#### A DECISION ANALYTIC MODEL FOR EARLY STAGE BREAST CANCER PATIENTS: LUMPECTOMY VS MASTECTOMY

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#### ABSTRACT

# A DECISION-ANALYTIC MODEL FOR EARLY STAGE BREAST CANCER PATIENTS: LUMPECTOMY VS MASTECTOMY

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The purpose of this study was to develop a decision model for early-stage breast cancer patients. This model provides an opportunity for comparing two main treatment options, mastectomy and lumpectomy, with respect to quality of life by making use of Decision Theoretic Techniques.

A Markov chain was constructed to project the clinical history of breast carcinoma following surgery. Then, health states used in the model were characterized by transition probabilities and utilities for quality of life. A Multi Attribute Utility Model was developed for outcome evaluation. This study was performed on the sample population of female university students, and utilities were elicited from these healthy volunteers. The results yielded by Multi Attribute Utility Model were validated by using Von Neumann-Morgenstern Standard Gamble technique. Finally, Monte Carlo Simulation was utilized in Treeage-Pro 2006 Suit software program in order to solve model and calculate expected utility value generated by each treatment option. The results showed that lumpectomy is more favorable for people who participated in this study. Sensitivity analysis on transition probabilities to local recurrence and salvaged states was performed and two threshold values

were observed. Additionally, sensitivity analysis on utilities showed that the model was more sensitive to no evidence of disease state; however, was not sensitive to utilities of local recurrence and salvaged states.

Key Words: Decision Analysis, Markov Chain, Breast Cancer, Quality of Life, Multi Attribute Utility Model.

# ERKEN EVRE MEME KANSERİ HASTALARI İÇİN ÇÖZÜMLEMELİ KARAR MODELİ: LUMPEKTOMİYE KARŞI MASTEKTOMİ

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Bu çalışmanın amacı, erken-evre meme kanseri hastaları için çözümlemeli karar modeli geliştirmekti. Bu model, meme kanseri hastalarına uygulanan iki temel tedavi şekli olan Mastektomi ve Lumpektomi operasyonlarını, teorik karar verme tekniklerini kullanarak yaşam kaliteleri açısından karşılaştırmaya olanak sağlar.

Operasyon sonrası meme kanserinin klinik sürecini yansıtmak için Markov zinciri oluşturuldu. Daha sonra, modelde tanımlanan sağlık durumları geçiş olasılıkları ve yaşam kalitesi için fayda değerleri ile nitelendirildi. Sonuç değerlendirmesi için Çok Kriterli Fayda Modeli geliştirildi. Bu çalışma bayan üniversite öğrencilerinden oluşan örnek nüfusa uygulandı ve fayda değerleri sağlıklı gönüllülerden oluşan bu örneklemeden çıkartıldı. Çok Kriterli Fayda Modelinden elde edilen sonuçlar Von Neumann-Morgenstern Standart Kumar tekniği ile doğrulandı. Son olarak, modeli çözmek ve her bir tedavi şekline ait tahmini fayda değerini hesaplamak için Treeage-Pro 2006 Suit bilgisayar yazılımında Monte Carlo Simülasyonu kullanıldı. Simülasyondan elde edilen sonuçlar, bu çalışmada yer alan katılımcıların Lumpektomi seçeneğini daha fazla tercih ettiğini gösterdi. Kanserin lokal tekrarı ve bu tekrardan sonraki iyileşme durumu olasılıkları üzerinde yapılan hassasiyet

çalışmaları sonucunda iki eşik değeri gözlendi. Ayrıca, fayda değerleri üzerinde yapılan hassasiyet çalışmaları, modelin hastalığın geçmiş olma durumundaki fayda değerlerindeki değişimlere karşı daha fazla hassas olduğunu; buna karşın hastalığın tekrar ettiği ve daha sonraki iyileşme durumlarındaki fayda değerlerindeki değişimlere karşı hassas olmadığını ortaya koymuştur.

Anahtar Kelimeler: Karar Analizi, Markov Zinciri, Meme Kanseri, Yaşam Kalitesi, Çok Kriterli Fayda Modeli. To My Family

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## LIST OF ABBREVIATIONS

OALY : Quality Adjusted Life Year HUI : Health Utilities Index QWB : Quality of Well Being MAUM : Multi Attribute Utility Model : Standard Gamble SG TTO : Time Trade Off RS : Rating Scale VAS : Visual Analogue Scale MUIS : Mishel Uncertainty in Illness Scale : Profile of Mood States POMS FACT-B : Functional Assessment of Cancer Therapy for Patients with Breast Cancer HUOH : Hacettepe University Oncology Hospital DM : Decision Maker NED : No Evidence of Disease NEDI : No Evidence of Disease but Having Hormone Therapy NEDII : No Evidence of Disease but Having Chemotherapy L-NED : No Evidence of Disease for Lumpectomy M-NED : No Evidence of Disease for Mastectomy L-NEDI : No Evidence of Disease but Having Hormone Therapy for Lumpectomy M-NEDI : No Evidence of Disease but Having Hormone Therapy for Mastectomy L-NEDII : No Evidence of Disease but Having Chemotherapy for Lumpectomy M-NEDII : No Evidence of Disease but Having Chemotherapy for Mastectomy MTMM : Multi Trait Multi Method

# **CHAPTER 1**

# **INTRODUCTION**

# **1.1 Objective of the Study**

Objective of this study is to analyze the decision context of early stage breast cancer patients in relation to two main treatment options, and to construct a decision making model that incorporates patient preferences over differing health state prospects as well as incorporating other typical complexities of such decision situations such as uncertainty.

The analysis focuses on early stage breast cancer patients, which means that patients are operable. Patients' age interval under consideration is 45-55, so that they are assumed to be pre-menopausal.

This study has two basic outcomes; first it demonstrates how Decision Theoretic Techniques can be utilized for critical health decisions, and second, the best treatment option can be determined by using the constructed instrument with respect to patients' individual values and preferences.

### **1.2 Problem Definition**

Today breast cancer is the most common type of cancer in women worldwide and its occurrence is steadily increasing. Every year more than 250,000 new cases of breast cancer are diagnosed in Europe, and approximately 175,000 in the United States, with a death rate of over 165,000 patients in Europe and 44,000 in the United States. Worldwide, more than 700,000 women die annually of breast cancer, and it is estimated that eight to nine percent of women will suffer from breast cancer in their lifetime (http://www.nationalbreastcancer.org, 2006). On the other hand, according to the statistics of Ministry of Health, in Turkey, approximately 30,000 women are diagnosed with breast cancer every year, and it is the most common cancer in women (http://www.saglik.gov.tr, 2006).

With technological advances, different types of treatment options have been adopted to extend survival of patients with breast cancer. Choosing the most appropriate cancer treatment is a decision that ideally should involve the patient, the family, and the health care team. Choice of treatment for early stage breast cancer depends on many factors, including size and stage of cancer, patient's age, and other health problems of patient, risks and advantages of treatments.

In the literature, when previously mentioned factors are taken into account, two basic treatment options are mentioned: lumpectomy and mastectomy. Briefly, mastectomy is the surgical removal of an entire breast, which contains cancer; on the other hand, lumpectomy, which is also called breast-conserving surgery, is the surgical removal of the tumor only (http://www.cancer.org, 2006). According to literature and experts' opinions both treatment options have benefits and drawbacks (Desch, et.al, 1999; Kiebert, 1991; Curran, et.al; 1998).

In general, surgeons recommend a treatment according to their experiences and the first thing taken into account is generally the survival of patient not the quality of life after surgery. However, their experiences may not always reflect the "best"

decision, and preferences of health professionals may conflict with patient preferences. Especially, when the chance of survival is nearly the same for both surgical treatment options, women's choice among these treatment options often focuses on quality of life issues. Thus, considerable amount of research has focused on the quality of life in breast cancer patients after surgery in order to make a better informed decision on treatment options.

Decision Making Techniques are useful for critical decisions in health care and have been used for over thirty years around the world. In fact, the idea of using decision theory in medical practice was first proposed by Ledley and Lusted (1959). However, decision analysis techniques have been used in clinical situations effectively only after the beginning of 1970's. In Turkey, health sector is unexplored territory with regard to such studies. The fundamental purpose of decision analysis is to provide useful strategies appropriate for dealing with complex clinical situations and opportunity for consideration of all possible outcomes.

In this study, we considered the patients for whom both treatment options can be applicable, and hence the patient preferences can legitimately make a difference if they could be modeled into the decision making process. For this purpose, we tried to create a quantitative representation of this decision situation involving both treatment choices. This quantitative representation of the breast cancer problem allowed for incorporating of choices, uncertainty and outcome measures. Expected value of outcomes that result from the two possible treatment options can be calculated and compared in order to decide on the best option for one patient. Similar studies from literature such as Lee (2002), who constructed a Markov model that describes clinical outcomes of breast carcinoma following mastectomy and performed cost-effectiveness evaluation of post mastectomy radiation therapy in high-risk premenopausal breast cancer patients, and Carter (1998), who and determined optimal treatment choice by examining quality adjusted life years (QALYs) among various treatment options, were used as reference.

Steps of the study can be followed in Figure 1.1. The first step in such a study is the modeling of disease progress for each treatment option. A decision model can be developed for the disease progress by using suitable decision-making techniques such as decision trees, influence diagrams or Markov models. The objective of this step is to identify possible outcomes associated with each treatment options so that by evaluating these outcomes the optimal decision about choices of treatment for breast cancer patient can be made. In this study, the central choice-making is between lumpectomy and mastectomy operation, the Markov process incorporates all events/decisions following a surgery and the decision analysis compares the values of two Markov processes. Sonnenberg (1993) developed a practical guide for using Markov Models in Medical Decision Making. By following this guide, all events were represented as transitions from one health condition (state) to another. Subjects (patients) were assumed to make transitions at discrete time intervals, at the end of each year, among the states relevant to the clinical problem. Since the breast cancer problem does not involve constant transition probabilities among the Markov states, the breast cancer problem was modeled as non-time homogeneous Markov chain. A Markov chain is constructed, and then it can be characterized for both treatment options with respect to transition probabilities and rewards. After measuring outcomes, outcome values can be assigned as reward for each markov state used in the model and the evaluation of the Markov chain on outcome values yields the expected reward. Then, two treatment options can be compared with respect to their expected rewards.

The focal step of this study is the evaluation of health outcomes. After identifying possible outcomes by suitable decision modeling technique, the next and the most important step is the modeling of outcome measure. A health outcome can be measured as a quantity or quality. Quantity represents life expectancy (life saved), on the other hand quality represents quality of life (utility of patient). In fact both

measures are important criteria, so combining quality (morbidity) and quantity (mortality) measures in a single metric is the best way for measuring health outcome. Quality Adjusted Life Years (QALYs) is such a metric. It reflects the expected utility of an intervention for an individual and allows us to formulate the patient's preferences in relation to probable outcomes under uncertainty. QALY is useful to measure the effects of different medical interventions in a comprehensive way since it combines quality and quantity (Drummond et al. 1987). Since QALY reflects the expected utility, Von Neumann-Morgenstern Utility Theory is considered to present the most suitable of measures for this health related quality of life. Hence, researchers in this field utilize utility assessment techniques to obtain patients' utilities in relation to health states probable along the path of their disease progress.

There are two main approaches in order to calculate QALY value of an outcome. The first approach is to develop outcome measure from people by direct assessment (primary data), which is what we performed in this study, and the second one is using ready-made generic measures (secondary data).

In the first approach, there are two basic strategies for deriving utility value for this outcome; holistic and decomposed. The holistic approach based on global rating and requires the decision maker, patient, physician or healthy volunteer, to consider the defined outcome and rate the outcome that reflects an overall assessment by using some specific techniques such as standard gamble, time trade off etc (Drummond et al., 1987). However determining utility value of an outcome by global rating may not be reliable. Thus, as first Fischer (1977) proposed that, applied decision analysts have shown considerable interest in decomposed evaluation procedures for theoretical as well as practical reasons. The decomposed approach is based multi-attribute utility assessment procedures and requires the decision maker to perform this evaluation task in more articulated way by using decision making techniques. In this procedure, the set of attributes are

specified and an outcome is defined in terms of these attributes. Then, the decision maker should assign relative values to each possible level of attributes. After eliciting individual values for each attribute, we need to aggregate these ratings in order to get overall utility value; thus, a composition rule for aggregating value across attributes should be specified to obtain an overall measure of worth.

As mentioned previously, the second approach to calculate QALY value of an outcome is using ready-made generic measures such as Health Utilities Index (Torrance, 1982), Quality of Well Being (Kaplan, 1988) or EQ-5D (Euroqol Group, 1990). These pre-scored multi attribute health status classification systems are developed by standardizing reference population assessments. In fact, these generic measures are results of multitude of studies on modeling outcome measure that had been previously conducted using versions of the first approach (from primary data). These ready-made measures are attractive due to practicality, and are being widely used for patient's preferences in the countries where they are available to use. However, depending on the population the utilities are assessed from, scoring systems of these measures are function of their own societal values. For instance, EQ-5D scoring system represents English society and using Turkish translation of this measure directly may not provide meaningful data due to cultural differences. On the other hand, let alone developing such scoring system, which represents Turkish society, even an outcome measure has not been developed yet.

In a study that deals with clinical decision making incorporating Turkish patient's preferences, therefore, we have only one choice, and that is implementing the first approach. For this purpose, after identifying all possible outcomes on the decision model developed as a Markov chain, a multi attribute utility model was constructed as described for measuring these outcomes. Suitable attributes were specified in order to define health states. Then we constructed scales for each attribute and assessed the location of all possible health states defined in the decision model along the scales of attributes. After assessing locations, individual values of the

patient can be obtained by direct assessment techniques. Then, overall utility values of the health states for both treatment options can be calculated for any patient.

This study was not performed on patients since they may be physically overtired or oversensitive and such interviews may affect them negatively if they are not applied by an analyst who is an expert on this area. We performed this study on a sample population of female university students, and aimed to obtain an indication of preferences of population at this specific age interval. For this purpose, individual utility values were elicited from university students and overall utility values were calculated for each possible health state. The consistency of these overall values was checked by the values yielded from global ratings.

In order to get transition probabilities among the health states in the Markov chain, subjective probability assignment method was used in this study. Probability estimates were based on a group of oncologists' consensus. Since transition probabilities among the health states are not constant over time, probabilities were estimated for each cycle (year) by considering 10-year survival for disease progression.

Final step is evaluation of the model according to data obtained from patient, obtaining QALY values that result from the two possible treatment options and deciding on optimal treatment option. Since the transition probabilities among the health states are time-dependent, it is impossible to evaluate the process with exact computation. Thus, a simulation method (Monte Carlo Simulation) was utilized in order to calculate the expected value (QALY) generated by each treatment option. The evaluation results showed that lumpectomy was more favorable for this sample population. Since we performed this study on a sample consisting of university students to generate QALY values, the results reflect their preferences.

This decision aid can be used either for taking the preferences of a single cancer patient into account in deciding on treatment, or for reflecting a reference population's preference structure on the issue. Its best use, however, may be in training physicians' judgment on the complexities of the decision space at hand so as to improve their chances of making a wise treatment decision.



Figure 1.1. Steps of the Study

### **1.3 Outline of the Study**

The outline of the thesis is as follows: After an introduction part in Chapter 1, we present a brief review of literature on decision making in health care, utility assessment techniques used in health care, and decision making and utility assessment applications on early breast cancer treatments in Chapter 2.

The model construction for the decision problem in Chapter 3 is the main part of the study. In the first section of this chapter, the rationale for and the construction of a Markov Tree for representing the decision process is presented. Then, we present the development of outcome evaluation process by means of a Multi Attribute Utility model. The chapter ends with presentation of probability assignment on the tree.

In Chapter 4, results of the simulation experiment are analyzed. Important findings from evaluation of the decision process are presented and computational results are discussed. In addition, sensitivity analysis results, performed in order to observe changes on the decision, are presented in this chapter.

Chapter 5 is devoted to the conclusions, summary of findings, and a discussion of limitations of the study. We also try to give directions for related future research studies.

### **CHAPTER 2**

#### LITERATURE REVIEW

### 2.1 Treatment Decisions in Health Care

In recent years, rising costs, advanced technologies, and increasing patient involvement in treatment decisions have contributed to the challenges faced by physicians in medical decision making. The physician has to recommend a treatment and the patient has to decide whether to go along with the treatment the physician recommends. Thus, decision analysis techniques have become standard techniques in analyzing uncertainties associated with complex medical problems.

The idea of using decision theory in medical practice was first proposed by Ledley and Lusted (1959). However, decision analysis techniques have been used in clinical situations effectively only after the beginning of 1970's. Fryback, studied subjective probability estimates (1974), decision theory (1978), and cost-benefit analysis (1977) in radiology. He pointed out that decision analysis techniques provide useful strategies for making complicated clinical decisions more manageable and rational, and improve clinician's judgments. Also Ransohoff (1976) discussed whether learning decision analysis technique is worthwhile for physicians in order to use in clinical medicine or not, and concluded that despite some problems, component parts of decision analysis is clinically helpful. Yoshimura et al. (1998) performed decision analysis to compare between two strategies for treatment of early stage prostate cancer.

Birkmeyer (1996) reviewed the medical literature (1966 to 1994) to identify surgical decision analysis studies and to assess trends over time. Results of his study showed that publication rates of surgical decision analysis have increased dramatically over time. Of the 86 total studies, only six were published before 1980. In contrast, 44 studies appeared between 1990 and 1994.

Decision analysis provides a methodology for comparing a set of clinical choices by calculating the expected value of outcomes. Mathematical representation of the decision problem is termed as decision model and there are many decision modeling techniques. Among those techniques especially, decision trees, Markov processes, influence diagrams are found very useful in evaluating clinical problems. In many studies, cost effectiveness analysis and sensitivity analysis are performed using these techniques.

The principles of using decision trees in clinical decision making were constructed and some diseases were examined as an application by Kassirer (1973, 1976) and Pauker (1976). When time horizon of problem is taken into consideration, decision trees may be inadequate for representing the problem, and may not be realistic. Thus, Markov Models are used in medical decision making when a decision problem involves risk that is continuous over time, when important events may happen more than once, and when the timing of events is important. Sonnenberg (1993) developed a practical guide for using Markov Models in Medical Decision Making.

Kassirer (1976) presented the principles of Clinical Decision Making. He pointed out that two basic elements for decision analysis are probabilities of various outcomes and utility values of final outcomes. Probabilities are obtained from literature, previous clinical studies, statistical data, or subjective judgments of clinicians. Utilities represent the strength of preference for the outcome and have become the standard measure of value in the analysis of health decisions. Von Neumann and Morgenstern (1944) first presented the fundamental axioms of utility theory under uncertainty, now called Expected Utility Theory. The axioms of Von Neumann and Morgenstern provide the foundation of modern decision theory, which has been widely applied in many fields for several decades. As mentioned, utility assignment is one of the basic elements of decision analysis, so various methods for measuring patient's utilities have been developed. In the next section, a detailed literature review on utility assessment in clinical studies is presented.

# 2.2 Utility Assessment in Clinical Studies

A patient's utility value or function can be elicited directly or indirectly. There are three basic approaches for direct evaluation: standard gamble technique (SG), time trade off technique (TTO) and rating scale (RS). SG technique is based on von Neumann and Morgenstern (1944) Utility Theory and it is the classical method for measuring preferences. Torrance (1972) developed the TTO method for use in health care in response to the burdensome nature of the SG. The third one is the scaling method that is the simplest one (Drummond et al., 1987). Torrance (1976) evaluated these three main techniques for different health states with respect to feasibility, validity, reliability, and comparability by using the general public as the subject population. He concluded that the TTO method was superior, since it was simpler and less costly than SG method for use on the general public. However, SG was found to be feasible for utilizing on educated people. Bass (1994) made a comparison of RS and SG in measuring patient preferences for outcomes of gallstone disease. Even though both scaling techniques yielded reliable results, the two methods did not produce equivalent scale values. However, SG values were highly correlated with, but significantly greater than, RS values. Also Bleichrodt (1997) compared the relative performance of quality weights elicited by RS, TTO and SG techniques for eight different health states about rheumatism. The results of the experiment reported in this paper showed that, the correlation between predicted and direct ranking was significantly higher for TTO values.

However, many researchers pointed out that using any of the above direct techniques for measuring preferences for health outcomes was very time consuming and complex. Thus, pre-scored multi-attribute health status classification systems were developed. Quality of Well Being (QWB) developed by Kaplan (1988), EQ-5D developed by EuroQol group (1990), and Health Utilities Index (HUI) developed by Torrance (1982) (and then extended as HUI2 and HUI3 in 1996), are three main classification systems. All these systems, also called "generic measures", are based on Multi Attribute Utility Theory. In Appendix A, original and Turkish version of EQ-5D can be examined.

These generic measures classify patients according to different attributes with multiple levels per attribute and social preference functions are used in order to evaluate each attribute. The general approach in determining social preference function is to define a set of health states of interest, to identify a group of subjects, to measure each subject's preferences by using preferences measurement techniques such as TTO, SG or RS for the health states, and to aggregate these measures across the subjects to determine overall social preferences function (Torrance et al. 1982). Then, researchers performing a decision analysis can use these ready-made utilities in his/her study.

Primary question in obtaining utilities is 'whose utilities should be used for Decision Analysis: patient, patient family, physician, hospital administration or general public?' Torrance (1978) suggested that general public could be used for utility measurement. Hadorn (1991) mentioned the role of public values in setting health care priorities. Also, Boyd (1990), Dolan (1999) and Cappelli (2001) compared the utility results obtained from different populations for various diseases. All these studies indicated that although health states were valued lower by general population than they would be valued by patients, the source of preference weights do not affect the base case results of comparison.

In addition, Cost Effectiveness Analysis is a widely used technique for economic evaluation of the clinical alternatives. It helps examine both value consumed (costs) and value produced (health outcome), and by this analysis, cost per unit health can be calculated. Namely, an incremental cost of a treatment is compared to incremental health effects. Unit of health outcome can be varied with respect to the objective such as blood pressure reduction, number of cases found, life years, lives saved, quality-adjusted life years (QALY) etc.

Räsänen et al. (2006) published a literature review to identify studies that used QALYs. A total of 3882 articles (from 1966 to 2004) were identified. Also it is pointed out that most of the identified studies also discussed cost per QALY (cost effectiveness). One of the most complex problems in QALY calculation is the assessment of quality of life. There are different methodological approaches for measurement of quality of life. The basic approach is obtaining quality of life values as scores by using the utility method, mentioned previously.

# 2.3 Decision Making and Utility Assessment Applications on Early Breast Cancer Treatments

Carcinoma of the breast is the most common cancer worldwide in women. The incidence has been steadily rising over the past few decades, and following lung cancer; breast cancer is today the most common cause of cancer death among women in most western countries. (http://www.nationalbreastcancer.org, 2006)

As advances have been made in medical technologies, several main treatment options have been developed to extend survival of breast cancer patients. Nissen (2001) pointed out that women with early stage breast carcinoma generally have the choice of three effective surgical options: lumpectomy (known as breast-

conserving surgery), mastectomy, and mastectomy plus reconstruction. Since all these options extend survival, the quality of life and costs of following the treatment has become topic of focus while deciding on the treatment. Considerable research has investigated quality of life in early stage breast cancer patients and studied cost effectiveness of these options.

Kiebert (1991) published a review on the impact of breast conserving treatment versus mastectomy on quality of life. He pointed out that the first study on the effect of different forms of surgical procedures in early breast cancer on quality of life was performed by Eisenberg and Goldenberg in 1966. After that, no significant report was published for 15 years. Then in 1980's researchers began to perform more studies, first in United States (Reznikoff, 1981; Steinberg, 1985; Taylor, 1985; Ganz, 1987; Wolberg, 1989; etc), and then in Denmark (Beckmann, 1983), the United Kingdom (Ashcroft, 1985; Fallowfield, 1986), and other countries. Also Ganz continued his studies and published several papers on quality of life of breast cancer patients.

Curran (1998) compared quality of life scores of early-stage breast cancer patients treated with radical mastectomy or breast conserving procedures, which were obtained via a questionnaire. Carter (1998) developed a Markov process model specific to early-stage breast cancer patients and determined optimal treatment choice by examining QALYs among various treatment options. Nissen (2001) applied MUIS (Mishel Uncertainty in Illness Scale), POMS (Profile of Mood States) and FACT-B (Functional Assessment of Cancer Therapy for Patients with Breast Cancer) measures to assess quality of life of early stage breast cancer patients who underwent breast conserving surgery, mastectomy alone or mastectomy plus reconstruction treatments. Cappelli (2001) performed a comprehensive study in which women's preferences for breast cancer treatments (lumpectomy plus radiation, double mastectomy plus chemotherapy or no treatment) were characterized by using standard gamble and rating scale techniques, and also, factors associated with quality of life were identified. Polsky

(2002) studied the impact of breast cancer treatment choice on patients' health state preferences. In this study, patient preferences for current health state, assessed with patient valuations using the visual analogue scale (VAS) from the EuroQol instrument and with general public valuations using the Health Utilities Index (HUI).

Cost effectiveness studies have become popular in health decisions in 1990's. In general, cost effectiveness studies were performed for comparison of lumpectomy and mastectomy and their derivatives, to decide whether any adjuvant therapy, which is the treatment given after the primary treatment to increase the chances of a cure, should be used or to compare of adjuvant therapies. Verhoef (1991) performed cost utility analysis (cost / QALY) for women receiving breast conserving surgery or mastectomy. Norum (1997) performed cost utility analysis for comparison of lumpectomy and mastectomy. In this study, costs (direct and indirect) were obtained from published literature and utilities were obtained with the use of EuroQol instrument. Hayman (1998) searched cost effectiveness of radiation therapy following conservative surgery and in his study; utilities were obtained by standard gamble technique. Hillner (1996) studied economic and cost effectiveness issues in breast cancer treatment. Additionally, Hillner and Smith performed series of studies in 1991-1993 on cost effectiveness of adjuvant therapies.

Cost effectiveness studies in breast cancer have increasingly continued in 2000's. Malin (2002), used cost effectiveness analysis to calculate the additional costs and benefits of various adjuvant therapy strategies, radiation after breast conserving surgery and reconstruction compared to those of surgery alone in order to define the most cost-effective breast cancer package for uninsured women. Lee (2002) constructed a Markov model that describes clinical outcomes of breast carcinoma following mastectomy and performed cost-effectiveness evaluation of post mastectomy radiation therapy in high-risk premenopausal breast cancer patients. Also Polsky (2003) studied incremental cost effectiveness analysis of breast

conservation and radiation versus mastectomy by using 5 years primary data. Naeim (2005) evaluated adjuvant treatment for early stage breast cancer with hormone therapy, chemotherapy or combination therapy to find out cost effectiveness in older patients. He concluded that decision-analytic models could help policy makers who are faced with decisions about adjuvant therapy in older breast cancer patients. Additionally, Hershman (2002) conducted a cost effectiveness analysis of tamoxifen for primary prevention in women at high risk for breast cancer. Markov modeling was used to estimate effects of tamoxifen on quality-adjusted survival, and preference ratings were elicited with time trade-off questionnaires.

Evidently, there is an increasing interest in quality of life research on breast cancer. Radice (2003) performed a study to provide a literature-based extensive overview of the quality-of-life and cost issues posed by the management of breast cancer. Mandelblatt (2004) published a descriptive review of the literature on breast cancer outcomes: 1990 through 2000. He summarized all measures and the instruments used in the studies of breast cancer outcomes. He studied 382 articles and summarized the characteristics of the studies, such as phase of care (screening, diagnosis, treatment, adjuvant therapy, survivor, etc.), study design, population, sample size, outcomes measures, and mode of assessment. This paper concluded that the most frequently reported outcomes were health-related quality of life (%54 of articles) followed by economic analysis (%38 of articles). It also points out that there was a wide variety of instruments used in the study sample for measuring preferences; however, given the complexity of breast cancer care and the heterogeneity in patient population, no single instrument is sufficiently comprehensive. Additionally, Mandelblatt (2003) reviewed research published between 1995 and June 2003 on breast cancer quality of life and outcomes among women aged 65 and older treated for breast cancer. He concluded that, few randomized trials or cohort studies that measured quality of life after treatment focused exclusively on older women; however, the processes of care, such as choosing therapy, good patient-physician communication, receiving treatment

concordant with preferences about body image, and low perceptions of bias, were associated with better quality of life and satisfaction.
## **CHAPTER 3**

# MODELING A BREAST CANCER PATIENT'S DECISION PROBLEM

As mentioned previously, in this study, the patients for whom both of two treatment options can be applicable were taken into consideration, and it was aimed to develop a model representing the decision situation of such a patient so as to help compare the two treatment options in terms of both the quantity and the quality of life promised by them. By using this decision aid, QALY value (quantity and quality aggregated) that result from the two possible treatment options can be calculated, and the decision can be made on the best option for her. Two important steps during this development task were the disease process modeling and the outcome measure modeling.

# **3.1** Decision Modeling of the Breast Cancer Progress

The fundamental purpose of decision modeling in clinical situations is to create a quantitative representation of a set of clinical choices. This quantitative representation allows for incorporating of choices (individual preferences), uncertainty (probabilities) and outcome measures. This section presents decision modeling of the process of disease progress for early breast cancer.

A decision model can be developed for the disease progress by using suitable decision-making techniques such as decision trees, influence diagrams or Markov models in order to identify possible outcomes. In this study, we tried to compare lumpectomy and mastectomy operation; thus, at first, a decision tree was constructed as a decision model for the breast cancer disease progress following surgery as in Figure 3.1.



Figure 3.1. Decision Tree Structure of Natural History of Breast Carcinoma

However, this tree did not meet our requirements. Since the paths that the patient follows are under consideration, there are too many health states to study. Also, most of the events recur over time, so there are too many repetitions and cycling occurs. Additionally, probabilities of events are time dependent but decision tree cannot reflect this property. Therefore, fidelity of modeling breast cancer problem as a decision tree is low for our study.

The central choice-making is between lumpectomy and mastectomy operation, for which a Markov tree is shown in Figure 3.2. As seen in the figure, the Markov process incorporates all events/decisions following a surgery and the decision tree analysis was reduced simply for comparing the values of two Markov processes.



Figure 3.2. A Process Model for the Breast Cancer Treatment Problem

The decision problem on breast cancer treatment following surgery, lumpectomy or mastectomy, was modeled as a Markov Tree (Sonneberg, 1993) because of its basic properties. First of all, clinical history of breast cancer is a stochastic process with the property that its future evolution can be reasonably assumed to be conditionally independent of its past provided that the present is known. Also,

decision problem of breast cancer treatment involves risk that is ongoing and varying over time, and finally, important events may happen more than once and hence cycling may occur.

The unqualified term "surgery" was used, because the history was the same for both treatment options. That means health states used in the model were the same. The differences were the parameter values such as transition probabilities, outcome values, etc. Thus, one Markov chain was constructed at first, and then it was characterized for both treatment options with respect to transition probabilities and rewards.

 $Y_t$  was referred to the health condition of the patient with breast cancer following surgery at time t, then

The stochastic process  $Y = \{Y_t, t \in N\}$  with a countable and finite state space S, is a Markov Chain provided that

$$P\{Y_{t+1} = j/Y_0, Y_1, ..., Y_t\} = P\{Y_{t+1} = j/Y_t = i\} \quad \forall i, j \in S \quad t \in N$$

In this process, all events were represented as transitions from one health condition (state) to another. Subjects (patients) were assumed to make transitions at discrete time intervals among the states relevant to the clinical problem. In reality, patients can make transition from one health condition to another at any time, which requires continuity; however, we restrict ourselves to a Markov chain for simplifying problem. Literature review shows that this in fact is a simplification commonly done in similar studies (Lee, 2002). Thus, for computational simplicity the problem was modeled as a Markov chain by assuming that patients make transitions at discrete time interval, at the end of each year.

