 used</td>
<td>Review of literature; source unclear</td>
<td>(Kievit et al., 1990)</td>
</tr>
<tr>
<td>Stage II–IV colorectal cancer patients (n=49; 34 completed both EQ-5D and TTO)</td>
<td>a) Current health; a) 0.82 (EQ-5D VAS - 78.4)</td>
<td>TTO (and EQ-5D to familiarize patients with valuing health states)</td>
<td>(Best et al., 2010)</td>
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</tr>
<tr>
<td>b) Adjuvant, no neuropathy; b) 0.67</td>
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<td>c) Adjuvant, mild neuropathy; c) 0.65</td>
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<td>d) Adjuvant, moderate neuropathy; d) 0.55</td>
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<tr>
<td>e) Adjuvant, severe neuropathy; e) 0.48</td>
<td></td>
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<td></td>
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<tr>
<td>f) Metastatic, stable; f) 0.46</td>
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<td>g) Metastatic, progressive g) 0.38</td>
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<tr>
<td>h) Remission h) 0.87</td>
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<tr>
<td>Colon cancer, Dukes C</td>
<td>chemotherapy, good scenario</td>
<td>0.8-1.0</td>
<td>TTO</td>
<td>(Smith, Hall, Gurney, &amp; Harnett, 1993)</td>
</tr>
<tr>
<td>Colon cancer, Dukes C</td>
<td>chemotherapy, medium scenario</td>
<td>0.88</td>
<td>TTO</td>
<td>(Smith et al., 1993)</td>
</tr>
<tr>
<td>Colon cancer, Dukes C</td>
<td>chemotherapy, &quot;bad&quot; scenario</td>
<td>0.80</td>
<td>TTO</td>
<td>(Smith et al., 1993)</td>
</tr>
<tr>
<td>Type of patients (sample size)</td>
<td>Description</td>
<td>Estimate (mean scores unless otherwise indicated)</td>
<td>Method of elicitation</td>
<td>Source</td>
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<tr>
<td>Colon cancer, Dukes C chemotherapy</td>
<td>Average of &quot;good&quot;, &quot;medium&quot; and &quot;bad&quot; scenario</td>
<td>0.87</td>
<td>TTO</td>
<td>(Smith et al., 1993)</td>
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<tr>
<td>Colon cancer patients (n=169)</td>
<td>Three time periods:</td>
<td></td>
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<tr>
<td></td>
<td>a) acute (&lt; 1 yr after diagnosis)</td>
<td>a) 0.67</td>
<td>HALex multi-attribute utility scaling</td>
<td>(Ko, Maggard, &amp; Livingston, 2003)</td>
</tr>
<tr>
<td></td>
<td>b) short-term (1-5 yrs)</td>
<td>b) 0.68</td>
<td></td>
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<tr>
<td></td>
<td>c) long-term (&gt;5 yrs)</td>
<td>c) 0.71</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer, colorectal</td>
<td>primary chemotherapy</td>
<td>0.74</td>
<td>expert judgment</td>
<td>(Glimelius et al., 1995)</td>
</tr>
</tbody>
</table>

### 2.3.2 Measuring HRQOL

The concept of the QALY was reviewed in the previous sections, including how it is calculated, its application and debates and critiques of the method. The following section focuses on the audience that can be used to measure HRQOL and provides the rationale for the perspective selected for this research study.

#### A question of perspective: individual or societal?

The perspective of utility measurement depends on the objectives of the research study. When undertaking a utility elicitation research study, one main question that needs to be considered is the perspective to be taken, that is, societal or individual, and whether it is important to consider the perspective of the individual who is currently experiencing the symptom (Buchanan et al., 2007); (Dolan, 1999). When assessing HRQOL, the question does not become a value-judgment as to whose perspectives matter more or less, but rather a question of the appropriateness of those being asked.

Decisions that affect the general public, such as policy decisions regarding the allocation of resources across various interventions that ultimately may affect different population groups,
should incorporate the public’s perspective and preferences (Dolan, 1999). On the other hand, surveying the health states of the population affected by the intervention may be most appropriate as their perspective reflects a ‘true’ preference directly experienced by the individual (Dolan, 1999). Understanding patient quality of life is important to a variety of audiences for various reasons: it can help bridge a barrier between clinicians and patients about how they are feeling; it can inform researchers about which healthcare interventions are most valuable or have the greatest positive impact to a patient’s well-being; and it can inform decision-makers about quality of life variations throughout the survivorship journey (Gandey, 2008). The choice of which audience to assess is important however, because of the applicability and also because there can be substantial differences in how each group values their health. The general public, who do not have experience with the disease, often overstate the severity of the hypothetical health state (Dolan, 2000). Conversely, those who are currently experiencing the diseased state have had the opportunity to adapt to their condition, including making adjustments to their life to return it to a state of normality.

The rationale for using patient-perspective utilities, or ‘experienced utilities’ as they are also referred to, for this research study is twofold: it enables the comparison against utility values generated in other CRC-related studies, an important consideration that informs instrument selection for capturing HRQOL (refer to Table 2); and it also enables end-users of this information to make treatment decisions for individual patient-care without engaging in the relatively lengthy process of gathering this information themselves.

2.3.3 Situating the Research Study

Some researchers estimate that between 75 and 80 percent of patients with colorectal cancer suffer from ‘significant co-morbidities’ (Gall et al., 2007; Ramsey et al., 2002). It is reasonable to state that some factors that influence HRQOL can be generalized to the experience of living with cancer, with certain factors specific to CRC. This can include long-term pain (Ko
et al., 2003), struggles with establishing (or re-establishing) normality to their lives with the presence of a stoma (i.e., a surgically-created opening in the large intestine that allows the removal of feces out of the body, to drain into a pouch external to the body) including being cautious and/or having reservations about going out into public because of physical issues related to the stoma (i.e., gas, erratic bowel movements, odour, etc), feelings of severe anxiety, dealing with altered self-image issues (i.e., perhaps related to presence of a stoma, but can include weight-loss and scarring) and the presence of co-morbidities that influence the types of treatments for which patients are eligible (Wilson et al., 2010).

By incorporating two generic health status measures for use in this research study, and exploring the factors that patients with CRC describe as important to their HRQOL, this research study presents a unique look at whether the current versions of the EQ-5D, VAS and HUI-III capture these factors and what some of the implications are of these findings to the policy and decision-making fields.
CHAPTER 3: RESEARCH METHODOLOGY

This chapter describes the research methodology of the study, providing a description of the study design, methods, sampling strategy, data analysis and research ethics.

3.1 Study Design

The overall aim of this thesis was to determine how well current health status measures capture HRQOL in a CRC population, as well as offer insights into the level of agreement between the EQ-5D, VAS and HUI-III utility assessments. To address this aim, a comprehensive understanding of the various factors that influence CRC patients’ HRQOL is required. This is achieved through the three research objectives and four research questions as presented in Chapter 1. To investigate these research questions, this study employed an exploratory case study design using two methods of data collection: self-completed health status surveys (i.e., quantitative data) and patient interviews (i.e., qualitative data). The strength of this research study lies in the integration of these two types of data. It is rare in the field of health economics to go beyond analyses of quantitative data to conduct deeper analyses using qualitative methods. Qualitative inquiry enables the exploration of the constructs and themes that fall outside the typical and oftentimes predetermined domains of inquiry. As the economist Paul Dolan (2000) explicitly states in the *Handbook of Health Economics*:

…qualitative data should provide insights into the cognitive processes that respondents use in order to arrive at their responses; thus enabling researchers to get a better understanding of why valuations differ in addition to how they differ…(Dolan, 2000).

Qualitative and quantitative data were analyzed separately and then were integrated at a later stage of the analysis to answer the research questions stated earlier. Patients who participated in the research study completed two generic, preference-based health status surveys,
the EQ-5D and HUI-III, as well as the VAS, in order to capture patient health status at the point in time that they were completed. The completion of these surveys resulted in 150 unique health states scores, or 3 sets of scores per patient (i.e., a utility estimate for each of the EQ-5D and HUI-III, and one VAS score). Qualitative interviews were conducted with a subset of the patient group who completed the surveys and were conducted either directly at the time of completion of the EQ-5D, VAS and HUI-III surveys or, in the case of participants from the OCC site, when a suitable time could be set up between the researcher and the patient which was usually a week or two after the completion of the surveys. These differences were due to differences in data collection approaches at the Odette Cancer Centre (OCC) and Princess Margaret Hospital (PMH) sites. Leech and Onwuegbuzie refer to this type of research design as a ‘partially mixed concurrent equal status design’ (see P1 in Figure 6) (Leech & Onwuegbuzie, 2009).

A partially mixed concurrent equal status design involves conducting a two-phase study where the phases occur concurrently, with the quantitative and qualitative phases having approximately equal weight (Leech & Onwuegbuzie, 2009). In the current research study, data were collected simultaneously, with the quantitative and qualitative portions of the study not integrated until the collection and analysis of the data were complete. The value of this approach is that it enables a continuous collection of data without a significant time lag in between rounds of collection and allows ongoing consideration of major themes from the analysis throughout the data collection process. Since this research study used two methods of data collection, it was beneficial from a resource (i.e. time) point-of-view to be able to collect the data without needing to analyze it at the time of collection.
Figure 6 - Typology of Mixed Methods

(M Leech & Onwuegbuzie, 2009)
3.1.1 Site and Participant Selection

Site

Given that the study was exploratory in nature, a convenience sampling strategy was used to collect the data. Data collection occurred at two of the largest academic cancer centres in Toronto, Ontario, the OCC and PMH, both of which are integrated with large academic health sciences centres. A medical oncologist specializing in the treatment of gastrointestinal cancer was identified at each site, and assumed responsibility for identifying patients who met the research study criteria.

During the research proposal stage, it was intended that data would only be collected at the OCC, however unanticipated obstacles with respect to ethics regulations and general operations issues at this site arose which greatly impacted the potential to collect data in a fairly straightforward and streamlined way. The limitations encountered with the OCC research setting prompted a re-design of the original study protocol to include a second site at PMH. Limitations with both study sites were encountered and are addressed further in Chapter 5, section 5.3.

At the OCC, eligible patients were identified by the supervising oncologist and recruited to participate in the study. Study packages that contained the EQ-5D, VAS and HUI-III surveys as well as an information letter were distributed to patients at the time of their clinic appointment by the oncologist. At PMH, I was directly involved in administering the survey to the patient once consent was given. Data collection occurred on the same day every week, when the gastroenterology clinic had the highest volume of CRC patients for the particular supervising oncologist. There are a number of advantages and disadvantages associated with different methods of data collection as used at the OCC and PMH sites as it applies to the overall
participation rate. These are outlined in Appendix J, reflecting my own experience with this research study.

Data collection at the OCC began in May 2010, with the last survey received in September 2010. At PMH, the data collection period was from August 2010 to October 2010. At both sites, data collection concluded when the majority of patients attending the clinics had been approached and/or already participated in the study.

Participants

Purposive sampling was used to select subjects for participation in the research study (Patton, 2002). Specifically, a criterion sampling strategy was used to select patients who met certain pre-determined criteria, primarily that they were CRC patients residing in Ontario, currently receiving treatment for their disease at either the OCC or PMH, and they had to be able to read and converse in English. The eligibility criteria was informed by a review of the relevant literature, awareness of the topic area in the Ontario context – for instance CRC has received much publicity in the news since the launch of prevention strategies targeted at the disease, including the recent launch of the ColonCancerCheck screening program (Ministry of Health and Long-Term Care, 2010) – and also in part due to the availability of patients with a specific stage of CRC from each of the research study sites.

3.2 Data Collection

3.2.1 Self-administered Health Status Surveys

An information letter was provided to all participants of the research study which outlined the name of the research study, the purpose of the study and how the data would be collected and stored (refer to Appendix B for a copy of the information letter). All participants who took part in completing the generic preference-based questionnaires were given the option to participate in the qualitative portion of the research study.
The EQ-5D includes five questions that are intended to represent dimensions of health-related quality of life, including Mobility, Self-Care, Usual Activities, Pain/Discomfort and Anxiety/Depression. For each question, there are three levels to choose from (i.e. no problems, some problems, extreme problems), classifying respondents into one of 243 possible health states (Drummond et al., 2005). The HUI-III health status survey has eight dimensions of health-related quality of life, including Vision, Hearing, Speech, Ambulation, Dexterity, Emotion, Cognition and Pain, and between five and six levels for scoring, for a total of 972,000 possible health states (Grutters et al., 2007) (Appendices C and D). Unique health states for the EQ-5D and HUI-III completed surveys were generated using a scoring algorithm (Appendix E).

Self-administered health status surveys were selected as the data collection method of choice for two main reasons: firstly, to contribute a pool of utility scores representative of a CRC patient population in Ontario to the literature; and secondly, to be used as a proxy measure of HRQOL whose internal validity in a CRC patient population could be challenged based on the findings from the interview phase.

### 3.2.2 Patient Interviews

One-on-one interviews represent one of the best ways to gather data on potentially sensitive subjects, such as may be experienced with CRC patients (Miles & Huberman, 1994). A semi-structured interview guide was used to help explore the subjects of interest to the research study (Patton, 2002) (see Appendix F). As Johnson and Turner (2003) state, interviewing as a data collection method permits the use of probing for more and/or in-depth insights into a particular subject (Johnson & Turner, 2003). Questions were asked in a sequential fashion as they were laid out in the interview guide. The timeframe available at PMH where interviews were conducted was approximately 10 to 15 minutes versus a much longer time frame at the OCC, which somewhat limited the degree to which themes could be explored in-depth.
Accommodations were made during the interviews to prioritize the questions asked. The potential limitations of this situation are further explored in Chapter 5, section 5.3.

The interview guide (Appendix F) was structured around the topic of HRQOL in CRC and the experience of completing the EQ-5D, VAS and HUI-III surveys as they relate to one’s perception of HRQOL. In the case of the current research study, the strength of a semi-structured approach as opposed to a purely guided or standardized open-ended approach is that it permitted flexibility to be able to probe various areas of interest more in-depth. In qualitative analysis, undertaking in-depth examination of a small number of subjects rather than by gathering standardized information from the entire population can actually be more informative than survey questions alone (Patton, 2002); (Miles & Huberman, 1994).

Patients from the OCC were invited to call and set up a time to conduct the interview, allowing the interview to be recorded. The response rate for participation in an interview was low at the OCC, with only three patients expressing interest. Conversely, the participation rate for interviews was higher at the PMH site, likely due to the fact that patient interviews were conducted immediately following the completion of the health status surveys, thereby eliminating the onus to call.

Before the larger research study was launched, a pilot study was conducted with four patients at the OCC in an attempt to gather information about the feasibility of the interview and its structure, including the number of and types of questions. Based on the findings from the pilot study, changes were made to the interview guide to make questions clearer and more specific and to improve the overall flow of the interview. For instance, there were a number of questions dealing with the concept of quality of life which were amalgamated into one main question after the pilot as it was felt that responses were beginning to be repetitive.

Although the original intent was to record all interviews as was the case for the OCC patients, it was found that the few patients at PMH who were asked to have the session recorded
refused and hence it was decided that hand notes only would be taken during the interviews. These differences in data collection methods resulted in two types of interview data – transcripts and hand notes. As it is difficult to record comprehensive notes during an interview while also asking questions, time was devoted immediately after each interview to supplement the hand notes with as many details as could be recalled. This process was used systematically after every interview as interviews were usually conducted with a significant (i.e. 1-2 hours) time lag between them depending on the operation of the clinic. Qualitative data collection was considered complete in the current research study when no new themes emerged from the interviews; this occurred after completion of 15 individual interviews.

3.3 Data Analysis

3.3.1 Quantitative analysis

Descriptive statistics were used to summarize the data collected from the EQ-5D, VAS and HUI-III surveys, for age, sex and time since diagnosis. These three factors were selected as this information is relatively easy-to-collect from participants as opposed to data that is potentially more problematic to collect (i.e. income or marital status could be interpreted as more sensitive information, or information on current chemotherapy regime which may not necessarily be accurate and may require validation by the supervising oncologist). Stage of cancer was considered as a potential focus of analysis, however it was decided that because the distribution of patients among various stages of cancer was limited (i.e. 78% of patients were diagnosed as stage IV), this factor was not included in the analysis of the data.

The survey responses were analyzed using the statistical program STATA (version 11). Descriptive statistics, including the mean and confidence interval, were calculated. Inferential statistics were also calculated and included a two-sample t-test to test the statistical significance of the results of the EQ-5D, VAS and HUI-III utility values and health status scores between
sub-groups (i.e., mean EQ-5D for patients aged 18-59 vs. 60-80+ years); a paired t-test to test the statistical significance of the means of each sub-group across the EQ-5D, VAS and HUI-III values (i.e., mean EQ-5D and mean HUI-III for patients aged 18-59 years); and an ANOVA to test the statistical significance between the three sub-groups of time since diagnosis (i.e., ≤ 12 months, 13-35 months, and ≥ 36 months).

3.3.2 Qualitative analysis

The interviews conducted with patients from the OCC site were audio recorded and transcribed verbatim by a professional transcriptionist and verified by reviewing the transcript while listening to the audio recording. The interviews conducted at the PMH site were not audio-recorded, however, notes were taken both during and immediately following the interview. Due to the limited time available to conduct the patient interviews (i.e. 10-15 minutes), there was little opportunity for patients to provide in-depth responses to questions. The majority of interviews followed a fairly structured approach, with the majority of patient responses directly addressing the questions asked. For this reason, the interview guide was used as an initial coding structure, with any emerging themes noted as coding of the transcripts and hand notes progressed (see Appendix G).

Themes from the interviews were determined by reviewing the notes and coding for similar themes that emerged. In cases where at least 20% (3 of 15) of participants described a similar phenomenon, this was highlighted as a theme in the analysis. A total of 12 themes were found to be relevant in the research study.

3.3.3 Integration of Findings

A mixed methods approach to the research study provides a comprehensive way to address the objectives of this thesis. This research study was guided by a naturalistic and interpretive paradigm, which gives recognition and value to the subjective experiences of people
as meaning is context-dependent and never absolute (Jang, 2009). Data triangulation was used to examine the research questions for this thesis, to better understand the context of the phenomenon, that of HRQOL in CRC. As Mathison (1988) states,

*(Triangulation)* is a technique which provides more and better evidence from which researchers can construct meaningful propositions about the social world (Mathison, 1988).

The process of comparing and analyzing the two data sets was conducted according to the ‘convergence model’ (see Figure 7) (Creswell & Piano Clark, 2007). The quantitative and qualitative data were collected and analyzed separately, and later analyzed together during what Creswell states as the ‘data interpretation phase’ (Creswell & Piano Clark, 2007). The results from the two sets of data were compared to each other by reviewing the results from each of the surveys to see whether the way in which patients rated their health status was aligned with the factors they described during the interviews as important to them.

**Figure 7 - Triangulation Design: Convergence Model**

![Triangulation Design: Convergence Model](image)

3.4 Research Ethics

Ethics approval for the OCC study site was obtained from the Sunnybrook Health Sciences Centre on August 28, 2009, with the final amendment to the protocol approved on April 26, 2010. Ethics approval for the second study site, PMH, was obtained from the University Health Network on July 19, 2010. As the research study took place at two teaching hospitals
affiliated with the University of Toronto, administrative study review approval was obtained from the University’s Research Ethics Board on January 29, 2010. Refer to Appendix H for a copy of the study approval letters from Sunnybrook Health Sciences Centre, UHN and the University of Toronto.
CHAPTER 4: RESULTS

This chapter begins with a review of health status scores and utility values generated from the EQ-5D, VAS and HUI-III generic preference-based surveys, as well as findings from participant interviews. Following this, I present an analysis of the quantitative data, with the themes from the qualitative interviews informing these results.

4.1 Results of the EQ-5D, VAS and HUI-III Health Status Measures

4.1.1 Participant Characteristics

A total of 50 participants completed the EQ-5D, VAS and HUI-III health status surveys, including 16 patients from the OCC and 34 from PMH. The majority of participants were between the ages of 18-59 years (52%), were male (58%) and had CRC for three years or less (84%). A greater proportion of females than males had been diagnosed with CRC between one and three years ago at the time of completion of the surveys (48% versus 38%, respectively), with more males than females having had CRC for 12 months or less (48% versus 33%). Although the sample population included a mix of patients with stage III and IV cancer, the majority of patients (78%) had stage IV cancer (i.e., advanced palliative disease). The disproportionately large number of patients with advanced stage of disease was due to site-specific bias, with the PMH site primarily treating patients with more advanced (i.e., stage IV) disease, while the OCC site treats a mix of stage III and IV patients (i.e., of the 16 patients who participated, 69% of them were categorized as stage III). There are some limitations associated with this difference in the patients from the various sites, which is acknowledged in Chapter 5.

Response Rate

The number of fully completed EQ-5D, VAS and HUI-III surveys (i.e. no blank responses) was higher at PMH compared to the OCC, with only four patients from PMH refusing
to participate due to reasons including survey fatigue (i.e., as a result of participating in “too many” research studies and surveys), general fatigue and time constraints. The overall participation rate at the OCC was difficult to determine as the method of collecting survey responses differed from that at PMH (i.e. indirect researcher involvement versus direct, respectively). There were a number of occurrences where survey responses were unclear, all of which occurred on surveys completed by patients from the OCC. These included three HUI-III surveys, two VAS surveys, and one EQ-5D survey (refer to Appendix I). Because surveys from the OCC were mailed in and hence the respondent is anonymous, it was not possible to contact the respondent directly for clarification. Therefore, assumptions were made when preparing the data for analysis.

4.1.2 Agreement between Health Status Measures

EQ-5D

A total of 18 unique health states from the EQ-5D surveys were generated based on patient responses. The most frequently observed health states generated on the EQ-5D were 11111 (utility weight of 1.0) with a total of 11 occurrences, and 11222 (utility weight of 0.69) with a total of 9 occurrences. The mean EQ-5D utility value was 0.76, with standard deviation of 0.194. The highest EQ-5D utility value was 1.00, and the lowest utility value was 0.16.

In the first case, both levels 2 and 3 were selected for the dimension Emotion on the HUI-III, with the respondent including a disclaimer that their response, “depends on the day!” Two other respondents also felt it necessary to include a similar disclaimer on their HUI-III surveys, assumingly in an attempt to explain how their response selection may have been different depending on how they were feeling at the time the survey was completed. In the second case, the participant selected both levels 1 and 2 for the dimension Anxiety/Depression on the EQ-5D. For analysis purposes, level 2 was used as the ‘selected’ response to this question as it represents a conservative reflection of health status. Finally, there were two instances of unclear responses on the VAS: in the first, the respondent differentiated their health status into physical and mental domains, and scored differently for both dimensions (i.e. physical, mental). In the other case, an arrow was used to indicate their “score” but the respondent did not explicitly indicate where on the scale they would rate their state of health. Refer to Appendix I for a copy of the surveys described here.
**HUI-III**

A total of 38 unique health states from the HUI-III surveys were generated based on patient responses. The most frequently observed health states were 11111111 (utility weight of 1.0) and 21111211 (utility weight of 0.91), each observed five and four times in the data set, respectively. The mean HUI-III utility value was 0.76 with standard deviation of 0.210. The highest HUI-III utility value was 1.00, and the lowest utility value was 0.03.

**VAS**

A total of nine unique health states were generated on the VAS based on patient responses. The most frequently selected health state value was 0.70, with 13 (26%) respondents, followed by 0.80 with nine (18%) respondents, and 0.90 with six (12%) respondents. The mean was 0.72, with standard deviation of 0.136. The highest VAS score was 0.90 and lowest was 0.40.

**Descriptive Statistics**

Descriptive statistics (e.g., mean, 95% confidence interval) were calculated for the EQ-5D and HUI-III utility scores for three univariate independent variables including age, sex, and time since diagnosis (refer to Table 3).
Table 3 - Descriptive Statistics for EQ-5D, VAS and HUI-III Scores

<table>
<thead>
<tr>
<th>Age</th>
<th>n (%)</th>
<th>mean EQ-5D (95% CI)</th>
<th>mean HUI-III (95% CI)</th>
<th>mean VAS (95% CI)</th>
<th>p-value EQ-5D/HUI-III</th>
<th>p-value EQ-5D/VAS</th>
<th>p-value HUI-III/VAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-59 y</td>
<td>26 (52%)</td>
<td>0.73 (0.65, 0.81)</td>
<td>0.74 (0.65, 0.83)</td>
<td>0.69 (0.63, 0.75)</td>
<td>0.810</td>
<td>0.194</td>
<td>0.261</td>
</tr>
<tr>
<td>60-80+ y</td>
<td>24 (48%)</td>
<td>0.79 (0.71, 0.86)</td>
<td>0.78 (0.71, 0.86)</td>
<td>0.75 (0.70, 0.80)</td>
<td>0.814</td>
<td>0.417</td>
<td>0.512</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>0.288</td>
<td>0.480</td>
<td>0.094</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th>n (%)</th>
<th>mean EQ-5D (95% CI)</th>
<th>mean HUI-III (95% CI)</th>
<th>mean VAS (95% CI)</th>
<th>p-value EQ-5D/HUI-III</th>
<th>p-value EQ-5D/VAS</th>
<th>p-value HUI-III/VAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>29 (58%)</td>
<td>0.76 (0.68, 0.84)</td>
<td>0.78 (0.71, 0.85)</td>
<td>0.73 (0.67, 0.78)</td>
<td>0.542</td>
<td>0.335</td>
<td>0.116</td>
</tr>
<tr>
<td>Female</td>
<td>21 (42%)</td>
<td>0.75 (0.68, 0.82)</td>
<td>0.73 (0.63, 0.84)</td>
<td>0.71 (0.66, 0.77)</td>
<td>0.743</td>
<td>0.251</td>
<td>0.693</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>0.855</td>
<td>0.466</td>
<td>0.704</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time since diagnosis</th>
<th>n (%)</th>
<th>mean EQ-5D (95% CI)</th>
<th>mean HUI-III (95% CI)</th>
<th>mean VAS (95% CI)</th>
<th>p-value EQ-5D/HUI-III</th>
<th>p-value EQ-5D/VAS</th>
<th>p-value HUI-III/VAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 12 mos</td>
<td>21 (42%)</td>
<td>0.75 (0.66, 0.84)</td>
<td>0.78 (0.71, 0.86)</td>
<td>0.7 (0.64, 0.76)</td>
<td>0.493</td>
<td>0.154</td>
<td>0.021*</td>
</tr>
<tr>
<td>13-35 mos</td>
<td>21 (42%)</td>
<td>0.79 (0.72, 0.86)</td>
<td>0.81 (0.74, 0.87)</td>
<td>0.73 (0.66, 0.79)</td>
<td>0.486</td>
<td>0.061</td>
<td>0.018*</td>
</tr>
<tr>
<td>≥ 36 mos</td>
<td>8 (16%)</td>
<td>0.7 (0.49, 0.91)</td>
<td>0.59 (0.31, 0.86)</td>
<td>0.76 (0.67, 0.84)</td>
<td>0.245</td>
<td>0.572</td>
<td>0.230</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>0.534</td>
<td>0.026*</td>
<td>0.630</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall</th>
<th>n (%)</th>
<th>mean EQ-5D (95% CI)</th>
<th>mean HUI-III (95% CI)</th>
<th>mean VAS (95% CI)</th>
<th>p-value EQ-5D/HUI-III</th>
<th>p-value EQ-5D/VAS</th>
<th>p-value HUI-III/VAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 (100%)</td>
<td>0.76 (0.70, 0.81)</td>
<td>0.76 (0.70, 0.82)</td>
<td>0.72 (0.68, 0.76)</td>
<td>0.921</td>
<td>0.142</td>
<td>0.193</td>
<td></td>
</tr>
</tbody>
</table>

*statistical significance at alpha level of 0.05
4.1.3 Impact of Age, Sex, and Time since Diagnosis on Utilities and VAS Scores

The dot plot in Figure 8 displays the frequency of EQ-5D, VAS and HUI-III utility scores for the entire sample population and reveals a number of insights about the index scores collected from participants. The frequency of scores on the EQ-5D was clustered around two main scores, 0.69 with 12 (24%) occurrences and 1.00 with 11 (22%) occurrences. On the HUI-III, scores were dispersed across the range of possible utility values, with the most popular score being 1.00 with five (10%) occurrences. The majority of VAS scores were clustered around 0.70, with 13 (26%) occurrences.