The next step was defining the state space, S, for this problem. In this study, the term "health state" is used as a markov state to describe the health status of an

individual at a particular point in time. Health states used in the model are conditions of being well (NED), having hormone therapy (NEDI) or chemotherapy (NEDII), having recurrent local disease (Local Recurrence), being salvaged after recurrence of disease (Salvaged), having distant disease (Metastasis) or death. Determination of these health states was challenging since describing clinical history of problem required serious support from medical experts. At first, detailed literature search was performed as a pre-study. Then, medical expert support was obtained from oncologists of Hacettepe University Oncology Hospital (HUOH). A series of meetings were held with oncologists through which a path of patient disease progress was represented. Then, the most basic health states that lie on the path of patient's disease progress were selected, relatively less significant ones were omitted in order to keep complexities manageable. Thus, if S denotes the countable state space, then

S = {NED, NEDI, NEDII, Local Recurrence, Salvaged, Metastasis, Death}

#### where

NED: No Evidence of Disease NEDI: No Evidence of Disease but Having Hormone Therapy NEDII: No Evidence of Disease but Having Chemotherapy

The next step in this analysis was to construct a state transition model to describe clinical history of breast carcinoma following a mastectomy or lumpectomy. At first, a natural evolvement pattern of breast cancer following surgery was developed. The principal analysis of the model focused on early stage breast cancer patients, between 45-55 years old (pre-menopausal), and therefore, operable. We analyze the process starting at the point immediately after patients have undergone curative surgery. At 1-year intervals, subjects may undergo transitions among the health states as mentioned previously. During each period, patients may remain in their current state or make transition to another health state. Obviously, death is an

absorbing state. All other states except death were transient states. The resultant state transition model is depicted in Figure 3.3.



Figure 3.3. State Transition Model of the Natural History of Breast Cancer Following Surgery

This model represents the state transition diagram for the stochastic process where,

 $Y = \{Y_t, t \in N\} \text{ with a countable state space S.}$  $Y_t = \text{Health state of the patient at time t,}$  $t \in N = \{0, 1, 2, 3...\}$ 

S = {NED, NEDI, NEDII, Metastasis, Local Recurrence, Death, Salvaged}

The stochastic process  $Y = \{Y_t, t \in N\}$  is a Markov Chain provided that

$$P\{Y_{t+1} = j/Y_0, Y_1, ..., Y_t\} = P\{Y_{t+1} = j/Y_t = i\}$$
  $\forall i, j \in S$   $t \in N$ 

For computational simplicity, in general, it is assumed that the conditional probability expressed above is independent of time, t, such that;

$$P\{Y_{t+1} = j/Y_t = i\} = P_{ij} \qquad \forall i, j \in S \qquad t \in N$$

P<sub>ij</sub>: Transition probabilities for the Markov chain X.

A Markov chain Y satisfying the condition of time independence is said to be timehomogeneous Markov chain. However, as in most medical processes, breast cancer problem does not involve constant probabilities, which means that the transition probabilities among the Markov states are not constant over time, and is not a time homogeneous process. Thus, in this study, the breast cancer problem was modeled as non-time homogeneous Markov chain and the conditional probability for this problem can be expressed as,

$$P\{Y_{t+1} = j/Y_t = i\} = P_t\{i,j\} \qquad \forall i, j \in S \qquad t \in \mathbb{N}$$

 $P_t{i,j}$ : Transition probabilities for the Markov chain Y at time t.

The assessment of transition probabilities among the health states was presented in detail at the end of this chapter.

As mentioned previously, in this study it was aimed to measure and compare outcomes related with each treatment options. After measuring outcomes, outcome values can be assigned as a reward for each markov state used in the model and the evaluation of a Markov chain on outcome values yield the expected reward. Suppose that at each time increment t, it is given a reward whose amount depends on that state Y. If Y = j, then the reward is denoted by  $R_t(j)$  depends on utility function of that state. Then, two treatment options can be compared with respect to their expected rewards. For this purpose, outcome measures assessed in Section 3.2 was assigned as state rewards.

#### **3.1.1** Description of Health States and Analysis of Transition Model

As seen in Figure 3.3, seven basic health states were defined along the path of disease progress of breast cancer patient. The state of "Death" was absorbing state and the all other states were transient states. Descriptions of these health states are as follows:

<u>NED (No Evidence of Disease) State:</u> All patients start in a "NED" state that represents no evidence of disease after mastectomy or lumpectomy, which means that they are free of cancer but remain at risk for reoccurrence. Target health states from the NED state include Metastasis, NEDI, NEDII, Local Recurrence and DEATH.

<u>NEDI</u> (No Evidence of Disease but Having Hormone Therapy) State: If the reoccurrence risk is low after surgery, patients can have hormone therapy as an adjuvant therapy in order to decrease reoccurrence risk although there is no evidence of disease. Hormone therapy is a cancer treatment that removes hormones or blocks their action and stops cancer cells from growing. After the surgery, patients are tested for hormone receptors. If the test is positive (ER+) which means that they have enough receptor to perceive estrogens and progesterone hormones, patients can undergo hormone therapy. In the following time interval, patients may remain in that state, may go into NED state after therapy is finished, may go to Local Recurrence or Metastasis state because of reoccurrence or may die.

<u>NEDII (No Evidence of Disease but Having Chemotherapy) State:</u> If the reoccurrence risk is relatively high after surgery, patients should have chemotherapy as an adjuvant therapy. Chemotherapy is a treatment program of cancer-fighting drugs. There are number of possible side effects of treatment: one can lose her hair but it is temporary, she can have stomach upset or vomiting, she can feel tired and unhappy which can interfere with her social life, her psychology. Following health states from the NEDII state may be Local Recurrence or Metastasis state if disease relapses, NEDI state if hormone receptor test is positive, NED state if hormone receptor test is negative and still no evidence of disease, or Death state.

<u>Metastasis State:</u> If the disease relapses in sites further away in the body such as bones, lung or liver, and there is no probability of being well, then patients go to Metastasis state, which means reoccurrence of disease distantly. The model assumes that, after the disease recurs distantly, no patient can be successfully treated and return to NED state. Patients may remain in Metastasis state or die from cancer.

Local Recurrence State: This state is presence of disease, which may be salvaged after curative treatments. In the following time interval, if there is no evidence of disease after curative treatment, patients go to Salvaged state, patients may remain in that state, may go to Metastasis state if disease gets worse, or death state.

<u>Salvaged State:</u> It means that there is no evidence of disease after curative and adjuvant treatments; thus, there is no need to carry out further therapy. However, they should be observed since there is a risk of reoccurrence. After this state, patients make transitions to Metastasis state or Death state.

<u>Death State:</u> Patients who die (absorbing state), make no further transition. During each period, patients may make transition to Death state. Patients may die from breast cancer or from other causes; however, in this study it was considered as

patients make transition to death state when they die from breast cancer, transition probability of death from other causes were not taken into consideration.

## **3.2** Modeling of the Outcome Evaluation Measure

As mentioned before, we are dealing with comparing two treatment methods of breast cancer disease on the basis of quantity and quality of life for the patient.

Evaluation of the Markov chain representing the disease progress yields the average number cycles spent in each (health) state. However, each state can be associated with a quality factor representing the quality of life in that state relative to perfect health. In this study, this quality of life is measured with patient's utility for each health state. The utility that was associated with spending one cycle in a particular state was referred to as incremental reward. Therefore, by assigning utility for each state, evaluation of Markov chain yields expected utility (QALY), total number of cycles spent in each state; each multiplied by the expected utility for that state.

Researchers in this field utilize utility (Von Neumann-Morgenstern) assessment techniques to obtain patients' utilities in relation to health states probable along the path of their disease progress. The main step for utility assessment is the determination of utility values of each health state. Within this general approach, a number of methods are available for assigning cardinal values to outcomes. Decision Maker (DM) can directly assign overall values to each outcome or on the other hand, divide the evaluation task into set of simple subtasks. Fischer (1977) proposed that, applied decision analysts have shown considerable interest in decomposed multi-attribute utility assessment procedures for theoretical as well as practical reasons. He claimed that decomposed evaluation procedures are much more systematic than holistic evaluations and so, the procedure permits the explicit consideration of a far larger number of outcome attributes than holistic approach. Since they describe the health states by a multi-attribute classification system, all

health state measurement systems mentioned in Chapter 2 (HUI, EQ-5D, QWB, etc) are based on multi-attribute utility theory. Thus, in this study Multi-Attribute Utility Method (Keeney and Raiffa, 1976) was used.

## 3.2.1 Multi-Attribute Utility Theory

Multi-Attribute Utility Modeling is concerned with expressing the utilities of multiple-attribute outcomes as a function of the utilities of each attribute taken singly. In this procedure, the DM must specify the set of attributes then must assign relative values to each possible state (level) of attribute and finally must specify composition rule for aggregating value across attributes to obtain an overall measure of worth. The composition function can be expressed as:

$$U(X_1, X_2, \dots, X_n) = f\{U_1(X_1), U_2(X_2), \dots, U_n(X_n)\} \qquad U, U_i \in [0, 100] \forall i$$

where,

The multi attribute utility theory specifies several possible forms of aggregate utility functions such as additive, multiplicative and multilinear. As a practical matter Keeney and Raiffa (1993) suggest that for  $n \ge 4$ , the reasonable models to consider are the additive and the multiplicative. Since we had 8 attributes in this study we concentrated on additive and multiplicative functions. Additionally, it was observed from the literature review that such studies have used one of these utility function types.

If mutual utility independence among attributes exits, that means every subset of  $\{X_1, X_2, ..., X_n\}$  is utility independent of its complement, then, the aggregate utility function is:

$$U(X) = \sum_{i=1}^{n} k_{i}U_{i}(X_{i}) + k\sum_{i=1;j>i}^{n} k_{i}k_{j}U_{i}(X_{i})U_{j}(X_{j}) + k^{2}\sum_{i=1;j>;l>j}^{n} k_{i}k_{j}k_{l}U_{i}(X_{i})U_{j}(X_{j})U_{l}(X_{l}) + \dots + k^{n-1}k_{1}k_{2}\dots k_{n}U_{1}(X_{1})U_{2}(X_{2})\dots U_{n}(X_{n})$$

where,

- ki : the scaling constant of the i<sup>th</sup> attribute
- k : additional the scaling constant

On the other hand, if additive independence exits among attributes, which means that the preferences over lotteries on  $X_1, X_2,..., X_n$  depend only on their marginal probability distributions for these attributes, then, the multi-attribute utility function can be expressed as an additive utility function as follows:

$$U(X_1, X_2, \dots, X_n) = k_1 U_1(X_1) + k_2 U_2(X_2) + \dots + k_n U_n(X_n)$$

Additive Independence among the attributes is the necessary and sufficient condition for the additive model. Independence among attributes can be improved by defining the dependence away, or by eliminating less important ones, or properly grouping some together. In this study additive utility function was used in order to aggregate utility values. Discussion on justifying additivity is given in Section 3.2.2.8.

#### 3.2.1.1 Determination of Attributes

Health states are generally defined in terms of several domains or dimensions of health such as pain level, emotional well being, and like that. The very first step in constructing an evaluation model for a health state requires that these domains or dimensions should be defined into a – preferably mutually independent and collectively exhausting – set of attributes.

On one hand; identifying attributes is probably best done by constructing an "objectives hierarchy" due to Keeney and Raiffa (1993). This method asks the analyst to assess the fundamental objectives of the decision maker in the decision context that is being considered. Then, by asking how this objective can be achieved, lower level objectives are identified. This hierarchy of objectives is worked through the lowest possible level where mostly *metrics* that collectively measure the fundamental objective are attained. This method makes perfect sense and it is usually very effective in the hands of a relatively experienced decision analyst.

On the other hand; the discourse of the thirty-odd years old Medical Decision Making community is beyond defining attributes, utility model building and assessment now. The standard practice is to use secondary data sources (generic preference measures, pre-assessed utility scores, established hospital records systems and nationwide data bases, etc.) which were mentioned before. Although the health state attributes used in these sources are not uniform, they share a common basis, which is accepted widely. Hence, there were two alternative ways in this study: To consider this basis as the starting point or to define attributes by constructing an objectives hierarchy while ignoring this common basis. Although defining attributes for health state evaluation from scratch by constructing an objectives hierarchy would have been very interesting and intellectually satisfying exercise, it might have been stretching the scope of this present study too much. Instead, a set of attributes commonly accepted in the related literature was adopted for the purposes of this study as a starting point. Mathematical properties of this set had to be scrutinized, and then the set accordingly had to be modified, as presented in this section.

In order to determine the attributes, at first, a thorough literature search was conducted for this purpose and all criteria related to health state designation of breast cancer patients were determined. Especially multi-attribute health status classification systems were taken as reference. Currently there are various systems available: Quality of Well Being (QWB) developed by Kaplan (1988), Health Utilities Indexes (HUI1, HUI2, HUI3) developed by Torrance (1982), EuroQol (EQ-5D) developed by EuroQol Group (1990), etc. All these systems are the "generic" measures, which means that they were generalized and can be applied to all kind of patients. These systems classify patients' health states according to different attributes. Attributes defined in some considerable generic measures are represented in Table 3.1. All attributes defined in these measures were studied and suitable attributes for designation of breast cancer were chosen. Also other medical studies conducted on QALY studies on breast cancer were studied and criteria taken into consideration in these studies were examined.

	А	ttributes		
QWB	EQ-5D	HUI1	HUI2	HUI3
Mobility	Mobility	Physical Function	Sensation	Vision
Physical Activity	Self-Care	Role Function	Mobility	Hearing
Social Activity	Usual Activities	Social-Emotional	Emotion	Speech
Symptom-Problem	Pain Function		Cognition	Ambulation
Complex	Anxiety	Health Problem	Self-Care	Dexterity
			Pain	Emotion
			Fertility	Cognition
				Pain

Table 3.1. Attributes Defined for Five Multi Attribute Classification Systems

After this pre-study, again medical expert support was obtained from the HUOH oncologist. In the first meeting, the attributes determined by pre-study were consulted, and expert opinion was taken into consideration. Then, the expert was

engaged in a brainstorming session to think of other attributes. During this initial idea generation no judgment was used. The purpose of this meeting was to identify as many attributes as possible to characterize any health state. In the next step of the study, some attributes were omitted since they seemed irrelevant or less important than the others. Also, in these meetings, independence property was taken into account to be able to aggregate the utility function in additive form. In order to get rid of dependencies among attributes and to achieve property of independence among them, some similar and dependent ones were grouped together by considering oncologist's suggestions. Finally, a number of attributes were determined in order to characterize health states. Specified attributes and their definitions are as follows:

#### Physical Function (X1)

The attribute of Physical Function reflects patient's ability for mobility and physical activities such as arm motion, walking, running, jumping etc.

#### Role Function Self Care (X<sub>2</sub>)

The attribute of Role Function reflects patient's role function and daily activities such as capability of eating, dressing, doing housework, bathing, cleaning etc.

#### Social Function (X<sub>3</sub>)

The attribute of Social Function reflects social activities of patient. Number of friends, relations with people, family relations, and hobbies are important criteria for determining this degree.

#### $\underline{Pain}(X_4)$

The attribute of Pain reflects pain level that patient has.

#### Psychological Discomfort (X<sub>5</sub>)

The attribute of Psychological Discomfort reflects patient's emotional status. For example, feeling happiness, sadness or depression, being anxious or angry etc. This

attribute is identified by three sub-attributes, body image, fears and concerns, and sexual function.

#### Body Image $(X_6)$

The attribute of Body Image reflects patient's satisfaction from her appearance. This attribute determines how disfigurement on her body affects patient such as if she feels ashamed or avoids nakedness or feels less attractive etc. This attribute affects Psychological Function, thus expressed as one of the sub attributes of this attribute.

## Fears and Concerns (X<sub>7</sub>)

The attribute of Fears and Concern reflects patient's fears and concerns about reoccurrence of disease or fear of death because of cancer. This attribute affects Psychological Function, thus expressed as one of the sub attributes of this attribute.

#### <u>Sexual Functioning $(X_8)$ </u>

The attribute of Sexual Function reflects the sexual interest and functioning of patient. Frequency, satisfaction, problems during relation, dysfunction etc. are determining factors to degree. This attribute affects Psychological Function, thus expressed as one of the sub-attributes of this attribute.

Finally, 5 main attributes and 3 sub-attributes were determined in order to characterize one health state. Multi-level attribute tree for determination of any health state can be seen in Figure 3.4.



Figure 3.4. Multi Level Attribute Tree for Determination of Any Health State

5-attribute additive utility function is:

$$U(X_1, X_2, ..., X_5) = k_1 U_1(X_1) + k_2 U_2(X_2) + k_3 U_3(X_3) + k_4 U_4(X_4) + k_5 U_5(X_5)$$

Since the attribute of Psychological Function  $(U_5)$  was defined by three subattribute, body image, fears and concerns, and sexual function, its utility value can be expressed as another additive multi attribute utility function:

$$U_{5}(X_{6}, X_{7}, X_{8}) = k_{6}U_{6}(X_{6}) + k_{7}U_{7}(X_{7}) + k_{8}U_{8}(X_{8})$$

Finally, the 8-attribute utility function for aggregate utility value can be written as:

$$U(X_1, X_2, ..., X_8) = k_1 U_1(X_1) + k_2 U_2(X_2) + k_3 U_3(X_3) + k_4 U_4(X_4) + k_5 (k_6 U_6(X_6) + k_7 U_7(X_7) + k_8 U_8(X_8))$$

Each attribute in the health state classification system is subdivided into a number of levels such that each health state can be defined by one level on each attribute. Thus, levels of attributes were made definite by the help of experts and literature search. The details of attributes' levels are in Appendix B. In summary, classification of any health state was based on the 8-dimensional system. From now on, any health state can be defined as a function of these 8 attributes. After identifying attributes, the next step is assessment of individual utility functions  $(U_i(X_i))$  for each attribute and scaling constants.

## 3.2.1.2 Assessment of Individual Utility Scales

An important part of the multi attribute model construction is the assessment of the single dimensional utility functions for each attribute. This was performed by a public survey (Appendix C). In this survey, clear and comprehensible definitions of each attribute and levels of these attributes were given. For each attribute a natural scale ("phrase-anchored" scale) was constructed and levels were pointed out on that scale as in Figure 3.5.



Figure 3.5. A Natural Scale for Sexual Function Attribute

As seen in Figure 3.5, the rating for the maximum level  $(U_7(X_7^{-1}))$  was predefined as 100 point for each attribute. The participants (Group 1) were requested to read the statements of each level, rate them according to personal judgments and write on the scale by considering that the best level was rated as 100 point and the death was rated as 0 point. Direct Rating Technique (Clemen, 1996) was used in for evaluation of each level. As mentioned in the previous chapter, standard gamble technique, time trade off technique and rating scale are the three basic approaches for direct evaluation. Rating Scale technique is the simplest one among these techniques, administered in less time, generally found easy to perform. There were total of 35 levels to be rated in the survey, and hence, the properties of direct rating technique mentioned previously were very persuasive for participants. For this reason, this technique was preferred in this survey.

This way, one-dimensional value scales were obtained for each participant. In fact, since the decision maker is uncertain about the outcome of the given action, this uncertainty should be expressed. Thus the next step was to turn from values to utilities in order to consider uncertainty. However, most practical elicitations of value and utility avoid this step, and value scale is directly taken as utility scale (Edwards et al., 1986); The value scales assessed in this study were also used as utility scale. All value scales for each attribute obtained from 30 participants can be observed in Figure 3.6 through Figure 3.13.

As can be seen in the graphs, most of the participants seemed to have a tendency of risk seeking behavior for the physical function and psychological function attributes. On the other hand, except for three, the participants showed risk neutral behavior for role function attribute. As for attributes of social function and pain, it was seen that there was tendency for risk averse behavior for almost all.



Figure 3.6. Individual Utility Function  $(U_1)$  (assessed from Group 1) for Attribute Physical Function  $(X_1)$ 



Figure 3.7. Individual Utility Function (U<sub>2</sub>) (assessed from Group 1) for Attribute Role Function (X<sub>2</sub>)



Figure 3.8. Individual Utility Function (U<sub>3</sub>) (assessed from Group 1) for Attribute Social Function (X<sub>3</sub>)



Figure 3.9. Individual Utility Function (U<sub>4</sub>) (assessed from Group 1) for Attribute Pain (X<sub>4</sub>)



Figure 3.10. Individual Utility Function  $(U_5)$  (assessed from Group 1) for Attribute Psychological Function  $(X_5)$ 



Figure 3.11. Individual Utility Function (U<sub>6</sub>) (assessed from Group 1) for Attribute Body Image (X<sub>6</sub>)



Figure 3.12. Individual Utility Function  $(U_7)$  (assessed from Group 1) for Attribute Fears & Concerns  $(X_7)$ 



Figure 3.13. Individual Utility Function (U<sub>8</sub>) (assessed from Group 1) for Attribute Sexual Function (X<sub>8</sub>)

## 3.2.1.3 Assessment of Individual Scaling Constants

Scaling constants (k<sub>i</sub>'s) indicate the relative importance of all attributes. The weight assigned to a criterion is a scaling factor which relates scores on that criterion to scores on all other criteria. In order to determine these scaling constants, a group of participants (Group 1) who performed the previous study were also asked to rank all attributes with respect to their relative importance by swing rating method (Clemen, 1996; Belton, 2002). In this method, DM is asked to consider all bottomlevel criteria simultaneously and to assess for which attribute changing its level from worst to best gives the greatest increase in overall value; this criterion will have the highest weight. The process is repeated on the remaining set of criteria until the order of benefit resulting from a changing from worst to best on each criterion has been determined. Then SMARTER (Edwards, 1994), an improved simple method for multi attribute utility measurement, was used in order to determine relative weights of attributes at each level. Relative weights were assessed within the families of criteria, which means that 3 sub-attribute sharing the same parent (Psychological Function) were assessed such that they sum to 1; 5 main attributes at the top of the tree in Figure 3.4, were assessed such that they sum to 1. These relative weights were obtained from Table D.1 (Edwards, 1994) shown in Appendix D. Then the cumulative weight of each criterion, that is the product of its relative weight in comparison with its siblings and the relative weights of its parent, was calculated. These cumulative weights are the scaling constants. In Appendix E all the individual utility values and importance order of attributes for all participants of public survey can be examined.

#### 3.2.1.4 Selection of Participants (Group 1) for Public Survey

In the ideal case, patients themselves should determine scaling constants and individual utility scales because these are the only people who know what is really like to be in those health states, and therefore, the only ones capable of expressing "true" preferences over different states of health. However, performing this

procedure with patients is generally not considered ethical or practical because patients may be physically overtired or oversensitive and such interviews may affect them negatively. For these reasons, generally physicians don't give permission for interviewing their patients.

On the other hand, many research studies have pointed out that it is possible to incorporate the values of general public into decision-making about health states. In some studies patient utility weights for various health states are generally higher than healthy volunteers' utility weights (Boyd, 1990; Cappelli, 2001). On the other hand, some studies suggest that there is no difference between valuation of patients and general public (Schackman, 2002). Almost all studies, which compare the utility values of various health states obtained by different groups such as patients, general public or physicians etc. indicated that although there are differences between valuations of different groups, these differences do not affect the results of the comparison. Thus, using public preferences are considered acceptable for making health decisions.

In this analysis it was decided to use a sample of healthy women for determination of scaling constants and individual utility scales for reasons mentioned above. For selection of the participants, there were some major criteria and limitations. First of all, the participants had to be well-educated people, and secondly, they should be familiar with techniques used in decision analysis for the ease of application of the assessment procedure. Thinking that it would take care of all these criteria, we decided to ask the 4<sup>th</sup> year, M.S. or new graduate female students from Industrial Engineering of Middle East Technical University to take part in our study. The participation was on voluntary basis. Meetings were held on one-to-one basis if possible or if not, the experiment were given to the participants before each meeting so that they became familiar with the task and the concepts. For this purpose, totally 45 participants took the survey for assessment of individual utility values and scaling constants. Seventeen of them performed the study by one-to-one

meetings and 28 of them by e-mail. However, the results of 15 participants had to be discarded since they performed the survey incorrectly.

#### 3.2.1.5 Assessment of Overall Utility Values of Health States

As mentioned before, in order to calculate utility value of any health state, Multi-Attribute Utility Model Assessment was used. Functional form is as follows:

$$U_{K} = k_{1}U_{1}(X_{1}^{j}) + k_{2}U_{2}(X_{2}^{j}) + k_{3}U_{3}(X_{3}^{j}) + k_{4}U_{4}(X_{4}^{j}) + k_{5}(k_{6}U_{6}(X_{6}^{j}) + k_{7}U_{7}(X_{7}^{j}) + k_{8}U_{8}(X_{8}^{j}))$$

where,

U <sub>K</sub>	: the aggregate value for K <sup>th</sup> health state
$X_i^j$	: measurement of X on $j^{th}$ level of $i^{th}$ attribute
$U_{i}\left(X_{i}^{j} ight)$	: the value of individual utility function $U_{j}  \text{at}  X_{i}^{ j}$
k <sub>i</sub>	: the scaling constant of the i <sup>th</sup> attribute

After eliciting individual utility values and scaling constants, by using these parameters for each attribute, utilities of each participant for each health state can be evaluated easily.

Implementation of the model based on assessing the location of health state along the scales of attributes. In this step, written description was developed for each health state by using location of attributes. For example, description of Health State A is shown in Table 3.2. In order to ensure accuracy of the resulting written description as much as possible, a group of ten oncologists from HUOH performed this experiment. A formal health state level evaluation form was designed for defining each health state with respect to identified attributes by self-completion of oncologists. Three main parts constituted this form. In the first part, introductory written information was given about health states, and oncologists were rendered familiar to the concept. After that, definitions of attributes and their levels, on which classification of health states were based, were given. Finally, evaluation sheet was given in the last part and for each health state they were asked to mark the suitable level that reflects the condition of that health state for each attribute. Ten oncologists performed this task individually. Evaluation sheets obtained from the oncologists can be seen in Appendix F. The modes of scores were taken and the descriptions of the health states were developed. All health state descriptions can be seen in Appendix G. According to those descriptions, twelve health states, six for mastectomy and six for lumpectomy, were defined by feasible combination of attribute levels and finally, multi attribute utility functions were formed for each health state.

As mentioned in Section 3.1 these utility functions were defined in order to assign a reward for each Markov state and the evaluation of a Markov chain on outcome measures yielded the expected reward. The reward for state j, and at time t was denoted by  $R_t(j)$ . All utility functions defined for rewards of twelve health states can be seen in Table 3.3.

Health State	A
Attribute1	Being able to get around house, yard, neighborhood or community WITHOUT help
	from another person; AND NEEDING mechanical aids walk or get around.
Attribute 2	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having
	NO limitations when playing, going to school, working or in other activities.
Attribute 3	Feeling ashamed of own body, feeling does not like herself.
Attribute 4	Feeling fear of recurrence and bothered by thoughts about the recurrence of cancer.
Attribute 5	Some changes in libido and frequency of sexual relationship negatively.

Table 3.2. An Example Health State Description

Rev	vard $(R_t(j))$	Multi Attribute Utility Function
	R <sub>t</sub> (NED)	$U_{1}=k_{1}U_{1}(X_{1}^{1})+k_{2}U_{2}(X_{2}^{1})+k_{3}U_{3}(X_{3}^{1})+k_{4}U_{4}(X_{4}^{3})+k_{5}(k_{6}U_{6}(X_{6}^{3})+k_{7}U_{7}(X_{7}^{1})+k_{8}U_{8}(X_{8}^{2}))$
ΜΥ	R <sub>t</sub> (NEDI)	$U_{2}=k_{1}U_{1}(X_{1}^{2})+k_{2}U_{2}(X_{2}^{1})+k_{3}U_{3}(X_{3}^{1})+k_{4}U_{4}(X_{4}^{3})+k_{5}(k_{6}U_{6}(X_{6}^{3})+k_{7}U_{7}(X_{7}^{1})+k_{8}U_{8}(X_{8}^{2}))$
CTO	R <sub>t</sub> (NEDII)	$U_{3}=k_{1}U_{1}(X_{1}^{2})+k_{2}U_{2}(X_{2}^{3})+k_{3}U_{3}(X_{3}^{2})+k_{4}U_{4}(X_{4}^{3})+k_{5}(k_{6}U_{6}(X_{6}^{3})+k_{7}U_{7}(X_{7}^{2})+k_{8}U_{8}(X_{8}^{3}))$
STE	R <sub>t</sub> (Loc Rec)	$U_{4} = k_{1}U_{1}(X_{1}^{2}) + k_{2}U_{2}(X_{2}^{3}) + k_{3}U_{3}(X_{3}^{2}) + k_{4}U_{4}(X_{4}^{3}) + k_{5}(k_{6}U_{6}(X_{6}^{3}) + k_{7}U_{7}(X_{7}^{3}) + k_{8}U_{8}(X_{8}^{3}))$
MA!	R <sub>t</sub> (Salvage)	$U_{5} = k_{1}U_{1}(X_{1}^{3}) + k_{2}U_{2}(X_{2}^{4}) + k_{3}U_{3}(X_{3}^{2}) + k_{4}U_{4}(X_{4}^{4}) + k_{5}(k_{6}U_{6}(X_{6}^{3}) + k_{7}U_{7}(X_{7}^{3}) + k_{8}U_{8}(X_{8}^{4}))$
	R <sub>t</sub> (Metas)	$U_{6} = k_{1}U_{1}(X_{1}^{4}) + k_{2}U_{2}(X_{2}^{5}) + k_{3}U_{3}(X_{3}^{2}) + k_{4}U_{4}(X_{4}^{5}) + k_{5}(k_{6}U_{6}(X_{6}^{3}) + k_{7}U_{7}(X_{7}^{4}) + k_{8}U_{8}(X_{8}^{4}))$
	R <sub>t</sub> (NED)	$U_{7}=k_{1}U_{1}(X_{1}^{1})+k_{2}U_{2}(X_{2}^{1})+k_{3}U_{3}(X_{3}^{1})+k_{4}U_{4}(X_{4}^{1})+k_{5}(k_{6}U_{6}(X_{6}^{1})+k_{7}U_{7}(X_{7}^{2})+k_{8}U_{8}(X_{8}^{1}))$
ΜΥ	R <sub>t</sub> (NEDI)	$U_{8} = k_{1}U_{1}(X_{1}^{1}) + k_{2}U_{2}(X_{2}^{1}) + k_{3}U_{3}(X_{3}^{1}) + k_{4}U_{4}(X_{4}^{2}) + k_{5}(k_{6}U_{6}(X_{6}^{1}) + k_{7}U_{7}(X_{7}^{2}) + k_{8}U_{8}(X_{8}^{1}))$
CTO	R <sub>t</sub> (NEDII)	$U_{9} = k_{1}U_{1}(X_{1}^{2}) + k_{2}U_{2}(X_{2}^{3}) + k_{3}U_{3}(X_{3}^{1}) + k_{4}U_{4}(X_{4}^{3}) + k_{5}(k_{6}U_{6}(X_{6}^{1}) + k_{7}U_{7}(X_{7}^{2}) + k_{8}U_{8}(X_{8}^{3}))$
APE	R <sub>t</sub> (Loc Rec)	$U_{10} = k_1 U_1(X_1^2) + k_2 U_2(X_2^3) + k_3 U_3(X_3^2) + k_4 U_4(X_4^3) + k_5(k_6 U_6(X_6^2) + k_7 U_7(X_7^3) + k_8 U_8(X_8^3))$
LUN	R <sub>t</sub> (Salvage)	$U_{11} = k_1 U_1(X_1^3) + k_2 U_2(X_2^4) + k_3 U_3(X_3^2) + k_4 U_4(X_4^4) + k_5(k_6 U_6(X_6^2) + k_7 U_7(X_7^3) + k_8 U_8(X_8^4))$
	R <sub>t</sub> (Metas)	$U_{12} = k_1 U_1(X_1^4) + k_2 U_2(X_2^5) + k_3 U_3(X_3^2) + k_4 U_4(X_4^5) + k_5(k_6 U_6(X_6^3) + k_7 U_7(X_7^4) + k_8 U_8(X_8^4))$

Table 3.3. Multi Attribute Utility Functions of Health States

After defining rewards for each state by 8-attribute utility functions, aggregate utility values were calculated with respect to data obtained from Group 1 by using Matlab Version 7.2.0.232 computer program. For this purpose, individual utility values and scaling constants for each attribute, given in Appendix E, were defined as input data for each participant. Then, utility functions were solved for each health state, and the overall utility values were found for all participants. Calculated overall utility values can be seen in Table 3.4.