Figure 8 - Frequency of EQ-5D, VAS and HUI-III utility scores (N=50)

The relationship between EQ-5D, VAS and HUI-III utility values and health status scores is plotted in Figure 9. In the first two graphs, it is apparent that for every VAS health status score, both the EQ-5D and the HUI-III result in a higher value until the point at which the two lines cross as indicated by the dotted vertical line in the Figures below. The estimate of the slope (i.e. coefficient) of the line for the EQ-5D/VAS plotted values is 0.688 (95% CI: 0.327 - 1.05), a steeper line than the estimated slope of the line for HUI-III/VAS plotted values that has a coefficient of 0.432 (95% CI: 0.012 - 0.853). The coefficient of the line for EQ-5D/HUI-III plotted values is 0.543 (95% CI: 0.320 - 0.766). Given that the 95% confidence interval for the
EQ-5D/VAS plotted values includes the value of 1.00, that is, the slope of the dotted line in Figure 9 below which represents an identical (i.e., 1:1 ratio) relationship between utility values and health status scores, we can conclude that the slope of the line is not statistically significant from 1.00. In contrast, the 95% confidence interval for the lines of the EQ-5D/HUI-III and HUI-III/VAS plotted values do not include the value of 1.00, and hence the slopes of these lines are statistically significantly different from 1.00.

Figure 9 - Relationship between EQ-5D, VAS and HUI-III Utility Values and Health Status Scores

![Graphs showing relationships between utility values and health status scores for EQ-5D/VAS, EQ-5D/HUI-III, and HUI-III/VAS.](image-url)
Age

For the EQ-5D, VAS and HUI-III health status surveys, mean values increase (i.e. closer to 1.00) with increasing age, implying that increasing age is positively associated with the valuation of health status (refer to Table 3). Mean EQ-5D and HUI-III scores were similar for younger and older age groups (0.73 and 0.74 for those 18-59 years, and 0.79 and 0.78 for those 60-80+ years). In terms of the VAS scores, mean scores increase with age, with the average VAS score of the age group of 60-80+ years 0.06 points greater than the average VAS score for the age group of 18-59 years.

To test whether the relationship between age and the mean EQ-5D, HUI-III and VAS scores was significant, a two-sample t-test was conducted between the age categories. For the EQ-5D, the results of the t-test indicate that the relationship is not statistically significant at an alpha level of 0.05 ($p=0.288$), similarly with the HUI-III ($p=0.480$) and the VAS ($p=0.094$).

However, the spread of these utility values and health status scores varies considerably between the age groups of “old” (i.e., age group of 60-80+ years) and “young” (i.e., between 18-59 years) participants (Figure 10). With the younger age group, the spread of EQ-5D, VAS and HUI-III utility values and scores is greater than for the older age group as is evident by the more stretched distribution. The median values for the older age group are consistently higher than the median values for the younger age groups for each of the three health status surveys.
In addition to the variation between mean EQ-5D, VAS and HUI-III scores, it is interesting to note differences with respect to the levels of health status selected on these surveys, based on the patient’s age, sex and time since diagnosis. As a designated proxy measure of health status variation, the proportion of participants who selected ‘some problems’ on each of the EQ-5D and HUI-III surveys, by age group, are showcased in Figure 11. For the purposes of this analysis, ‘some problems’ is identified as any level greater than 1, i.e.:

1) “I have *some* problems with self-care” (EQ-5D - dimension 2, level 2)
2) “Able to see *well enough* to read ordinary newsprint and recognize a friend on the other side of the street, *but with* glasses” (HUI-III dimension 1, level 2)
Figure 11 - Proportion of Respondents Reporting ‘Some Problems’ on EQ-5D and HUI-III, by Age Group

**EQ-5D**

<table>
<thead>
<tr>
<th>Attribute</th>
<th>18-59 y</th>
<th>60-80+y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobility</td>
<td>19%</td>
<td>17%</td>
</tr>
<tr>
<td>Self-Care</td>
<td>15%</td>
<td>4%</td>
</tr>
<tr>
<td>Usual Activities</td>
<td>69%</td>
<td>54%</td>
</tr>
<tr>
<td>Pain/Discomfort</td>
<td>62%</td>
<td>38%</td>
</tr>
<tr>
<td>Anxiety/Depression</td>
<td>58%</td>
<td>63%</td>
</tr>
</tbody>
</table>

**HUI-III**

<table>
<thead>
<tr>
<th>Attribute</th>
<th>18-59 y</th>
<th>60-80+y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vision</td>
<td>62%</td>
<td>71%</td>
</tr>
<tr>
<td>Hearing</td>
<td>0%</td>
<td>4%</td>
</tr>
<tr>
<td>Speech</td>
<td>15%</td>
<td>8%</td>
</tr>
<tr>
<td>Ambulation</td>
<td>46%</td>
<td>29%</td>
</tr>
<tr>
<td>Dexterity</td>
<td>19%</td>
<td>21%</td>
</tr>
<tr>
<td>Emotion</td>
<td>73%</td>
<td>67%</td>
</tr>
<tr>
<td>Cognition</td>
<td>50%</td>
<td>38%</td>
</tr>
<tr>
<td>Pain</td>
<td>62%</td>
<td>46%</td>
</tr>
</tbody>
</table>
For four of the five dimensions on the EQ-5D, the younger age group (18-59 years) reported a higher percentage of ‘some problems’ than did their older (60-80+ years) counterparts, with the exception of the dimension Anxiety/Depression. Similarly on the HUI-III, other than the dimensions Vision and Hearing where the older age group reported a higher number of having ‘some problems’, the younger age group reported experiencing a greater number of ‘some problems’ on the five remaining dimensions.

Sex

Utility values for EQ-5D and HUI-III were relatively similar between men and women (refer to Table 3). Mean health status scores for men were consistently higher on all three health status surveys compared to women. To test the association between sex and the mean EQ-5D, VAS and HUI-III scores, a two-sample t-test was conducted between sex categories. For the EQ-5D, the results of the t-test indicate that the relationship was not statistically significant \((p=0.855)\), similarly with the HUI-III \((p=0.466)\) and the VAS \((p=0.704)\). The average VAS scores were similar between males and females, at 0.73 and 0.71 respectively.

The spread of the utility values and health status scores varies between males and females across the various health status surveys, with males consistently having higher median scores than their female counterparts do (Figure 12). For utility values generated using the EQ-5D, the spread of these values is greater as evidenced by the size of the box plot, however for the HUI-III, the spread of these values are similar between females and males. On the VAS, the spread of health status scores for females is much greater than the spread of scores for males.
Figure 12 - EQ-5D, VAS and HUI-III Utility Values and Scores, by Sex

In terms of the proportion of respondents who reported having some problems, females more often reported having problems on both the EQ-5D and HUI-III surveys than males did (refer to Figure 13). There are notable differences between the proportion of males and females who responded as having ‘some problems’ on seven dimensions in particular – Self-Care, Usual Activities, and Anxiety/Depression on the EQ-5D, and Vision, Speech, Ambulation and Emotion on the HUI-III.
Figure 13 - Proportion of Respondents Reporting ‘Some Problems’ on EQ-5D and HUI-III, by Sex

**EQ-5D**

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Mobility</th>
<th>Self-Care</th>
<th>Usual Activities</th>
<th>Pain/Discomfort</th>
<th>Anxiety/Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>female</td>
<td>14%</td>
<td>5%</td>
<td>71%</td>
<td>52%</td>
<td>67%</td>
</tr>
<tr>
<td>male</td>
<td>21%</td>
<td>14%</td>
<td>55%</td>
<td>48%</td>
<td>55%</td>
</tr>
</tbody>
</table>

**HUI-III**

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Vision</th>
<th>Hearing</th>
<th>Speech</th>
<th>Ambulation</th>
<th>Dexterity</th>
<th>Emotion</th>
<th>Cognition</th>
<th>Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>female</td>
<td>81%</td>
<td>0%</td>
<td>5%</td>
<td>43%</td>
<td>24%</td>
<td>81%</td>
<td>48%</td>
<td>52%</td>
</tr>
<tr>
<td>male</td>
<td>55%</td>
<td>3%</td>
<td>17%</td>
<td>34%</td>
<td>17%</td>
<td>62%</td>
<td>41%</td>
<td>55%</td>
</tr>
</tbody>
</table>
Time since Diagnosis

Time since diagnosis is divided into three categories, including (1) less than 12 months since diagnosis with CRC ($\leq 12$ months), (2) between one and three years since diagnosis (13-35 months), and (3) more than three years since diagnosis ($\geq 36$ months). Being diagnosed between 13 and 35 months ago at the time of the study was associated with higher mean EQ-5D and HUI-III scores, except for the VAS, where the highest mean VAS score was for patients who had been diagnosed more than 36 months ago (refer to Table 3). To test the relationship between time since diagnosis and the mean EQ-5D, HUI-III and VAS scores, an ANOVA was conducted between the three categories. For the EQ-5D, the results indicate that the relationship is not statistically significant, at an alpha level of 0.05 ($p=0.534$), similarly with the VAS ($p=0.630$). Conversely for the HUI-III, the relationship was statistically significant ($p=0.026$). Mean VAS scores increased with increasing time since diagnosis, with the mean VAS score of those diagnosed more than three years ago 0.06 points higher than for patients who had been diagnosed less than 12 months ago.

The spread of the utility values and health status scores varies between the various time since diagnosis categories. For utility values generated using the EQ-5D, the spread of scores is relatively consistent across categories; the median value was greatest for patients who received a diagnosis between 13 and 35 months ago. For utility values generated using the HUI-III, the spread of scores is the greatest for patients who received a diagnosis of CRC more than 36 months ago as is shown by the size of the box plot in Figure 14; the median value was greatest for patients who received a diagnosis of less than 12 months ago. For health status scores generated using the VAS, the spread of scores was greatest for patients who received a diagnosis less than 12 months ago, with the median value greatest for patients who received a diagnosis of between 13 and 35 months ago.
The proportion of patients who reported having some problems on the health status surveys varied. Patients frequently mentioned having experienced ‘some problems’ on the Anxiety/Depression dimension of the EQ-5D, although less than half (43%) of patients who had been diagnosed between 13 and 35 months ago reported experiencing ‘some problems’. Problems with Usual Activities rose steadily with increasing time since diagnosis. Similarly to Anxiety/Depression, patients in age categories (1) and (3) reported experiencing ‘some problems’ more than patients in category (2) for Pain/Discomfort.

On the HUI-III, Cognition, like Usual Activities on the EQ-5D, showed a steady increase in the percentage of patients reporting ‘some problems’ as time since diagnosis increased. On the
other hand, for *Emotion* and *Pain*, like the *Anxiety/Depression* and *Pain/Discomfort* dimensions on the EQ-5D, patients in category (1) and (3) of time since diagnosis reported experiencing more problems than the patients in category (2) (refer to Figure 15).

**Figure 15 - Proportion of Respondents Reporting ‘Some Problems’ on EQ-5D and HUI-III, by Time since Diagnosis**

![EQ-5D and HUI-III Diagrams](image-url)
4.2 Patient Interviews

4.2.1 Participant Characteristics

Participants who completed the three health status instruments, the EQ-5D, VAS and HUI-III had the option to participate in an in-person or phone interview (for OCC patients). The intent of the semi-structured interviews was to gain insight into the patients’ experience of living with a diagnosis of CRC and gain insights into the HRQOL factors that are important to them.

A total of 15 interviews were conducted over the period May 2010 to October 2010. Five participants were male, and 10 were female. Of the patients who participated in interviews, seven had received their diagnosis of CRC less than one year ago, seven had received it between one and two years ago, and one person received her diagnosis between two and three years ago. Every patient but one, who recently completed her treatment, was on active chemotherapy treatment when the interview was conducted. Three interviews were conducted with patients from the OCC and 12 from PMH. The duration of the interviews ranged from 10 to 45 minutes each. The variation in the interview time is attributed to the circumstances and constraints unique to each data collection site as described in Chapter 3 and further in the Limitation section of Chapter 5. Table 4 provides details for patients who participated in the interviews.

For the three interviews that were recorded, the files were transcribed as text documents by a professional transcriptionist who was external to the study. These transcripts were verified while listening to the interview recording. All qualitative interview data, including transcribed and hand-written notes, were coded for major themes.
### Table 4 - Patient Characteristics for Interview Participants

<table>
<thead>
<tr>
<th>PATIENT ID (PI)</th>
<th>DURATION (APPROXIMATE)</th>
<th>PRIMARY SITE AND FORMAT OF INTERVIEW</th>
<th>LOCATION</th>
<th>CHARACTERISTICS</th>
<th>AGE</th>
<th>SEX</th>
<th>TIME SINCE DIAGNOSIS (MONTHS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>30 min.</td>
<td>Telephone</td>
<td>OCC</td>
<td></td>
<td>60-79 y</td>
<td>Female</td>
<td>≤ 12 mos</td>
</tr>
<tr>
<td>10</td>
<td>30 min.</td>
<td>Telephone</td>
<td>OCC</td>
<td></td>
<td>60-79 y</td>
<td>Female</td>
<td>13-35 mos</td>
</tr>
<tr>
<td>13</td>
<td>45 min.</td>
<td>Telephone</td>
<td>OCC</td>
<td></td>
<td>60-79 y</td>
<td>Male</td>
<td>≤ 12 mos</td>
</tr>
<tr>
<td>51</td>
<td>10 mins.</td>
<td>In-person</td>
<td>PMH</td>
<td></td>
<td>40-59 y</td>
<td>Female</td>
<td>13-35 mos</td>
</tr>
<tr>
<td>58</td>
<td>15 mins.</td>
<td>In-person</td>
<td>PMH</td>
<td></td>
<td>40-59 y</td>
<td>Female</td>
<td>13-35 mos</td>
</tr>
<tr>
<td>59</td>
<td>10 mins.</td>
<td>In-person</td>
<td>PMH</td>
<td></td>
<td>40-59 y</td>
<td>Female</td>
<td>≥ 36 mos</td>
</tr>
<tr>
<td>60</td>
<td>15 mins.</td>
<td>In-person</td>
<td>PMH</td>
<td></td>
<td>18-39 y</td>
<td>Female</td>
<td>13-35 mos</td>
</tr>
<tr>
<td>61</td>
<td>15 mins.</td>
<td>In-person</td>
<td>PMH</td>
<td></td>
<td>40-59 y</td>
<td>Female</td>
<td>13-35 mos</td>
</tr>
<tr>
<td>62</td>
<td>10 mins.</td>
<td>In-person</td>
<td>PMH</td>
<td></td>
<td>40-59 y</td>
<td>Male</td>
<td>≤ 12 mos</td>
</tr>
<tr>
<td>72</td>
<td>15 mins.</td>
<td>In-person</td>
<td>PMH</td>
<td></td>
<td>40-59 y</td>
<td>Female</td>
<td>≤ 12 mos</td>
</tr>
<tr>
<td>73</td>
<td>10 mins.</td>
<td>In-person</td>
<td>PMH</td>
<td></td>
<td>40-59 y</td>
<td>Male</td>
<td>≤ 12 mos</td>
</tr>
<tr>
<td>74</td>
<td>10 mins.</td>
<td>In-person</td>
<td>PMH</td>
<td></td>
<td>80+ y</td>
<td>Male</td>
<td>≤ 12 mos</td>
</tr>
<tr>
<td>81</td>
<td>10 mins.</td>
<td>In-person</td>
<td>PMH</td>
<td></td>
<td>80+ y</td>
<td>Male</td>
<td>13-35 mos</td>
</tr>
<tr>
<td>97</td>
<td>10 mins.</td>
<td>In-person</td>
<td>PMH</td>
<td></td>
<td>60-79 y</td>
<td>Female</td>
<td>≤ 12 mos</td>
</tr>
<tr>
<td>100</td>
<td>10 mins.</td>
<td>In-person</td>
<td>PMH</td>
<td></td>
<td>40-59 y</td>
<td>Female</td>
<td>13-35 mos</td>
</tr>
</tbody>
</table>

**Disease Diagnosis and Treatment**

The majority (8/15 = 53%) of patients who received a diagnosis of CRC were asymptomatic, with abnormal results from a routine screening test such as the Fecal Occult Blood Test (FOBT) or a colonoscopy leading to the diagnosis. All patients who reported undergoing a regular screening test were female. Two patients reported having seen blood in their stool in the past and experienced some mild pain in the abdomen area, raising suspicions
that something was ‘not right’ and prompting them to seek medical advice. One patient was treated for CRC after cancerous polyps were detected during a routine surgery, with previous colonoscopies never having detected the disease.