	•			•		•						
			MASTE	CTOMY					LUMPE	CTOMY		
Participant	U1	<b>U2</b>	U3	<b>U4</b>	<b>US</b>	<b>U</b> 6	<b>U7</b>	<b>U</b> 8	<b>U9</b>	<b>U10</b>	U11	U12
1	88	81	65	64	40	25	66	95	71	66	42	25
2	75	74	60	58	47	39	66	96	83	71	60	39
3	95	88	67	65	46	32	95	93	68	65	46	32
4	75	72	56	54	29	13	98	91	59	55	30	13
5	94	83	68	66	50	35	66	98	70	67	51	35
9	83	83	60	48	33	16	94	92	70	49	34	16
7	81	78	55	47	31	13	90	86	58	48	32	13
8	06	86	58	57	39	25	66	66	64	60	42	25
6	86	82	56	54	32	17	66	94	58	55	32	17
10	93	84	68	99	47	29	67	94	71	67	47	29
11	06	80	99	99	44	31	100	98	68	67	44	31
12	89	77	68	67	45	33	66	95	70	67	45	33
13	93	87	60	57	41	25	86	85	62	58	42	25
14	84	82	70	70	51	25	100	93	74	72	52	25
15	95	06	68	99	40	30	<i>L</i> 6	96	76	68	42	30

Table 3.4. Utility Results Obtained by Multi-Attribute Utility Model

	/		2		•		'n					
			MASTE	CTOMY					LUMPE	CTOMY		
Participant	U1	<b>U2</b>	U3	<b>U</b> 4	<b>US</b>	<b>U6</b>	U7	<b>U8</b>	<b>U9</b>	U10	<b>U11</b>	U12
16	85	82	58	50	36	18	86	84	66	52	38	18
17	93	84	70	67	52	29	98	95	72	68	53	29
18	94	81	61	61	47	17	100	98	65	61	47	17
19	93	84	63	59	41	25	95	93	65	60	43	25
20	06	89	68	59	52	39	86	83	73	60	53	39
21	92	69	42	39	19	10	97	94	43	39	19	10
22	98	86	65	64	44	33	98	97	72	64	44	33
23	95	91	61	56	39	20	98	96	63	57	40	20
24	91	88	64	60	30	20	99	97	65	61	31	20
25	93	83	55	54	29	18	98	67	61	55	30	18
26	89	89	75	73	63	47	98	95	77	74	63	47
27	75	71	60	59	36	18	100	88	62	60	37	18
28	96	86	73	70	45	28	97	96	76	71	45	28
29	80	79	70	68	52	27	99	92	79	74	58	27
30	77	76	66	63	43	25	98	96	75	69	48	25
MEAN	88	82.03	63.07	60.07	41.20	25.13	96.6	93.37	67.67	61.83	42.77	25.13

Table 3.4. (continued) Utility Results Obtained by Multi-Attribute Utility Model

#### 3.2.1.6 Results of Multi-Attribute Utility Model

A total of 45 participants performed the survey for the assessment of individual utility values and scaling constants; however, a total of 30 participants' responses were used. Distributions of utility values obtained from these participants can be observed in Appendix K.

Utility values assessed for the health state of No Evidence of Disease (NED) vary between 75-100 and the mean value is 88 if the patient has mastectomy operation; 96.6 if she has lumpectomy operation, which means that, in general, they feel healthy if the operation is successful. Utility values of 26 participants were evaluated higher for the health state of No Evidence of Disease for lumpectomy (L-NED). This result indicates that, for almost all, if her health state is well after surgical operation, she attaches more importance to her body appearance than their fears about reoccurrence. Remaining 2 participants' data gave equal results for both operations, and interestingly according to other 2 participants' data, utility of L-NED is lower than No Evidence of Disease for mastectomy (M-NED). The reason for that is, for L-NED the only attribute whose level is lower than M-NED is Fears and Concerns. According to these two participants, the importance weight of the attribute of Fears and Concerns was so high that it compensated the low levels of other attributes in M-NED.

Calculated NED-I (No Evidence of Disease but Having Hormone Therapy as an adjuvant therapy) utility values vary between 69-98 and the mean values are 82.03 and 93.37 with respect to mastectomy and lumpectomy operations. As seen, according to opinion of general population, hormone therapy as an adjuvant therapy, does not affect quality of life significantly. All utility values of L-NEDI are higher than M-NEDI except for two participants. L-NEDI values are lower for the same two people because of the same reason mentioned above.

Utility values in NED-II (No evidence of disease but having chemotherapy as an adjuvant therapy) vary between 42-83 and the mean values are 63.07 and 67.67 for mastectomy and lumpectomy operations, respectively. Although there is no evidence of disease after surgery, which means that patient is free of cancer, utility values decreased dramatically for this state. The reasons for that may be a number of side effects of this treatment, which affect patient's life negatively. As expected, evaluated utility values of all participants for L-NEDII are higher than M-NEDII. As we examine health state descriptions for NED II, it is seen that, Fears and Concerns are at the same level for mastectomy and lumpectomy; on the other hand, levels of Body Image and Social Function are at the upper levels for Impectomy. So theoretically it is impossible to assign higher utility values for M-NEDII.

Utility values assessed for the health state of Local Recurrence vary between 39-74 and 19-63 for the health state of Salvaged. As seen the utilities are observed relatively low for these health states since this means the disease has come back. Utility values assessed for lumpectomy are higher with respect to both health states, but differences are negligible. The reason for that is clear: the oncologists consider both treatment options equal with respect to attribute level except for body image and importance weights obtained from almost all participants for body image cause only 1-2 point variations between treatments.

Examining the health state descriptions indicates that, all attributes are at the same level for mastectomy and lumpectomy, which means that there is no difference between the two treatments for this state. Thus, all utility values for the health state of Metastasis are equal for both treatment options. In this health state, it is observed that, the utility value decreased down to 10. When the utility of death, which is 0, taken into consideration, it is clearly realized that participants believed that Metastasis is really an adverse state with respect to quality of life.

As a result, utility values obtained using multi attribute utility model shows that at every state of the breast cancer disease, utility values assigned by participants are higher for lumpectomy operation. However, it should be made clear that after reoccurrence of the disease utility values for both treatment options are equal or very close to each other. That is to say, if cancer comes back, the only thing to consider as important is to survive, so participants do not care much about the surgical treatment option that they are offered. This point is one of the most important results of this study.

In conclusion, analysis in Table 3.5 indicates that there are statistically significant differences between utility values obtained by lumpectomy health states and mastectomy health states, and it is clear that most of the participants believe that lumpectomy provides better quality of life. In particular, if there is no evidence of disease, utility differences between them increase.

PA	AIR	MEAN		MEAN DIFF	T VALUE	P VALUE
Mastec.	Lumpec.	Mastec.	Lumpec.			
NED	NED	88.00	96.60	-8.60	-5.53	< 0.001
NEDI	NEDI	82.03	93.37	-11.33	-9.12	< 0.001
NEDII	NEDII	63.07	67.67	-4.60	-5.67	< 0.001
Local Rec.	Local Rec.	60.07	61.83	-1.77	-3.79	0.001
Salvage	Salvage	41.20	42.77	-1.57	-3.32	0.002
Metastasis	Metastasis	25.13	25.13	0	-	-

Table 3.5. Statistical Analysis of Results Obtained from Multi Attribute Utility Model (MAUM)

In summary, in this section health states of interest (total of 12 health states) were defined, then a group of subjects, for performing utility assessment procedure, were identified and each subject's preferences was measured by using preference

measurement technique. The next section is devoted for validity check of overall utility values obtained by Multi-Attribute Utility Model by means of comparing with global (holistic) ratings.

## 3.2.2 Validity Check of Multi Attribute Utility Model

The utility values for each health state were assessed using Multi Attribute Utility Model. Now, we must deal with one difficult question: Do the numerical values obtained from multi attribute utility model provide valid outcomes? In order to answer this question, the validity of these values should be checked. The term "validity" was meant in this study as the consistency check of the results, utility values for each health state, obtained from the Multi Attribute Utility Model. Anastasi (1997) states that fundamentally all procedures for determining test validity are concerned with the relationships between performance on the test and other independently observable facts about the behavior characteristics under consideration.

In order to perform validation process, global (holistic) ratings for each health state were obtained from interview results of a control group (Group 2), and the values yielded by the model and the global ratings were compared. In addition to comparison of two samples (Group 1 & Group 2), in order to assess degrees to which values of health states derived by the multi-attribute utility model were consistent with the values derived by holistic procedure, a random sample was drawn from control group (Group 2), and they were also applied Multi Attribute Utility Model assessment procedures (which was the task of Group 1). So, using the sample that performed both assessment methods, "construct validation" was used to determine whether subjects' holistic preference judgments are consistent with an algebraic utility model (Anastasi, 1997).
#### 3.2.2.1 Selection of Participants for Control Group – Group 2

In order to implement this experiment, 34 participants (Group 2) were used. At first, it was decided to use different participants for this experiment because participant's concentration could wane when both techniques were used on the same participant. Also they couldn't be objective after the first experiment, so the resulting data couldn't provide an effective validity check. The same criteria as with Group 1 were taken into consideration for selection of participants for Group 2. Similar type of participants was employed for comparison of utility values obtained from the model, versus those obtained from global ratings.

Again, the participation was on voluntary basis. At this time, all meetings were held on one-to-one basis because the method used in validation assessment was more complicated than direct rating method which was used in MAUM in terms of understanding and applying the procedure correctly. The written instructions and the information about experiment were given to the participants before each meeting so that they became familiar with the task and the concepts.

#### 3.2.2.2 Global Rating

Von Neumann and Morgenstern Standard Gamble technique was employed for global rating because of its widespread use and its well-established reputation as the classical method of measuring preferences (utilities). Torrance (1976) proved that this method gives feasible and reliable results and has been claimed to be gold standard in terms of validity. Bennett (1996) stated that, because it involves uncertainty, a characteristic of practically all medical decisions, it is a true utility assessment method. Additionally, Ross (2003) mentioned that the reliability of the SG was very good and it is the only method consistent with the von Neumann and Morgenstern axioms of decision theory and the only utility measure for which expected value is meaningful.

The Standard Gamble technique was first proposed by von Neumann and Morgenstern. The heart of this measurement process is a paired comparison in which the participant is presented with two alternatives and asked to select the preferred one. One alternative offers the participant a particular outcome with certainty while the other alternative offers a gamble with specified probabilities for two possible outcomes (Torrance, 1976). Illustration for this method can be seen in Figure 3.14.

In this experiment, the participants were asked to think really hard and try to imagine that they are in Health State A, and are offered a choice between two alternatives. One is associated with the certainty that the participant continues to live in Health State A. The other alternative involves a gamble (Figure 3.14) in which there is a probability (p) of attaining perfect health (utility = 1) and a complementary probability (1-p) of immediate death (utility =0). In other words, in this alternative participant should accept a (1-p) risk of death in order to have a p-chance for perfect health. The participant was asked what the value of p, such that she accepts a (1-p) % risk of death in order to obtain perfect health, was. In other words, for which probability of p, the participant is indifferent between two alternatives? The indifference probability gives the utility for Health State A. This procedure was applied to every participant for each health state. Worksheet for utility assessment of health state of NED following mastectomy can be seen in Appendix H.



Figure 3.14. Representation of Standard Gamble Method for Obtaining Utilities

By applying this experiment it is aimed to obtain global (holistic) utility values for health states defined previously. In this experiment, this procedure was applied to each participant for twelve health states: six were for after mastectomy operation and six were for after lumpectomy operation. The health state of "Death" was not included in the experiment since its utility was assigned as 0 by default. The results of this experiment are tabulated in Table 3.6.

			MASTE	CTOMY					LUMPE	CTOMY		
Participant	U1	<b>U2</b>	U3	<b>U4</b>	U5	<b>U</b> 6	<b>U7</b>	<b>U8</b>	<b>U9</b>	U10	<b>U11</b>	U12
1	95	95	87	85	75	70	98	97	85	85	75	70
2	83	80	77	78	70	66	89	88	84	79	72	69
3	80	75	70	70	60	50	85	90	75	65	55	45
4	98	90	80	95	85	80	95	90	80	97	85	80
5	100	95	97	75	70	09	67	97	85	70	70	50
9	70	09	70	40	30	30	66	80	80	50	40	50
7	60	40	50	30	30	20	06	60	50	30	30	20
8	95	66	95	85	85	30	66	98	66	87	81	30
9	85	75	70	75	65	58	95	90	73	70	60	50
10	80	65	55	55	50	40	66	80	60	55	50	40
11	95	90	80	85	50	10	06	97	80	80	50	10
12	80	75	70	60	57	30	85	80	72	55	55	20
13	97	06	75	50	60	30	66	97	68	55	55	35
14	95	80	70	60	45	20	85	80	70	55	45	20
15	06	06	85	80	50	20	95	92	85	80	50	15

Table 3.6. Global Utility Results Obtained by Global Rating

			MASTE	CTOMY					LUMPE	CTOMY		
Participant	Ul	U2	U3	U4	US	U6	U7	<b>U8</b>	<b>6</b> 0	U10	U11	U12
16	95	98	96	97	90	92	90	89	88	89	87	86
17	06	95	80	75	60	70	57	55	52	50	45	45
18	80	66	75	66	50	50	50	50	40	45	10	15
19	80	95	75	80	65	70	75	80	60	65	60	65
20	85	80	78	75	70	68	67	66	65	63	62	60
21	66	66	76	98	96	96	06	92	85	87	80	80
22	86	66	96	100	06	92	88	85	09	65	50	53
23	98	66	98	66	95	95	93	93	06	90	88	88
24	66	100	98	66	95	97	95	96	92	94	86	86
25	66	66	85	90	80	85	65	65	55	55	30	30
26	75	95	70	90	50	55	40	35	30	25	15	10
27	06	97	88	95	80	85	70	75	65	65	45	45
28	70	98	65	95	40	80	30	40	32	32	5	9
29	80	75	70	65	60	50	95	90	83	65	65	40
30	06	85	30	20	10	5	65	60	45	20	15	5
MEAN	87.70	82.00	73.07	67.27	58.87	44.40	93.77	88.60	76.97	67.30	59.27	43.93

Table 3.6. (continued) Global Utility Results Obtained by Global Rating

#### 3.2.2.3 Results of Global Rating

As mentioned, 34 participants took part in this experiment but results of 4 participants were not taken into consideration during evaluations, since they performed the experiment incorrectly. Thus, totally 30 results were evaluated. Distributions of these results was depicted in Appendix K.

Examining No Evidence of Disease health states, 22 participants assigned higher utility for lumpectomy while 6 participants assigned higher utility for mastectomy. That means, according to the participants' beliefs, after surgical operation, if the health state of patient is well, body image is more important than fears about reoccurrence.

24 participants assigned higher utility and 4 participants assigned lower utility for lumpectomy if they are in health state of No Evidence of Disease but Having Hormone Therapy as an adjuvant therapy. As in NED state, during hormone therapy, participants believed that they are free of cancer and body image is more important than fears and concerns about reoccurrence of cancer. Almost all participants assigned high utilities for that health state, which means that this therapy does not affect the quality of life significantly; however, when compared with NED state, assigned values were quite lower. The reason for that may be feeling little amount of pain during the therapy and being affected physically during the therapy.

During chemotherapy, as a result of side effects, utility scores decreased for all participants. 18 of participants assigned higher utility for lumpectomy. Although there was no evidence of disease, number of participants, who preferred lumpectomy, decreased. The reason for that may be that all attributes are in their lower levels and as a result, the participants are not interested in their body image as much as the previous states. Nevertheless, lumpectomy was still preferred much more than mastectomy at this state.

As expected, in Local Recurrence state, utility scores fell down. An interesting point is that some participants assigned higher utilities for that health state than Chemotherapy although the cancer is back. Probably the reason for this is that as the participants read the probable side effects of chemotherapy, they were affected negatively and they felt worse than they felt about reoccurrence. In this health state, the most important point was that when the cancer came back, popularity of lumpectomy decreased, only 10 of them assigned higher utility to lumpectomy. This means that the participants believed that when the disease is reoccurred the patient who had mastectomy feels more comfortable while the patient who had lumpectomy is affected negatively. The breaking point is reoccurrence of disease.

In the health state of Salvaged, the utility scores were lower than Local Recurrence. At first glance, having higher utility values while the patient is ill can be considered illogical but in fact it is possible because the results of having a second surgical operation can be more adverse than having cancer with respect to quality of life. Also after the first operation, reoccurrence of the cancer may cause lack of confidence, and although she is salvaged after second operation she might not believe that she is well. Since the second operation is more severe, the levels of all attributes are very low. The utility scores for lumpectomy and mastectomy are very close. The reason is simple; the second surgical operation is always mastectomy, which means that although the patient had lumpectomy at first, if the cancer comes back, she should have mastectomy. In other words, during second surgical operation, the patient has an operation for an entire breast removal and from then on there is no superiority for lumpectomy with respect to body image.

During Metastasis stage, the assigned utility scores decreased dramatically since there is no hope to recover. Because of fears about death, and severe conditions of disease, participants believed that treatment option that she has is unimportant in that state, so most of the participants assigned the same utility values for mastectomy and lumpectomy. However, 7 participants assigned higher utility for lumpectomy. The reason may be that the people with less intense fear of death may feel better about their body image if they have only lumpectomy. On the other hand 8 participants assigned higher utility for mastectomy. They may feel that they didn't have to give up their breast, so they were operated by lumpectomy; but the cancer comes back, so they may regret this decision and assign fewer score for lumpectomy.

An interesting result is that 5 participants assigned all utility scores between 80-100. This attitude can arise from their high level of fears about death, which may stem from risk averse behavior. When they saw probability of death in Alternative 1, they hesitated to take the risk of death, and so they accepted very low risk of death (1-p) in order to have a p-chance for perfect health. Thus, they overestimated the p value, which is the utility of health state under consideration. This result can be considered as a downside of Standard Gamble Technique.

On the other hand, 8 participants assigned utility scores between 0-20 for Metastasis, which indicated that they rejected to live in that condition and accepted a high risk of death for a chance to have perfect health.

Statistical analysis of results can be examined in Table 3.7. As seen, except for two, there are no statistically significant differences between utility values obtained by lumpectomy health states and mastectomy health states, and it is clear that similar to Multi-Attribute Utility Model results, most of the participants believe that, lumpectomy provides better quality of life.

P	AIR	M	EAN	MEAN DIFF	T VALUE	P VALUE
Mastec.	Lumpec.	Mastec.	Lumpec.		,112.02	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
NED	NED	87.70	93.77	-6.07	-2.79	0.009
NEDI	NEDI	82.00	88.60	-6.60	-3.42	0.002
NEDII	NEDII	73.10	77.00	-3.90	-2.46	0.020
Local Rec.	Local Rec.	67.30	67.30	-0.03	-0.04	0.964
Salvage	Salvage	58.90	59.30	-0.40	-0.62	0.540
Metastasis	Metastasis	44.40	43.90	0.46	0.45	0.655

Table 3.7. Statistical Analysis of Results Obtained from Global Rating

The comparison of general results obtained from Standard Gamble (SG) method and Multi-Attribute Utility Model (MAUM) indicates that utility scores obtained from MAUM are lower than SG method. When the participant evaluates attributes one by one she may assign lower utilities than she might holistically (SG), but when confronted with risk of death, she cannot take that risk easily, and so the worth of health state seems more valuable than otherwise. Thus, it can be concluded that MAUM results are more realistic as should be hoped and expected.

#### 3.2.2.4 Statistical Analysis of Two Sample Data

A statistical analysis was conducted for comparing results obtained from MAUM and SG. Table 3.8 shows the descriptive statistics results for both data sets. As seen in the table, for the first two health states after mastectomy and lumpectomy, mean utility values are nearly the same in both measurements; also for the next two health states, mean values are close to each other; but for the last two health states, mean value differences are significantly higher. As the standard deviations in both measurements were compared, it was observed that standard deviations were not so similar. There was a tendency for SG values to show more variation than MAUM values.

Var	iable	MAUM	N=28)			GLOBAL	RATIN	G (N=30)	
				I	I				1
		MEAN	SD	MEDIAN	SE	MEAN	SD	MEDIAN	SE
					MEAN				MEAN
	U1	88.00	7.10	90.00	1.30	87.70	10.46	90.00	1.91
Ŋ	U2	82.03	5.89	83.00	1.07	82.00	13.59	82.50	2.48
ctom	U3	63.07	6.68	64.00	1.22	73.07	17.46	72.50	3.19
aste	U4	60.07	7.66	60.50	1.40	67.27	20.80	70.00	3.80
Σ	U5	41.20	9.11	41.00	1.66	58.87	20.39	60.00	3.72
	U6	25.13	8.54	25.00	1.56	44.40	25.84	45.00	4.72
	U7	96.600	4.149	98.000	0.757	93.77	7.59	96.00	1.39
ŋy	U8	93.367	4.351	94.500	0.794	88.60	10.93	90.00	2.00
cton	U9	67.67	7.95	68.00	1.45	76.97	14.47	80.00	2.64
umpe	U10	61.83	8.25	61.50	1.51	67.30	20.30	68.00	3.71
Lu	U11	42.77	9.84	42.50	1.80	59.27	19.95	57.50	3.64
	U12	25.13	8.54	25.00	1.56	43.93	25.89	45.00	4.73

Table 3.8. Descriptive Statistics of Utility Values

Before validity check of this model, normality of the data obtained from both experiment was checked. In what follows, histograms of data for each health state, given in Appendix I, were examined and it was seen that their shapes were not exactly bell-shaped. Normal probability plots, sample versus normal scores of samples, were obtained in order to see normality of distributions. This plot should be approximately a straight line if the sample is from a normal population but exhibits curvature if the population is not normal. As seen in Appendix J, most of the data sets are very close to linearity. Thus, it was considered that normality assumption was meaningful and normal curves were assigned as in Appendix K. However, since the normality test yielded doubtful results for three health states, the analysis was repeated using nonparametric tests and results were compared.

The next step was to investigate if there is a statistical difference between two population means by analyzing two independent samples for each health states, sample of which MAUM was performed and the sample of which SG was performed. It is known that both samples were drawn from the same population; thus, theoretically if the MAUM results are consistent, result of the t-test should demonstrate this fact, which means that the t-test should say that there isn't statistically significant evidence that two populations differ for each health state. According to Sincich (2003), test of hypothesis can be represented as follows:

Null Hypothesis: $H_0: (\mu_1 - \mu_2) = D_0$ Alternative Hypothesis: $H_a: (\mu_1 - \mu_2) \neq D_0$ 

where  $D_0$  = Hypothesis difference between the means. Since our null hypothesis is difference between the means is 0, then  $D_0 = 0$ 

Test statistics:

$$z = \frac{\left(\overline{x_1} - \overline{x_2}\right) - D_0}{\sigma_{\left(\overline{x_1} - \overline{x_2}\right)}}$$

where,

$$\sigma_{(\overline{x_1}-\overline{x_2})} = \sqrt{\frac{\sigma_1^2}{n_1} + \frac{\sigma_2^2}{n_2}}$$

*Rejection region:*  $|z| > z_{\alpha/2}$ 

Assumptions: The two samples are randomly selected in an independent manner from two populations. The sample sizes  $n_1$  and  $n_2$  are large enough so that  $\overline{x_1}$  and  $\overline{x_2}$  both have approximately normal sampling distributions and so that  $s_1^2$  and  $s_2^2$ provide good approximations to  $\sigma_1^2$  and  $\sigma_2^2$ . This will be true if  $n_1 \ge 30$  and  $n_2 \ge 30$ . The statistical significance of difference in utility values for each health state between two experiments was assessed with two-sample t-test, using statistical software package MINITAB Release 14.20. Test results are displayed in Table 3.9 and MINITAB printouts are given in Appendix L.1. According the results of six health states, p values are higher than  $\alpha$  for %95 and %99 confidence intervals and so there is no statistically significant evidence that two populations are different. Thus for these health states it can be concluded that MAUM results match the SG results. On the other hand, for the rest of six health states, p values are smaller than  $\alpha$ , and so there is a strong evidence to reject null hypothesis and conclude that MAUM results do not match the SG.

PA	AIR	ME	CAN	MEAN DIFFERENCE	T-VALUE	P-VALUE
MAUM	GR	MAUM	GR			
U1	U1	88.00	87.70	0.30	0.13	0.897
U2	U2	82.03	82.00	0.03	0.01	0.990
U3	U3	63.07	73.10	-10.03	-2.93	0.006
U4	U4	60.07	67.30	-7.23	-1.78	0.084
U5	U5	41.20	58.90	-17.70	-4.33	< 0.001
U6	U6	25.13	44.40	-19.27	-3.88	< 0.001
U7	U7	96.60	93.77	2.83	1.79	0.080
U8	U8	93.37	88.60	4.77	2.22	0.033
U9	U9	67.67	77.00	-9.33	-3.09	0.003
U10	U10	61.83	67.30	-5.47	-1.37	0.180
U11	U11	42.77	59.30	-16.53	-4.06	< 0.001
U12	U12	25.13	43.90	-18.77	-3.78	0.001

Table 3.9. MINITAB Results of Pairwise Comparison by Two-Sample t-Test

In order to perform two-sample t-test it was assumed that samples show normal sample distribution property; however, as mentioned there was a doubt about normality so that the analysis was repeated using nonparametric tests and the results were compared. The nonparametric Wilcoxon rank sum test (also called Mann-Whitney for independent sampling) was used to test the hypothesis that probability distributions associated with two populations are equivalent.

The results obtained from two-sample t-test, were unchanged when the analysis was repeated using the nonparametric Wilcoxon rank sum test (Mann-Whitney). Results of this test can be seen in Table 3.10 and MINITAB printouts are given in Appendix L.2.

PA	AIR	MEI	DIAN	W-VALUE	<b>P-VALUE</b>
MAUM	GR	MAUM	GR		
U1	U1	90	90	954.0	0.5692
U2	U2	83	82.5	947.0	0.6414
U3	U3	64	72.5	1131.0	0.0014
U4	U4	60.5	70.0	1061.5	0.0309
U5	U5	41	60	1177.5	0.0001
U6	U6	25	45	1118.5	0.0027
U7	U7	98	96	804.5	0.1039
U8	U8	94.5	90	839.5	0.2675
U9	U9	68	80	1127.5	0.0017
U10	U10	61.5	68	1010.5	0.1602
U11	U11	42.5	57.5	1168.5	0.0002
U12	U12	25	45	1108.5	0.0043

Table 3.10. MINITAB Results of Pairwise Comparison by Mann-Whitney Test

According to these statistical results MAUM results do not entirely match the SG results but it is an expected result! It is interesting that the model results match the global ratings results especially for the no-evidence of disease health states. As the condition of the patient becomes worse, p-values become poorer. The reason for that is if assessing health state condition is similar to participants' current conditions, they can evaluate the condition more realistically. However, as the health state condition that they are assessed for becomes different from their current condition, imagining being in that remote health state and assessing the condition objectively becomes difficult. Namely, extreme states are difficult to estimate overall utility value by global rating. Because of that valuation could be different in global rating since the healthy volunteers performed the study; however as mentioned, differences between valuation obtained from patients and healthy volunteers do not affect ranking. In what follows, it is claimed that MAUM yields more realistic results since it analyzes health states in their attribute levels. This result is the one of the most crucial results obtained in this study.

#### 3.2.2.5 Statistical Analysis of One Sample Data

In addition to the mean comparison of two samples, as mentioned at the beginning of this section, in order to assess degrees to which values of health states derived by the multi-attribute utility model were consistent with the values derived by standard gamble, a random sample was drawn from control group (Group 2) and they were also applied Multi Attribute Utility Model assessment procedures (which was applied to Group 1). So, one sub-sample performed both of the assessment methods and the results of one sample were also analyzed with paired difference experiments, in which observations are paired and the differences are analyzed. The idea is to compare population means by comparing the differences between pairs of experimental units (subjects) that were very similar prior to the experiment. Sincich (2003), points out that in many cases a paired difference experiment can provide more information about the difference between the population means than an independent samples experiment. Test results are displayed in Table 3.11 and

MINITAB printouts are given in Appendix L.3. The paired difference experiment showed that for all health states, p values are higher than  $\alpha$  for %95 and %99 confidence intervals and so, there is no statistically significant evidence that two populations are different. Thus, for these health states it can be concluded that MAUM results are consistent with the results of SG.

Again, random sample from Group 2 was also considered as nonparametric and Wilcoxon rank sum test was used in order to test for a difference when the data is considered nonparametric. The results of this test are tabulated in Table 3.12 and MINITAB printouts are given in Appendix L.4. The results obtained from paired difference experiment were unchanged when the analysis was repeated using the nonparametric Wilcoxon rank sum test like the previous study. Namely, for all health states, T values are higher than  $T_0$  values for %95 and %99 confidence intervals. Thus, for these health states it can be concluded that MAUM results are consistent with the results of SG method.

PA	AIR	ME	CAN	MEAN DIFF.	<b>T-VALUE</b>	<b>P-VALUE</b>
MAUM	GR	MAUM	GR			
U1	U1	90.18	88.91	1.27	0.34	0.739
U2	U2	87.00	83.73	3.73	0.92	0.377
U3	U3	69.64	72.46	-2.82	-0.5	0.625
U4	U4	67.55	69.55	-2.00	-0.29	0.781
U5	U5	53.00	60.82	-7.82	-1.12	0.291
U6	U6	32.27	46.91	-14.64	-1.41	0.189
U7	U7	98.09	92.91	5.18	3.14	0.011
U8	U8	94.91	89.36	5.55	1.88	0.089
U9	U9	74.73	78.36	-3.63	-0.71	0.493
U10	U10	68.64	69.73	-1.09	-0.15	0.881
U11	U11	54.09	60.36	-6.27	-0.84	0.420
U12	U12	33.18	46.55	-13.36	-1.24	0.244

Table 3.11. MINITAB Results of Paired Difference Experiment

Table 3.12. MINITAB Results of Wilcoxon Rank Sum Test

PA	AIR	T-VALUE	W-VALUE	P-VALUE
MAUM	GR			
U1	U1	25	25	0.813
U2	U2	22	44	0.351
U3	U3	27	27	0.625
U4	U4	29.5	29.5	0.790
U5	U5	22	22	0.351
U6	U6	20	20	0.266
U7	U7	7	59	0.023
U8	U8	16.5	49.5	0.155
U9	U9	16.5	16.5	0.515
U10	U10	30	30	0.824
U11	U11	25	25	0.505
U12	U12	19.5	19.5	0.248

#### 3.2.2.6 Simple Validation

The common validity check for this type of decomposition model is so-called "convergent validity" (Fischer, 1977; Krabbe et al., 1997) and its measure is the correlation between the results of the methods, based on the mean values of the health states. When alternatives are characterized by a small number of attributes, information overload should not be serious problem, so it is reasonable to expect high degree of consistency between the two types of judgments.