### 4.2.2 HRQOL Factors for CRC patients

This section states the factors that patients described as being part of their HRQOL, including physical side effects, feelings about the disease itself, and family and friend support. The main HRQOL factors are outlined in Table 5.

**Physical Side effects**

Physical side effects are defined as any side effect that impacts patients’ health and/or well-being, including their ability to perform usual and daily activities of life. The most predominant side effect that patients reported feeling was fatigue and weakness as a result of the chemotherapy regime (6/15 = 40%); this side effect was equally reported among males and females. For one patient, the treatments were so aggressive they were described as being unbearable:

I collapsed because I couldn’t take the stronger dose…he (the doctor) didn’t tell me it was aggressive…I couldn’t put up with it (PI: 2).
Table 5 - HRQOL Factors in CRC Patients

<table>
<thead>
<tr>
<th>Physical Side Effects</th>
<th>Emotional and Mental Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Fear/Axiety</td>
</tr>
<tr>
<td>Fatigue/Weakness</td>
<td>Acceptance/Coping</td>
</tr>
<tr>
<td>Trouble Eats/Weight Loss</td>
<td>Feeling Grateful</td>
</tr>
<tr>
<td>Change from Usual Activities</td>
<td>Depression/Sadness</td>
</tr>
<tr>
<td>Guilt</td>
<td>Loss of Control over one’s life</td>
</tr>
<tr>
<td>Self-Image</td>
<td>Feeling rejected by others</td>
</tr>
</tbody>
</table>

Pain (73%), trouble eating and weight loss (47%) were the two most frequently mentioned physical side effects. Changes from usual activities were also described as being a prevalent feeling in the patient’s life (33%), as with changing jobs or having to quit a job altogether because of the limitations associated with treatment and/or illness. To a lesser degree, patients’ physical and emotional side effects also include insomnia (13%), diarrhea (13%), nausea (7%), and feelings of confusion (7%). Patients would describe the fatigue as being so significant that it routinely prevented them from participating in their usual daily activities (4/15 = 27%):

(P) I’ve had two of these now…I guess the first four (treatments) were…I wasn’t tired at all. Well, I was tired, but not tired like I am now  
(I) Something you weren’t used to, I’m assuming, from before  
(P) That’s correct, yeah  
(I) A big change?  
(P) Yeah (PI: 13).

*P – Patient/Participant; I – Interviewer*
Although male patients would just as often describe feeling fatigued or tired as female patients, their experiences with physical side effects differed. For instance males would express feeling tired but focus on the activities they still could do since their diagnosis, such as cutting the grass (PI: 73), exercising (PI: 74), and working but at a reduced workload (PI: 73). It is interesting to note that the dimension Usual Activities on the EQ-5D had the greatest proportion of males (55%) and females (71%) reporting some problems (i.e. scoring a level greater than 1), compared to any other dimension on this survey.

Another physical side effect that patients frequently described during the interviews was pain, usually mild, a feeling of numbness in their extremities (i.e. fingers and toes), and mouth sores. Experiences of pain were more often reported by female than male patients. Males and females similarly reported ‘some problems’ with pain/discomfort on the health status surveys.

In addition to fatigue/weakness and pain, some patients reported having trouble eating, in some cases leading to weight loss (PI: 51, 60, 62). Trouble eating was often attributed to the presence of mouth sores, nausea, and/or gas/discomfort (PI: 10, 51). One patient described the “fear” associated with eating solid food, because of the pain she felt when going to the washroom (PI: 51). Only one patient reported having problems with either diarrhea or constipation (PI: 59); other informants mentioned it as something they had to deal with in the past (i.e., when initially beginning treatment), but that it was not a concern presently.

Confusion and ‘not thinking clearly’ was a point raised among some patients during the interviews, but it was not a strong theme. Only one patient discussed feeling generally confused (PI: 2), but it was unclear whether the confusion was attributed to having CRC and/or its associated treatments, or whether it was due to the presence of a co-morbidity, i.e. diabetes.

Some patients stated during the interview that they had a colostomy bag inserted into their abdomen after surgery, although this was not a direct question that was asked as part of the interview guide. For patients with a colostomy bag, changes to their quality of life seemed to be
most significant. For instance, patients expressed that they often need to be near a washroom, could not go on long trips, and felt that having the colostomy bag even prevented them from taking part in regular activities: “I don’t even want to go out sometimes” (PI: 59).

**Emotional and Mental Side Effects**

Emotional and mental side effects are described as the feelings and attitudes of patients as they undergo changes to their lives as a result of the cancer. Patients react to changes in their bodies as a result of the cancer and/or its treatment, the fear and anxiety associated with having cancer, coping strategies, and finally, describe the reactions of others to their diagnosis.

There is a spectrum of feelings that CRC patients experience, with the disease affecting some patients more than others. Having a diagnosis of CRC can change not only one’s physical well-being, but also their outlook on life. How patients cope with their disease, changes to their body and how they view their body, and feelings of fear and anxiety about the future were very predominant themes in patients’ valuation of their quality of life. For some, a diagnosis meant taking action if one was to survive:

There’s ways to get around things if you work at it…you’re the boss so it’s up to you…if you’re going to sit there like a bump on a log, then you’re going to put up with whatever they (doctors) do to you (PI: 13).

Descriptions of acceptance, coping and perseverance were frequently mentioned in the patient interviews (8/15 = 53%):

(1) I don’t want to go through it anymore (chemotherapy). I’m going to do it, but I don’t want to go through all this anymore…I have to do it. I’m going to do it. I’m not going to back off. If I have reached this far, let me go to the end…I’ve accepted what the doctors tell me, which I could not accept before…If he (the doctor) tells me I have to take one more (chemotherapy), then, I have to do it! I have no choices at all in me anymore” (PI: 2).

(2) I have to be strong, I have to be independent (PI: 51).

(3) …I can’t give up (PI: 58)
Other feelings that patients described that were associated with coping included having a positive outlook on their prognosis (PI: 73), being grateful for a “new lease on life” and for still being alive (PI: 51, 72), and the cancer being a “milestone” in their life that they have chosen to overcome (PI: 61). Learning to cope with the disease in their life was one factor that the majority (53%) of patients in the interviews described as important to them. Patients described a feeling of ownership over their care, a ‘take charge’ attitude, and a determination to continue with their care despite feelings of wanting to give up. Some patients describe having a ‘positive’ attitude toward their disease as the most important factor that helps them cope, and that feeling happy and interested in life was necessary in order to deal with the complications associated with their treatment and the newfound changes in their life because of their illness.

A loss of control over the disease and its effect on their body were also described by patients (33%), as well as feelings of guilt at enabling the disease to take over one’s life which was described as a negative factor in the patients’ lives (20%).

Changes to how one views their body and how others view their body were a main theme that arose from the interviews. Patients described their body as “deformed”, no longer feeling “normal”, and wanting to avoid looking at oneself in the mirror. Although women were more likely than men to raise this as a topic of discussion during the interviews, it was apparent that this was a particularly sensitive topic especially for those patients who had undergone surgery prior to chemotherapy and were living with a colostomy bag. Patients reported that the colostomy bag is visible underneath clothes, making it especially difficult to cover up in the summer, and causes feelings of discomfort and self-consciousness (PI: 59, 61).

Feelings of fear and anxiety were predominant among patients. One patient described feeling anxious about the guilt she felt with causing pain and anguish to her family members:
I’m taking it out on my children, and it’s not very fair to (them), and I cry because I’m really taking it out on them; they do not deserve what I am doing…I wish I could forgive myself and then I’d tell them I’m sorry (P: 2).

Another patient described shock, anxiety, and fear with the disease, something she didn’t expect to feel: “… (it is) the first time in your life that you are faced with your own mortality” (PI: 10). Fear was associated with the disease itself, rather than with the treatment or other factors that play into patients’ experience with CRC: “Cancer is a very scary sickness” (PI: 51). Uncertainty and anxiety about the future were themes that were expressed by patients, and more so by those who had young families. Overall, fear and anxiety were predominant themes among patients: “Cancer makes you anxious” (PI: 97).

One patient felt that the dimension Anxiety/Depression on the EQ-5D survey should be separated and asked as two distinct questions rather than one and was unsure how to answer the question with the two seemingly disconnected concepts combined (PI:10).

In addition to feelings of fear and anxiety, patients expressed a significant change in their overall quality of life. For one patient, it was difficult to describe life without cancer, as it seemed to infiltrate and affect everything in her life: “When you have this sickness, it affects your outlook on life…you don’t seem normal anymore” (PI: 51). Every patient interviewed, regardless of their age, sex or time since diagnosis described a change that occurred in their lives as a result of the disease. Most described feelings of sadness (in one case, described as “overwhelming sadness”), loss or grief for the life they had before CRC, and changes to their outlook in life, whether negative or positive. Many were frightened of the unknown and what the future held for them. It should be noted that while prompts were used during the interviews to encourage patients to discuss their experiences in the relatively short time frame (i.e. diarrhea, constipation, trouble eating), other questions were left completely open-ended (i.e. describing quality of life).
Family/friend support

The majority of participants stated that their friends and family offer a significant amount of support to them during the course of their illness; all participants claimed that this was important to them. For some however, family and friends retreated and withdrew their support for various reasons, for instance (PI: 51, 59):

...They (family/friends) are afraid they are going to catch it (CRC)...they only drink bottled water when they come here because they’re afraid of catching the disease – they won’t drink our tap water if they do come over…they don’t even call – maybe they are afraid they are going to catch it (CRC) through the phone (PI: 59).

It is clear from discussions with the patients that living with a diagnosis of CRC affects the entire social circle of the individual, including family, friends, work relationships and any other support groups that individuals may be a part of.

4.2.3 Experience with Health Status Measures

The physical, mental and emotional factors that patients describe as part of their HRQOL were stated in the previous section. In this section, the themes generated from patient interviews are contrasted against responses to the EQ-5D, VAS and HUI-III health status surveys to better understand the degree of congruence between what patients express as factors of HRQOL that are important to them, and what HRQOL dimensions the generic health status surveys capture.

Experience with completing the EQ-5D, VAS, and HUI-III

Generally, patients felt that the EQ-5D, VAS and HUI-III surveys were relatively easy to complete (“Well, there’s nothing to it” (PI: 10)). However, some minor difficulties were stated such as the ambiguity of the questions, or the feeling that response choice is highly dependent on how and whether the patient’s health status changed on a day-to-day basis.

The majority of participants struggled somewhat with completing the VAS, expressing that they felt that the task of selecting one value on the ‘feeling thermometer’ was difficult.
Many stated that they would prefer to select a range to express the variability in how they feel on a day-to-day basis. One patient expressed that a number (i.e. VAS score) could not reflect the complexities of his feelings, and although a score was provided, it is uncertain whether this value was a true reflection of the patient’s health status:

I don’t know how to compare those numbers, really, because tomorrow I might be so down I’ll stay in bed the whole day (PI:2).

Other participants initially refused to even select a score altogether, for instance, one participant expressed that a number could not reflect the complexities of his feelings, stating, “how would you feel if your doctor told you you had five to seven months left to live?” (PI: 73). Another participant was hesitant to provide a score on the VAS, stressing she “does not feel normal” with having this disease, and equated being normal (i.e. disease-free) with a perfect score (1.00); a score of 0.80 was selected by this participant (PI: 51). Some patients also struggled with the concept that the score on the VAS incorporates all aspects of their health and well-being. Patients felt that the concept of HRQOL was complex and multi-faceted, and struggled with how to express all the factors that they associate with this concept into a single score. For one patient, she had wanted to score her “mental” state as separate and distinct from her “physical” state, and provided a score of 0.70 although she stressed that her “mental state was much worse than a score of 0.70”.

It was suggested from a number of participants that the EQ-5D and HUI-III surveys include a section where qualitative responses can be captured, to allow a better exploration of the themes and concept of quality of life. This idea is further explored in the discussion section in Chapter 5.

Interview participants were asked whether they would be willing to shorten the length of their life if it meant they could eliminate any unfavourable side effects associated with their disease (see Appendix F - 1.4, c). It is interesting to note that none of the patients responded that
they would be willing to sacrifice length of life for improved quality of life – albeit, one patient expressed some uncertainty in their response:

…if there is anything available to get rid of the tiredness that would shorten my life, I don’t know whether I’d trade it or not…because right now they say that the tumours are shrinking…and I’m happy with what they’re (doctors) telling me (PI: 13).

Despite the finding that patients experience side effects with the disease – in some cases with more significant effects on quality of life than for others – the average overall VAS score was 0.72, with the average score per sub group of analysis ranging from a low of 0.69 for the younger age group (18-59 years), to a high of 0.76 for patients who received a diagnosis of CRC more than three years ago.

While there are likely many other factors that may influence a person’s HRQOL, those brought to light in this research study help to explain and contextualize some of the reasons for the variations in scores between the various sub-groups. In the next Chapter, the implications of using these health status surveys in a CRC population are discussed, as well as some considerations for future research in this area.
CHAPTER 5: DISCUSSION

Incorporating findings from the health status surveys, the EQ-5D, VAS and HUI-III, as well as themes about HRQOL as informed by patient interviews, the previous chapter described the major results and findings that arose from an analysis of these data. This chapter considers how these results inform the overall aim of this research study, which was to determine how well current health status measures capture HRQOL in a CRC population, as well as offer insights into the level of agreement between the EQ-5D, VAS and HUI-III utility assessments. The emergent themes from the patient interviews help further our understanding of HRQOL in CRC patients, and in light of this, suggest how the EQ-5D and HUI-III surveys capture HRQOL in CRC. The chapter concludes with considerations of the limitations of the study.

5.1 Main Results and Findings

This is the first study to collect and report on HRQOL and health state utilities for stage III and IV CRC patients using three health status instruments, the EQ-5D, VAS, and HUI-III, as well as accompanied by patient interviews. This section will provide an overview for each of the four research questions of this study and discuss the main results and findings compared to what is already known about HRQOL in CRC.

5.1.1 Utilities

Using and comparing utilities generated from two different preference-based measures of health for the same population, as has been done in this research study, is important in economics as it informs the discussion about whether utilities are sensitive to the choice of health status instrument ((Brazier, Roberts, Tsuchiya, & Busschbach, 2004); (Djalalov, Hoch, & Tomlinson, 2010); (McDonough & Tosteson, 2007); (Sach et al., 2009); (Pickard et al., 2007); (Konerding et al., 2009); (Conner-Spady & Suarez-Almazor, 2003)).
**RQ-1.** *Are there differences in utility scores in a sample of CRC patients when using the EQ-5D and the HUI-III?*

In the current research study, the mean utility scores generated by the EQ-5D and HUI-III for a sample of CRC patients in Ontario were identical (both means were 0.76). This is a reassuring finding as the EQ-5D and HUI-III measures are intended to be used interchangeably when collecting utility weights. However, within-group means differed between the EQ-5D and HUI-III surveys (i.e. younger versus older patients, male versus female, etc.), although only one of the results was statistically significant at a level of significance of 0.05. The largest differences were seen between the mean EQ-5D score for patients experiencing a diagnosis of cancer for three years or more and the average HUI-III value for the same group of patients, by a value of 0.11. Similarly, average VAS scores between younger patients (18-59 years) and older patients (60-80+ years) also differed (but not statistically significantly) with the younger patients scoring on average 0.06 more points than their older counterparts.

Although the overall mean utility scores with the EQ-5D and HUI-III were identical, differences were apparent with respect to an estimate of the trend, or slope of the line, between EQ-5D, VAS and HUI-III plotted utility values. A slope value of 1.00 was selected as it represents the slope of the line for a situation whereby the plotted values are identical and a one unit change in one utility instrument is associated with a one unit change in another. This scenario is indicated with the dotted lines seen in Figure 9 in Chapter 4, section 4.1.3. For instance, a 0.1 change on the HUI-III results in an approximate 0.05 change on the EQ-5D, essentially implying that for every increase in the HUI-III score the corresponding increase in the EQ-5D score is half of this value.
These results can be compared to the literature for utility estimation in CRC. In Best et al. (2010), current health status for patients was valued at 0.82, with the unadjusted range at a high of 0.67 to a low of 0.38 (Best, Garrison, Hollingworth, Ramsey, & Veenstra, 2010). For Krabbe et al. (2004), CRC patients with liver metastases were surveyed post-intervention (i.e., liver resection). Results at baseline and post-6 month time points were almost identical, with the average VAS score at 0.76 and 0.75, respectively, and EQ-5D at 0.84 for both time periods (Krabbe, Peerenboom, Langenhoff, & Ruers, 2004). The VAS score determined here for a sample of 75 patients at baseline is closely aligned with the average VAS score found in the current research study, at 0.72, whereas average EQ-5D score was lower, at 0.76.

In Hamashima et al. (2002), the focus of the research study was on determining whether differences exist between patients that do and do not have a stoma. While the presence of a stoma was not a factor included in the analysis of this research study, some of the patients in the current research study expressed in the interview that they did not have a stoma. That factor aside, it is apparent that vast differences exist between Hamashima’s findings with respect to the proportion of respondents who reported having ‘some problems’ on the EQ-5D (identified as selecting level 2 or 3 for each dimension) and the current research study most especially with respect to three attributes: Usual care, where 62% of all patients interviewed in the current study reported some problems with this attribute whereas for Hamashima, only 29% of patients without stoma reported issues; Pain/Discomfort, where 50% of patients in the current study reported some problems but only 21% did the same in Hamashima’s study; and finally, Anxiety/Depression, where 60% of patients reported some problems in the current study, with a fraction of that, only 14%, claiming some problems in Hamashima et al (Hamashima, 2002). Three patients who participated in interviews in the current research study had a colostomy bag, all of whom described this as affecting their overall HRQOL because of changes they had to
make in their day-to-day activities. However, the range of average utility scores between these three patients make it difficult to allude to the effect that the colostomy bag has on HRQOL (0.93, 0.71, and 0.58, respectively), unlike Ramsey et al. (2002) who claim their findings support the fact that the presence of a colostomy does in fact affect HRQOL.

Finally, in Norum et al. (1996) and (1997), EQ-5D average score were 0.79 and 0.78 respectively, with an average VAS score of 0.80 (1996). These average EQ-5D scores most closely align with the findings in the current research study (Norum, Angelsen, Wist, & Olsen, 1996), (Norum, Vonen, Olsen, & Revhaug, 1997).

An interesting conclusion in Ramsey et al. (2000) is the finding that CRC patients’ valuation of HRQOL is higher than age-matched community members who do not have the diagnosis. The authors presumed it may have to do with the fact that a diagnosis of cancer makes people appreciate day-to-day life more so than for the average person (Ramsey et al., 2000). With the findings from the current research study, there is support for this claim. One of the major themes which arose from an analysis of the patient interviews was strategies to cope with the disease, including feelings of hope for a cure, perseverance at continuing with the treatment despite the negative side effects and gratitude for being alive.

*The concept of ‘trade-off’*

The techniques used to convert EQ-5D and HUI-III responses to utility values differ. In the EQ-5D, the conversion of a health state into a single index value is based on the TTO technique versus the SG technique for the HUI-III (Conner-Spady & Suarez-Almazor, 2003). For the individual completing either of the health status surveys, the concept of “trade off”, which is the decision about how much one would be willing to give up in order to gain an improvement in quality of life, is not made explicit but rather is embedded. When patients were asked during
their interview whether they would be willing to trade length of life for an improvement in the quality of their life, all but one respondent replied that they would not. A major source of inconsistency lies with this observation in that only one of the 15 sets of utility and health scores generated for patients who participated in the interviews resulted in a score of perfect health (i.e., 1.00), with the majority of scores less than 0.80 on all health status surveys. This observation clearly shows a disconnect between the individual interpretation of sacrifice in terms of improved quality of life and the established method for eliciting this information via commonly used health status surveys, and highlights a major issue with respect to the fact that respondents may not be valuing what the researcher or health-care decision maker thinks they are.

Although the average utility score for the entire sample in the current research study was identical, the differences across sub-groups are indicative of the fact that not all health status measures are necessarily created equally. Some attention should be given to differences between sub-groups, as important insights may be gained.

**RQ-2. How do various factors impact the utility scores generated using the EQ-5D and the HUI-III?**

When comparing the effects of age on mean utility scores and VAS scores, older age is positively associated with better health status, although compared to their younger counterparts, the results are not statistically significant. This may imply a number of insights about older patients, for instance as a group they may have either better adapted to living with a diagnosis of CRC and the accompanying changes this brings, have a more positive outlook on life and their prognosis, or have fewer physical side-effects that if present, could affect their quality of life. While the precise reason for this difference cannot be known with certainty, similar findings have been found in other research studies in colorectal and rectal cancers, with some support that
physical side effects including fatigue, insomnia, and diarrhea, were highest among youngest age
groups and decreased with older age (Wilson et al., 2006; Arndt, Merx, Stegmaier, Ziegler, &
Brenner, 2004).

Other research studies have evaluated the HRQOL of CRC patients at various stages of
disease progression. Ramsey et al. (2000) found that the mean utility score for a sample of CRC
patients obtained using the HUI-III tool was 0.84 for patients with stage IV disease progression,
but that average utility scores varied by time since diagnosis within that stage of disease
progression (Ramsey et al., 2000). The greatest average utility score in Ramsey et al. (2000) was
found to be for those who had been diagnosed within the past 13 to 24 months (0.95). While this
score is higher than the average score in the current research study for patients diagnosed within
a similar time period, 13 to 35 months since diagnosis (0.79 and 0.81 for EQ-5D and HUI-III,
respectively), both the EQ-5D and HUI-III average utility scores were higher in earlier versus
later stages of disease diagnosis, as was the case in Ramsey’s study. The lowest utility score in
Ramsey et al. (2002) was found to be for those diagnosed between 37 and 60 months ago (0.76),
a similar finding to the current research study where the average utility scores were also lower
for the patients with the diagnosis for 36 months or more.

Other findings from published studies on utility elicitation for health states associated
with CRC report that the acute period (i.e., one year or less after diagnosis) had the lowest utility
scores, although this improved over time (Ko et al., 2003). These findings are not consistent with
results from this research study. One possible reason for improvement over time of utility scores
could be improvements in pain management for instance (Ko et al., 2003). Also on the EQ-5D,
VAS and HUI-III, utility and health status scores for men were higher than for women, although
the results were not statistically significant. This may be due to the fact that more women than
men reported having ‘some problems’ on the surveys with respect to the dimensions of Emotion,
Usual Activities, Ambulation and Cognition, among others. More women than men tended to
discuss feelings of fear and anxiety, guilt, issues with body image, and pain in the interviews than did their male counterparts, which may also have contributed to the finding that utility, overall, is higher for men than women. This is an example of the value of qualitative data in research on HRQOL, as it allows for a more in-depth exploration of information that otherwise would not be possible with quantitative data alone.

Differences do exist in the utility scores generated on the EQ-5D, VAS and HUI-III health status scores depending on the factors of analysis. Qualitative data provide another layer of analysis that can potentially offer insights into utility assessments such as the case when analyzing differences in health status scores between males and females. Patients are more liberated to discuss openly about their feelings without the limitations of predetermined questions as they experience on the EQ-5D, VAS and HUI-III. While utility assessments are needed in economic evaluations as they inform the researcher of the benefits and drawbacks of a certain therapy or intervention on day-to-day activities, their results can potentially be misleading as they are limited to the parameters of a strictly quantitative analysis, and if possible, should be investigated further to avoid potential misinterpretation.

5.1.2 HRQOL Factors

A number of factors important to patient HRQOL were described during the patient interviews. Patient responses were categorized into two main themes: physical side effects and emotional/mental side effects.

RQ-3. What are the factors of HRQOL that CRC patients describe as important to them?

It is evident from the HRQOL factors described earlier in Chapter 4 that living with a diagnosis of CRC affects a number of facets in a patient’s life. The impact of cancer is expressed through its effects on patients’ physical and emotional well-being, how they have experienced
the disease and how it has affected their and their families’ lives, and its overall effect on their quality of life. Factors including pain, fatigue, changes from usual activities, learning to cope with the disease, and a loss of control over one’s life were all described as important to patient’s experience with CRC, some of which have been identified in previous studies as well (Wilson et al., 2010). The relatively limited number of dimensions on the EQ-5D and HUI-III instruments means that those who are completing these surveys must force their plethora of HRQOL experiences into a few pre-determined questions. By helping to shed light on these factors, this research study helps to inform areas where the EQ-5D, VAS and HUI-III are lacking in their ability to accurately capture HRQOL.

For some of these factors, the relative weight is so great that it is hard to imagine that an instrument that claims to assess HRQOL would not include these factors found to be important in a patient’s life. This is a theme that will be discussed in the next section.

5.1.3 Representation of HRQOL Factors on Health Status Surveys

It is important to have confidence in the health status instruments that are used to capture HRQOL. As with any generic instrument, dimensions are not specific to any particular disease but rather are intended to be useful in a variety of circumstances and enable the comparison of health status scores and utility values across a variety of different diseases and conditions.

RQ-4. Do the EQ-5D and the HUI-III satisfactorily capture patient-described HRQOL factors in their respective survey dimensions?

Figure 16 provides an overview of physical and emotional HRQOL factors found to be prevalent and meaningful to CRC patients and attempts to map them onto the five dimensions of the EQ-5D and the eight dimensions of the HUI-III. Physical, emotional and mental side effects
that have a corresponding dimension on the EQ-5D and HUI-III surveys are shaded grey in the figure, while the factors that are not shaded are not sufficiently represented on the surveys.

The results from the qualitative interviews indicate that there are a variety of factors that an individual with CRC associates with their HRQOL. Context variables such as age, sex, and time since diagnosis do impact how patients tend to value their own health. The finding that there are more emotional and mental side effects than physical side effects that encompass patient’s HRQOL is an important finding of this research study, especially given the fact that the majority of dimensions on the EQ-5D and HUI-III are related to physical well-being. As is apparent from Figure 16, the majority of the HRQOL factors that patients describe as important to them do not directly relate to the dimensions of the EQ-5D and HUI-III health status instruments. These instruments tend to focus on physical parameters, and more so with the HUI-III than the EQ-5D. For instance, six of the eight dimensions on the HUI-III predominately deal with physical attributes while for the EQ-5D, three of five dimensions do. For some of the most frequently mentioned HRQOL factors such as trouble eating, acceptance/coping, and changes in self image, no obvious corresponding item on the scale exists. For others such as depression/sadness, a HRQOL factor, a relationship to Emotion on the HUI-III is presumed (hence the dotted line connecting this factor to the dimension). Neither the EQ-5D nor the HUI-III includes a dimension that directly captures ‘fatigue’ or ‘feeling weak’. Hence, of the 12 total HRQOL factors for patients with CRC, eight are not represented on these surveys.