Correlation coefficients for convergent validity were all computed based on the mean values for 12 health states and represented in Figure 3.15. This correlation analysis demonstrated that the mean utility values yielded by Multi-Attribute Model were highly correlated with the mean utility values yielded by global rating by Standard Gamble.



Figure 3.15. Correlation Coefficients Based on the Mean Values for 12 Health States

#### 3.2.2.7 Construct Validation

A joint committee of the American Psychological Association, the American Education Research Association, and the National Council on Measurement in Education, in their Standards for Educational and Psychological Tests defined three basic types of validity: criterion, content, and construct (Kaplan, Bush and Berry, 1976). The criterion validity is comparison of method to be tested (predictor), with the reference method (criterion). In criterion validity the coefficient of validity is determined as the correlation coefficient between predictor and criterion; however, Kaplan, Bush and Berry (1976) argue that criterion validity is not possible for a broad health status measure because no well-accepted criterion exists that accurately measures the phenomena of interest. In this respect, the construct validity was studied for the two valuation methods.

A framework within which to conduct construct validation was proposed by Campbell and colleagues, who pointed out that in order to demonstrate construct validity it should be shown not only that a test correlates highly with other variables it would be theoretically expected to, but also that it does not correlate highly with variables with which it would be expected to differ (Campbell and Fiske, 1959; Anastasi, 1997). Campbell and Fiske (1959) proposed a systematic method for exploring this, the Multitrait-Multimethod (MTMM) Matrix method, which entails the assessment of two or more constructs by two or more methods.

They identified four classes of correlation coefficients. First one is, monotraitmonomethod reliability correlations, in which health states are measured twice for each method separately: test-retest. Second one is, convergent validity (monotraitheteromethod) correlations, which is between measures of same health state using different methods. Third one is heterotrait-monomethod correlation, in which different health states are assessed by the same method. The last one is, heterotraitheteromethod correlations, in which different health states are assessed by different methods. The third one or the last one is called as discriminant validity coefficients. A synthetic MTMM matrix is represented in Appendix M.

For satisfactory construct validity, in the first place, convergent validity coefficients should be different from zero and sufficiently large to encourage further examination of validity. Second, convergent validity coefficients should be higher than discriminant validity coefficients lying in the same column and the row in the triangles.

The MTMM matrix for this study can be seen in Figure 3.16. As seen, convergent validation correlations different from zero are moderately high for all health states across the methods Multi-Attribute Utility Model and Standard Gamble (global rating) (average= 0.518). Anastasi (1997) points out that, such correlations should be moderately high but not too high, for otherwise the new test represents needless duplication (unless it is e.g. briefer, or easier to administer). In addition, because these correlation coefficients are based on the analysis of individual values for 12 health states of the two methods, such correlations are therefore always lower than correlation coefficients based on aggregated mean data (e.g. Figure 3.15). We can conclude that, these moderately high correlation coefficients can be acceptable for validity.

Secondly, convergent validity coefficients were compared with the discriminant validity coefficients. As seen in Figure 3.14, not all of the validity values meet this requirement. Some of the validity values are lower than the correlations obtained between that variable and any other variable having neither state nor method in common. However, Campbell and Fiske (1959) claimed that this requirement might seem so minimal and so obvious as to not need stating; yet an inspection of the literature shows that it is frequently not met.

In conclusion, after a series of statistical analysis and validation studies it can be concluded that Multi Attribute Utility Model results are reasonably valid. Hence, the model is ready for implementation.

Π	<u></u>		-9			8	() ()		-2	-3		<u></u>			-2	-2		<u></u>			-2	-2		Ş	
	12	-											_										_		
	11						-						2						-	_					0.994
	10							s						s										1260	9260
	6																						0972	0.955	1960
	8																					0.839	0830	0.803	0.802
ATTNG	7																				100	0.835	0.856	1210	1221
BAL R																				628	1837 (	0.270	783	1291	644 (
G	0																		932	839 0	844 C	847 C	804	305	709 0
	5	-											1					281	169 0	201 0	201 0	196 0	154	044 0	087 0
	4					<u></u>											511	368 0.	728 0.	714 0.	730 0.	599 0.	530	535 0.	576 01
	m							1 10 2 1								2	t2 0.	10 01	) 8	29 0.	03 0.	17 01	õ	16 0.	18 0.
	7	-						0							<i>u</i>	2 03	3 0.84	6 02	0.10	8 -0.0	7 -0.0	4 0.1.	000	10 Q	8 0.02
_	1					3		i - 11	-2			5			9.42	0.86	1 0.44	8 0.76	0.60	8 0.46	5 0.45	5 0.46	035	027	031
	12							s. 7		2				0.16	200	021	0 -0.12	03%	0.495	03%	038	0.40	0.45	0.47)	0.43
	11							0					0982	0.129	0.126	0.178	-0.14	0321	0.456	0304	0330	0.414	0.466	0.504	0.468
	10											0.861	0.895	0.241	220.0	0.391	-0.045	0.537	0.665	0.593	0.631	0.605	0.641	0.627	0.593
	٩										9260	0.848	0.879	0316	0.153	0.427	0.054	0.636	0.723	0.639	0.639	0.682	0.694	0.673	0.638
	80							_		0.878	0.873	0.857	0.852	0.149	0350	0310	0.191	0345	0.433	0365	0386	0.477	0.499	850	0.486
MU	6	-							0260	0.865	0.745	0.762	0.753	0.237	0.444	0334	0 295	0.455	0.485	0.402	0369	0.541	053	0.520	050
M	9							0.750	0925	0.813	0.888	0.836	0.842	0.023	0.121	0.224	-0.031	0.257	0.396	0304	0.347	0369	0.425	0.416	0386
	S						0.750	0.983	0.905	0.906	0.790	0.751	0.762	0279	0320	0.393	0.227	0.536	0.549	0.512	0.469	0.610	0.589	0.578	0.561
	4					0.115	0.243	0.168	0.224	0.089	0.106	0.180	0.248	0.278	0383	0.142	0.434	-0.041	-0.095	-0.113	-0.126	-0.175	-0.171	-0257	-0236
	e				0800	6090	0.270	0.498	0316	0.624	0.474	0306	0384	0.512	-0.128	0.472	-0.033	0.737	0.633	0.637	0.534	0.585	0.516	0.458	0.439
	2			-0.427	0.609	0.165	0.299	0 295	0374	0.038	0.062	0.167	0/1/0	-0.064	9690	-0.041	0.642	-0.291	-0217	-0310	-0.276	-0.305	0.270	-0337	-0326
			0276	. 790	308	348	0.038	312 (	1062	328	1137	1.160	161.0	629	103	414	0510	. 619	1487	365	1280	1374	1324	1245	1251
	1	1	2 -1	3 0	4	S O	9	7 0	8	9 0	10 0	11 0	12 0	1 0	2 0	0 0	4 0	s o	0	7 0	8	9	10 0	11 0	12 0
							WIN	ΑM									Ð	ILL	ΥR.	IA8	IO1	Ð			1

Figure 3.16. MTMM (Multi-Trait Multi-Method) Matrix for Construct Validation

#### 3.2.3 Additivity Discussion

As mentioned previously, the reasonable multi attribute utility functions can be additive and multiplicative if the number of attributes  $n \ge 4$ . In order to be able to apply these functions, necessary independence conditions should be established and verified as the first step of the study. As mentioned previously, mutual utility independence conditions are needed for using multiplicative utility function; on the other hand, additive utility independence conditions are needed for using additive utility function. Additive utility function is the specific case of the multiplicative form, and more preferable because of its relative simplicity to elicit. On the other hand verifying additive independence is a more challenging task. As Torrance (1982) mentioned the establishment and verification of the independence conditions is normally a tedious, exacting and time-consuming task.

Edwards (1986), ignored measurement theory and nonadditivities, and instead relied on simple additive models. He claimed that best thing is defining away dependencies, and suggested that fist step is to define such attributes that they are independent anyway. This way the model is always simple to deal with. As discussed in Section 3.2.1.1, the set of attributes to be used in this study was adopted from multi-status classification systems were established in the medical decision making literature. All these multi-status classification systems are based on multi attribute utility theory and use multiplicative or additive utility functions as multi-attribute utility model, as attributes in these systems are shown to be mutually independent. Additive independence has been proven for only some, not all. Hence, we need to check for additive independence condition in the specific set of attributes, some similar and dependent attributes were grouped together and the model was re-structured as discussed in Section 3.2.1.1; but additive independence should be checked on the resultant set.

In medical decision making literature, the ideal way to check additive independency is to check whether the sum of global ratings assigned to the "corner outcomes" is 1 or not. Corner outcome is increasing any attribute's level to its best level while holding all other attributes constant at their worst level. In this study since 8 attributes were defined, there are 8 corner points, which are:

1 <sup>st</sup> corner point:	$(X_1^*, X_2^0, X_3^0, X_4^0, X_5^0, X_6^0, X_7^0, X_8^0)$
2 <sup>nd</sup> corner point:	$(X_1^0, X_2^*, X_3^0, X_4^0, X_5^0, X_6^0, X_7^0, X_8^0)$
3 <sup>rd</sup> corner point:	$(X_1^{\ 0}, X_2^{\ 0}, X_3^{\ *}, X_4^{\ 0}, X_5^{\ 0}, X_6^{\ 0}, X_7^{\ 0}, X_8^{\ 0})$
4 <sup>th</sup> corner point:	$(X_1^{\ 0}, X_2^{\ 0}, X_3^{\ 0}, X_4^{\ *}, X_5^{\ 0}, X_6^{\ 0}, X_7^{\ 0}, X_8^{\ 0})$
5 <sup>th</sup> corner point:	$(X_1^{\ 0}, X_2^{\ 0}, X_3^{\ 0}, X_4^{\ 0}, X_5^{\ *}, X_6^{\ 0}, X_7^{\ 0}, X_8^{\ 0})$
6 <sup>th</sup> corner point:	$(X_1^0, X_2^0, X_3^0, X_4^0, X_5^0, X_6^*, X_7^0, X_8^0)$
7 <sup>th</sup> corner point:	$(X_1^{\ 0}, X_2^{\ 0}, X_3^{\ 0}, X_4^{\ 0}, X_5^{\ 0}, X_6^{\ 0}, X_7^{\ *}, X_8^{\ 0})$
8 <sup>th</sup> corner point:	$(X_1^{\ 0}, X_2^{\ 0}, X_3^{\ 0}, X_4^{\ 0}, X_5^{\ 0}, X_6^{\ 0}, X_7^{\ 0}, X_8^{\ *})$

where,

 $X_i^*$ : the best level of  $i^{th}$  attribute.

 $X_i^0$ : the worst level of  $i^{th}$  attribute.

Application of this ideal method was impossible for this study because, the worst levels of attributes were defined as "death", which means that assigning a utility value for the best level of any attribute while considering all other attributes are in their "death" levels is meaningless.

On the other hand, a common way to check independence is, as Torrance (1982) suggested, to assume the existence of additive independence property and then to test this assumption later with the data obtained. In what follows, it is assumed that multi-attribute utility function is additive and 5-attribute additive utility function was used and overall utility values were obtained. Later, the multi-attribute utility model results was tried to be validated by global ratings. In the end of validation process, although it was concluded that the multi-attribute utility model results

were reasonably valid, there were some statistically significant differences for some states during statistical analyses. It was considered that, these differences could be arising from failure in additivity assumption. Thus, the existence of additive independence property was tested by using individual utility values and global ratings obtained from the random sample drawn from the control group (Group2)

As mentioned before, the family of functions that are typically used for aggregate (multi attribute) utility functions has the following general form:

$$U(X) = \sum_{i=1}^{n} k_{i}U_{i}(X_{i}) + k \sum_{i=1; j > i}^{n} k_{i}k_{j}U_{i}(X_{i})U_{j}(X_{j})$$
  
+  $k^{2} \sum_{i=1; j >; i > j}^{n} k_{i}k_{j}k_{l}U_{i}(X_{i})U_{j}(X_{j})U_{l}(X_{l}) + ... + k^{n-1}k_{1}k_{2}...k_{n}U_{1}(X_{1})U_{2}(X_{2})...U_{n}(X_{n})$ 

As Keeney and Raiffa (1993) present, if  $\sum_{i=1}^{n} k_i = 1$ , then k = 0 and then this utility function written above reduces to an additive utility function,

$$U(X) = \sum_{i=1}^{n} k_i U_i(X_i)$$

The k values can be obtained from the equation above by using overall utility values obtained from global ratings and individual utility values and scaling constants. If the k values are near zero, we can conclude that using additive utility function is reasonable.

In what follows, the utility function expressed above was re-formulated by considering 5 attributes,

$$U(X) = \sum_{i=1}^{5} k_{i}U_{i}(X_{i}) + k \sum_{i=1; j > i}^{5} k_{i}k_{j}U_{i}(X_{i})U_{j}(X_{j})$$
  
+  $k^{2} \sum_{i=1; j > ; l > j}^{5} k_{i}k_{j}k_{l}U_{i}(X_{i})U_{j}(X_{j})U_{l}(X_{l})$   
+ ... +  $k^{4}k_{1}k_{2}k_{3}k_{4}k_{5}U_{1}(X_{1})u_{2}(X_{2})U_{3}(X_{3})U_{4}(X_{4})U_{5}(X_{5})$ 

re-arrange as follows:

$$U(X) = \beta_0 + \beta_1 k + \beta_2 k^2 + \beta_3 k^3 + \beta_4 k^4$$

where,

$$\begin{split} \beta_0 &= \sum_{i=1}^5 k_i U_i(X_i) \\ \beta_1 &= \sum_{i=1; j>i}^5 k_i k_j U_i(X_i) U_j(X_j) \\ \beta_2 &= \sum_{i=1; j>i; l>j}^5 k_i k_j k_l U_i(X_i) U_j(X_j) U_l(X_l) \\ \beta_3 &= \sum_{i=1; j>i; l>j; m>l}^5 k_i k_j k_l k_m U_i(X_i) U_j(X_j) U_l(X_l) U_m(X_m) \\ \beta_4 &= k_1 k_2 k_3 k_4 k_5 U_1(X_1) U_2(X_2) U_3(X_3) U_4(X_4) U_5(X_5) \end{split}$$

The equation expressed above is quadratic. The roots of this equation give k values. In this equation, U (X) is the overall utility value obtained from global rating for any health state and  $\beta$  values are the constants calculated using individual utility values and scaling constants. Hence, the only unknown here is k.

This quadratic equation was written for each health state of each participant who performed the both utility assessment procedures. There are 12 health states and 15 participants' data; thus 12x15 quadratic equations were written and solved for their roots. This process was performed with using Matlab Version 7.2.0.232. All calculated k values are given in Appendix N. As examined the k values, almost all values (except 8 data among 180 data), are nearly zero. Hence we can conclude that

multi attribute utility function defined for mutually additive independent attributes nearly gave the same results with our additive utility function. Thus, it is reasonable to use additive one.

# **3.3 Probability Assignment**

One of the challenges in decision analysis is to ascertain the values of the probabilities in the model. There are a number of methods of probability assignment. Empirical clinical studies and statistical data obtained from literature are the most manageable sources for probability assignment. In this study, relying on past records of Hacettepe University Oncology Hospital (HUOH) would have been the most desireable way to pursue. Unfortunately, this was not possible because the hospital records needed to estimate probabilities are not yet kept adequately. Moreover, some records are confidential documents since they include patients' personal information, and revealing them may be considered as unethical.

On the other hand, as Kassirer (1976) points out, when the literature provides unsatisfactory answers, the situation requires the "judgment of an experienced clinician," applying his "common sense" as he has done in the past. This means that it is possible to carry out decision analysis, deriving the probability values from subjective estimates. In what follows, in this study subjective probability assignment method was used in order to get transition probabilities among the health states in Markov chain.

There are a number of approaches for subjective probability assessment in conventional decision analysis approaches that are based on comparing bets or lotteries. We consulted a group of experts for assessing the transition probability values that we needed for our model to be complete. Probability estimates were based on their common evaluation. The experts used for this study are oncologists at Hacettepe University Oncology Hospital (HUOH).

As mentioned previously, transition probabilities among the health states are not constant over time. Thus, we need probability assessment for each cycle. Since a Markov chain through 10-year survival was used to model disease progression, for probability data at most 10 cycles was needed for both treatment options. There are 25 transitions in our base case, so total of 25\*2\*10=500 probability data was needed. Therefore, some steps had to be taken to bring this tremendous task down to manageable magnitudes. Below are assumptions and simplifications made to this end.

#### Assumptions and Simplifications

• The first and the most important assumption is that, transition probabilities among the health states are the same for mastectomy and lumpectomy. This is a safe assumption since the expert asserted that option of surgery does not affect these probabilities significantly. There definitely are some differences; such as probability of local recurrence being higher for lumpectomy, or probability of salvage after local recurrence being higher for lumpectomy. However, these differences were not taken into account at the first stage and analysis was performed by considering the same transition probabilities. Afterwards, sensitivity analysis was performed in order to observe the effect of differences in transition probabilities (see Chapter 4).

• The simulation begins in NED state after surgery. The first year, patient makes transition into every state except for Salvaged state. Transitions to NEDI or NEDII state can take place only in the first year. The reason for this is that it was assumed that these therapies are carried out if there is a risk of recurrence after surgery and if she does not accept these adjuvant therapies at the beginning of the first year, there is no reason to carry out these treatments in following years.

• Hormone therapy was assumed to last for approximately 5 years and thus a patient remains in that state at most 5 times. After that, transition probability to remain in that state and consequently in other states are 0 for following years.

- In addition, it was assumed that a patient does not have to complete treatment in order to go to another state, so during treatment of hormone therapy, a patient can make transition to any state.
- Chemotherapy was assumed to last for approximately 1 year and all assumptions made for hormone therapy are valid for chemotherapy.
- Death state was considered as death from breast cancer, so probability of death from other causes was not taken into consideration.
- For the states of Local Recurrence and Salvaged, transition probabilities were considered as constant except for the first cycle. In these states, the transition probabilities do not change unless patient makes transition to other states.

By considering the assumptions and the simplifications mentioned above, transition probabilities among health states were determined by expert opinion. All probabilities among health states were tabulated in Table 3.13. In this table cycles do not represent time of the process; instead, it represents number of times. For instance, if the patient goes into state NEDII in the forth stage of the process (t = 4) at first time, then, from Table 3.13 1<sup>st</sup> cycle probabilities should be considered for the transition probabilities from NEDII to the other possible states.

The transition probabilities into other states at time t is  $P_t(i,j)$ , where

$$P_{t}(i, j) = P\{Y_{t+1} = j/Y_{t} = i\} \qquad \forall i, j \in S$$
$$P_{t}(i, j) \ge 0$$
$$\sum_{j \in S} P_{t}(i, j) = 1 \qquad \forall i \in S; \forall t \in N$$

IIC	NED	0.42	0	0	0	0	0	0	0	0	0	TASIS	DEAD	0.10	0.2	0.2	0.3	0.3	0.3	0.3	0.4	0.5	0.5
NEI	NEDII	0	0	0	0	0	0	0	0	0	0	METAS	META	0.90	0.8	0.8	0.7	0.7	0.7	0.7	0.6	0.5	0.5
	DEAD	0.01	0.01	0.01	0.01	0.01	0	0	0	0	0		DEAD	0	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
	META.	0.04	0.08	0.08	0.06	0.05	0	0	0	0	0	ALVAGED	META.	0.80	0.09	60.0	60.0	60.0	60.0	60.0	0.09	0.09	0.09
	LOC. R.	0.03	0.05	0.05	0.06	0.05	0	0	0	0	0	S	SALVA	0.20	06.0	06.0	06.0	06.0	06.0	06.0	06.0	06.0	0.90
NEDI	NED	0.05	0.05	0.05	0.05	0.89	0	0	0	0	0	Ш	DEAD	0.05	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
	NEDI	0.87	0.81	0.81	0.82	0	0	0	0	0	0	URRENCI	META	0.7	0.85	0.85	0.85	0.85	0.85	0.85	0.85	0.85	0.85
	DEAD	0	0.0035	0.0035	0.0035	0.0035	0	0	0	0	0	OCAL REC	SALVA	0.1	0	0	0	0	0	0	0	0	0
	META.	0	0.024	0.0275	0.0275	0.024	0.0175	0.014	0.0205	0.017	0.0135	D	LOC R.	0.15	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
	LOC. R.	0	0.0135	0.017	0.017	0.0135	0.0135	0.01	0.0035	0.0035	0		DEAD	0.02	0	0	0	0	0	0	0	0	0
NED	NEDII	0.75	0	0	0	0	0	0	0	0	0		LOC. R.	0.05	0	0	0	0	0	0	0	0	0
	NEDI	0.2	0	0	0	0	0	0	0	0	0	VEDII	META.	0.10	0	0	0	0	0	0	0	0	0
	NED	0.05	0.9625	0.952	0.952	0.959	0.969	0.976	0.976	0.9795	0.9865	~	NEDI	0.41	0	0	0	0	0	0	0	0	0
Ì	J	1	2	3	4	5	9	7	8	6	1	Ì		1	2	3	4	5	9	7	8	6	0
							Ξ	CLI	YЭ											ΓE	ЭX	C	

Table 3.13. Transition Probabilities among the Health States

## **CHAPTER 4**

### ANALYSIS OF EXPERIMENTAL RESULTS

In this section, experimental results and the effects of factors on the results were analyzed. In previous sections, the Markov chain was constructed for the problem, reward and probability assessment were performed, and so, the development of this model was completed. The next step was evaluation of the model according to the data that was collected from participants, and therefore evaluation of the alternative treatments with respect to the quality adjusted life years to be gained with each.

### 4.1 Evaluation of Decision Model

As mentioned previously, evaluation of the Markov chain developed for the disease progress yields QALY, which is total number of cycles spent in each state, each multiplied by the reward for that state, since the reward was assigned to the each health state.

$$QALY = \sum_{j=1}^{7} t_j \times R_j$$

where

t<sub>j</sub> : time spent in state j.

 $R_j$  : reward (utility) for state j.

Since the transition probabilities among the health states are time-dependent, it is impossible to evaluate the process with exact method. Additionally, the utility values in relation to health states should be defined as distributions with respect to data obtained from the participants. Since there was uncertainty involved in reward values, it was considered to use simulation method in order to calculate the expected utility value (QALY) generated by each treatment option.

Design and evaluation of the model were performed by making use of Treeage-Pro 2006 Suit software. The constructed model is in Figure 3.3. The configuration of the model for mastectomy option can be seen in Figure 4.1. As mentioned previously, the history is the same for the both treatment options. Thus, the basic configurations are the same and the only difference is the parameter values such as utility values.

As seen in the Figure 4.1, the model representation looks like a decision tree. In the original graphical representation of a Markov model, each state is represented by using circle and arrows represents transitions. However, Treeage does not employ this representation of a Markov model. Instead, Treeage uses "Cycle Tree" which is based on a node and a branch framework, making it easily integrated into standard decision tree structures. Sonnenberg (1993) presented a practical guide, which includes representation of Markov models in medical decision-making.

In the Figure 4.1, the seven branches emanating from Markov node enumerate the Markov states (health states). Later, the subtree emanating from each state is used to represent the possible transitions from that state. A state out of which transitions are not possible has no transition subtree, which is the absorbing state (Dead). To the right of the each transition node's symbol is displayed the name of the state to jump to at the beginning of the next stage (terminal node).

The utilities of each health state were assigned as an incremental reward that reflected the value of being in that state for one cycle. The incremental reward was

accrued by the membership of the state at each subsequent stage of the process, starting at stage 1 and continuing until the process terminates. Instead of assigning utilities as certain numbers, they were defined as normally distributed random values with mean and standard deviations, which were, calculated in Chapter 3. Hence, for each simulation trial, a random number was generated for each utility value from the related distribution. Also, since all patients start in NED state, initial reward was assigned for that state, which was a one-time adjustment to the incremental reward that was made at the beginning of the simulation experiment. It was used to implement half cycle correction and therefore, its value was set to half of the incremental reward of NED state (Sonnenberg, 1993).

Since the stages were represented by survival years, the total reward was the quality of life for each health state is multiplied by the time spent in that state. The total reward is expressed as the quality adjusted life years (QALY) as mentioned previously. Thus, the total reward evaluated from simulation represents QALY value of that treatment option.

As seen in Figure 4.1, since all patients start in a NED state after the surgery, initial probabilities were assigned as 0, for all states except NED state. On the other hand, transition probabilities were represented by variables. Since transition probabilities vary with time, they referenced the probability tables of stage dependent values by using appropriate Markov keywords, which are called *tracker variables*. Thus, for this purpose, a tracker variable was defined for each health state. These variables count the number of visits to each possible state. For instance, a tracker variable defined for the NED state was NT. If a subject encounters a node NED containing a tracker variable definition NT=NT+1, the Treeage takes the current global value of NT for that individual's trial, add 1 to it, and store the new global value. Thus, the tracker variable NT counts the number of visits to NED state during the process and when the subject visits NED state, the program checks the tracker variable NT and according to value of NT variable, the following transition probabilities from NED state to other states were taken from related probability tables.

To sum up three different kinds of variables were defined in this program. First one was defined as an incremental reward for utility values, which were referred to appropriate distributions for each health state. The second kind of variables was defined for transition probabilities, which were referred to probability tables. And the last one was tracker variables defined for counting number of visits to each possible state during simulation.



Figure 4.1. Configuration of Cycle Tree for Mastectomy

## 4.2 **Results**

Time-dependent Markov chains could be simulated by a cohort simulation (one trial, multiple subjects) or by a Monte Carlo simulation (many trials, single subject for each) (Chapman and Sonnenberg, 2000). Cohort simulation and Monte Carlo simulation to the Markov process are illustrated graphically in Figure 4.2.



Figure 4.2. A) Cohort Simulation B) Monte Carlo Simulation

One of the important assumptions in a cohort analysis is that the model maintains no memory of previous events. However, in our model, state's transition probabilities depend on prior events. Since they vary with time, it is important to know how many times a subject visits a state previously. Thus, the simulation should allow tracking transition probabilities. In what follows, cohort analysis is not suitable for this analysis since the histories of the different components of the cohort are not maintained in this simulation type. On the other hand, Monte Carlo simulation is the most common and efficient method for introducing detailed
memory into Markov processes; because, in this simulation, one individual at a time is placed into the process, and that person is followed from state to state until a terminal state is reached and thus, one can keep track of the complete history of state membership as the individual moves through the process. Hence, the model in this study was evaluated by Monte Carlo simulation.

Monte Carlo simulation determines prognosis of a large number of individual subjects. Each subject starts in the starting state, NED state, and at the end of each cycle, a random number generator is used together with the transition probabilities to determine in which state the patient will begin the next cycle, and the subject is given reward for each cycle spent. When the subject enters the death state or satisfies the termination condition, the simulation is stopped. The process is repeated a very large number of times, and each trial generates a quality adjusted survival time. After a large number of trials, these constitute a distribution of survival values. The mean value of this distribution will be similar to the expected utility.

10-year survival was considered, so the cycle length was defined as 10 cycles, and termination condition was set as 10 stages. Total of 200 samples, recalculation of the model based on a randomly generated set of utility values from normal distribution, and 1000 trials for each sample were performed (total of  $2x10^5$  trials). Firstly, the simulation was performed for mastectomy. The analysis output showed that if the subject is operated with mastectomy, mean value for the gained quality adjusted life years was 641.62. On the other hand, the data were revised according to lumpectomy option and then, the model was simulated again. The mean value for the gained quality adjusted life years was 700.72 at this time. The results showed that, as expected, quality adjusted life years for lumpectomy is higher than mastectomy. Simulation statistics were tabulated in Table 4.1 for lumpectomy and Table 4.2 for mastectomy. Since the transition probabilities were assumed to be same for each treatment option, number of visits to each health states was also same as expected. The maximum average number of visits were observed into

NED state and the minimum ones were observed into Salvaged state. The detailed text reports of 200 samples' outcomes can be examined in Appendix O.

Statistic	Value	NEDII	NEDI	Loc. Rec.	Metastasis	NED	Salvaged
Mean	700.72	0.748755	1.83733	0.194275	1.555685	5.20046	0.029165
Std Dev	22.79	0.012594	0.069082	0.013442	0.069153	0.107992	0.010391
Min	644.68	0.717	1.653	0.153	1.407	4.93	0.009
Median	703	0.749	1.84	0.194	1.551	5.191	0.028
Max	762.89	0.79	2.04	0.23	1.762	5.505	0.062

Table 4.1. Simulation Statistics for Lumpectomy

Table 4.2. Simulation Statistics for Mastectomy

Statistic	Value	NEDII	NEDI	Loc. Rec.	Metastasis	NED	Salvaged
Mean	641.62	0.752275	1.829435	0.19361	1.564415	5.19829	0.02913
Std Dev	32.9	0.013761	0.068402	0.015686	0.073146	0.119534	0.009774
Min	565.06	0.718	1.622	0.155	1.396	4.913	0.01
Median	641.32	0.751	1.83	0.195	1.56	5.199	0.027
Max	736.96	0.794	2.017	0.241	1.784	5.524	0.058

Cumulative distributions of the outcomes for 200 samples were represented in Figure 4.3 and Figure 4.4. It was observed that, the outcomes were also distributed normally. Also, QALY values versus years can be seen in Figure 4.5. The difference in the total reward between lumpectomy and mastectomy increases each year.



Figure 4.3. Monte Carlo Simulation at Mastectomy



Figure 4.4. Monte Carlo Simulation at Lumpectomy



Figure 4.5. Projected Overall Quality Adjusted Life Years

# 4.3 Sensitivity Analysis

Neither probabilities nor the utilities are certain quantities. Utilities of health states were estimated on the basis of general population preferences and survey results; on the other hand, transition probabilities were estimated on the basis of experience of clinicians and literature review. Thus, it is important to study how our decision might be affected by changes in those parameters.

In this section, a series of one-way sensitivity analyses were run in order to check whether changes in the value of a variable have the anticipated effect on the results. One-way sensitivity analyses were performed on utility and probability data.

As mentioned, transition probabilities among the health states were assumed to be equal for options of mastectomy and lumpectomy for the purpose of simplification. However, it is known that the probability of transition from any state to local recurrence state (if possible) is actually higher for lumpectomy. This difference decreases total reward for lumpectomy. On the other hand, the probability of salvaged after local recurrence is also higher for lumpectomy and as estimated, this difference increases total reward for lumpectomy. Thus, one-way sensitivity analysis was performed in order to observe the effect of the differences in those probabilities.