While certain studies have found that the adequacy of the EQ-5D and HUI-III are acceptable as a generic measure of health, for this particular study the findings are important in that they shed light on many elements that are missing from these surveys as important to CRC patients (Devlin, Hansen, & Selai, 2004). The exclusion of these dimensions could imply that utility values as they are currently being measured may be overstating health status, and that by
including dimensions that are important to CRC patients such as those uncovered in this research study, a score that better represents health status would be generated.

**Figure 16 - Representation of HRQOL Factors in CRC Patients on EQ-5D and HUI-III**

Dimensions of the HUI-III
- Vision
- Hearing
- Speech
- Ambulation
- Dexterity
- Emotion
- Cognition
- Pain

HRQOL Factors Identified by Interviewees
- Physical Side Effects
  - Pain
  - Usual Activities
  - Trouble Eating/Weight Loss
  - Fatigue/Weakness

- Emotional and Mental Side Effects
  - Depression/Sadness
  - Fear/Anxiety
  - Self-Image
  - Feeling Rejected
  - Acceptance/Coping
  - Feeling Grateful
  - Guilt
  - Loss of Control

Dimensions of the EQ-5D
- Mobility
- Self-Care
- Usual Activities
- Pain/Discomfort
- Anxiety/Depression

HRQOL factors not represented as dimensions on EQ-5D and HUI-III

HRQOL factors represented as dimensions on EQ-5D and HUI-III

Dimensions on EQ-5D and HUI-III not identified as HRQOL factors

Direct relationship / Presumed relationship
5.2 Study Limitations

There are a number of limitations with the present research study with respect to the richness and amount of data collected, the robustness of the analysis of the data, and the generalizability of the findings.

Study setting

Due to restrictions with respect to ethics regulations and the general clinic operation at the OCC, participants were recruited to participate in the study by the supervising oncologist. For instance, ideally patients could have been approached during their time in the waiting room to participate in the research study. However, standard ethics regulations prohibit interaction with patients for research purposes unless the researcher is first introduced to the patient by a member of the patient’s circle of care, for instance their overseeing medical oncologist or the clinic nurse. Given the generally fast-paced environment of a high-volume clinic such as the Gastrointestinal (GI) clinic at the OCC, it was not feasible to expect that the oncologist or nurse would be available to introduce the research study to every eligible patient; hence, another option was explored. After patients are brought into the medical examination room but before the oncologist comes in to see them an interview could occur. Patients are generally waiting in this examination room for anywhere from five to 20 minutes depending on how busy the clinic is. This is an ideal time period to have the study introduced to the patient with the assistance of the clinic nurse, conduct the surveys (which on average, can take anywhere from five to ten minutes), and if there is time remaining, conduct a brief in-person interview with the patient in the time remaining. However, the supervising oncologist at the OCC did not feel the use of this setting for conducting the research was appropriate, and hence an alternate method was found (i.e. distribution of survey packages to patients in the clinic). Surveys were colour-coded to identify
which patients had stage III and which had stage IV cancer. Patients had the option of either
dropping off the survey to the clinic nurse or mailing in the surveys using a self-addressed
envelope included in the survey package. As can be expected, there were significant limitations
with this method in terms of patient enrollment, nature of survey completion (i.e. conflicting
responses to survey questions) and willingness to participate in the qualitative interviews. These
limitations encountered prompted a search for alternate sources of eligible patients at PMH.

While the move to include PMH as a secondary study site helped to alleviate some of the
issues associated with the OCC including a low participation rate for the surveys and participant
interviews, better control over the research process (i.e. survey distribution and collection was
researcher-controlled as opposed to controlled by the supervising oncologist) and a higher survey
completion rate (i.e. fewer unclear or confusing responses), the ensuing trade-off of using PMH
as a secondary study site was the fact that the richness and depth of qualitative data that was
collected was limited by the setting where the interviews were conducted. For instance,
interviews with patients from the OCC site lasted 30 to 45 minutes, enabling more in-depth
analysis of the data and more opportunity for the exploration of broader themes and issues, while
interviews at PMH lasted between 10 and 15 minutes. It is possible that this relatively brief time
period allotted for the interviews could have resulted in misinterpretation of the question(s) by
the patient, or could have resulted in brief responses that were relatively superficial, or “surface
level” in their depth and breadth. Faced with these constraints however, I decided to continue
with the approach that offered me greater patient access at the expense of additional time with
the participants, a process that still enabled me to ask the majority of questions needed during the
interview. For future research studies that utilize qualitative methodology as part of the research
design, it is advisable that more time be allotted for patient interviews to allow more in-depth
exploration of responses.
Sample size and generalizability of results

The setting where the data were collected (i.e., Toronto, Ontario) somewhat limits the generalizability of the study findings and results. It is very possible that the same research study conducted within a different setting of the province or country (i.e., mix of rural and urban sites) could have produced different results. However, given the exploratory nature of this study, basing this study in Toronto is justified in that it offers an initial look at these data in a relatively homogenous setting.

Analysis of the data

Another main limitation related to the amount of information collected from study participants that could be used in the analysis. For instance, the fact that demographic information, information on treatment regime, and information regarding the presence of comorbidities, was not collected for the patient population of interest restricts the level of insight that could be gained regarding the influence of various factors on HRQOL. However, the combination of a high participation rate and the mixed methods approach to the research question enabled rich inquiry into patients’ experienced quality of life while undergoing treatment for CRC.

The coding of the interview data was undertaken by one person only. Most interviews followed a fairly structured approach, more so than is typical of most ‘semi-structured’ interviews, with most responses directly addressing the specific question asked. Therefore, the coding of the patient responses generally followed the interview guide structure. For this reason, the need for multiple coders was considered less necessary than in other interview contexts, where responses are more open-ended. That being said, preliminary findings were reviewed with the research committee to help guide the analysis.
CHAPTER 6: IMPLICATIONS

The previous chapter discussed some of the limitations of the current research study. The final chapter of this thesis is a reflection on the study design, sampling technique and biases of the current research study and how these might inform future research studies. Insight into potential extensions of this work in policy and decision-making arenas is also offered.

6.1 Study Considerations

6.1.1 Study Sample

The study design used for this research study was an exploratory study design using a combination of qualitative and quantitative methods. There were some aspects of the study design and sampling techniques that limited the generalizability of the findings and may have contributed to the introduction of biases within the study. A reflection on the limitations discussed in Chapter 5 and the significance of these limitations will be further explored in the following sections.

Sample Size

A total of 50 patients participated in the completion of the EQ-5D, VAS and HUI-III surveys at two study sites, the Odette Cancer Centre and Princess Margaret Hospital. Of those 50 patients, 15 also participated in qualitative interviews following the completion of the health status surveys. Site-specific (i.e. number of eligible patients being seen by the participating medical oncologist) and other resource constraints (i.e. time to conduct the multi-site study) somewhat limited the capacity to expand this sample size. Yet, this sample size was determined to be reasonable and appropriate for this research study based on previous studies on utility
elicitation for CRC patients whereby a sample size of between 40 and 62 was used (Ness et al., 1999; Best et al., 2010), (Norum et al., 1997). In addition to this, experts in the field agreed the sample size was reasonable given the scope of the research questions.

The size of the study sample limits statistical significance when conducting comparative analyses. As the research study was exploratory in nature, however, and not intended for hypothesis testing, this was not a priority for the research study. Also, considering that the overall means of the EQ-5D and HUI-III were identical, a larger sample size would not have influenced these findings in a significant way if the results would have been equivalent to what had already been achieved. Means between subgroups of analysis (age, sex and time since diagnosis) were similar but not identical, and additional study participants probably would not have changed these estimates of the means. This design is satisfactory for an exploratory study such as this research study; however, future studies that wish to test for differences in the means should consider larger sample sizes.

The benefits of a larger sample size must be acknowledged to inform future research studies. Larger sample sizes are usually more generalizable to the population of interest, help to ensure statistical significance of research findings, and may be more representative of the sample population at large (Jang, 2009). Ensuring statistical significance of findings would be helpful for studies that wish to evaluate statistical relationships. For this research study, it is difficult to assert with confidence that the results are generalizable all CRC patients receiving treatment in Ontario.
6.1.2 Generalizability of findings

A sample of 50 patients could be criticized for having limited generalizability to a broader CRC patient population. The sample of 50 patients included an uneven number of males and females, with 10 females and five males participating in the qualitative interviews, as well as an uneven number of patients categorized as stage III and IV. All study participants were residents of the Greater Toronto Area (GTA), and attended either the OCC or PMH sites for treatment. The study sampling criteria were broad, stating that patients must have a current diagnosis of stage III or IV CRC, must be residents of Ontario, and must be currently receiving treatment for their disease at either the OCC or PMH sites. These criteria resulted in a relatively homogenous group of patients who participated in the research study, with the majority of participants having a diagnosis of stage IV CRC and recruited from the PMH site.

With such a homogenous group, it is difficult to determine whether the results are due to the surroundings and/or context, and whether we would see different results if more patients were available.

There is uncertainty whether similar results would have been found with a more structured approach and patients with different characteristics. Had these considerations been incorporated into the study design/sampling criteria, it would have allowed for cross-group analysis and examination and broadened the scope of understanding with respect to the results.

The mix of patients in the two groups was not adequate enough to enable between-group analysis, for instance to test for differences between males and females, or between stage III and IV cancer patients. In addition, the analysis is limited to the characteristics of the demographic who reside in the GTA. Future studies could consider expanding the inclusion criteria to include patients from more geographically-dispersed areas, and using cancer centres located in more remote areas to gain further insights into how these variations influence the findings.
6.1.3 Participation Rate

The participation rate in a research study is determined by the ratio of the proportion of participants who took part in the study compared to the number of potential participants who meet the study criteria but did not participate in the research study. Understanding the participation rate in a research study is helpful because it can provide some insight into the effectiveness of study recruitment strategies as well as the population of interest.

In the current research study, the number of potential study participants at both study sites that were eligible to participate but did not is unknown. Patients were selected to participate on an ad-hoc basis, with the supervising oncologist informing the research student on a regular (i.e. daily at the PMH site) basis from their patient roster which patients could be approached to participate in the study. Due to ethics regulations as well as guidance from the oncologist, the oncologist was the only member of the research team who was privy to the patient roster list and knew which patients should be approached and which should not. This made it impossible to know the number of eligible patients that were not approached from these two sites as well as the number of non-responders from the OCC site specifically, although survey response rate is one way of assessing this information.

Although the number of non-respondents was not captured this number is expected to be quite low. At the PMH site, all patients who were identified by the oncologist as eligible to participate in the study were approached with four patients refusing to participate. This likely is a testament to having direct researcher involvement in the design and implementation of the study, as the researcher has more time to sit with patients and explain the intent of the research, what is involved, how the findings will be used, and also gain some rapport with the patient who is participating. All of these factors likely had a positive influence on the participation rate at the PMH versus OCC site.
Not knowing the participation rate prohibits an understanding of the potential reach of the study. For this particular research study, it is unknown whether the participation rate would have differed had alternate methods been used which did not involve direct oncologist involvement. For instance, a mail-out survey would have provided all potential participants an equal opportunity to respond to the survey without the influence of their oncologist, which was the circumstance at the OCC site. Information about non-responders including their reasons for not participating were unfortunately not captured in this current research design. Future studies are cautioned to understand and become familiar with the patient mix at the site of interest, for instance, how well or sick patients are which will affect participation rates. This information was not captured at the research sites prior to the start of the study although it would have been greatly advantageous to have it.

6.1.4 Recruitment Strategy

A combination approach to recruitment of participants for the research study was undertaken. Patients at the OCC site were recruited by the participating medical oncologist as it was felt to be a more feasible approach that the oncologist also preferred. Ethics regulations with respect to study recruitment strictly prohibited recruitment of patients without initial introduction by a member of the patient’s ‘circle of care’.

Although sampling criteria had been established to guide the research study, selection of patients for participation in the study was determined by the participating medical oncologist at both study sites. Therefore, the strategy for recruiting patients closely resembles a convenience sampling strategy as participants were approached to participate only if they were present (i.e. had an appointment with the medical oncologist at their clinic) during the time that recruitment was taking place. Therefore, not all potential participants who met the study criteria had an equal chance to participate.
Qualitative interviews were also conducted with a subset of the study sample. All participants were offered an opportunity to participate in the qualitative interviews. Participants from the OCC site were provided with an information letter which they could use to call the researcher to set up a time for an interview. At the PMH site, participants were directly asked after they completed the surveys whether they would be willing to participate in an interview.

The level of researcher involvement differed between the OCC and PMH sites, with varying levels of involvement from the researcher. For instance at the OCC site, the oncologist was primarily responsible for not only identifying the patients but also for distributing and collecting the surveys, although patients had the option of mailing back completed health status surveys. At PMH, the oncologist only helped to identify which patients would be eligible for participation, while the rest of the research was carried out by the research student. The impact of these varying approaches is that it limits the ability to make informed inferences about the findings.

Suggestions for future research include having more specific sampling criteria to adhere to ensuring that in the event that someone external to the research study is involved in subject recruitment, that subjects are continued to be recruited based on a strict set of criteria which would eliminate the opportunity for interpretation. The primary researcher should be as involved as possible in the recruitment of subjects, as important information is revealed at these times. Finally, taking note of the number of non-respondents and their reasons for not participating in the research study is extremely beneficial to informing the success or failure of the recruitment strategy. This information will assist in the design of studies, especially those employing a mail-out option for data collection.

6.2 Policy and Research Implications

The study of HRQOL is complex, as it incorporates emotional, social, mental, physical, as well as other dimensions, all of which are theoretically captured by preference-based HRQOL
measures. This thesis is the first study based in Ontario that investigates HRQOL among CRC patients using two generic measures, with findings from qualitative interviews informing these results. There is no doubt that a diagnosis of CRC significantly changes the lives of the people it affects, and it is important that the complexity of these changes be accurately captured to enable informed decision-making. The available chemotherapy, surgery and radiotherapy treatments help to prolong cancer-free survival, and yet CRC still remains the second leading cause of death from cancer in Canadian men and women combined. Increasing attention to this disease in terms of screening and early detection likely means that economic analyses will be sought to help inform decisions regarding the relative cost-effectiveness of certain techniques and/or therapies related to CRC. With decision-making sensitive to a cost-effectiveness threshold, the inclusion of certain parameters such as those identified in this research study may have a significant impact on the results of such analyses. It is for this reason that recommendations for the research and policy realm are suggested in the next section.

6.2.1 Policy and Decision-Making

This research study found certain HRQOL dimensions that were important to quality of life of CRC patients but were not included on the EQ-5D and HUI-III health status surveys. Decision-making in health care should not necessarily be entirely predicated on the value of these utilities as there is evidence that they may not be reflective of the patient experience. However, the policy implications of these findings could be significant enough that decisions regarding whether to fund a certain drug or intervention change based on the relative weight of these missing parameters.

These dimensions, although important to CRC patients, may not necessarily change the results of cost-utility analyses if surveying of these dimensions does not influence the overall
QALY. More research is needed on estimating the potential weight of these missing HRQOL dimensions and how their inclusion could affect final cost-utility analyses.

6.2.2 Future Research

In this research study, results from the utility scores and interview transcripts indicate that most of the patients experience side effects that affect their quality of life to differing degrees of severity. These findings are consistent with findings from focus group research conducted with CRC patients by Ness et al. (1998), whereby the number and intensity of symptoms reported by stage III patients treated with chemotherapy was bimodal – that is, half the participants reported significant symptoms while on chemotherapy (i.e. nausea, mouth sores, severe diarrhea) whereas the other half did not (Ness, Holmes, Klein, Greene, & Dittus, 1998). With such a volume of patients reporting side effects, consideration must be given to integrating a method for capturing this information on current generic preference-based surveys.

One possible suggestion is the pairing of disease-specific instruments with generic, preference-based surveys, such as the Functional Assessment of Cancer Therapy for Colorectal Cancer, or FACT-C. The FACT tools are a series of quality of life questionnaires targeted to the management of chronic illness, with the FACT-C specifically tailored to CRC. With a total of 36 questions covering areas such as physical well-being, social and family well-being, emotional well-being, functional well-being, and additional concerns including questions about diarrhea, appetite, body appearance, and feelings about patient ostomy, this questionnaire covers many of the areas of HRQOL that generic health status surveys do not. The main limitation however with this disease-specific instrument is that the scores do not produce utilities, thereby limiting its use to a purely information-gathering and supportive purpose.
In a recent study by Wilson et al. (2010), HRQOL factors that CRC patients describe as important to them were compared to the dimensions on the FACT-C tool. While there was a fairly significant degree of overlap between what was described in the interviews and the FACT-C tool, certain other criteria such as information about the disease and/or the side effects, and normality and daily routine, were not included (Wilson et al., 2010). For these reasons, the authors suggested that currently used instruments that collect information on health status should be supplemented with additional questions. While Wilson et al. conclude that such augmentation could be useful in a clinical setting to prompt clinicians to be alerted to possible changes in patient’s health status, developing a more comprehensive utility score may be more useful and informative in economic studies where the utility score is thought to represent HRQOL.

Alternatively, disease-specific questions could be added to generic, preference-based surveys such as the EQ-5D and HUI-III. The advantages of this option include a more informative utility value which captures the aspects that are important to CRC patients. However, the disadvantage of this option is predominately the time that it would take to incorporate these dimensions into the surveys. Additional research would be required into how to convert the valuation on these dimensions into utility scores, as well as time to validate such a revised health status instrument within a CRC population.

Finally, if it is not feasible to incorporate the use of disease-specific questions when using generic surveys for reasons such as cost and time constraints, then users of these preference-based utility scores should approach their results with caution. Utility scores generated this way may be misleading as they could be either over-representing or under-representing HRQOL. This has the potential to significantly impact the results of the cost-utility analysis and hence, final decision-making related to this.
6.3 Implications

The comprehensiveness of generic instruments such as the EQ-5D and HUI-III in accurately capturing HRQOL in the study of cancer have not been well studied, at least not to the extent of the current research study. Utilizing qualitative inquiry to investigate more thoroughly the factors of HRQOL that are important to CRC patients is unique to a study of preference-based utility, and one that has revealed important insights about the kinds of factors that should be included in a HRQOL assessment.

The QALY is a concept that is far from being free from controversy. Combining quality and quantity of life in a single index is fairly straightforward and easy-to-calculate and enables broad comparisons of results. However, this relatively streamlined approach is limited by the tools which are used to capture the quality aspect of one’s life. The findings from this research study will be of interest to researchers who collect and use these utility scores for cost-utility analyses, as well as policy makers who use the results of these economic analyses to make informed decisions about treatment modalities and/or interventions. Developers of these generic preference-based surveys can also draw important conclusions from these findings that could help inform the development and refinement of future instruments. Clinicians and healthcare professionals who are involved in the treatment of CRC patients may also find this information of great value as potential users of these surveys to assess changes in health status of their patients. The insights gained from the questions that are asked alongside these generic surveys provide a look into the current health status of patients that clinicians may not necessarily have a chance to ask the patient, but are worthwhile and informative nonetheless. These questions may reveal underlying side effects that could be worsening, for instance, underlying depression or extreme stress and/or fatigue that could be significantly impacting patient quality of life. Future research can provide answers as to the extent that these issues affect the QALY.
APPENDICES
Appendix A – Direct Preference-Based Health Status Instruments

1. The Standard Gamble (SG) technique

“Using the SG technique to obtain utility values, respondents are presented with a choice between an intermediate, guaranteed health state and a gamble between full health and death. The probability of death (1 - P) is varied until a point of indifference is reached between the two choices. The value of P gives the utility value. The Figure below illustrates the SG technique” (Yorkshire & Humber Public Health Observatory, 2009).

2. Time trade-off (TTO) technique

Time is varied until the point of indifference (x/t = value for state i) (Vergel & Sculpher, 2008).
Appendix B – Study Information Letter

<<Cancer Centre letterhead>>

Hello,

I would like to invite you to participate in a study about quality of life for colorectal cancer patients currently undergoing treatment, or being monitored, in Ontario at the Odette Cancer Centre. Sarah Costa is a University of Toronto graduate student conducting this study as part of her thesis project. The main purpose of the study is to determine details about quality of life that are important to colorectal cancer patients, and to determine whether these factors are adequately being captured by current health status surveys.

If you would like to participate in the study, you would be completing two self-administered surveys. The surveys will take about 10 minutes total to complete. Please note that by completing these surveys, your informed consent is assumed to be given. If you choose to, you may also participate in an in-person interview where Sarah will explore more in-depth the impact of various factors affecting your quality of life. There is no risk involved in participating in the study. Your participation is completely voluntary, and you are under no obligation to participate. Please note that all of the information obtained during the survey and/or interview sessions is strictly confidential, and will be reported only at aggregate levels. Any interview that is conducted will be recorded using a digital recorder and deleted once the interview has been transcribed. All digital recordings as well as transcribed documents will be uploaded to a secure network and password protected. Ethics approval for the study has been obtained from the University of Toronto and the Sunnybrook Health Sciences Centre.

If you would like more information about the study, or to book a half-hour interview, please call Sarah Costa at (416) 971-9800 x 3319, or you can also reach her at sarah.costa@utoronto.ca.

Thank you for your consideration of participation in this study. Your perceptions and insights are invaluable to the research project. If you have any questions about your rights as a research participant, please contact (Name), Chair of the (Hospital Name) Research Ethics Board, at (xxx) xxx-xxxx.

Yours sincerely,

(Supervising Medical Oncologist and Researcher to sign)
Appendix C – EQ-5D and VAS Survey Instrument

By placing a check-mark in one box in each group below, please indicate which statements best describe your own state of health today.

**Mobility**
I have no problems in walking about
I have some problems in walking about
I am confined to bed

**Self-Care**
I have no problems with self-care
I have some problems washing or dressing myself
I am unable to wash or dress myself

**Usual Activities** *(e.g. work, study, housework, family or leisure activities)*
I have no problems with performing my usual activities
I have some problems with performing my usual activities
I am unable to perform my usual activities

**Pain/Discomfort**
I have no pain or discomfort
I have moderate pain or discomfort
I have extreme pain or discomfort

**Anxiety/Depression**
I am not anxious or depressed
I am moderately anxious or depressed
I am extremely anxious or depressed
**Visual Analog Scale**

To help people say how good or bad their state of health is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your state of health is today.
Appendix D – HUI-III Survey Instrument

HUI3 Multi-Attribute Health Status Classification System

Please circle the most appropriate answer for each question

Vision:
1. Able to see well enough to read ordinary newsprint and recognize a friend on the other side of the street, without glasses or contact lenses.
2. Able to see well enough to read ordinary newsprint and recognize a friend on the other side of the street, but with glasses.
3. Able to read ordinary newsprint with or without glasses but unable to recognize a friend on the other side of the street, even with glasses.
4. Able to recognize a friend on the other side of the street with or without glasses but unable to read ordinary newsprint, even with glasses.
5. Unable to read ordinary newsprint and unable to recognize a friend on the other side of the street, even with glasses.
6. Unable to see at all.

Hearing:
1. Able to hear what is said in a group conversation with at least three other people, without a hearing aid.
2. Able to hear what is said in a conversation with one other person in a quiet room without a hearing aid, but requires a hearing aid to hear what is said in a group conversation with at least three other people.
3. Able to hear what is said in a conversation with one other person in a quiet room with a hearing aid, and able to hear what is said in a group conversation with at least three other people, with a hearing aid.
4. Able to hear what is said in a conversation with one other person in a quiet room, without a hearing aid, but unable to hear what is said in a group conversation with at least three other people even with a hearing aid.
5. Able to hear what is said in a conversation with one other person in a quiet room with a hearing aid, but unable to hear what is said in a group conversation with at least three other people even with a hearing aid.
6. Unable to hear at all.

Speech:
1. Able to be understood completely when speaking with strangers or friends.
2. Able to be understood partially when speaking with strangers but able to be understood completely when speaking with people who know me well.
3. Able to be understood partially when speaking with strangers or people who know me well.
4. Unable to be understood when speaking with strangers but able to be understood partially by people who know me well.
5. Unable to be understood when speaking to other people (or unable to speak at all).
Ambulation:
1. Able to walk around the neighbourhood without difficulty, and without walking equipment.
2. Able to walk around the neighbourhood with difficulty, but does not require walking equipment or the help of another person.
3. Able to walk around the neighbourhood with walking equipment, but without the help of another person.
4. Able to walk only short distances with walking equipment, and requires a wheelchair to get around the neighbourhood.
5. Unable to walk alone, even with walking equipment. Able to walk short distances with the help of another person, and requires a wheelchair to get around the neighbourhood.
6. Cannot walk at all.

Dexterity:
1. Full use of two hands and ten fingers.
2. Limitations in the use of hands or fingers, but does not require special tools or help of another person.
3. Limitations in the use of hands or fingers, is independent with use of special tools (does not require the help of another person).
4. Limitations in the use of hands or fingers, requires the help of another person for some tasks (not independent even with use of special tools).
5. Limitations in use of hands or fingers, requires the help of another person for most tasks (not independent even with use of special tools).
6. Limitations in use of hands or fingers, requires the help of another person for all tasks (not independent even with use of special tools).

Emotion:
1. Happy and interested in life.
2. Somewhat happy.
3. Somewhat unhappy.
4. Very unhappy.
5. So unhappy that life is not worthwhile.

Cognition:
1. Able to remember most things, think clearly and solve day to day problems.
2. Able to remember most things, but have a little difficulty when trying to think and solve day to day problems.
3. Somewhat forgetful, but able to think clearly and solve day to day problems.
4. Somewhat forgetful, and have a little difficulty when trying to think or solve day to day problems.
5. Very forgetful, and have great difficulty when trying to think or solve day to day problems.
6. Unable to remember anything at all, and unable to think or solve day to day problems.

Pain:
1. Free of pain and discomfort.
2. Mild to moderate pain that prevents no activities.
3. Moderate pain that prevents a few activities.
4. Moderate to severe pain that prevents some activities.
5. Severe pain that prevents most activities.
### Appendix E – Scoring Algorithms for EQ-5D and HUI-III Surveys

#### EQ-5D Algorithm

<table>
<thead>
<tr>
<th>Dimension</th>
<th>Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>0.081</td>
</tr>
<tr>
<td>1. Mobility</td>
<td></td>
</tr>
<tr>
<td>Level 1</td>
<td>0</td>
</tr>
<tr>
<td>Level 2</td>
<td>0.089</td>
</tr>
<tr>
<td>Level 3</td>
<td>0.314</td>
</tr>
<tr>
<td>2. Self-care</td>
<td></td>
</tr>
<tr>
<td>Level 1</td>
<td>0</td>
</tr>
<tr>
<td>Level 2</td>
<td>0.104</td>
</tr>
<tr>
<td>Level 3</td>
<td>0.214</td>
</tr>
<tr>
<td>3. Usual Activity</td>
<td></td>
</tr>
<tr>
<td>Level 1</td>
<td>0</td>
</tr>
<tr>
<td>Level 2</td>
<td>0.036</td>
</tr>
<tr>
<td>Level 3</td>
<td>0.094</td>
</tr>
<tr>
<td>4. Pain/Discomfort</td>
<td></td>
</tr>
<tr>
<td>Level 1</td>
<td>0</td>
</tr>
<tr>
<td>Level 2</td>
<td>0.123</td>
</tr>
<tr>
<td>Level 3</td>
<td>0.386</td>
</tr>
<tr>
<td>5. Anxiety/Depression</td>
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</tr>
<tr>
<td>Level 1</td>
<td>0</td>
</tr>
<tr>
<td>Level 2</td>
<td>0.071</td>
</tr>
<tr>
<td>Level 3</td>
<td>0.236</td>
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<tr>
<td>N3</td>
<td>0.259</td>
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#### HUI-III Algorithm