First of all, the transition probabilities from NED, NEDI, and NEDII states to Local Recurrence state increased 1%, 5%, 10%, 20% and 50% systematically and the differences were analyzed. The results of this analysis are shown in Table 4.3. As seen, the result was not affected up to 5%; the QALY value was still higher than that of mastectomy. However, when the change was increased to %5, the QALY value for lumpectomy became equal and when it was increased to %10, it became lower than mastectomy. It means that, threshold value was observed at 5%. Threshold value can be observed in Figure 4.6 distinctly.

Table 4.3. One-way Sensitivity Analysis for Transition Probability of Local Recurrence

Lumpectomy	QALY	
Adjustment	MEAN	SD
Baseline	700.72	22.79
1%	687.47	22.82
5%	641.11	25.09
10%	596.16	22.2
20%	530.56	28.54
50%	409.41	32.4



Figure 4.6. One-way Sensitivity Analysis on Local Recurrence Probability

Secondly, since the probability of salvaged after local recurrence is also higher for lumpectomy, two-way sensitivity analysis was performed on probabilities of local recurrence and salvage in order to observe the effect of these probabilities simultaneously. Transition probabilities from Local Recurrence to Salvage state increased systematically while holding local recurrence increase at specific values. The results of this analysis can be seen in Table 4.4. Since increasing transition probability from local recurrence to salvage cause increasing the total reward, it can be observed more than one threshold values at different points. In this analysis, only two threshold values were observed. First one was observed when the probability of local recurrence was increased to 5% and the probability of local recurrence was increased to 6% and the probability of salvage was increased to 25%. As seen from the table, the probability of salvage does not affect QALY results as much as the probability of local recurrence.

		Local Recurrence Probability Change (%)							
		4	4 5 6 7						
ity	0	654.96	641.11	634.35	622.43				
abili %)	5	657.29	645.12	635.76	623.43				
robs se (9	10	656.61	646.4	635.96	624.13				
ge P nang	15	657.36	648.8	637.35	626.66				
lva Cl	20	657.89	649.98	639.45	627.65				
Sa	25	662.63	650.21	641.17	627.91				

Table 4.4. Two-way Sensitivity Analysis on Local Recurrence and Salvage Probability

After studying the probability data, one-way sensitivity analysis was performed on the utility data for lumpectomy and mastectomy in order to observe the effect of each utility of health states. This study was performed by evaluating QALY values for minimum and maximum utility values of health states which were observed in the public preferences. The analysis results are tabulated in Table 4.5. The model was much more sensitive for utility of no evidence of disease state, as expected. The utilities of no evidence of disease but having hormone therapy state, chemotherapy state and metastasis state also affected the model relatively. However, the model was not sensitive for the other parameters, utilities of local recurrence stage and salvaged stage.

Health States	MEAN-Lum	MEAN-Lumpectomy		MEAN-Mastectomy	
Baseline	700	).72	641	.62	
	Min	Max	Min	Max	
U1	651.16	718.93	580.52	687.25	
U2	686.08	708.21	616.39	652.67	
U3	682.17	713.25	621.39	647.6	
U4	693.46	703.61	631.3	642.6	
U5	695.2	703.11	638.98	640.13	
U6	683.37	732.03	617.44	671.57	

Table 4.5. Sensitivity Analysis on Utility Values

# **CHAPTER 5**

### **CONCLUSIONS AND FURTHER RESEARCH AREAS**

The main objective of this study was to analyze the decision context of early stage breast cancer patients in relation to two main treatment options, and to construct a decision making model that incorporates patient preferences over differing health state prospects as well as incorporating other typical complexities of such decisions situations such as uncertainty.

### 5.1 Summary of Study and Findings

In the first part of the study definition of the problem and the reasons of studying this problem were given. Then, in the second part, review of a comprehensive literature search that covers decision making techniques used in health care systems, utility assessment techniques and their applications on early breast cancer treatments were presented.

Two important steps during this development task, the disease process modeling and the outcome measure modeling, were represented in the Chapter 3. In the first section of this chapter, regardless of clinical history of the breast cancer following surgery, type of surgery is mastectomy or lumpectomy, was modeled as a Markov Tree. Natural history of the breast carcinoma was defined by seven basic health states in the model. All events were represented as transitions from one health state to another.

Health states used in the model were characterized by transition probabilities into other states and by utilities as a measure of quality of life gained by the transitions. The multi-attribute utility model, as an outcome evaluation measure, was constructed for utility attributed to health states. Five main attributes and 3 subattributes were determined in order to characterize health states. Healthy volunteers assigned individual utility values and scaling constants of attributes for each health state. Overall utilities of each participant for each health state were evaluated by using their results obtained from public survey as data in the multi-attribute utility model. According to the results obtained from multi attribute utility model, average overall utility values assigned by participants were higher for lumpectomy operation, especially if there was no evidence of disease. When the cancer came back, participants did not care what surgical treatment option she was operated with, which means that after reoccurrence of disease, utility values for both treatment options were equal or very close to each other.

Another important section of this chapter was validity check of multi-attribute utility model. This process was performed by comparison between multi-attribute utility results and global ratings for each health state, which were obtained by another survey (Group 2). In the second survey standard gamble technique was used to get global ratings of each health state. Descriptive statistics showed that obtained mean utility values obtained from this method were higher than multiattribute utility model results for most health states. Additionally, it was observed that after mastectomy and lumpectomy, for the first four health states mean utility values are nearly same or close to each other in both measurements; but for the last two health states, mean value differences are significantly higher. Then, in the next step, statistical difference between two population means was analyzed for each health states by considering samples both normally distributed and nonparametric. According to two-sample t-test and Wilcoxon rank sum test results, for six health states, multi-attribute utility model results match global ratings. On the other hand, for the rest of six health states, values from multi-attribute utility model and global ratings do not match. An important result from this analysis was that multi-attribute utility model gave highly correlating results especially for the no-evidence of disease health states. On the other hand, as the health state got worse, consistency of results became poorer. The reason for that may be use of general population in the analysis, because if assessing health state condition is similar to participants' current conditions, they can evaluate more objectively. However, as the assessing health state condition becomes different from their current condition, imagining being in that health state and assessing the condition objectively becomes difficult.

In addition to comparison of two samples statistically, in order to perform more effective consistency check, a random sample of 15 was drawn from control group (Group 2) and they were also applied multi attribute utility model assessment procedures, so one sample was performed the both of the assessment methods and by using their results whether a subject's holistic preference judgments are consistent with an algebraic utility model was determined by "construct validation". A systematic method, Multitrait-Multimethod (MTMM) Matrix method, was performed for construct validation. In this method different classes of correlation coefficients were identified and compared with each other and some necessity conditions were looked for validation. Results were sufficient to accept that multi attribute utility method is reasonably valid.

Finally, after development of the decision model and assigning utility values and transition probabilities, the process was represented in Treeage-Pro 2006 Suit software, simulated by Monte Carlo Simulation. Results of this simulation were analyzed and necessary sensitivity analyses were performed in order to observe the effects of parameters. The output was quality adjusted life years (QALY) during 10-year survival. The runs showed that, if the subject had mastectomy, mean value for the quality adjusted life years gained (QALY-gain) was 641.62; on the other hand, if the preference was lumpectomy, the mean value for the QALY-gain was

700.44 at this time. The results showed that, quality adjusted life years for lumpectomy is higher than mastectomy on the average. That means, according to the preferences of participants, decision model points to lumpectomy for surgical operation. Since the utility values and transition probabilities were not certain in the model, one-way and two-way sensitivity analysis were performed. Threshold values for optimal decisions were: 641.11 if the probability of local recurrence was increased up to 5% and 641.17 if the probability of local recurrence was increased up to 6% while salvage probability was increased up to 25% for lumpectomy option. Secondly, effects of utility were analyzed, and observed that the model was much more sensitive to utility of no evidence of disease, relatively sensitive to the utilities of no evidence of disease but having hormone therapy stage, chemotherapy stage and metastasis stage, however, was not sensitive to utilities of local recurrence stage and salvaged stage.

In conclusion, the decision model was developed with reasonable success for early stage breast cancer patients, and tested by using general public data. The results obtained from these data showed that lumpectomy was more favorable for these participants. The most important result was that the model is applicable for determining patient preference by considering their personal parameters such as, individual utility values, and scaling constants. This model is also of help for surgeons' decisions. As Fryback (1974, 1978) and Ransohof (1976) pointed out, decision analysis improves physicians' intuition or judgment and increases the attention focused to anticipate all possible outcomes. Thus, the assessment process performed in this modeling effort prepares the mind for making a correct decision. It should be noted that we do not imply that physicians currently make bad decisions; rather, we interpret our study to show that good decisions may be improved, on the average, by making use of such decision theory concepts. This model can be applied to patients by an expert or surgeon and according to results of the model, they can decide more easily for treatment option. Needless to say, the results of the model cannot be compulsory decision; it only gives an opinion or

guides for correct decision. Briefly, the application of the decision tool is as follows:

Step 1. Assessment of Individual Utility Scales

The first step is the assessment of the person's dimensional utility function for each attribute. This is achieved by performing a survey given in Appendix C to the patient.

Step 2. Assessment of Individual Scaling Constants

The next step is, determining scaling constants in order to indicate the relative importance of all attributes. First of all, Swing Rating Method is applied, as in Appendix C, to the patient for this purpose and the attributes are ranked. After ranking procedure, relative weights are obtained by SMARTER, from Table D.1 shown in Appendix D.

Step 3. Assessment of Overall Utility Values of Health States

After the assessment of individual utility values and scaling constants, the next step is assessment of overall utility values of health states by using 8-attribute additive utility function as follows:

$$U_{K} = k_{1}U_{1}(X_{1}^{j}) + k_{2}U_{2}(X_{2}^{j}) + k_{3}U_{3}(X_{3}^{j}) + k_{4}U_{4}(X_{4}^{j}) + k_{5}(k_{6}U_{6}(X_{6}^{j}) + k_{7}U_{7}(X_{7}^{j}) + k_{8}U_{8}(X_{8}^{j}))$$

All aggregate utility values for twelve health states are calculated from utility functions given in Table 3.2.

### Step 4. Evaluation of the Decision Model

Final step in this tool is defining utility values and probabilities in the Markov Tree, and executing evaluation of this model. Results provide the gained quality adjusted life years for each treatment option, and the patient can see which one provides higher QALY value with respect to her parameters, and gives her decision by considering this result.

The model is not perfect and cannot be considered as generic measure such as HUI indexes or QWB scales. We performed this study to take the first steps in this area and to attract attention for using decision theoretic techniques in health care in Turkey.

# 5.2 Limitations of the Study

There were a number of factors that defined some boundaries or limitations on this study. Below is a brief discussion of these limitations.

### • Model

The disease progress was represented by a Markov chain and seven basic health states were designated. In the real context of such a problem, there are many more health states. For example, in reality hormone therapy can be carried on up to five years. In the model it was considered that if the patient is in the health state of NED I and in the next interval she remains in the same state, the utility of that state remains the same since she is in the same state. However, this is not entirely right. In the second year of adjuvant therapy, patient's utility is lower, so that another health state should be defined for each year of adjuvant therapy. However, it was assumed that these utility differences were negligible with respect to other transitions between health states and considered as only one state.

The principal analysis of the model focuses on early stage breast cancer patients. Patients' age interval is considered between 45-55 year-old so that they are assumed to be premenopausal. The model has been structured for defined breast cancer patients, and therefore usage of the model is limited to these patient

characteristics. Although many facets of the model are similar to other types of breast cancers, the results cannot be directly applied as a policy guideline.

### • Attributes

Another limitation that should be considered was the attributes used in the Multi Attribute Utility Model. In order to characterize health states a number of attributes identified in the literature. A number of health status classification systems were studied and the suitable attributes for our problem were selected from these metrics (see Chapter 3). Then by consulting oncologists, some attributes were omitted since they seem irrelevant or less important than others, so that model was simplified. However, these omitted attributes could make some differences and because of that number of attributes could limit the results.

A valuable improvement to the present study would be to generate the outcome measure attributes entirely anew, tailored to our culture. For this purpose, as mentioned previously, identifying attributes is best done using the "objectives hierarchy" (due to Keeney and Raiffa (1993)) uniquely constructed for this decision context.

### Population

Utility assessment of the health states in the model and the validation of the model were performed on university students (a segment from general population). Ideally, the utilities of the health states ought to belong to the patients, because these are the only people who know what is really like to be in these health states and therefore the only ones capable of expressing "true" preferences over them. However, this procedure may not be considered as ethical because patients may be oversensitive and such interviews may affect their psychology negatively. Because of these reasons, sometimes physicians don't give permission for interviewing their patients. For this reason, using public preferences are considered acceptable for

making health decisions (Torrance, 1978; Boyd, 1990; Dolan, 1999; Cappelli, 2001).

Although, it is believed that the source of preference weights do not affect the base case results of comparison, the research shows that healthy volunteers underestimate the value of health state; because, assessing the health state condition objectively becomes difficult for people without direct experience of the health state. Thus, some deviations could be observed in results if early stage breast cancer patients performed the study.

### Probabilities

Transition probabilities in the markov model were obtained by using subjective probability assessment techniques. These probabilities were acquired by using expert judgments. Although subjective probability is scientific and accepted as a method for probability assignment, using "objective" probabilities based on hospital records could provide more realistic results. However, the data that we need was not kept entirely and reliably. We, researchers in this field, should help design ways for hospitals to keep such data for future studies to be more robust.

### Validation

The validity check was performed by correlating the values obtained from model and the global ratings. Standard gamble technique was preferred for the global rating because of the certain properties of this method, which were mentioned previously. However, the standard gamble was time consuming, it can only be handled in face to face interview and it required well trained members as participants with high level of education. These factors limited the characteristic of general population and the group size, which affected the study efficiency. Additionally, during utility assessment procedure, direct rating technique was performed for assessment of individual utility values. On the other hand, during validation of process standard gamble technique was performed for global ratings. Thus, using different techniques for assigning utility in the multi attribute utility model and in the global ratings could cause some errors such that risk of death preference could affect participants' assessment in standard gamble technique. So, this point should be taken into account while validation results are studied.

### • Reliability

Health states should ideally be measured second time with the same measurement method after a period of time, re-tested, and then we can conclude that our measurement technique is reliable if the results are consistent. Reliability is an important concept in validation such that correlation coefficients obtained from reliability data are used for construction of MTMM matrix. However, the analysis of the reliability could not be performed for this study because of practical difficulties. As mentioned previously, second measurement should be performed at least after 6 months for effective study. However, to reach same participants and perform the study is almost impossible during our study period.

# **5.3** Suggestions for Further Research

This study can be extended through a number of research studies, some of which are mentioned in this section. Naturally, the first suggestion that comes to mind is to work to eliminate the limitations that were discussed above. More detailed Markov model can be developed; more health states can be defined and observed if the detailed model affects the main results of the study. Patient characteristics can be extended and the model can be adapted to other presentations of breast cancer. Real patients can perform utility assessment and validation process, and results can be compared. More generalized multi-attribute utility model can be developed in order to observe effect of additive independence property on the results. And finally reliability analysis can be performed in the future.

In addition to eliminating the limitations of the study, we have some other suggestions in order to extend this study. As mentioned previously, the health sector is an open area for the industrial engineers, and this study is the very first in our country. So, this instrument can be improved in order to increase its performance. This model was performed on particular university students and it reflected their preferences. However, attaining generalizable results is the purpose of scientific research, therefore, by further research, this instrument can be generalized for Turkish people like health status classification systems developed by Torrance (1982), Kaplan (1988), and the like.

In this study, breast cancer patients' preferences for health outcomes were evaluated with respect to quality adjusted life years (QALY). Using these study results, a cost effectiveness analysis can be performed. As known, cost effectiveness analysis is a very useful technique for the economic evaluation of the clinical alternatives. It examines both value consumed (costs) and value produced (health outcome), and by this analysis cost per unit health is calculated. Thus, patient preferences can be determined by considering both quality of life and cost of the treatment.

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# **APPENDIX A**

# **ORIGINAL AND TURKISH VERSIONS OF EQ-5D**

Original and Turkish versions of EQ-5D, which is one of the pre-scored multi attribute health status classification systems and developed by EuroQol group (1990), can be examined in this part. This generic measure is used in order to evaluate patient's preferences for health outcomes.

The EuroGol Group	FQ - 5D
The EuroQol Group is an international group of researchers who co-operate in the field of measuring health-related quality of life. Membership requires active contribution to the development of the EQ-5D. The annual EuroQol meeting provides an opportunity to share results of investigations and experiences in the field.	A Measure of Health-related
Information	Quality of Life
<ul> <li>To obtain an EQ-5D User Guide</li> <li>To add your name to the EuroQol Group's mailing list</li> <li>Regarding membership of the EuroQol Group</li> </ul>	from the EuroQol Group
Please contact:	
rrank de Charro EuroQol Group Business Manager Centre for Health Policy and Law Erasmus University Rotterdam	X
P.O. Box 1738 3000 DR Rotterdam The Netherlands	
clephone +31 10-408-2364 av +31 10-452-5303	
e-mail deCharro@gbr.fig.cur.nl	
Bada X, Fernandez E, Segura A, Influence of socio domographic and heulth status anattaes or e-aluation of health states in a Sparser population. European Buotana O Factor Health vol 5 (1958) pp 69: 93. Buotana O Factor Health vol 5 (1958) pp 69: 93. Dooran P, Macterio M, and 10 (1958) pp 60: 50 (2010) Pocy Vol 37 (1956) pp 503 (2010) EuroColi health states. Meadu, Cure Vol 35 (1957) pp 1055 (100) et al. CureColi health states. Meadu Cure Vol 35 (1957) pp 1055 (100) EuroColi health states. Meadu Cure Vol 35 (1957) pp 1055 (100) EuroColi health states. Meadu Cure Vol 35 (1957) pp 1055 (100) EuroColi health states. Meadu Cure Vol 35 (1957) pp 1025 (100) EuroColi health states. Meadures on fraethistics (cure-triat and the EuroColi et al. Cure Vol 25 (1957) pp 1025 (100) EuroColi et al. 2010) EuroColi et al. 2010 (1957) pp 1025 (100) EuroColi et al. 2010) EuroColi et al. 2010 (1957) pp 1025 (100) EuroColi et al. 2010) EuroColi et al. 2010 (1957) pp 1025 (100) EuroColi et al. 2010) EuroColi et al. 2010 (1957) pp 1025 (100) EuroColi et al. 2010) EuroColi et al. 2010 (1957) pp 1025 (100) EuroColi et al. 2010) EuroColi et al. 2010 (1957) pp 1025 (100) EuroColi et al. 2010) EuroColi et al. 2010 (1957) pp 1025 (100) EuroColi et al. 2010) EuroColi et al. 2010 (1957) pp 1025 (100) EuroColi et al. 2010) EuroColi et al. 2010 (1957) pp 1025 (100) EuroColi et al. 2010) EuroColi et al. 2010 (1957) EuroColi et al. 2010) EuroColi et al. 2010 (1957) EuroColi et al. 2010) EuroColi et al. 2010 (1957) EuroColi et al. 2010) EuroColi et al. 2010 (1957) EuroColi et al. 2010) EuroColi et al. 2010 (1957) EuroColi et al. 2010) EuroColi et al. 2010 (1957) EuroColi et al. 2010) EuroColi et al. 2010 (1957) EuroColi et al. 2010) EuroColi et al. 2010 (1957) EuroColi et al. 2010) EuroColi et al. 2010 (1957) EuroColi et al. 2010) EuroColi et al. 2010 (1957) EuroColi et al. 2010) EuroColi et al. 2010 (1957) EuroColi et al. 2010) EuroColi et al. 2010 (1957) EuroColi et al. 2010) EuroColi et al. 2010 (1957) EuroColi et al. 2010) EuroColi et al. 20	EQ-5D
(193) p. 237-246 Kind P. Dalan P. Gudet C. Williama A. Varattoris in population health stutus results from a United KingSam national questionitaine survey. Birlinsh Medical Journal Vol. 216 (1956) p. 736 740-736.	A generic, single index measure Validated in several countries
Ohinnaa A. Sintonen H. Olaviy of life of the Frontin population measured by EuroOon EuroOot Jeensy meeting Barcelood Discussion Parietis. Eds. Buolu X. Heriorani J. Segura A. Inshidi Umeetistan de Salua Pudica de Curduniya (1995) juj. 16.1.172	Measuring health for clinical and economic apprais. Supported by an international research proving

> each with 3 levels) and a visual analogue scale on which The EQ-5D consists of a questionnaire which classifies the patient into one of 243 health states (5 dimensions,

Background

Introduction

patients rate their own health between 0 and 100.

As well as self-rated health status, valuations can be generated for other EQ-5D health states from different

valuing EQ-5D health states

- . .

Values for a subset of health states have been derived from the general public in Finland. Germany, the Netherlands, Norway, Spain, Sweden, the UK and the

health professionals; general public.

patients;

.

groups:

carers;

US. For all the 243 possible EQ-5D health states, values have been derived using modeling and statistical

techniques.

purpose

The EQ-5D generates a single numeric index of health status. It therefore can be used as a measure of health outcome in both clinical and economic evaluation. It is recommended for use alongside other more detailed generic measures such as the SF-36, the NHP or the SIP.

or disease-specific measures.

usage

The EQ-5D is being widely used throughout Europe as well as in Australia, Canada and the US.

-

# 118





The EQ-5D instrument was simultaneously developed in the following languages: *Dutch* • *English* • *Finnish* • *Norvegian* • *Swedish* 

Provides a simple descriptive profile and an overall

numeric estimate of health-related quality of life which can be used for both elinical and economic

Designed for use alongside disease-specific or

evaluations of health care.

other generic measures of quality of life.

Applicable for use in a wide range of health con-

ditions and treatments.

Contents

Other versions available: Auxtralian • Catalan • Croatian • Czech • Danish • French • German • Italian • Palish • Québéroixe • Spanish • Turkish.

Versions in preparation: *Hebrew* • Japanese • Portuguese • US.

# EQ-5D in practice

- Designed for self-completion by patients.
- Cognitively simple, taking only a few minutes to complete, and suitable for use as a postal questionnaire.
- Classification of health based on a five-dimensional system (see below).
- Valuation on a 0 to 100 scale by means of a visual analogue scale (see figure on the right).

		Г
Mobility I have no problems in waiking about. I have some problems in waiking about. I am confined to bed.	000	
Self-Care Thave no problems with self-care. I have some problems washing or dresing myself. I am unable for wash or dress myself.	000	
Usual Activities (eg. work, study, housework, lamily or leisure activities) Thave on problems with performing my usual activities. Thave some groblems with performing any usual activities. I am unable loperform my usual activities.	000	
Pairvdiscomfort Thave no pain or discomfort. Thave moderate pain or discomfort. Thave extreme pain or discomfort.	000	
Anxlety/depression I am noi anxious or depressed. I am moderately anxious or depressed. I am extremely anxious or depressed.	000	



Dr. F. Th. de Charro EuroQol Group Business Manager PO Box 4443, 3006 AK Rotterdam, Netherlands: E-mail fdecharro@csi.com www.euroqol.org



### NOTES ON THE USE OF EQ-5D DEVELOPED BY THE EUROQOL GROUP May 2000

### Clinical use of the EQ-5D

In most clinical uses, only pages 2 and 3 of EQ-5D are used. Patients are asked to assess their own health by way of the descriptive statements on page 2 (EQ-5D self-classifier) and then on a visual analogue scale (EQ-VAS) on page 3. On page 2, answers are coded as 1 (no problem), 2 (some or moderate problems), or 3 (unable or extreme problem). These are not added together, but act as a description of a health state, e.g. state 22213 indicates some problems with mobility. self care and usual activities, no pain or discomfort but extremely anxious or depressed. A health state score is obtained from the EQ-VAS "thermometer" on page 3 by asking the respondent to draw a line from the box marked "your own health state today" to the appropriate point on the EQ-VAS. Leading zeros should be included, e.g. a health state could be rated 070. Brief demographic information is requested on page 4 of EQ-5D.

### Economic use of EQ-5D

In the economic evaluation of health care such as cost-effectiveness analyses, Quality Adjusted Life Years (QALY's) are sometimes used to compare the results of different health programmes. QALY calculations are based on information generated from quality of life indices combined with information about the number of life years gained.

One method of using EQ-SD for economic evaluation would be to use the patients' own estimates of their quality of life derived from the page EQ-VAS as described above. However, EQ-SD health states, defined by the health state classification on page 2 may also be converted to a score using "sets of values" derived from general population samples.

Over the past few years, the EuroQol Group has been engaged in several research projects exploring this issue using different methods, for example, the EQ-5D valuation questionnaire has been used to generate values elicited from general population samples for a subset of health states in Finland, Germany, Greece, Netherlands, Spain, Sweden, UK and US. More recent research has concentrated on statistical modeling to generate values for all the 243 theoretically possible health states defined by EQ-5D.

The Business Management of the EuroQol Group acts as an intermediary supplying information on the background to research in the various countries. However to date, the research carried out as part of the MVH Project at York University, UK, using the Time Trade-Off method (TTO) has been underpinned by the most elaborate research effort. Values for the 243 possible EQ-5D health states plus unconscious are available, based on data collected from a representative survey of the UK general public'. Please contact Paul Kind directly for this information. His details are: Paul Kind, Centre for Health Economics, University of York, UK (Tel: +44 1904 433653, Fax: +44 1904 433644, E-mail: pk1@york.ac.uk)

### Data analysis

An "off the shelf" software package such as SPSS, SAS or BMDP may be used to analyse EQ-5D data.

### Further information

A full user guide is available on request from the EuroQol Business Management in Rotterdam, NL.

### Conditions for usage

EQ-5D may be used without cost provided that the research is not being undertaken for commercial purposes, e.g. the testing of a new product by the Pharmaceutical Industry. More information on the Group's policy in these instances can be obtained from the EuroQol Business Management.

For non-commercial academic and clinical use, the EQ-5D is freely available, however the Group does require that only official language versions of EQ-5D are used and that users register their project. Free use of EQ-5D also implies that users are willing to share their knowledge with the Group regarding the application of EQ-5D as well as information that adds to the methodological knowledge of EQ-5D, e.g., issues surrounding validity and reliability. The Group is also particularly interested in demographic data, comparative data (where EQ-5D has been used alongside other instruments) and valuation data as well as data relating to the EQ-5D self-classifier and the EQ-VAS rating scale.

<sup>&</sup>lt;sup>1</sup> Dolan P. Modeling valuations for EuroQol health states. <u>Medical Care</u> Vol 35, No. 11, pp. 1095-1108. 1997.

EuroQol Group Business Management

April 2002

Scoring EQ-5D: Notes

The information derived from the descriptive system (Page 2 of EQ-5D) may be converted to a score using "sets of values" derived from population samples. A number of different "sets" have been derived in different countries using different techniques. EU funding has enabled the EuroQol Group to harmonize this work with a view to producing a European set of values. Papers have been submitted to journals but until this work has been published (and in the absence of a national value set), The EQ Group would recommend using the data collected in the UK. This research carried out as part of the MVH Project at York University, UK, using the Time Trade-Off method (TTO) has been underpinned by the most elaborate research. Mean observed values for the 243 possible EQ-5D health states plus unconscious are available, based on data collected from a representative survey of the UK General public. (Dolan P. Modeling valuations for EuroQol health states. Medical Care Vol 35, No. 11, pp. 1095-1108. 1997)

A WORD document is available that can be used to convert the 5 dimensional 3 level system into a single index utility score calibrated in terms of the UK population survey mentioned above. An SPSS syntax file that will make matters easier is also available.

If you would like more specific details about the scoring, and/or a copy of the UK EQ-5D information package (that includes the UK value set) please contact EQ researcher Paul Kind directly. His details are: Paul Kind, Centre for Health Economics University of York, UK. Tel: +44 1904 433653; Fax: +44 1904 433644; e-mail: <u>pk1@york.ac.uk</u>.

> Frank de Charro, EuroQol Group Business Manager PO Box 4443, 3006 AK Rotterdam, The Netherlands

# Scoring EQ-5D health states

Values for the 243 health states defined by the EuroQoL classification have been calculated using a regression model. The following worked example indicates how these coefficients are to be used so as to compute the estimated values for each state.

EuroQoL dimension	Level 2	Level 3
Mobility	0.069	0.314
Self-care	0.104	0.214
Usual activity	0.036	0.094
Pain / discomfort	0.123	0.386
Anxiety / depression	0.071	0.236
	Constant = 0.081	N3 = 0.269

Calcula	ting H	<u>EQ-5D</u>	state	scores	- a	worked	example	e
Calcula	ungi	10-20	State	scores	- a	worked	example	e

The arithmetic needed to recover the estimated value for any health state from this table of decrements is given by the following example:

Taking health state 1 1 2 2 3

Full health (1 1 1 1 1) = 1.0

Constant term (for any dysfunctional state)(subtract 0.081)

Mobility. level 1(subtract 0) Self-care. level (subtract 0) Usual activity. level 2(subtract 0.036) Pain / discomfort. level 2(subtract 0.123) Anxiety / depression. level 3(subtract 0.236)

Level 3 occurs within at least 1 dimension(subtract N3 parameter 0.269).

Hence the estimated value for state 1 1.2 3 3 is given by

1.0 - 0.081 - 0.036 - 0.123 - 0.236 - 0.269 = .255

Estimated weights for EQ- 5D health states 1 1 1 1 1 2 0.848 1 1 1 1 2 0.796 1 1 2 2 0.725 1 1 1 2 3 0.291 1 1 2 3 0.291 1 1 3 1 0.264 1 1 3 2 0.193 1 1 3 3 0.028 1 2 1 2 0.812 1 2 1 2 0.812 1 2 2 1 0.760 1 2 2 2 0.689 1 2 2 1 0.760 1 2 2 2 0.689 1 2 2 3 0.255 1 1 2 3 1 0.228 1 1 2 3 2 0.157 1 2 3 3 -0.008 1 3 1 1 0.556 1 3 1 2 0.485 1 3 1 2 0.485 1 3 1 3 0.320 1 3 2 1 0.433 1 3 2 2 0.362 1 3 2 2 0.362 1 3 3 2 0.099 1 3 3 1 0.170 1 3 3 2 0.099 1 3 3 1 0.170 1 3 3 2 0.099 1 1 3 3 2 0.099 1 1 3 3 2 0.099 1 1 3 3 2 0.099 1 1 3 3 2 0.099 1 1 3 3 2 0.099 1 1 3 3 2 0.099 1 1 3 3 2 0.099 1 2 1 2 0.744 1 2 1 1 0.815 1 2 1 1 0.815 1 2 1 2 1 0.692 1 2 1 2 1 0.692 1 2 1 2 1 0.692 1 2 1 2 1 0.692 1 2 1 2 1 0.692 1 2 1 2 1 0.692 1 2 1 2 1 0.779 1 2 2 1 2 0.788 1 2 2 1 0.056 1 2 2 1 1 0.779 1 2 2 1 2 0.788 1 2 2 1 0.056 1 2 2 1 0.056 1 2 2 1 1 0.779 1 2 2 1 2 0.053 1 2 2 3 0.151 1 2 2 3 0.151 1 2 2 3 0.151 1 2 3 1 0.124 1 2 3 1 0.124 1 2 3 2 0.053 1 2 3 2 0.053 1 2 3 2 0.053 1 2 3 2 0.053 1 2 3 2 0.053 1 2 3 2 0.053 1 2 3 2 0.053 1 2 3 2 0.053 1 2 3 3 0.016 1 2 3 3 0.016 1 2 3 3 0.016 1 2 3 3 0.016 1 2 3 3 0.0216 1 2 3 2 0.053 1 2 3 3 0.0216 1 3 0.026 1 2 3 3 0.0216 1 3 0.026 1 3 0.026 1 3 0.026 1 3 0.026	1       3       1       1         1       3       1       2         1       3       1       2         1       3       1       2         1       3       1       2         1       3       1       2         1       3       1       3         1       3       1       3         1       3       1       3         1       3       1       3         1       3       1       3         1       3       2       1         1       3       2       1         1       3       2       1         1       3       2       2         1       3       2       2         1       3       2       2         1       3       3       2         1       3       3       2         1       3       3       2         1       3       3       2         1       3       3       3         1       3       3       3         1	0.365 0.200 0.313 0.242 0.077 0.050 -0.021 -0.186 0.400 0.329 0.164 0.277 0.206 0.041 0.014 -0.057 -0.222 0.342 0.271 0.106 0.219 0.148 -0.017 -0.044 -0.115 -0.280 0.850 0.779 0.345 0.727 0.656 0.222 0.195 0.124 -0.041 0.814 0.743 0.309 0.691 0.620 0.186 0.159 0.088 -0.077 0.487 0.416 0.251 0.364 0.293 0.128 0.101 0.030 -0.135 0.746 0.675 0.241 0.623 0.552 0.118	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
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•

$\begin{array}{cccccccccccccccccccccccccccccccccccc$	3 3 2 3 2 -0.371 3 3 2 3 3 -0.536 3 3 3 1 1 0.028 3 3 3 1 2 -0.043 3 3 3 1 3 -0.208 3 3 3 2 1 -0.095 3 3 2 2 -0.166 3 3 3 2 2 -0.166 3 3 3 2 3 -0.331 3 3 3 1 -0.358 3 3 3 2 -0.429 3 3 3 3 2 -0.429 3 3 3 3 -0.594 Unconscious [ -0.402 ] Note : this value is the mean observed score. It does not result from the regression model.
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Source : A1 TARIFF BASED ON UK SURVEY (1993)
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	an an an an an an an an an an an an an a
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	t e a Ser to a to a to a to a to a to a to a to
3       2       3       2       3       -0.221         3       2       3       3       1       -0.248         3       2       3       3       2       -0.319         3       2       3       3       3       -0.484	* * <u>*</u> * *
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
3 3 2 3 1 -0.300	

```
pute value = 1.0.
if (mob eq 2) value = value - .069.
If (mob eq 3) value = value - .314.
if (selfc eq 2) value = value - .104.
if (selfc eq 3) value = value - .214.
if (uact eq 2) value = value - .036. if (uact eq 3) value = value - .094.
if (pain eq 2) value = value - .123.
if (pain eq 3) value = value - .386.
if (mood eq 2) value = value - .071.
if (mood eq 3) value = value - .236.
if (mob ne 1 or uact ne 1 or selfc ne 1 or pain ne 1 or mood ne 1)
value = value - .081.
if (mob eq 3 or selfc eq 3 or uact eq 3 or mood eq 3 or pain eq 3)
value = value - .269.
if (missing(mob) or missing(uact) or missing(selfc) or missing(pain) or missing(mood))
value = 9.
                                                 .
missing values value (9).
```



# Sağlık Anketi

Turkish version

Aşağıda, her grubun karşısında bulunan kutulardan birine yandaki gibi bir işaret koyarak (⊠ bu şekilde), bugünkü sağlık durumunuzu en iyi ifade eden cümleciği işaretleyiniz.

-

Hareket edebilme		
Yürürken, hiç bir güçlük çekmiyorum		
Yürürken bazı güçlüklerim oluyor		i k
Yatalağım		
Kendi Kendine Bakabilme		
Kendime bakmakta güçlük çekmiyorum		
Kendi kendime yıkanırken veya giyinirken bazı güçlüklerim oluyor		
Kendi kendime yıkanancak veya giyinebilecek durumda değilim		
Olağan işler (örneğin ; iş, ders çalışma, ev işleri, aile içi veya		
boş zaman faaliyetleri)		
Olağan işlerimi yaparken herhangi bir güçlük çekmiyorum		
Olağan işlerimi yaparken bazı güçlüklerim oluyor		
Olağan işlerimi yapabilecek durumda değilim		
Ağrı/Rahatsızlık	_	
Ağrı veya rahatsızlığım yok		
Orta derecede ağrı veya rahatsızlıklarım var		
Aşırı derecede ağrı veya rahatsızlıklarım var		
Endişe / Moral Bozukluğu		
Endişeli veya moral bozukluğu içinde değilim		
Orta derecede endişeliyim veya moralim bozuk		
Aşırı derecede endişeliyim veya moralim çok bozuk		
Hayal edilebilecek en iyi sağlık durumu 100 9 🛉 0 8 = 0 7 🛓 0 5 0 4 0 3 = 0 

> Hayal edilebilecek en kötü sağlık durumu

0

Sağlık durumunun ne kadar iyi veya kötü olduğunu ifade edebilmede yardımcı olabilmek için, üzerinde hayal edilebildiğiniz en iyi sağlık durumunu 100 ile, ve hayal edilebildiğiniz en kötü sağlık durumunu ise 0 ile gösterebileceğiniz, (termometreye oldukça benzeyen) bir ölçek çizdik.

Bu ölçek üzerinde, bugünkü sağlığınızın kendi düşüncenize göre ne kadar iyi veya kötü olduğunu işaretlemenizi istiyoruz. Lütfen, bunu; alttaki kutucuktan, şu anki sağlık durumunuzun ne kadar iyi veya kötü olduğunu gösteren noktaya kadar bir çizgi çizerek yapınız. Çizginiz ölçek üstündeki bir noktayı mutlaka kesmelidir.

> Bugünkü sağlık durumunuz

### **APPENDIX B**

# **DEFINITION OF ATTRIBUTES' LEVELS**

#### 1. Physical Function: Mobility and Physical Activities

<u>Level 1.</u> Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift, walk, run, jump or bend.

<u>Level 2.</u> Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend.

Level 3. Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND NEEDING mechanical aids walk or get around.

Level 4. NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND having SOME limitation in physical ability to lift, walk, run, jump or bend.

<u>Level 5.</u> NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NEEDING mechanical aids walk or get around. <u>Level 6.</u> NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NOT being able to use or control the arms and legs.

### 2. Role Function Self Care (Daily Activities)

Level 1. Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities.

Level 2. Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having SOME limitations when playing, going to school, working or in other activities.

<u>Level 3.</u> Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND NOT being able to play, attend school or work.

<u>Level 4.</u> NEEDING HELP to eat, dress, bath and go to the toilet; AND having SOME limitations when playing, going to school, working or in other activities.

Level 5. NEEDING HELP to eat, dress, bath and go to the toilet; AND NOT being able to play, attend school or work.

### 3. Psychological Discomfort (Emotional)

Level 1. Generally happy and free from worry

Level 2. Occasionally fretful, angry, irritable, anxious, depressed or suffering "night terrors"

Level 3. Often fretful, angry, irritable, anxious, depressed or suffering "night terrors"

Level 4. Almost always fretful, angry, irritable, anxious, depressed

<u>Level 5.</u> Extremely fretful, angry, irritable, anxious, depressed usually requiring hospitalization or psychiatric institutional care.

#### 4. Pain

Level 1. Free of pain and discomfort

<u>Level 2.</u> Occasional pain. Discomfort relieved by nonprescription drugs or selfcontrol activity without disruption of normal activities.

<u>Level 3.</u> Frequent pain. Discomfort relieved by oral medicines with occasional disruption of normal activities.

<u>Level 4</u>. Frequent pain; frequent disruption of normal activities. Discomfort requires prescription narcotics for relief.

Level 5. Severe pain. Pain not relieved by drugs and constantly disrupts normal activities.

### 5. Social Function

Level 1. Having an average number of friends and contacts with others.

Level 2. Having a few friends and contacts with others.

Level 3. Having no friends and contacts with others.

### 6. Body Image

<u>Level 1.</u> Having no concern about your appearance, do not feel like yourself and still feeling attractive

<u>Level 2.</u> Feeling self-conscious about your appearance, discomfort about scar, some problems on nakedness.

Level 3. Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes.

Level 4. Feeling ashamed of own body, feeling does not like yourself.

### 7. Fears and Concerns

Level 1. Feeling difficulties with your illness are over and no concern about recurrence

Level 2. Having some concerns about recurrence and feeling uneasy about future health

Level 3. Feeling fear of recurrence and bothered by thoughts about the recurrence of cancer.

Level 4. Feeling fear of death.

### 8. Sexual Functioning

Level 1. Having no problems about sexual relationship and sexual attractiveness

<u>Level 2.</u> Some changes in libido and frequency of sexual relationship negatively.

Level 3. Problems in sexual relationship, lack of sexual interest

Level 4. Loss of libido and sexual dysfunction.

### **APPENDIX C**

# PUBLIC SURVEY FOR ASSESSMENT OF INDIVIDUAL UTILITY SCALES AND SCALING CONSTANTS

# PART I

### SINGLE DIMENSION UTILITY VALUES

Classification of any health state is based on 8 dimensional systems. Thus we can define any health state as a function of these 8 attributes. The aim of this study is to assess the one-dimensional value function for each attribute. In each page you will read about one dimension. Please read definitions and procedures carefully; after that, consider and evaluate each attribute individually.

#### **ATTRIBUTE 1. PHYSICAL FUNCTION**

The degree to health states which reflects patient ability for mobility and physical activities such as arm motion, walk, run, jump etc.



where:

- Level 1: Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift, walk, run, jump or bend.
- Level 2: Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend.
- Level 3: Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND NEEDING mechanical aids walk or get around.
- Level 4: NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND having SOME limitation in physical ability to lift, walk, run, jump or bend.
- Level 5: NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NEEDING mechanical aids walk or get around.
- Level 6: NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NOT being able to use or control the arms and legs.

The aim of this stage of the process is to assess the one-dimensional value function for the attribute of "Physical Function". This will be done by rating the anchor points. As described, this attribute has 6 anchor points (Level 1, Level 2,..., Level 6) and the rating for the Best Level is predetermined: the rating for the Level 1 is 100 (as seen on scale). Now, please read the statements of EACH LEVEL, think carefully and **RATE (between 0–100) EACH LEVEL** (other than Level 1) according to your beliefs. For example after reading definition of Level 2, if you feel that your rating for that level is 80, write as "80" for Level 2 on scale, after definition of Level 3, if you feel that your rating for that level is 65, write as "65" for Level 3 on scale and continue like that.

#### **ATTRIBUTE 2. ROLE FUNCTION**

The degree to health states which reflects patient role function and daily activities such as ability level of eating, dressing, doing housework, bathing, cleaning etc.



The aim of this stage of the process is to assess the one-dimensional value function for the attribute of "Role Function". This will be done by rating the anchor points. As described, this attribute has 5 anchor points (Level 1, Level 2,..., Level 5) and the rating for the Best Level is predetermined: the rating for the Level 1 is 100 (as seen on scale). Now, please read the statements of EACH LEVEL, think carefully and **RATE (between 0–100) EACH LEVEL** (other than Level 1) according to your beliefs. For example after reading definition of Level 2, if you feel that your rating for that level is 80, write as "80" for Level 2 on scale, after that reading definition of Level 3, if you feel that your rating for that level is 65, write as "65" for Level 3 on scale and continue like that.

#### ATTRIBUTE 3. PSYCHOLOGICAL DISCOMFORT

The degree to health states which reflects patient emotional feelings. For example feeling happiness, sadness or depression, being anxious or angry etc.



- Level 1: Generally happy and free from worry.
- **Level 2:** Occasionally fretful, angry, irritable, anxious, depressed or suffering "night terrors".
- Level 3: Often fretful, angry, irritable, anxious, depressed or suffering "night terrors".
- Level 4: Almost always fretful, angry, irritable, anxious, depressed.

**Level 5:** Extremely fretful, angry, irritable, anxious, depressed usually requiring hospitalization or psychiatric institutional care.

The aim of this stage of the process is to assess the one-dimensional value function for the attribute of "Psychological Discomfort". This will be done by rating the anchor points. As described, this attribute has 5 anchor points (Level 1, Level 2,..., Level 5) and the rating for the Best Level is predetermined: the rating for the Level 1 is 100 (as seen on scale). Now, please read the statements of EACH LEVEL, think carefully and **RATE (between 0–100) EACH LEVEL** (other than Level 1) according to your beliefs. For example after reading definition of Level 2, if you feel that your rating for that level is 80, write as "80" for Level 2 on scale, after that reading definition of Level 3, if you feel that your rating for that level is 65, write as "65" for Level 3 on scale and continue like that.

#### **ATTRIBUTE 4. PAIN**

The degree to health states that reflects pain level that patient has.



where:

- Level 1: Free of pain and discomfort.
   Level 2: Occasional pain. Discomfort relieved by nonprescription drugs or self-control activity without disruption of normal activities.
   Level 3: Frequent pain. Discomfort relieved by oral medicines with occasional disruption of normal activities.
   Level 4: Frequent pain; frequent disruption of normal activities. Discomfort requires
  - prescription narcotics for relief.Level 5: Severe pain. Pain not relieved by drugs and constantly disrupts normal activities.

The aim of this stage of the process is to assess the one-dimensional value function for the attribute of "Pain". This will be done by rating the anchor points. As described, this attribute has 5 anchor points (Level 1, Level 2,..., Level 5) and the rating for the Best Level is predetermined: the rating for the Level 1 is 100 (as seen on scale). Now, please read the statements of EACH LEVEL, think carefully and **RATE (between 0–100) EACH LEVEL** (other than Level 1) according to your beliefs. For example after reading definition of Level 2, if you feel that your rating for that level is 80, write as "80" for Level 2 on scale, after that reading definition of Level 3, if you feel that your rating for that level is 65, write as "65" for Level 3 on scale and continue like that.

#### **ATTRIBUTE 5. SOCIAL FUNCTION**

The degree to health states which reflects social activities of patient. Number of friends, relations with people, family relations, and hobbies are important criteria for determining this degree.

SC	CALE:	
(1	00)	
<b>↓</b>	↓	•
Level 1	Level 2	Level 3
(Best)		(Worst)
where:		
Level 1:	Having an average number of friends and contacts with others.	
Level 2:	Having a few friends and contacts with others.	
Level 3:	Having no friends and contacts with others.	

The aim of this stage of the process is to assess the one-dimensional value function for the attribute of "Social Function". This will be done by rating the anchor points. As described, this attribute has 3 anchor points (Level 1, Level 2, Level 3) and the rating for the Best Level is predetermined: the rating for the Level 1 is 100 (as seen on scale). Now, please read the statements of EACH LEVEL, think carefully and **RATE (between 0–100) EACH LEVEL** (other than Level 1) according to your beliefs. For example after reading definition of Level 2, if you feel that your rating for that level is 80, write as "80" for Level 2 on scale.

#### **ATTRIBUTE 6. BODY IMAGE**

The degree to health states which reflects patient satisfaction from her appearance. This attribute determine how disfigurement on her body affects patient such as if she feels ashamedness or avoids nakedness or feels less attractive etc.

ALE:		
0)		
↓		•
Level 2	Level3	Level 4
		(Worst)
Having no concern about your body attractive.	appearance, like yourself a	nd still feeling
Feeling self-conscious about my approblems on nakedness.	pearance, discomfort about	scar, some
Having concerns about appearance, discomfort because of body changes	feeling clothes don't look g s.	good and
Feeling ashamed of own body, feeli	ng does not like yourself.	
	ALE: <b>0</b> ) Level 2 Having no concern about your body attractive. Feeling self-conscious about my app problems on nakedness. Having concerns about appearance, discomfort because of body changes Feeling ashamed of own body, feeli	ALE: <b>0)</b> Level 2 Level3 Having no concern about your body appearance, like yourself a attractive. Feeling self-conscious about my appearance, discomfort about problems on nakedness. Having concerns about appearance, feeling clothes don't look g discomfort because of body changes. Feeling ashamed of own body, feeling does not like yourself.

The aim of this stage of the process is to assess the one-dimensional value function for the attribute of "Body Image". This will be done by rating the anchor points. As described, this attribute has 4 anchor points (Level 1, Level 2,..., Level 4) and the rating for the Best Level is predetermined: the rating for the Level 1 is 100 (as seen on scale). Now, please read the statements of EACH LEVEL, think carefully and **RATE (between 0–100) EACH LEVEL** (other than Level 1) according to your beliefs. For example after reading definition of Level 2, if you feel that your rating for that level is 80, write as "80" for Level 2 on scale, after that reading definition of Level 3, if you feel that your rating for that level is 65, write as "65" for Level 3 on scale and continue like that.

#### **ATTRIBUTE 7. FEARS AND CONCERNS**

The degree to health states which reflects patient fears and concerns about reoccurrence of disease or fear of death because of cancer.



- Level 1: Feeling difficulties with your illness are over and no concern about recurrence
- Level 2: Having some concerns about recurrence and feeling uneasy about future health
- **Level 3:** Feeling fear of recurrence and bothered by thoughts about the recurrence of cancer.
- Level 4: Feeling fear of death.

The aim of this stage of the process is to assess the one-dimensional value function for the attribute of "Fears and Concerns". This will be done by rating the anchor points. As described, this attribute has 4 anchor points (Level 1, Level 2,..., Level 4 and the rating for the Best Level is predetermined: the rating for the Level 1 is 100 (as seen on scale). Now, please read the statements of EACH LEVEL, think carefully and **RATE (between 0–100) EACH LEVEL** (other than Level 1) according to your beliefs. For example after reading definition of Level 2, if you feel that your rating for that level is 80, write as "80" for Level 2 on scale, after that reading definition of Level 3, if you feel that your rating for that level is 65, write as "65" for Level 3 on scale and continue like that.

#### **ATTRIBUTE 8. SEXUAL FUNCTIONING**

The degree to health states which reflects sexual interest and functioning of patient. Frequency, satisfaction, problems during relation, dysfunction etc. are determining factors to degree.



Level 4: Loss of libido and sexual dysfunction.

The aim of this stage of the process is to assess the one-dimensional value function for the attribute of "Sexual Functioning". This will be done by rating the anchor points. As described, this attribute has 4 anchor points (Level 1, Level 2,..., Level 4) and the rating for the Best Level is predetermined: the rating for the Level 1 is 100 (as seen on scale). Now, please read the statements of EACH LEVEL, think carefully and **RATE (between 0–100) EACH LEVEL** (other than Level 1) according to your beliefs. For example after reading definition of Level 2, if you feel that your rating for that level is 80, write as "80" for Level 2 on scale, after that reading definition of Level 3, if you feel that your rating for that level is 65, write as "65" for Level 3 on scale and continue like that.

### PART II

# **SWING-WEIGHTING**

The table below was created for your health states. As you known from the previous part, we have 8 main attributes to determine health states. You read definitions of attributes in previous section. Now we aim to assess the relative contribution of individual attribute to the overall evaluation of alternatives.

As you see the "worst case" provides a benchmark and it will rank seventh (worst) overall. Now imagine that you are allowed to increase just one criterion from worst to best (its maximum level) on the relevant. Which would you choose? Please rank your option as "1" in the table.

Now imagine that you are in a situation where the maximum possible score is achieved on this criterion, but all others remain at their worst. You can now select a second criterion to be raised to the maximum level. What would it be this time? Please rank your option as "2" in the table.

If both of these criteria were raised to the maximum score, what would be the next most important swing? Go on like that and fill the "Rank" column in Table.

Attribute Swung from	Consequence to Compare	Rank
Worst to Best		
Benchmark	$(X_1, X_2, X_3, X_4, X_5, X_6, X_7, X_8)$	9
Physical Function	$(X_1^+, X_2^-, X_3^-, X_4^-, X_5^-, X_6^-, X_7^-, X_8^-)$	
Role Function	$(X_1, X_2^+, X_3, X_4, X_5, X_6, X_7, X_8)$	
Social Function	$(X_1, X_2, X_3^+, X_4, X_5, X_6, X_7, X_8)$	
Pain	$(X_1, X_2, X_3, X_4^+, X_5, X_6, X_7, X_8)$	
Body Image	$(X_1, X_2, X_3, X_4, X_5^+, X_6, X_7, X_8)$	
Fears and Concern	$(X_1, X_2, X_3, X_4, X_5, X_6^+, X_7, X_8)$	
Sexual Function	$(X_1, X_2, X_3, X_4, X_5, X_6, X_7, X_8)$	
Psychological Funct.	$(X_1, X_2, X_3, X_4, X_5, X_6, X_7, X_8^+)$	

Table C.1. Attribute Importance Level Table.

 $X_1$  = Physical Function

X<sub>2</sub> = Role Function (Daily Activities)

 $X_3 =$  Social Function

 $X_4 = Pain$ 

 $X_5 = Body Image$ 

 $X_6 =$  Fears and Concerns

 $X_7$  = Sexual Function

 $X_8$  = Psychological Function

 $X_i^-$  = The worst level on  $i^{th}$  attribute  $X_i^+$  = The best level on  $i^{th}$  attribute

i = 1,2,..., 7

# **APPENDIX D**

# **ROC WEIGHTS FOR INDICATED NUMBER OF ATTRIBUTES**

Rank		Number of Attributes										
	9	8	7		6	5		4		3	2	
1	.3143	.3397	.3704	1.4	083	.45	67	.520	8	.6111	.750	0
2	.2032	.2147	.2276	5 .2	417	.25	67	.270	8	.2778	.250	0
3	.1477	.1522	.1561	l .1	583	.15	67	.145	8	.1111		
4	.1106	.1106	.1085	5 .1	028	.09	00	.062	5			
5	.0828	.0793	.0728	3 .0	611	.04	00					
6	.0606	.0543	.0442	2 .0	278							
7	.0421	.0335	.0204	1								
8	.0262	.0156										
9	.0123											
Rank			-	Numł	oer of	f Attr	ibu	tes				
	16	15		14	1	3		12		11	10	
1	.2113	.2212	.2	323	.24	146	.4	2586		.2745	.2929	)
2	.1488	.1545	.0	1608	.16	577	.1	1753		.1836	.1929	)
3	.1175	.1212	.1	251	.12	292	.1	1336		.1382	.1429	)
4	.0967	.0990	.1	013	.10	)36	.1	1058		.1079	.1096	5
5	.0811	.0823	.0	834	.08	344	.(	)850		.0851	.0846	5
6	.0686	.0690	0.	692	.06	590	.(	)683		.0670	.0646	5
7	.0582	.0579	0.	573	.05	562	.(	)544		.0518	.0479	)
8	.0492	.0484	.0	471	.04	152	.(	)425		.0388	.0336	5
9	.0414	.0400	0. (	381	.03	356	.(	)321		.0275	.0211	l
10	.0345	.0326	.0	302	.02	270	.(	)299		.0174	.0100	)
11	.0282	.0260	0.	230	.01	93	.(	)145		.0083		
12	.0226	.0199	0.	165	.01	23	.(	)069				
13	.0173	.0143	.0	106	.00	)59						
14	.0125	.0092	.0	051								
15	.0081	.0044										
16	.0039											

# Table D.1. ROC Weights for Indicated Number of Attributes

# **APPENDIX E**

# INDIVIDUAL UTILITY VALUES AND RELATIVE IMPORTANCE ORDER OF ATTRIBUTES

Table E. 1. Individual Utility Values of 8 Attributes for Participant 1.

Participant 1	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	85	60	40	20	2
Role	100	80	50	25	10	-
Social	100	60	20	-	-	-
Pain	100	75	50	10	2	-
Body	100	60	20	5	-	-
Fears	100	60	20	10	-	-
Sex	100	70	40	10	-	-
Psychological	100	90	60	30	10	-

Table E. 2. Individual Utility Values of 8 Attributes for Participant 2.

Participant 2	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	90	50	10	5	1
Role	100	90	60	30	5	-
Social	100	80	5	-	-	-
Pain	100	80	50	20	0	-
Body	100	90	10	1	-	-
Fears	100	80	10	5	-	-
Sex	100	50	20	1	-	-
Psychological	100	70	30	5	1	-

Table E. 3. Individual	Utility	Values of 8	Attributes	for Participant 3

Participant 3	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	85	60	50	30	10
Role	100	60	40	20	5	-
Social	100	95	60	-	-	-
Pain	100	80	70	40	20	-
Body	100	90	80	70	-	-
Fears	100	50	30	0	-	-
Sex	100	60	40	30	-	-
Psychological	100	50	30	20	15	_

Participant 4	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	80	60	30	15	5
Role	100	75	50	20	10	-
Social	100	70	40	-	-	-
Pain	100	85	50	20	3	-
Body	100	70	40	20	-	-
Fears	100	60	25	10	-	-
Sex	100	70	50	30	-	-
Psychological	100	90	60	25	15	-

Table E. 4. Individual Utility Values of 8 Attributes for Participant 4.

### Table E. 5. Individual Utility Values of 8 Attributes for Participant 5.

Participant 5	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	75	60	50	30	10
Role	100	75	50	30	5	-
Social	100	85	10	-	-	-
Pain	100	90	60	20	5	-
Body	100	85	60	40	-	-
Fears	100	90	70	40	-	-
Sex	100	80	40	20	-	-
Psychological	100	90	50	30	15	-

# Table E. 6. Individual Utility Values of 8 Attributes for Participant 6.

Participant 6	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	90	50	40	30	0
Role	100	90	50	20	0	-
Social	100	50	0	-	-	-
Pain	100	90	60	30	5	-
Body	100	60	40	10	-	-
Fears	100	80	40	10	-	-
Sex	100	70	30	5	-	-
Psychological	100	80	40	30	5	-

# Table E. 7. Individual Utility Values of 8 Attributes for Participant 7.

Participant 7	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	60	30	20	10	0
Role	100	85	40	20	5	-
Social	100	90	10	-	-	-
Pain	100	85	55	25	0	-
Body	100	65	45	25	-	-
Fears	100	65	35	5	-	-
Sex	100	65	40	25	-	-
Psychological	100	70	30	10	0	-

		5				
Participant 8	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	75	50	30	20	5
Role	100	80	55	35	15	-
Social	100	75	20	-	-	-
Pain	100	85	65	35	15	-
Body	100	85	50	10	-	-
Fears	100	70	40	15	-	-
Sex	100	70	40	15	-	-
Psychological	100	85	65	35	10	-

Table E. 8. Individual Utility Values of 8 Attributes for Participant 8.

Table E. 9. Individual Utility Values of 8 Attributes for Participant 9.

Participant 9	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	75	50	30	10	0
Role	100	80	50	25	10	-
Social	100	60	20	-	-	-
Pain	100	80	50	25	10	-
Body	100	75	50	25	-	-
Fears	100	80	50	25	-	-
Sex	100	80	50	25	-	-
Psychological	100	80	50	25	10	_

Table E. 10. Individual Utility Values of 8 Attributes for Participant 10.

Participant 10	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	80	60	40	15	10
Role	100	80	55	30	10	-
Social	100	65	35	-	-	-
Pain	100	80	65	40	20	-
Body	100	75	55	35	-	-
Fears	100	50	20	5	-	-
Sex	100	75	50	40	-	-
Psychological	100	75	50	25	15	-

 Table E. 11. Individual Utility Values of 8 Attributes for Participant 11.

Participant 11	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	80	50	35	25	15
Role	100	75	50	30	20	-
Social	100	85	50	-	-	-
Pain	100	90	50	30	10	-
Body	100	80	60	50	-	-
Fears	100	80	65	50	-	-
Sex	100	70	60	50	-	-
Psychological	100	95	70	50	30	-

		5				1
Participant 12	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	75	55	45	30	10
Role	100	80	60	30	15	-
Social	100	70	30	-	-	-
Pain	100	85	60	30	15	-
Body	100	80	50	25	-	-
Fears	100	85	60	30	-	-
Sex	100	80	50	25	-	-
Psychological	100	80	50	35	20	-

Table E. 12. Individual Utility Values of 8 Attributes for Participant 12.

Table E. 13. Individual Utility Values of 8 Attributes for Participant 13.

Participant 13	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	60	40	20	10	5
Role	100	80	60	30	5	-
Social	100	90	30	-	-	-
Pain	100	90	70	50	40	-
Body	100	70	60	50	-	-
Fears	100	50	40	20	-	-
Sex	100	80	65	40	-	-
Psychological	100	75	50	10	1	-

Table E. 14. Individual Utility Values of 8 Attributes for Participant 14.

Participant 14	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	85	70	60	40	15
Role	100	85	65	45	15	-
Social	100	65	25	-	-	-
Pain	100	85	70	45	10	-
Body	100	95	65	35	-	-
Fears	100	80	55	25	-	-
Sex	100	80	55	30	-	-
Psychological	100	85	65	40	15	-

Table E. 15. I	Individual	Utility	Values of	8 Attributes	for	Participant	15.
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Participant 15	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	90	40	35	25	5
Role	100	70	45	40	25	-
Social	100	50	5	-	-	-
Pain	100	80	45	15	5	-
Body	100	90	40	5	-	-
Fears	100	70	45	5	-	-
Sex	100	80	60	15	-	-
Psychological	100	75	40	15	0	-

		5				1
Participant 16	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	85	50	25	15	8
Role	100	85	50	25	15	-
Social	100	90	65	-	-	-
Pain	100	80	50	25	15	-
Body	100	95	90	70	-	-
Fears	100	70	20	5	-	-
Sex	100	85	70	55	-	-
Psychological	100	95	85	40	20	-

Table E. 16. Individual Utility Values of 8 Attributes for Participant 16.

Table E. 17. Individual Utility Values of 8 Attributes for Participant 17.

Participant 17	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	80	65	40	25	5
Role	100	80	60	35	5	-
Social	100	80	20	-	-	-
Pain	100	70	45	25	5	-
Body	100	85	70	50	-	-
Fears	100	75	45	20	-	-
Sex	100	75	50	20	-	-
Psychological	100	75	60	40	15	_

Table E. 18. Individual Utility Values of 8 Attributes for Participant 18.

Participant 18	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	70	60	20	15	0
Role	100	60	40	30	0	-
Social	100	60	10	-	-	-
Pain	100	90	70	30	5	-
Body	100	90	70	25	-	-
Fears	100	75	55	25	-	-
Sex	100	75	40	15	-	-
Psychological	100	85	60	30	10	-

Table E. 19. Individual Utility Values of 8 Attributes for Participant 19	ividual Utility Values of 8 Attributes for Parti	cipant 19
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Participant 19	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	80	60	40	20	1
Role	100	60	40	20	1	-
Social	100	85	10	-	-	-
Pain	100	80	50	20	1	-
Body	100	80	50	10	-	-
Fears	100	50	10	1	-	-
Sex	100	80	50	25	-	-
Psychological	100	80	50	20	1	-

		5				1
Participant 20	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	95	90	75	70	65
Role	100	98	90	88	80	-
Social	100	50	5	-	-	-
Pain	100	80	60	40	10	-
Body	100	90	80	70	-	-
Fears	100	50	20	5	-	-
Sex	100	80	60	40	-	-
Psychological	100	50	20	10	1	-

Table E. 20. Individual Utility Values of 8 Attributes for Participant20.

Table E. 21. Individual Utility Values of 8 Attributes for Participant 21.

Participant 21	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	50	25	10	5	1
Role	100	50	10	5	1	-
Social	100	80	50	-	-	-
Pain	100	80	50	5	1	-
Body	100	90	80	70	-	-
Fears	100	50	5	1	-	-
Sex	100	90	70	50	-	-
Psychological	100	80	60	50	30	_

Table E. 22. Individual Utility Values of 8 Attributes for Participant 22.