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<th>Dimension</th>
<th>Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Vision</td>
<td></td>
</tr>
<tr>
<td>Level 1</td>
<td>1.00</td>
</tr>
<tr>
<td>Level 2</td>
<td>0.98</td>
</tr>
<tr>
<td>Level 3</td>
<td>0.89</td>
</tr>
<tr>
<td>Level 4</td>
<td>0.84</td>
</tr>
<tr>
<td>Level 5</td>
<td>0.75</td>
</tr>
<tr>
<td>Level 6</td>
<td>0.61</td>
</tr>
<tr>
<td>2. Dexterity</td>
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</tr>
<tr>
<td>Level 1</td>
<td>1.00</td>
</tr>
<tr>
<td>Level 2</td>
<td>0.95</td>
</tr>
<tr>
<td>Level 3</td>
<td>0.88</td>
</tr>
<tr>
<td>Level 4</td>
<td>0.75</td>
</tr>
<tr>
<td>Level 5</td>
<td>0.65</td>
</tr>
<tr>
<td>Level 6</td>
<td>0.56</td>
</tr>
<tr>
<td>3. Emotion</td>
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</tr>
<tr>
<td>Level 1</td>
<td>1.00</td>
</tr>
<tr>
<td>Level 2</td>
<td>0.95</td>
</tr>
<tr>
<td>Level 3</td>
<td>0.85</td>
</tr>
<tr>
<td>Level 4</td>
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<tr>
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<td>0.46</td>
</tr>
<tr>
<td>Level 6</td>
<td>N/A</td>
</tr>
<tr>
<td>4. Cognition</td>
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<tr>
<td>Level 1</td>
<td>1.00</td>
</tr>
<tr>
<td>Level 2</td>
<td>0.92</td>
</tr>
<tr>
<td>Level 3</td>
<td>0.95</td>
</tr>
<tr>
<td>Level 4</td>
<td>0.83</td>
</tr>
<tr>
<td>Level 5</td>
<td>0.60</td>
</tr>
<tr>
<td>Level 6</td>
<td>0.42</td>
</tr>
<tr>
<td>5. Pain</td>
<td></td>
</tr>
<tr>
<td>Level 1</td>
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</tr>
<tr>
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<td>0.93</td>
</tr>
<tr>
<td>Level 3</td>
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</tr>
<tr>
<td>Level 4</td>
<td>0.77</td>
</tr>
<tr>
<td>Level 5</td>
<td>0.55</td>
</tr>
<tr>
<td>Level 6</td>
<td>N/A</td>
</tr>
</tbody>
</table>

### Example

On the EQ-5D, a health state of 12112 would be scored the following way:

**Perfect Health:** 1.0  
**Constant (for any dysfunctional state):** 0.081  
**Level 1:** 0  
**Level 2:** 0.104  
**Level 3:** 0  
**Level 4:** 0  
**Level 5:** 0.071

\[
1.0 - (0.104 + 0.071) = 0.825 - (0.081) = 0.74
\]
Appendix F – Interview Guide

Preamble
- The intent of this research study is to determine quality of life for colorectal cancer patients currently undergoing treatment at the Odette Cancer Centre in Toronto, Ontario
- This study is funded by The University of Toronto. The research student, Sarah Costa, is completing this research study as part of her thesis for the degree of Masters of Health Services Research with the Department of Health Policy, Management and Evaluation at the University of Toronto. The supervising professor is Dr. Jeffrey Hoch, PhD

Permission/Consent to Record Key Informant Interview
- I would like to reiterate that participation in this study is completely voluntary and that you may choose to withdraw at any time or choose not to answer any questions. I would like to record this interview to assist with analysis later on. Is this acceptable to you?

Section 1 – Characteristics of the Disease

1.1. How long ago were you diagnosed with CRC?

1.2. How did you find out of your diagnosis? 
   *i.e. regular screening, symptoms, etc.*

1.3. Are you currently on treatment?

1.4 When you were on treatment/if you are on treatment now:
   a. did you have side effects?
   b. what sorts of side effects did you have? *i.e. pain, trouble eating, diarrhea*
   c. were any of the side effects so bad that you if it were possible, you would be willing to shorten your life to get rid of the side effect?

1.5 Did you feel like you had support from your friends and family during the time you were receiving treatment that made it easier to cope with the disease and the side effects it had? How important was that to you, to have that support?

Section 2 – Interpretation of the Surveys

2.1 Is there anything you don’t like about these surveys? Why or why not?

2.2 Did you feel there was anything missing from these surveys? For example, we talked a lot earlier in this interview about some of your side effects, the effect the disease had/has on you, your support system including family and the effect they’ve had on you during this time. Did you feel with these surveys you could express those things?

Section 3 – Perspectives on Health

3.1 Do you feel that these surveys accurately captured your current state of “health”, however you would define that?
## Appendix G – Major themes from Qualitative Analysis

<table>
<thead>
<tr>
<th><strong>Time Since Diagnosis</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 12 months</td>
<td></td>
</tr>
<tr>
<td>13-35 months</td>
<td></td>
</tr>
<tr>
<td>≥ 36 months</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th><strong>How the Diagnosis of CRC was Detected</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptomatic</strong></td>
<td>(i) blood in stool</td>
</tr>
<tr>
<td><strong>Asymptomatic</strong></td>
<td>(i) family history</td>
</tr>
<tr>
<td></td>
<td>(ii) regular screening</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Physical Side Effects from Treatment</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue/weakness</td>
<td></td>
</tr>
<tr>
<td>Trouble eating</td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
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</tr>
<tr>
<td>Diarrhea</td>
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<td>Confusion</td>
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</tr>
<tr>
<td>Pain</td>
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</table>

<table>
<thead>
<tr>
<th><strong>Feelings about the Disease</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptance</td>
<td></td>
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<tr>
<td>Change from usual activities</td>
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<tr>
<td>Coping</td>
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<tr>
<td>Grateful</td>
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<tr>
<td>Loss of control</td>
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<tr>
<td>Guilt</td>
<td></td>
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<tr>
<td>Fear</td>
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<td>Body image</td>
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<table>
<thead>
<tr>
<th><strong>Interpretation of Health Status Surveys: EQ-5D, VAS and HUI-III</strong></th>
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<tbody>
<tr>
<td>VAS score</td>
<td></td>
</tr>
<tr>
<td>EQ-5D dimensions</td>
<td></td>
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<tr>
<td>HUI-III dimensions</td>
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<table>
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<tr>
<th><strong>Family/Friend Support</strong></th>
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<tbody>
<tr>
<td>Increased support</td>
<td></td>
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<tr>
<td>Decreased support</td>
<td></td>
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<tr>
<td>Changes to family/friend dynamics</td>
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</tr>
</tbody>
</table>
Appendix H – Ethics Approval Letters

Odette Cancer Centre at Sunnybrook Health Sciences Centre

To: Dr. Linda Rabeneck
   Medicine/Oncology
   Room T2 025

From: Dr. Philip Hébert

Date: August 28, 2009

Subject: Assessing Quality of Life for Colorectal Cancer Patients in Ontario Using a Mixed Methodology Approach

Project Identification Number: 190-2009
Approval Date: August 28, 2009
Expiry date: August 28, 2010

The Research Ethics Board of Sunnybrook Health Sciences Centre has conducted a Delegated Board review of the research protocol referenced above and approved the involvement of human subjects as specified in the protocol on the above captioned date. The quantum for approval did not involve any member associated with this project.

The approval of this study includes the following documents:

- Protocol dated August 12, 2009
- Information Letter and Consent Form for the surveys dated August 12, 2009
- Information Letter and Consent Form for the interview dated August 12, 2009
- Interview Guide dated August 12, 2009
- HUI3 Multi-Attribute Health Status Classification System (received June 12, 2009)
- EQ-5D Health Questionnaire (received June 12, 2009)

The above Project Identification Number has been assigned to your project. Please use this number on all future correspondence. Should your study continue for more than one year you must request a renewal on or before one year from the approval date. Please advise the Board of the progress of your research annually and/or any adverse events or deviations which may occur in the future.

Approval of this study by the Sunnybrook REB entails that this study complies with current legislation as outlined in the Ontario Personal Health Information Protection Act (PHIPA) and all policies and guidelines established by Sunnybrook Health Sciences Centre. All applicable

The Research Ethics Board of Sunnybrook Health Sciences Centre operates in compliance with the Tri-Council Policy Statement, ICH GCP Guidelines, Part C Division 5 of the Food and Drug Regulations, Part 4 of the Natural Health Products Regulations, and the Medical Devices Regulations. All Health Canada regulated trials at Sunnybrook are conducted by a Qualified Investigator.

Fully affiliated with the University of Toronto
Princess Margaret Hospital

University Health Network
Research Ethics Board
10th Floor, Room 1056
700 University Ave
Toronto, Ontario, M5G 1L6
Phone: (416) 581-7860

Notification of REB Initial Approval

Date: July 19th, 2010
To: Dr. Monika Krajczarowski
Rm 227, 5th Floor, 610 University Ave, PMH

Re: 09-0807-AE
Assessing Quality of Life for Colorectal Cancer Patients in Ontario Using a Mixed Methodology Approach

REB Review Type: Expedited
REB Initial Approval Date: July 19th, 2010
REB Expiry Date: July 19th, 2011

Documents Approved:
- Protocol
- Recruitment Materials - Invitation Letter
- Questionnaire - Baseline Demographics
- Questionnaire - EQ-5D
- Questionnaire - Health Utilities Index
- Interview Guide

Version date: June 18th, 2010
Version date: July 10th, 2010
Version date: July 10th, 2010
Version date: 1990
Version date: 2002
Version date: August 12th, 2009

The above named study has been reviewed and approved by the University Health Network Research Ethics Board. If, during the course of the research, there are any serious adverse events, confidentiality concerns, changes in the approved project, or any new information that must be considered with respect to the project, these should be brought to the immediate attention of the REB. In the event of a privacy breach, you are responsible for reporting the breach to the UHN REB and the UHN Corporate Privacy Office (in accordance with Ontario health privacy legislation - Personal Health Information Protection Act, 2004). Additionally, the UHN REB requires reports of inappropriate/unauthorized use of the information.

Please be aware that it is UHN policy that research-related activities involving an external party require a research agreement. An 'external party' refers to a corporation other than UHN or an individual who is not UHN personnel. Should a research agreement be required in this case, the study may not begin at UHN until the agreement has been signed by all parties. Should the negotiation process raise concerns, the REB reserves the right to reconsider its approval.

If the study is expected to continue beyond the expiry date, you are responsible for ensuring the study receives re-approval. The REB must be notified of the completion or termination of this study and a final report provided. As the Principal Investigator, you are responsible for the ethical conduct of this study.

The UHN Research Ethics Board operates in compliance with the Tri-Council Policy Statement, ICH/GCP Guidelines, the Ontario Personal Health Information Protection Act (2004), and Part C, Division 5 of the Food and Drug Regulations of Health Canada.

There's always an answer. We'll find it.
University of Toronto

Office of the Vice-President, Research
Office of Research Ethics

PROTOCOL REFERENCE #24001

January 23, 2010

Dr. Jeffrey Hoch
Health Policy, Management and Evaluation
St. Michael’s Hospital
30 Bond St.
Toronto, ON M5B 1W8

Ms. Sarah Costa
Health Policy, Management and Evaluation
St. Michael’s Hospital
30 Bond St.
Toronto, ON M5B 1W8

Dear Dr. Hoch and Ms. Costa:

Re: Administrative Approval of your research protocol entitled, “Assessing Quality of Life for Colorectal Cancer Patients in Ontario Using a Mixed Methodology Approach”

We are writing to advise you that the Office of Research Ethics has granted administrative approval to the above-named research study. The level of approval is based on the following role(s) of the University, as you have identified with your submission:

• Graduate Student research – hospital-based only
• Storage or analysis of De-identified Personal Information (data)

This approval does not substitute for ethics approval, which has been obtained from your hospital Research Ethics Board. Please note that you do not need to submit Annual Renewals, Study Completion Reports or Amendments to the ORE unless the involvement of the University changes so that ethics review is required. Please contact the ORE to determine whether a particular change to the University’s involvement requires ethics review.

Best wishes for the successful completion of your project.

Yours sincerely,

S. Lanthier
Research Ethics Coordinator

McMurrich Building, 12 Queen's Park Cres. W, 2nd Floor Toronto, ON M5S 1S9
TEL: 416-946-3273 FAX: 416-946-5763 EMAIL: ethics.review@utoronto.ca
Appendix I – Sample EQ-5D, VAS and HUI-III Surveys

**HUI-III**

Emotion:
1. Happy and interested in life.
2. Somewhat happy.
3. Somewhat unhappy.
4. Very unhappy.
5. So unhappy that life is not worthwhile.

**EQ-5D**

Anxiety/Depression

- I am not anxious or depressed
- I am moderately anxious or depressed
- I am extremely anxious or depressed
VAS

Best imaginable state of health

Worst imaginable state of health

Physically

Mentally
### Appendix J – Differences between Direct and Indirect Data Collection Methods

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Direct (researcher-administered)</th>
<th>Indirect (no direct researcher involvement)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method of data collection</td>
<td>Researcher administered and/or self-administered; collected at time of completion (i.e., no time lag between survey completion and collection)</td>
<td>Self-administered without the assistance of the researcher; collected indirectly (i.e. member of patient’s circle of care; surveys are mailed in or dropped-off)</td>
</tr>
<tr>
<td>Locus of control</td>
<td>High - significant degree of control over data collection process</td>
<td>Low - limited control over data collection process&lt;br&gt;- recruitment of participants is responsibility of designated member</td>
</tr>
<tr>
<td>Interviewer/researcher bias</td>
<td>Potential for interviewer bias high - interpretation of questions influenced by researcher and may have impact on how question is answered</td>
<td>Free of interviewer bias - designated member of research study is at ‘arm’s length’ with study results</td>
</tr>
<tr>
<td>Participation/response rate</td>
<td>Generally high(er) - direct encouragement to participate in study&lt;br&gt;- availability of researcher to answer questions and provide clarification&lt;br&gt;- researcher intervention allows for probing and/or explanation&lt;br&gt;- fewer incomplete responses&lt;br&gt;- allows for additional information to be collected from participant, i.e. nuances about disease state, quality of life, etc., and/or</td>
<td>Generally low(er) - encouragement to participate remains outside of control of researcher&lt;br&gt;- greater potential to lose, misplace, or provide incomplete responses on survey(s)&lt;br&gt;- greater perceived barriers to survey completion, i.e. researcher not readily available to provide clarification&lt;br&gt;- no researcher intervention available to</td>
</tr>
<tr>
<td>Characteristics</td>
<td>Method</td>
<td>Direct (researcher-administered)</td>
</tr>
<tr>
<td>-----------------</td>
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<tr>
<td></td>
<td></td>
<td>encouragement in participation in in-person interview (part of data collection process)</td>
</tr>
</tbody>
</table>
| Resource burden | Time: high  
Cost: low  
- researcher time  
- person from patient’s *circle of care* must be involved in process by introducing study to patient and obtain consent | Time: low/medium  
Cost: medium  
- distribution of surveys remains solely in control of clinic staff (oncologist and nurse)  
- less direct researcher time required  
- cost of postage stamps required for mail-in surveys |
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Ref Type: Online Source (www.colorectal-cancer.ca)


Ref Type: Abstract


Ref Type: Unpublished Work


Ref Type: Online Source


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Ref Type: Unpublished Work


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Ref Type: Pamphlet


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Ref Type: Personal Communication


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