Participant 22	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	75	50	40	20	5
Role	100	80	50	20	5	-
Social	100	60	30	-	-	-
Pain	100	80	70	50	20	-
Body	100	90	70	50	-	-
Fears	100	60	40	20	-	-
Sex	100	80	60	40	-	-
Psychological	100	90	70	50	10	_

Table E. 23.	Individual	Utility	Values of	of 8 A	Attributes	for	Particip	oant 1	23.
		2							

Participant 23	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	85	60	35	20	15
Role	100	80	40	20	5	-
Social	100	80	25	-	-	-
Pain	100	80	70	60	20	-
Body	100	80	30	10	-	-
Fears	100	80	30	5	-	-
Sex	100	80	70	50	-	-
Psychological	100	90	70	40	10	-

Participant 24	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	90	60	40	10	5
Role	100	80	50	10	5	-
Social	100	90	30	-	-	-
Pain	100	90	50	25	10	-
Body	100	90	50	20	-	-
Fears	100	75	20	1	-	-
Sex	100	90	70	50	-	-
Psychological	100	80	60	40	20	-

Table E. 24. Individual Utility Values of 8 Attributes for Participant 24.

Table E. 25.	Individual	Utility V	Values of 8	Attributes	for Participant 2	5
		2				

Participant 25	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	80	40	20	15	10
Role	100	40	30	15	10	-
Social	100	40	5	-	-	-
Pain	100	90	50	20	10	-
Body	100	80	60	30	-	-
Fears	100	50	30	20	-	-
Sex	100	50	20	5	-	-
Psychological	100	80	60	40	10	_

Table E. 26. Individual Utility Values of 8 Attributes for Participant 26.

Participant 26	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	90	75	60	50	40
Role	100	80	60	55	35	-
Social	100	60	30	-	-	-
Pain	100	80	65	50	30	-
Body	100	80	60	50	-	-
Fears	100	60	40	30	-	-
Sex	100	80	60	50	-	-
Psychological	100	65	60	50	30	-

Table E. 27.	Individual	Utility	Values	of 8	Attributes	for	Particip	oant 27	'.
		~							

Participant 27	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	85	55	40	25	5
Role	100	75	45	30	10	-
Social	100	60	20	-	-	-
Pain	100	75	50	25	1	-
Body	100	90	70	30	-	-
Fears	100	85	60	35	-	-
Sex	100	75	50	20	-	-
Psychological	100	80	60	40	15	-

		5				1
Participant 28	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	80	50	30	20	5
Role	100	85	60	15	5	-
Social	100	60	15	-	-	-
Pain	100	90	70	40	15	-
Body	100	90	60	25	-	-
Fears	100	80	60	40	-	-
Sex	100	90	60	30	-	-
Psychological	100	90	60	35	15	-

Table E. 28. Individual Utility Values of 8 Attributes for Participant 28.

Table E. 29. Individual Utility Values of 8 Attributes for Participant 29.

Participant 29	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	85	75	50	30	5
Role	100	80	60	40	10	-
Social	100	80	15	-	-	-
Pain	100	85	75	50	15	-
Body	100	85	50	10	-	-
Fears	100	85	65	35	-	-
Sex	100	85	50	20	-	-
Psychological	100	80	55	20	5	_

Table E. 30. Individual Utility Values of 8 Attributes for Participant 30.

Participant 30	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Physical	100	90	60	40	10	5
Role	100	90	60	35	5	-
Social	100	80	20	-	-	-
Pain	100	95	70	40	20	-
Body	100	85	50	20	-	-
Fears	100	70	30	5	-	-
Sex	100	60	20	5	-	-
Psychological	100	80	40	10	2	-

Table E. 31. Importance Order of Attributes for Participants 1 to 5.

Rank			Attribute		
	Part. 1	Part.2	Part. 3	Part. 4	Part. 5
1	Physical	Social	Physical	Pain	Physical
2	Role	Pain	Fears	Role	Role
3	Pain	Body	Role	Physical	Psychological
4	Psychological	Physical	Psychological	Fears	Pain
5	Social	Role	Sex	Psychological	Social
6	Body	Sex	Pain	Social	Fears
7	Fears	Fears	Body	Body	Body
8	Sex		Social	Sex	Sex

	Rank	Attribute						
Γ		Part. 6	Part. 7	Part. 8	Part. 9	Part.10		
Γ	1	Fears	Psychological	Role	Role	Fears		
Γ	2	Psychological	Fears	Psychological	Pain	Physical		
Γ	3	Pain	Pain	Physical	Physical	Role		
Γ	4	Sex	Role	Social	Psychological	Pain		
	5	Social	Physical	Sex	Social	Psychological		
	6	Body	Social	Body	Fears	Social		
	7	Role	Sex	Pain	Sex	Body		
Γ	8	Physical	Body	Fears	Body	Sex		

Table E. 32. Importance Order of Attributes for Participants 6 to 10.

|--|

Rank			Attribute		
	Part. 11	Part. 12	Part. 13	Part. 14	Part. 15
1	Physical	Physical	Psychological	Pain	Physical
2	Role	Pain	Role	Role	Role
3	Pain	Role	Physical	Physical	Psychological
4	Psychological	Psychological	Fears	Psychological	Social
5	Sex	Fears	Pain	Social	Fears
6	Social	Social	Social	Body	Pain
7	Body	Sex	Sex	Sex	Body
8	Fears	Body	Body	Fears	Sex

Table E. 34. Importance Order of Attributes for Participants 16 to 20.

Rank			Attribute		
	Part. 16	Part. 17	Part. 18	Part. 19	Part. 20
1	Pain	Physical	Physical	Physical	Psychological
2	Physical	Role	Role	Role	Physical
3	Role	Psychological	Pain	Psychological	Fears
4	Social	Pain	Social	Fears	Pain
5	Psychological	Social	Psychological	Pain	Social
6	Fears	Fears	Sex	Body	Role
7	Sex	Body	Body	Social	Sex
8	Body	Sex	Fears	Sex	Body

Ta	ole E. 35. Importance Orde	er of Attributes for Participants 21 to 25.
Da	m]-	Attailanta

Rank			Attribute		
	Part. 21	Part. 22	Part. 23	Part. 24	Part. 25
1	Pain	Physical	Role	Role	Physical
2	Role	Role	Physical	Physical	Role
3	Physical	Psychological	Psychological	Fears	Psychological
4	Fears	Social	Pain	Pain	Social
5	Psychological	Pain	Fears	Psychological	Sex
6	Social	Fears	Social	Body	Pain
7	Sex	Body	Sex	Social	Body
8	Body	Sex	Body	Sex	Fears

Rank			Attribute		
	Part. 26	Part. 27	Part. 28	Part. 29	Part. 30
1	Physical	Pain	Physical	Pain	Physical
2	Role	Physical	Psychological	Psychological	Role
3	Pain	Role	Role	Role	Pain
4	Fears	Psychological	Pain	Physical	Psychological
5	Body	Social	Social	Social	Social
6	Psychological	Sex	Fears	Body	Sex
7	Social	Body	Sex	Fears	Body
8	Sex	Fears	Body	Sex	Fears

Table E. 36. Importance Order of Attributes for Participants 26 to 30.

### **APPENDIX F**

# HEALTH STATE EVALUATIONS OF ONCOLOGISTS

A formal health state level evaluation form was designed for defining each health state with respect to identified attributes by self-completion of oncologists. Three main parts constituted this form. In the first part, introductory written information was given about health states, and oncologists were familiar to the concept. After that, definitions of attributes and their levels, on which classification of health states were based, were given. Finally, evaluation sheet was given in the last part and for each health state they were asked to mark the suitable level that reflects the condition of that health state for each attribute. In this part, you can examine evaluation sheets obtained from ten oncologists performed this task.

			HEALTH STATE LEVEL EVALUA	TIC	DN	FOJ	RM	1							
				MA	STI	ECT	OM	Y		LU	MPI	ECT	OM	Y	
Attribute		Level	Definition	NED	NED I	VED II	Local Recurr.	Saşvaged	Metastasis	NED	NED I	NED II	Local Recurr.	Salvaged	Metastasis
	1	l	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift, walk, run, jump or bend	Х	Х					X	X				
uo	2	2	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend			χ	ĩχ					Х	Х		
Functi	3	3	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND NEEDING mechanical aids walk or get around			,		X						X	
iysical	4	1	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND having SOME limitation in physical ability to lift, walk, run, jump or bend						χ						X
Ph	5	5	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NEEDING mechanical aids walk or get around				5								
	6	5	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NOT being able to use or control the arms and legs												
	1	1	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities	X	X					Х	X				
lction	2	2	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having SOME limitations when playing, going to school, working or in other activities			×									
e Fur	1	3	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND NOT being able to play, attend school or work			X	Х	X				Х	Х	Х	
Rol	4	4	NEEDING HELP to eat, dress, bath and go to the toilet; AND having NO limitations when playing, going to school, working or in other activities												
	5	5	NEEDING HELP to eat, dress, bath and go to the toilet; AND NOT being able to play, attend school or work						X						Х
al	<u>.</u> ]	1	Having an average number of friends and contacts with others	X	X	X	Х			X	Х	X	Х		
0 ci	Fun	2	Having a few friends and contacts with others	<u> </u>			<u> </u>	X	X					X	X
<b>0</b> , 1		3	Having no friends and contacts with others	-	-	-				<u> </u>	-				
	1	1 2	Free of pain and discomfort Occasional pain. Discomfort relieved by nonprescription drugs or self-control activity without disruption of normal activities							X					
ain	3	3	Frequent pain. Discomfort relieved by oral medicines with occasional disruption of normal activities	X	X	Х	X			褒	Х	Х	χ		
E	4	4	Frequent pain; frequent disruption of normal activities. Discomfort requires prescription narcotics for relief					Х						X	
	-	5	Severe pain. Pain not relieved by drugs and constantly disrupts normal activities						Х						X
ae		1	Having no concern about my body appearance, like myself and still feeling attractive							X	X	Х			
Ima	2	2	Feeling self-conscious about my appearance, discomfort about scar, some problems on nakedness										Х	Х	
Body	3	3	Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes	Х	X	Х	Х	Х	Х						Х
	4	4	Feeling ashamed of own body, feeling does not like herself												
ŝ	1 L	1	Feeling difficulties with her illness are over and no concern about recurrence	X	Х	N					5.				
ears	once	2	future health			X	5.7			X	Х	X			
ΕŬ		3	Feeling fear and bothered by thoughts about the recurrence Feeling fear of death				X	IX.	X				X	Х	$\nabla$

Table F.1. Health State Evaluation Form of 1<sup>st</sup> Oncologist

		HEALTH STATE LEVEL EVALUA	TIC	DN	FOI	RM								
			MA	STI	ECT	OM	Y		LU	MP	ECT	OM	Y	
Attribute	Level	Definition	VED	VED I	VED II	ocal Recurr.	aşvaged	Metastasis	VED	VED I	VED II	ocal Recurr.	salvaged	Metastasis
	1	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift, walk, run, jump or bend	Х						X	-	-			F.
uo	2	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend		Х						Х				
Functi	3	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND NEEDING mechanical aids walk or get around			Х						Х			
ıysical	4	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND having SOME limitation in physical ability to lift, walk, run, jump or bend				Х						Х		
Id	5	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NEEDING mechanical aids walk or get around					X						Х	
	6	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NOT being able to use or control the arms and legs						Х						X
	1	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities	Х						X					
nction	2	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having SOME limitations when playing, going to school, working or in other activities		X						X				
le Fu	3	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND NOT being able to play, attend school or work			Х						Х			
Ro	4	NEEDING HELP to eat, dress, bath and go to the toilet; AND having NO limitations when playing, going to school, working or in other activities					Х						Х	
	5	being able to play, attend school or work						Х						Х
cial nc.	1	Having an average number of friends and contacts with others	X	4					X		-			
Sou	3	Having no friends and contacts with others	$\vdash$	r				X		X				X
	1	Free of pain and discomfort	X		-	-	-	<u> </u>	X	-				
	2	Occasional pain. Discomfort relieved by nonprescription drugs or self-control activity without disruption of normal activities		Х					Ĺ	Х				
Pain	3	Frequent pain. Discomfort relieved by oral medicines with occasional disruption of normal activities Frequent pain: frequent disruption of normal activities. Discomfort	_			X				• (	XX			
	5	requires prescription narcotics for relief Severe pain. Pain not relieved by drugs and constantly disrupts					$\wedge$	X	-		$\sim$			
ag	1	Having no concern about my body appearance, like myself and still feeling attractive	X		Ÿ				Х					
Ima	2	Feeling self-conscious about my appearance, discomfort about scar, some problems on nakedness		`	X					X				
Body	3	Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes					Х					×.	X	
	4	reeiing asnamed of own body, reeling does not like herself	L	-				X		-				X
s &	1	Feeling difficulties with her illness are over and no concern about recurrence Having some concerns about recurrence and feeling uneasy about	X					•	X		V			
ear	2	future health	-				Å				X		10	
	4	Feeling fear of death		-	-	-		X	-	-		-	F	X

Table F.2. Health State Evaluation Form of 2<sup>nd</sup> Oncologist

		HEALTH STATE LEVEL EVALUA	TIC	DN I	FOI	RM								
			MA	STI	ECT	OM	Y		LU	MPI	ECT	OM	Y	
Attribute	Level	Definition	VED	NED I	NED II	Local Recurr.	Saşvaged	Metastasis	VED	VED I	VED II	ocal Recurr.	Salvaged	Metastasis
	1	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift, walk, run, jump or bend	X	~	~			4	X	4	4	I	5	R
no	2	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend		Χ		1	21			$\times$	Ø			3
Functi	3	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND NEEDING mechanical aids walk or get around									X			
nysical	4	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND having SOME limitation in physical ability to lift, walk, run, jump or bend			X	X						X		
łd	5	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NEEDING mechanical aids walk or get around					X						X	
	6	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NOT being able to use or control the arms and legs						X						X
	1	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities	X						X					
nction	2	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having SOME limitations when playing, going to school, working or in other activities		X						X				
e Fu	3	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND NOT being able to play, attend school or work			X						X			
Rol	4	NEEDING HELP to eat, dress, bath and go to the toilet; AND having NO limitations when playing, going to school, working or in other activities					X						K	
	5	NEEDING HELP to eat, dress, bath and go to the toilet; AND NOT being able to play, attend school or work						X						X
al	; 1	Having an average number of friends and contacts with others	K						X					
joci Tur	2	Having a few friends and contacts with others		1	L	×	X	ļ.,	Ĺ	X	$\prec$	X		,
01 -	3	Having no friends and contacts with others	┝					1					$\times$	X
	1	Free of pain and discomfort	X				<u> </u>			-				
	2	self-control activity without disruption of normal activities		X		ļ ,				X				
ain	3	occasional disruption of normal activities			X	X					X			
	4	Frequent pain; frequent disruption of normal activities. Discomfort requires prescription narcotics for relief					K					X	X	
	5	Severe pain. Pain not relieved by drugs and constantly disrupts normal activities						Х						X
ae	1	Having no concern about my body appearance, like myself and still feeling attractive	X						Х	X				
Ima	2	Feeling self-conscious about my appearance, discomfort about scar, some problems on nakedness		X	Х				Ĺ		X			
sody	3	Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes				X	R					X	X	
<sup>m</sup>	4	Feeling ashamed of own body, feeling does not like herself						X						$\checkmark$
	1	Feeling difficulties with her illness are over and no concern about	$\checkmark$	•										
ars &	2	Having some concerns about recurrence and feeling uneasy about future health	Ĺ	7	X	$\mathbf{x}$	7		X	X	X			
Fe	3	Feeling fear and bothered by thoughts about the recurrence			-		X		Ĺ	1		Х	${ \times }$	
	4	Feeling fear of death						X						Х

Table F.3. Health State Evaluation Form of 3<sup>rd</sup> Oncologist

			HEALTH STATE LEVEL EVALUA	TIC	ON I	FOI	RM								
	Τ			MA	ASTI	ECT	OM	Y		LU	MPI	ЕСТ	OM	Y	
Attribute		Level	Definition	NED	NED I	NED II	Local Recurr.	Salvaged	Metastasis	NED	NED I	NED II	Local Recurr.	Salvaged	Metastasis
		1	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift, walk, run, jump or bend	X	X					X	X				
u		2	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend			X	X	20 °.				X	X		
Functio		3	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND NEEDING mechanical aids walk or get around					X						X	
iysical		4	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND having SOME limitation in physical ability to lift, walk, run, jump or bend						X						Х
Ph		5	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NEEDING mechanical aids walk or get around												
		6	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NOT being able to use or control the arms and legs												
		1	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities	X	X					X	Y				
nction		2	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having SOME limitations when playing, going to school, working or in other activities			X	X	X				X	×	X	
ole Fu		3	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND NOT being able to play, attend school or work												
Rc		4	having NO limitations when playing, going to school, working or in other activities												
		5	NEEDING HELP to eat, dress, bath and go to the toilet; AND NOT being able to play, attend school or work						$\times$						X
cial	nc.	1	Having an average number of friends and contacts with others	X	X	X	X	~		X	X	X	Х	/	-
So	Fu	3	Having no friends and contacts with others	$\vdash$	+	+	-		<u>-</u>					×	_X
<u> </u>	+	1	Free of pain and discomfort	$\vdash$	+	+	-	-				-			
		2	Occasional pain. Discomfort relieved by nonprescription drugs or self-control activity without disruption of normal activities												
Pain		3	Frequent pain. Discomfort relieved by oral medicines with occasional disruption of normal activities	X	X	×	X			X	K	1	X		
		4	Frequent pain; frequent disruption of normal activities. Discomfort requires prescription narooties for relief					X						X	
		5	Severe pain. Pain not relieved by drugs and constantly disrupts normal activities						×						Х
ge		1	Having no concern about my body appearance, like myself and still feeling attractive			11				X	X	Х			
Ima		2	Feeling self-conscious about my appearance, discomfort about scar, some problems on nakedness										X	X	
Body		3	Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes	×	X	X	X	X	X						X
		4	Feeling ashamed of own body, feeling does not like herself												
æ	irn	1	Feeling difficulties with her illness are over and no concern about recurrence	Х	X										
ears	once	2	future health			K	L ,			X	X	X			
F		3	Feeling fear of death	-	-	-	X	X	V				X	×	J

Table F.4. Health State Evaluation Form of 4<sup>th</sup> Oncologist

		HEATTH STATE I EVEL EVALUA	TI		FOI	2 M								
		HEALTH STATE LEVEL EVALUA	M	STI		OM	v		III	MDI	ECT	OM	v	
			1412	1.511						IVII I			1	
Attribute	Level	Definition	NED	NED I	NED II	Local Recurr	Saşvaged	Metastasis	NED	NED I	NED II	Local Recurr	Salvaged	Metastasis
	1	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift, walk, run, jump or bend	$\checkmark$	$\checkmark$	$\checkmark$	1			$\vee$	$\checkmark$		$\langle \rangle$		
u	2	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend				-	V	V	ł				$\checkmark$	V
Functio	3	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND NEEDING mechanical aids walk or get around												
iysical	4	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND having SOME limitation in physical ability to lift, walk, run, jump or bend												
Ph	5	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NEEDING mechanical aids walk or get around												
	6	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NOT being able to use or control the arms and legs												
	1	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities	$\sim$	$\sim$	$\sim$	$\sim$	-		$\checkmark$	$\sim$	$\sim$	~	ł	
nction	2	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having SOME limitations when playing, going to school, working or in other activities					$\vee$	1					$\checkmark$	V
le Fu	3	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND NOT being able to play, attend school or work												
Ro	4	having NO limitations when playing, going to school, working or in other activities												
	5	NEEDING HELP to eat, dress, bath and go to the toilet; AND NOT being able to play, attend school or work	L				_							
ial	1	Having an average number of friends and contacts with others	$\bowtie$	$\vee$		$\sim$			$[\vee$	$ \vee$		$\vee$		
Soc	2	Having a few friends and contacts with others					V	$1^{\vee}$	1	<u> </u>	-	-	~	V
	3	Free of nois and discomfort			-									-
	2	Occasional pain. Discomfort relieved by nonprescription drugs or				~	~		ľ			$\overline{\mathbf{k}}$		-
ain	3	Frequent pain. Discomfort relieved by oral medicines with occasional disruption of normal activities					$\vee$	-			v		$\overline{\vee}$	ł
P	4	Frequent pain; frequent disruption of normal activities. Discomfort requires prescription narcotics for relief						$\checkmark$	t		-			
	5	Severe pain. Pain not relieved by drugs and constantly disrupts normal activities												
ge	1	Having no concern about my body appearance, like myself and still feeling attractive		,	1									
Ima	2	Feeling self-conscious about my appearance, discomfort about scar, some problems on nakedness	$\vee$	1					$\vee$	1				
Body	3	Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes												
	4	Feeling ashamed of own body, feeling does not like herself												
ઝા	1	Feeling difficulties with her illness are over and no concern about recurrence												
ears	2	Having some concerns about recurrence and feeling uneasy about future health	$\vee$	$\sim$	V	1	/		$\vee$	$\vee$	1	1		
F O	3	Feeling fear of death	-	-		$\vee$			ł			V	$\vee$	
	14	r soning real of ucaul	1	1		1	1	IV	1	1	1	1	1	N

Table F.5. Health State Evaluation Form of 5<sup>th</sup> Oncologist

			HEALTH STATE LEVEL EVALUA	TIC	DN	FOI	RM								
	Τ			MA	STI	ECT	OM	Y		LU	MPI	ECT	OM	Y	
Attribute		Level	Definition	NED	NED I	NED II	Local Recurr.	Saşvaged	Metastasis	NED	NED I	NED II	Local Recurr.	Salvaged	Metastasis
		1	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift, walk, run, jump or bend	X						X	Par			01	1
u		2	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend		X			.1			χ				
Junctio		3	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND NEEDING mechanical aids walk or get around			γ						X			
ysical I		4	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND having SOME limitation in physical ability to lift walk run jump or bend				χ						χ		
Phy		5	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NEEDING machanical aida walk or act around					χ						χ	
		6	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NOT being able to use or control the arms and legs						χ					/	χ
		1	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities	X	N.	1				Х					
nction		2	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having SOME limitations when playing, going to school, working or in other activities	X	χ					χ					
e Fur		3	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND NOT being able to play, attend school or work			Х						Х	χ		
Rol		4	NEEDING HELP to eat, dress, bath and go to the toilet; AND having NO limitations when playing, going to school, working or in other activities			χ								χ	
		5	NEEDING HELP to eat, dress, bath and go to the toilet; AND NOT being able to play, attend school or work						X						X
ial	IC.	1	Having an average number of friends and contacts with others	•	Х					Х					
Soc	Fur	2	Having a few friends and contacts with others	<u> </u>	-	IX.		-	$\mathbf{k}$	_	X	<u> </u>			
		3	Free of pain and discomfort		-			-	X		-				$\times$
		2	Occasional pain. Discomfort relieved by nonprescription drugs or self-control activity without disruption of normal activities		χ					X	Х				
ain		3	Frequent pain. Discomfort relieved by oral medicines with occasional disruption of normal activities			Х						χ			
[		4	Frequent pain; frequent disruption of normal activities. Discomfort requires prescription narcotics for relief					Х						Х	
		5	Severe pain. Pain not relieved by drugs and constantly disrupts normal activities						X						χ
age		1	Having no concern about my body appearance, like myself and still feeling attractive			1			X	Х				X	Х
y Im		2	reging self-conscious about my appearance, disconfort about scar, some problems on nakedness	a.		χ						_			
Bod		<u> </u>	and discomfort because of body changes	X							Х	Х			
		4	Feeling ashamed of own body, feeling does not like herself		Х		Х						X		
ŝ	ern	1	Feeling difficulties with her illness are over and no concern about recurrence Having some concerns about recurrence and feeling uneasy about	X	X					X	Х				
ears	onc	2	future health			X						X			
		4	Feeling fear of death	-		X	X	X	X	-		X	X	X	Х

Table F.6. Health State Evaluation Form of 6<sup>th</sup> Oncologist

		HEALTH STATE LEVEL EVALUA	TIC	)N I	FOI	RM					1			
			MA	STE	ECT	OM	Y		LU	MPF	ECT	OM	Y	
Attribute	Level	Definition	NED	NED I	NED II	Local Recurr.	Saşvaged	Metastasis	NED	NED I	NED II	Local Recurr.	Salvaged	Metastasis
	1	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift, walk, run, jump or bend	X						X					
uo	2	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend		$\times$						2				
Functi	3	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND NEEDING mechanical aids walk or get around			K						X			
nysical	4	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND having SOME limitation in physical ability to lift, walk, run, jump or bend				X						X		
PI	5	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NEEDING mechanical aids walk or get around					X						X	
	6	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NOT being able to use or control the arms and legs						X						X
	1	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities	X						X					
nction	2	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having SOME limitations when playing, going to school, working or in other activities		X						Х				
e Fu	3	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND NOT being able to play, attend school or work			$\times$						X	X		
Rol	4	NEEDING HELP to eat, dress, bath and go to the toilet; AND having NO limitations when playing, going to school, working or in other activities				X	X						X	
	5	NEEDING HELP to eat, dress, bath and go to the toilet; AND NOT being able to play, attend school or work						Х						X
[a]	1	Having an average number of friends and contacts with others	X	X					X				2	
Soci	2	Having a few friends and contacts with others			K	×.	X			$\times$	X	K.	X	
	1	Free of pain and discomfort			-	-		K		/	-	-	-	X
	2	Occasional pain. Discomfort relieved by nonprescription drugs or self-control activity without disruption of normal activities	$\left[ \right]$	X					×	X				
ain	3	Frequent pain. Discomfort relieved by oral medicines with occasional disruption of normal activities			Х						X			
	4	Frequent pain; frequent disruption of normal activities. Discomfort requires prescription narcotics for relief				X	Х					X	K	
	5	normal activities						X						X
ge	1	Having no concern about my body appearance, like myself and still feeling attractive					X		X	n			Х	X
Ima	2	Feeling self-conscious about my appearance, discomfort about scar, some problems on nakedness			X									
Body	3	Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes	X	,						X	Х	,		
	4	reeiing ashamed of own body, feeling does not like herself		Х		X			<u> </u>			X		-
æ		Feeling difficulties with her illness are over and no concern about recurrence Having some concerns about recurrence and feeling uneasy about	X	X		_				۶×				
ears		future health			X	-				_	X	-	_	
E C	4	Feeling fear of death	$\vdash$	+	$\vdash$	X	1	X	$\vdash$	-	-	X	Z	X

Table F.7. Health State Evaluation Form of 7<sup>th</sup> Oncologist

		HEALTH STATE LEVEL EVALUA	TIC	)N I	FOF	RM								
			MA	STE	СТ	OM	Y		LU	MPI	ECTO	OMY	Y	
Attribute	Level	Definition	NED	NED I	NED II	Local Recurr.	Saşvaged	Metastasis	NED	NED I	NED II	Local Recurr.	Salvaged	Metastasis
	1	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift, walk, run, jump or bend	X	X	X		X		X	K	X		X	
uo	2	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend				X				2		X		
Functio	3	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND NEEDING mechanical aids walk or get around												
ıysical	4	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND having SOME limitation in physical ability to lift, walk, run, jump or bend						X						X
łł	5	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NEEDING mechanical aids walk or get around												
	6	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NOT being able to use or control the arms and legs												
	1	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities	×	X			X		X	X			$\boldsymbol{\swarrow}$	
nction	2	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having SOME limitations when playing, going to school, working or in other activities											1	
tole Fu	3	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND NOT being able to play, attend school or work NEEDING HELP to eat, dress, bath and go to the toilet; AND	-		X	X					X	メ		
R	5	having NO limitations when playing, going to school, working or in other activities NEEDING HELP to eat, dress, bath and go to the toilet; AND NOT												~
	-	being able to play, attend school or work	-		_	-		$\wedge$	-		-			$\wedge$
cial nc.	1	Having an average number of mends and contacts with others		1	1	X	$\overline{\mathbf{x}}$	-	~	2	×	Z	Z	-
South	3	Having no friends and contacts with others	F				$ \land$	X	F		1	<u> </u>		X
	1	Free of pain and discomfort	1	2		-	2	F	2	6	K		$\overline{\mathbf{v}}$	$\cap$
	2	Occasional pain. Discomfort relieved by nonprescription drugs or self-control activity without disruption of normal activities			$\bigcap$	Х					$\square$	×		
ain	3	occasional disruption of normal activities												
<b> </b>	4	Frequent pain; frequent disruption of normal activities. Discomfort requires prescription narcotics for relief						X						Х
	5	normal activities												
ae	1	Having no concern about my body appearance, like myself and still feeling attractive												
Ima	2	Feeling self-conscious about my appearance, discomfort about scar, some problems on nakedness							K	X	Х			
Body	3	Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes	1	X	Х							Х	•	
	4	Feeling difficulties with her illness are even and no concern shout	+	-	-	A	P	4X	+	-	+		X	X
s &	2	recurrence Having some concerns about recurrence and feeling uneasy about	X	X	1	-			X	X	×	-	-	
Fear	3	future health Feeling fear and bothered by thoughts about the recurrence	-	-	P	X	1	-	-	-	$\uparrow$	X		-
175	4	Feeling fear of death	$\vdash$	1	-	1	1	X	1	-	-	$\vdash$	r	Z

Table F.8. Health State Evaluation Form of 8<sup>th</sup> Oncologist

		HEALTH STATE LEVEL EVALUA	TIC	)N I	FOF	RM								
			MA	STE	СТ	OMY	Y		LUI	MPE	CT	OM	Y	
Attribute	Level	Definition	VED	VED I	VED II	Local Recurr.	sașvaged	Metastasis	VED	VED I	VED II	Local Recurr.	Salvaged	Metastasis
	1	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift, walk, run, jump or bend	X	F	<b>F</b>	_		H	X	-	Fa	_		
uo	2	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend		Х	X	1	-			χ	X			
Functi	3	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND NEEDING mechanical aids walk or get around				Х						X		
hysical	4	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND having SOME limitation in physical ability to lift, walk, run, jump or bend												
P	5	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NEEDING mechanical aids walk or get around						X						χ
	6	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NOT being able to use or control the arms and legs					X						Х	
	1	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities	X						X					
nction	2	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having SOME limitations when playing, going to school, working or in other activities		X						X				
e Fu	3	Being able to eat, dress, bath and go to the toilet WITHOUT HELP, AND NOT being able to play, attend school or work			X	Х					X	K		
Rol	4	NEEDING HELP to eat, dress, bath and go to the toilet; AND having NO limitations when playing, going to school, working or in other activities					X						X	
	5	NEEDING HELP to eat, dress, bath and go to the toilet; AND NOT being able to play, attend school or work						Х						X
ial of	1	Having an average number of friends and contacts with others												x
Soc	2	Having a few menus and contacts with others	$\vdash$		$\sim$		$ \land$	$\sim$	$\square$		X	$ \vdash \frown$	$\wedge$	
	1	Free of pain and discomfort	5						×	×				-
	2	Occasional pain. Discomfort relieved by nonprescription drugs or self-control activity without disruption of normal activities			$\times$						X			
ji.	3	Frequent pain. Discomfort relieved by oral medicines with				X						X		
P	4	Frequent pain; frequent disruption of normal activities. Discomfort requires prescription narcotics for relief					X	X					Х	X
	5	Severe pain. Pain not relieved by drugs and constantly disrupts normal activities												
Ige	1	Having no concern about my body appearance, like myself and still feeling attractive												
Ims	2	Feeling self-conscious about my appearance, discomfort about scar, some problems on nakedness	X	X	K				17	X	X			
Body	3	Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes				$\checkmark$	K	Х	Ĺ			X	X	X
	4	Feeling ashamed of own body, feeling does not like herself				-			<u> </u>			-		_
S.	1	Feeling difficulties with her illness are over and no concern about recurrence Having some concerns about recurrence and feeling uneasy about	j#						$\lambda$	X				
ears		future health	1X	X					1º	FA.				
I E C	3	Feeling fear and bothered by thoughts about the recurrence Feeling fear of death	-		14	1	X	X	-	-	12		K	V

Table F.9. Health State Evaluation Form of 9<sup>th</sup> Oncologist
			HEALTH STATE LEVEL EVALUA	TI	ON	FO	RM						_	_	
				MA	AST	ECT	ОМ	Y		LU	MPI	ECT	OM	Y	
Attribute		Level	Definition	VED	NED I	VED II	ocal Recurr.	aşvaged	Metastasis	VED	VED I	VED II	ocal Recurr.	alvaged	Metastasis
		1	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift walk run jump r head		-	E	I	02	R	L	V	4	H	<u>6</u>	E
uo		2	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend	V	V							L			
Functi		3	Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND NEEDING mechanical aids walk or get around			L	L	if.					L		
iysical		4	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND having SOME limitation in physical ability to lift, walk, run, jump or bend					L						L	
Pł		5	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NEEDING mechanical aids walk or get around						L						V
		6	NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND NOT being able to use or control the arms and legs												
		1	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities							Ŀ	V				
ction		2	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having SOME limitations when playing, going to school, working or in other activities	V	V						×	V			
e Fun		3	Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND NOT being able to play, attend school or work			V	Ł						L		
Rol		4	NEEDING HELP to eat, dress, bath and go to the toilet; AND having NO limitations when playing, going to school, working or in other activities					V						V	
		5	NEEDING HELP to eat, dress, bath and go to the toilet; AND NOT being able to play, attend school or work						L						5
al	c.	1	Having an average number of friends and contacts with others	L	V					L	V	V			
oci	un	2	Having a few friends and contacts with others			V	V	4	14				V	V	
91	-	3	Having no friends and contacts with others						L						V
		1	Free of pain and discomfort							V	V				
u		2	Occasional pain. Discomfort relieved by nonprescription drugs or self-control activity without disruption of normal activities Frequent pain. Discomfort relieved by oral medicines with	V	V	V						V			
Pai	-	4	occasional disruption of normal activities Frequent pain: frequent disruption of normal activities. Discomfort			/	V	V					V	V	
	-	5	requires prescription narcotics for relief					5	V				_	ø	V
		5	normal activities												
agi		1	Having no concern about my body appearance, like myself and still feeling attractive							V	V				
Ima		2	Feeling self-conscious about my appearance, discomfort about scar, some problems on nakedness	V	6	V				1		V		1	
sody		3	Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes				V	2					L	L	E
H	T	4	Feeling ashamed of own body, feeling does not like herself						V						-
		1	Feeling difficulties with her illness are over and no concern about recurrence							1:2	-V	-			
ars &	ncer	2	Having some concerns about recurrence and feeling uneasy about future health	V	V						1				
Fe	S	3	Feeling fear and bothered by thoughts about the recurrence Feeling fear of death			L	1	L	1.			V	V	V	1
	_	т							V						V

Table F.10. Health State Evaluation Form of 10<sup>th</sup> Oncologist

## **APPENDIX G**

## **DEFINITION OF HEALTH STATES**

#### **Reference State: Perfect Health**

- Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift, walk, run, jump or bend

- Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities

- Having an average number of friends and contacts with others

- Free of pain and discomfort

- Having no concern about your body appearance, like yourself and still feeling attractive

- Feeling difficulties with your illness are over and no concern about recurrence
- Having no problems about sexual relationship and sexual attractiveness

#### 1. <u>Mastectomy - No Evidence Of Disease (NED)</u>

- Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift, walk, run, jump or bend

- Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities

- Having an average number of friends and contacts with others

- Frequent pain. Discomfort relieved by oral medicines with occasional disruption of normal activities

- Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes

- Feeling, difficulties with your illness are over and no concern about recurrence
- Some changes in libido and frequency of sexual relationship negatively.

### 2. <u>Mastectomy - No Evidence of Disease But Having Hormontherapy</u>

- Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend

- Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities

- Having an average number of friends and contacts with others

- Frequent pain. Discomfort relieved by oral medicines with occasional disruption of normal activities

- Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes

- Feeling difficulties with your illness are over and no concern about recurrence

- Some changes in libido and frequency of sexual relationship negatively.

## 3. <u>Mastectomy - No Evidence of Disease But Having Chemotherapy</u>

- Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend

- Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND NOT being able to play, attend school or work

- Having a few friends and contacts with others

- Frequent pain. Discomfort relieved by oral medicines with occasional disruption of normal activities

- Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes

- Having some concerns about recurrence and feeling uneasy about future health
- Problems in sexual relationship, lack of sexual interest

## 4. <u>Mastectomy – Local Recurrence (may be salvaged)</u>

- Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend

- Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND NOT being able to play, attend school or work

- Having a few friends and contacts with others

- Frequent pain. Discomfort relieved by oral medicines with occasional disruption of normal activities

- Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes

- Feeling fear and bothered by thoughts about the recurrence
- Problems in sexual relationship, lack of sexual interest

### 5. <u>Mastectomy – Salvaged</u>

- Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND NEEDING mechanical aids walk or get around

- NEEDING HELP to eat, dress, bath and go to the toilet; AND having SOME limitations when playing, going to school, working or in other activities

- Having a few friends and contacts with others

- Frequent pain; frequent disruption of normal activities. Discomfort requires prescription narcotics for relief

- Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes

- Feeling fear and bothered by thoughts about the recurrence

- Loss of libido and sexual dysfunction.

### 6. <u>Mastectomy – Metastasis</u>

- NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND having SOME limitation in physical ability to lift, walk, run, jump or bend

- NEEDING HELP to eat, dress, bath and go to the toilet; AND NOT being able to play, attend school or work

- Having a few friends and contacts with others

- Severe pain. Pain not relieved by drugs and constantly disrupts normal activities

- Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes

- Feeling fear of death

- Loss of libido and sexual dysfunction.

## 7. <u>Lumpectomy - No Evidence Of Disease (NED)</u>

- Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift, walk, run, jump or bend

- Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities

- Having an average number of friends and contacts with others
- Free of pain and discomfort

- Having no concern about your body appearance, like yourself and still feeling attractive

- Having some concerns about recurrence and feeling uneasy about future health
- Having no problems about sexual relationship and sexual attractiveness

#### 8. <u>Lumpectomy - No Evidence of Disease But Having Hormontherapy</u>

- Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having NO limitation in physical ability to lift, walk, run, jump or bend

- Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND having NO limitations when playing, going to school, working or in other activities

- Having an average number of friends and contacts with others

- Occasional pain. Discomfort relieved by nonprescription drugs or self-control activity without disruption of normal activities

- Having no concern about your body appearance, like yourself and still feeling attractive

- Having some concerns about recurrence and feeling uneasy about future health

- Having no problems about sexual relationship and sexual attractiveness

## 9. <u>Lumpectomy - No Evidence of Disease But Having Chemotherapy</u>

- Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend

- Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND NOT being able to play, attend school or work

- Having an average number of friends and contacts with others

- Frequent pain. Discomfort relieved by oral medicines with occasional disruption of normal activities

- Having no concern about your body appearance, like yourself and still feeling attractive

- Having some concerns about recurrence and feeling uneasy about future health

- Problems in sexual relationship, lack of sexual interest

## 10. <u>Lumpectomy - Local Recurrence (may be salvaged)</u>

- Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND having SOME limitation in physical ability to lift, walk, run, jump or bend

- Being able to eat, dress, bath and go to the toilet WITHOUT HELP; AND NOT being able to play, attend school or work

- Having a few friends and contacts with others

- Frequent pain. Discomfort relieved by oral medicines with occasional disruption of normal activities

- Feeling self-conscious about your appearance, discomfort about scar, some problems on nakedness

- Feeling fear and bothered by thoughts about the recurrence

- Problems in sexual relationship, lack of sexual interest

#### 11. <u>Lumpectomy – Salvaged</u>

- Being able to get around house, yard, neighborhood or community WITHOUT help from another person; AND NEEDING mechanical aids walk or get around

- NEEDING HELP to eat, dress, bath and go to the toilet; AND having SOME limitations when playing, going to school, working or in other activities

- Having a few friends and contacts with others

- Frequent pain; frequent disruption of normal activities. Discomfort requires prescription narcotics for relief

- Feeling self-conscious about your appearance, discomfort about scar, some problems on nakedness

- Feeling fear and bothered by thoughts about the recurrence

- Loss of libido and sexual dysfunction.

### 12. Lumpectomy – Metastasis

- NEEDING HELP from another person in order to get around house, yard, neighborhood or community; AND having SOME limitation in physical ability to lift, walk, run, jump or bend

- NEEDING HELP to eat, dress, bath and go to the toilet; AND NOT being able to play, attend school or work

- Having a few friends and contacts with others

- Severe pain. Pain not relieved by drugs and constantly disrupts normal activities

- Having concerns about appearance, feeling clothes don't look good and discomfort because of body changes

- Feeling fear of death

- Loss of libido and sexual dysfunction.

## **APPENDIX H**

#### WORKSHEET FOR UTILITY ASSESSMENT

In this part, you can examine the introductory page of worksheet for utility assessment, and application of one of the health states as an example.

#### WORKSHEET FOR UTILITY ASSESSMENT

Using Decision Making tools in health decisions usually requires measuring a decision maker's perception of his/her quality of life while he/she is in a certain "health state". Familiar concept of "utility" (Von Neumann-Morgenstern) is considered to be the most suitable of measures for this health related quality of life. Hence, researchers in this field utilize utility assessment techniques to obtain patients' utilities in relation to health states probable along the path of their disease progress. However, since patients usually do not feel well enough to conduct such assessment procedures on them, researchers must resort to implement these on healthy people as proxy. Standardized descriptions of health states are presented to healthy people and they are asked to think hard and imagine being in the health state that is being described to them.

In what follows, you will be asked to go through such descriptions of a number of health states during the progress of (God forbid!) breast cancer. Upon reading each one of these descriptions, you are asked to imagine being in that health state, and to answer the related questions. As unpleasant as it is to imagine having such a serious disease, we hope this feeling will be compensated by the knowledge that these studies hopefully will eventually yield better health services for all of us.

Today breast cancer is the most common cancer in women worldwide, and considerable research has especially focused on the quality of life in breast cancer patients after surgery. However in our country, health sector is an unbeaten area for such studies. Thus, your effort will contribute significantly in one of the very few studies conducted in our country

Your concentrated effort is very important for this study. There are 12 health state descriptions presented to you below to be evaluated. Please, read carefully the description of each health state, concentrate on that definition, and while answering the questions, imagine that you are in that health state.

Let's look at the descriptions of the 12 health states one by one:

#### Health State (1)- Mastectomy - No Evidence Of Disease (NED)

**Definition:** Imagine that you have been diagnosed as having breast cancer and you had an operation for an entire breast removal (Mastectomy). There is no evidence of disease after surgery, which means that you are free of cancer but remain at risk for reoccurrence. This Health State is characterized by 7 attributes in Table 1. Perfect Health State is also defined in Table 1. in order to provide comparison.

Table 1. Description of Health State (1) &	Perfect Health characterized by 7 attributes
Mastectomy - No Evidence Of Disease	Perfect Health
*Being able to get around house, yard,	*Being able to get around house, yard,
neighborhood or community WITHOUT help	neighborhood or community WITHOUT help
from another person; AND having NO limitation	from another person; AND having NO limitation
in physical ability to lift, walk, run, jump or bend	in physical ability to lift, walk, run, jump or bend
*Being able to eat, dress, bath and go to the toilet	*Being able to eat, dress, bath and go to the toilet
WITHOUT HELP; AND having NO limitations	WITHOUT HELP; AND having NO limitations
when playing, going to school, working or in	when playing, going to school, working or in
other activities	other activities
*Having an average number of friends and	*Having an average number of friends and
contacts with others	contacts with others
*Frequent pain. Discomfort relieved by oral	*Free of pain and discomfort
medicines with occasional disruption of normal	*Having no concern about my body appearance,
activities	like myself and still feeling attractive
*Having concerns about appearance, feeling	
clothes don't look good and discomfort because	*Feeling difficulties with your illness are over
of body changes	and no concern about recurrence
*Feeling, difficulties with your illness are over	*Having no problems about sexual relationship
and no concern about recurrence	and sexual attractiveness
*Some changes in libido and frequency of sexual	
relationship negatively.	

Now, imagine that you have two choices. In the first choice you live in Health State(1) for certain. In the second choice, you have a chance of living in perfect health with probability of p and a chance of death with complementary probability (1-p). Namely in this alternative you should accept a (1-p) risk of death in order to have a p-chance for perfect health. (Figure 1)



**P** = ?

Figure 1. Standard Gamble Representation

Think carefully, for which probability of (p), you are indifferent between two alternatives? In other words, what is the value of p that you accept a (1-p) % risk of death in order to obtain perfect health?

## **APPENDIX I**

## **DOTPLOT GRAPHS OF UTILITY VALUES**



Figure I.1. Dotplot graphs of NED, NEDI, NEDII states of Mastectomy utility values obtained from MAUM.



Figure I.2. Dotplot graphs of Local Recurrence, Salvaged, Metastasis states of Mastectomy utility values obtained from MAUM.



Figure I.3. Dotplot graphs of NED, NEDI, NEDII states of Lumpectomy utility values obtained from MAUM.



Figure I.4. Dotplot graphs of Local Recurrence, Salvaged, Metastasis states of Lumpectomy utility values obtained from MAUM.



Figure I.5. Dotplot graphs of NED, NEDI, NEDII states of Mastectomy utility values obtained from Standard Gamble.



Figure I.6. Dotplot graphs of Local Recurrence, Salvaged, Metastasis states of Mastectomy utility values obtained from Standard Gamble.



Figure I.7. Dotplot graphs of NED, NEDI, NEDII states of Lumpectomy utility values obtained from Standard Gamble.



Figure I.8. Dotplot graphs of Local Recurrence, Salvaged, Metastasis states of Lumpectomy utility values obtained from Standard Gamble.

## **APPENDIX J**

## NORMAL PROBABILITY PLOTS



Figure J.1. Normal Probability Plots for Utility Data Sets Obtained by MAUM.



Figure J.2. Normal Probability Plots for Utility Data Sets Obtained by Validation Model

## **APPENDIX K**

## **GRAPH SUMMARY OF UTILITY VALUES**



Figure K.1 Graph Summary of utility values through U1 to U3 obtained from MAUM



Figure K.2 Graph Summary of utility values through U4 to U8 obtained from MAUM



Figure K.3 Graph Summary of utility values through U9 to U12 obtained from MAUM



Figure K.4 Graph Summary of utility values through U1 to U4 obtained from Global Rating



Figure K.5 Graph Summary of utility values through U5 to U8 obtained from Global Rating



Figure K.6 Graph Summary of utility values through U9 to U12 obtained from Global Rating

### **APPENDIX L**

## STATISTICAL ANALYSIS RESULTS

### 1. Minitab Outputs for Two Sample T-Test

```
Table L.1. T-test results for Mastectomy-NED states.
Two-Sample T-Test and CI: U1-MNED; U1-MNED 1
```

Two-sample T for U1-MNED vs U1-MNED\_1 N Mean StDev SE Mean U1-MNED 30 87.7 10.5 1.9 U1-MNED\_1 30 88.00 7.10 1.3 Difference = mu (U1-MNED) - mu (U1-MNED\_1) Estimate for difference: -0.300000 95% CI for difference: (-4.934467; 4.334467) T-Test of difference = 0 (vs not =): T-Value = -0.13 P-Value = 0.897 DF = 51

```
Table L.2. T-test results for Mastectomy-NEDI states.
```

```
Table L.3. T-test results for Mastectomy-NEDII states.
```

Table L.4. T-test results for Mastectomy-Local Recurrence states.

Table L.5. T-test results for Mastectomy-Salvaged states.

Table L.6. T-test results for Mastectomy-Metastasis states.

```
Table L.7. T-test results for Lumpectomy-NED states.
```

Table L.8. T-test results for Lumpectomy-NEDI states.

Table L.9. T-test results for Lumpectomy-NEDII states.

Table L.10. T-test results for Lumpectomy-Local Recurrence states. Two-Sample T-Test and CI: U10-LLR; U10-LLR\_1

Table L.11. T-test results for Lumpectomy-Salvaged states. Two-Sample T-Test and CI: U11-LS; U11-LS\_1

Table L.12. T-test results for Lumpectomy-Metastasis states.

```
Two-Sample T-Test and CI: U12-LM; U12-LM_1
Two-sample T for U12-LM vs U12-LM 1
         N Mean StDev SE Mean
U12-LM
                          4.7
         30
             43.9
                    25.9
                   8.54
U12-LM 1 30 25.13
                             1.6
Difference = mu (U12-LM) - mu (U12-LM_1)
Estimate for difference: 18.8000
95% CI for difference: (8.6959; 28.9041)
T-Test of difference = 0 (vs not =): T-Value = 3.78 P-Value = 0.001 DF =
35
```

### 2. Minitab Outputs for Mann Whitney Test

Table L.13. Mann Whitney Test results for Mastectomy-NED states. Mann-Whitney Test and CI: U1-MNED; U1-MNED\_1

```
N Median

U1-MNED 30 90.000

U1-MNED_1 30 90.000

Point estimate for ETA1-ETA2 is 1.000

95.2 Percent CI for ETA1-ETA2 is (-4.002; 5.001)

W = 954.0

Test of ETA1 = ETA2 vs ETA1 not = ETA2 is significant at 0.5692

The test is significant at 0.5679 (adjusted for ties)
```

Table L.14. Mann Whitney Test results for Mastectomy-NEDI states. Mann-Whitney Test and Cl: U2-MNED1; U2-MNED1\_1

```
N Median
U2-MNED1 30 82.500
U2-MNED1_1 30 83.000
Point estimate for ETA1-ETA2 is 2.000
95.2 Percent CI for ETA1-ETA2 is (-4.997;6.998)
W = 947.0
Test of ETA1 = ETA2 vs ETA1 not = ETA2 is significant at 0.6414
The test is significant at 0.6410 (adjusted for ties)
```

Table L.15. Mann Whitney Test results for Mastectomy-NEDII states.

```
Mann-Whitney Test and CI: U3-MNED2; U3-MNED2_1

N Median

U3-MNED2 30 72.50

U3-MNED2_1 30 64.00

Point estimate for ETA1-ETA2 is 12.00

95.2 Percent CI for ETA1-ETA2 is (5.00;19.00)

W = 1131.0

Test of ETA1 = ETA2 vs ETA1 not = ETA2 is significant at 0.0014

The test is significant at 0.0014 (adjusted for ties)
```

Table L.16. Mann Whitney Test results for Mastectomy-Local Recurrence states. Mann-Whitney Test and CI: U4-MLR; U4-MLR\_1

N Median U4-MLR 30 70.00 U4-MLR\_1 30 60.50 Point estimate for ETA1-ETA2 is 10.00 95.2 Percent CI for ETA1-ETA2 is (1.00;19.01) W = 1061.5 Test of ETA1 = ETA2 vs ETA1 not = ETA2 is significant at 0.0309 The test is significant at 0.0308 (adjusted for ties)

Table L.17. Mann Whitney Test results for Mastectomy-Salvaged states. Mann-Whitney Test and CI: U5-MS; U5-MS 1

```
N Median
U5-MS 30 60.00
U5-MS_1 30 41.00
Point estimate for ETA1-ETA2 is 18.00
95.2 Percent CI for ETA1-ETA2 is (10.00;26.00)
W = 1177.5
Test of ETA1 = ETA2 vs ETA1 not = ETA2 is significant at 0.0001
The test is significant at 0.0001 (adjusted for ties)
```

Table L.18. Mann Whitney Test results for Mastectomy-Metastasis states.

```
Mann-Whitney Test and CI: U6-MM; U6-MM_1
```

```
N Median
U6-MM 30 45.00
U6-MM_1 30 25.00
Point estimate for ETA1-ETA2 is 18.50
95.2 Percent CI for ETA1-ETA2 is (4.99;32.00)
W = 1118.5
Test of ETA1 = ETA2 vs ETA1 not = ETA2 is significant at 0.0027
The test is significant at 0.0026 (adjusted for ties)
```

Table L.19. Mann Whitney Test results for Lumpectomy-NED states.

Table L.20. Mann Whitney Test results for Lumpectomy-NEDI states. Mann-Whitney Test and CI: U8LNED1; U8LNED1\_1

```
N Median
U8LNED1 30 90.000
U8LNED1_1 30 94.500
Point estimate for ETA1-ETA2 is -2.000
95.2 Percent CI for ETA1-ETA2 is (-6.001;0.999)
W = 839.5
Test of ETA1 = ETA2 vs ETA1 not = ETA2 is significant at 0.2675
The test is significant at 0.2659 (adjusted for ties)
```

Table L.21. Mann Whitney Test results for Lumpectomy-NEDII states.

```
Mann-Whitney Test and CI: U9-LNED2; U9-LNED2_1
```

N Median U9-LNED2 30 80.00 U9-LNED2\_1 30 68.00 Point estimate for ETA1-ETA2 is 10.00 95.2 Percent CI for ETA1-ETA2 is (5.00;16.00)W = 1127.5 Test of ETA1 = ETA2 vs ETA1 not = ETA2 is significant at 0.0017 The test is significant at 0.0017 (adjusted for ties)

Table L.22. Mann Whitney Test results for Lumpectomy-Local Recurrence states. Mann-Whitney Test and CI: U10-LLR; U10-LLR\_1

N Median U10-LLR 30 68.00 U10-LLR\_1 30 61.50 Point estimate for ETA1-ETA2 is 7.00 95.2 Percent CI for ETA1-ETA2 is (-2.00;16.00)W = 1010.5 Test of ETA1 = ETA2 vs ETA1 not = ETA2 is significant at 0.1602 The test is significant at 0.1595 (adjusted for ties) Table L.23. Mann Whitney Test results for Lumpectomy-Salvaged states.

Table L.24. Mann Whitney Test results for Lumpectomy-Metastasis states. Mann-Whitney Test and CI: U12-LM; U12-LM\_1

```
N Median
U12-LM 30 45.00
U12-LM_1 30 25.00
Point estimate for ETA1-ETA2 is 18.00
95.2 Percent CI for ETA1-ETA2 is (5.00;29.00)
W = 1108.5
Test of ETA1 = ETA2 vs ETA1 not = ETA2 is significant at 0.0043
The test is significant at 0.0043 (adjusted for ties)
```

#### 3. Minitab Outputs for Paired T-Test

```
      Table L.25. Paired T-Test results for Mastectomy-NED states.

      Paired T-Test and CI: U1-MNED; U1-VAL

      N Mean StDev SE Mean

      U1-MNED
      15
      89.5333
      6.1975
      1.6002

      U1-VAL
      15
      91.4667
      6.6961
      1.7289

      Difference
      15
      -1.93333
      5.57375
      1.43914

      95% CI for mean difference:
      (-5.01997; 1.15331)
      T-Test of mean difference = 0 (vs not = 0):
      T-Value = -1.34
      P-Value = 0.201
```

```
Table L.26. Paired T-Test results for Mastectomy-NEDI states.
```

```
Paired T-Test and CI: U2-MNED1; U2-VAL

Paired T for U2-MNED1 - U2-VAL

N Mean StDev SE Mean

U2-MNED1 15 85.0667 5.4046 1.3955

U2-VAL 15 86.6667 7.9252 2.0463

Difference 15 -1.60000 7.17934 1.85370

95% CI for mean difference: (-5.57578; 2.37578)

T-Test of mean difference = 0 (vs not = 0): T-Value = -0.86 P-Value =

0.403
```

#### Table L.27. Paired T-Test results for Mastectomy-NEDII states. **Paired T-Test and CI: U3-MNED2; U3-VAL**

Paired T for U3-MNED2 - U3-VAL N Mean StDev SE Mean U3-MNED2 15 70.2667 7.7687 2.0059 U3-VAL 15 75.3333 13.5524 3.4992 Difference 15 -5.06667 11.45467 2.95758 95% CI for mean difference: (-11.41005; 1.27672) T-Test of mean difference = 0 (vs not = 0): T-Value = -1.71 P-Value = 0.109

#### Table L.28. Paired T-Test results for Mastectomy-Local Recurrence states. **Paired T-Test and CI: U4-MLR: U4-VAL**

Paired T for U4-MLR - U4-VAL N Mean StDev SE Mean U4-MLR 15 68.6000 8.2358 2.1265 U4-VAL 15 68.3333 16.3037 4.2096 Difference 15 0.266667 15.026009 3.879699 95% CI for mean difference: (-8.054460; 8.587793) T-Test of mean difference = 0 (vs not = 0): T-Value = 0.07 P-Value = 0.94

Table L.29. Paired T-Test results for Mastectomy-Salvaged states. **Paired T-Test and CI: U5-MS: U5-VAL** 

Paired T for U5-MS - U5-VAL N Mean StDev SE Mean U5-MS 15 52.2667 11.0095 2.8426 U5-VAL 15 59.8667 17.9955 4.6464 Difference 15 -7.60000 13.22228 3.41398 95% CI for mean difference: (-14.92225; -0.27775) T-Test of mean difference = 0 (vs not = 0): T-Value = -2.23 P-Value = 0.043 Table L.30. Paired T-Test results for Mastectomy-Metastasis states.

```
Paired T-Test and Cl: U6-MM; U6-VAL
Paired T for U6-MM - U6-VAL

N Mean StDev SE Mean
U6-MM 15 33.9333 13.5355 3.4948
U6-VAL 15 42.1333 29.2816 7.5605
Difference 15 -8.20000 25.32136 6.53795

95% CI for mean difference: (-22.22250; 5.82250)
T-Test of mean difference = 0 (vs not = 0): T-Value = -1.25 P-Value =
0.230
```

#### Table L.31. Paired T-Test results for Lumpectomy-NED states. **Paired T-Test and CI: U7-LNED; U7-VAL**

Paired T for U7-LNED - U7-VAL N Mean StDev SE Mean U7-LNED 15 98.2000 1.7403 0.4493 U7-VAL 15 95.8667 5.4493 1.4070 Difference 15 2.3333 4.41858 1.14087 95% CI for mean difference: (-0.11359; 4.78026) T-Test of mean difference = 0 (vs not = 0): T-Value = 2.05 P-Value = 0.060

Table L.32. Paired T-Test results for Lumpectomy-NEDI states.

Paired T-Test and CI: U8-LNED1; U8-VAL

Paired T for U8-LNED1 - U8-VAL N Mean StDev SE Mean U8-LNED1 15 95.5333 2.3865 0.6162 U8-VAL 15 93.7333 6.7662 1.7470 Difference 15 1.80000 6.12022 1.58024 95% CI for mean difference: (-1.58927; 5.18927) T-Test of mean difference = 0 (vs not = 0): T-Value = 1.14 P-Value = 0.274

```
Table L.33. Paired T-Test results for Lumpectomy-NEDII states.
```

```
Paired T-Test and CI: U9-LNED2; U9-VAL
Paired T for U9-LNED2 - U9-VAL
           Ν
                           StDev SE Mean
                  Mean
              75.3333
                         7.4226
U9-LNED2
           15
                                 1.9165
3 4209
          15 77.4000 13.2493
U9-VAL
                                   3.4209
Difference 15 -2.06667 12.36046 3.19146
95% CI for mean difference: (-8.91166; 4.77833)
T-Test of mean difference = 0 (vs not = 0): T-Value = -0.65 P-Value =
0.528
```

## Table L.34. Paired T-Test results for Lumpectomy-Local Recurrence states. **Paired T-Test and CI: U10-LLR; U10-VAL**

Paired T for U10-LLR - U10-VAL N Mean StDev SE Mean U10-LLR 15 70.2667 7.5920 1.9602 U10-VAL 15 69.6667 15.0317 3.8812 Difference 15 0.600000 13.978555 3.609247 95% CI for mean difference: (-7.141066; 8.341066) T-Test of mean difference = 0 (vs not = 0): T-Value = 0.17 P-Value = 0.870

```
Table L.35. Paired T-Test results for Lumpectomy-Salvaged states.
Paired T-Test and CI: U11-LS; U11-VAL
```

Paired T for Ull-LS - Ull-VAL N Mean StDev SE Mean Ull-LS 15 53.8000 10.9427 2.8254 Ull-VAL 15 61.2667 17.1692 4.4331 Difference 15 -7.46667 13.17935 3.40289 95% CI for mean difference: (-14.76515; -0.16819) T-Test of mean difference = 0 (vs not = 0): T-Value = -2.19 P-Value = 0.046

#### Table L.36. Paired T-Test results for Lumpectomy-Metastasis states. **Paired T-Test and CI: U12-LM; U12-VAL**

```
Paired T for U12-LM - U12-VAL

N Mean StDev SE Mean

U12-LM 15 34.6000 12.8163 3.3092

U12-VAL 15 41.9333 28.5218 7.3643

Difference 15 -7.33333 25.73121 6.64377

95% CI for mean difference: (-21.58280; 6.91614)

T-Test of mean difference = 0 (vs not = 0): T-Value = -1.10 P-Value =

0.288
```

### 4. Minitab Outputs for Wilcoxon Signed Rank Test

Table L.37. Wilcoxon Signed Rank Test results for Mastectomy-NED states Wilcoxon Signed Rank Test: U1-DIFF

Test of median = 0.000000 versus median not = 0.000000 N for Wilcoxon Estimated N Test Statistic P Median U1-DIFF 15 14 32.5 0.221 -2.500

## Table L.38. Wilcoxon Signed Rank Test results for Mastectomy-NEDI states. Wilcoxon Signed Rank Test: U2-DIFF

Test of median = 0.000000 versus median not = 0.000000

		Ν			
		for	Wilcoxon		Estimated
	Ν	Test	Statistic	P	Median
U2-DIFF	15	14	36.5	0.331	-2.000

# Table L.39. Wilcoxon Signed Rank Test results for Mastectomy-NEDII states. Wilcoxon Signed Rank Test: U3-DIFF

Test of median = 0.000000 versus median not = 0.000000 N for Wilcoxon Estimated N Test Statistic P Median U3-DIFF 15 15 34.5 0.156 -4.750

## Table L.40. Wilcoxon Signed Rank Test results for Mastectomy-Local Rec. states. Wilcoxon Signed Rank Test: U4-DIFF

Test of median = 0.000000 versus median not = 0.000000

N for Wilcoxon Estimated N Test Statistic P Median U4-DIFF 15 15 62.5 0.910 1.250

Table L.41. Wilcoxon Signed Rank Test results for Mastectomy-Salvaged states. Wilcoxon Signed Rank Test: U5-DIFF

Test of median = 0.000000 versus median not = 0.000000

		N			
		for	Wilcoxon		Estimated
	Ν	Test	Statistic	P	Median
U5-DIFF	15	14	22.0	0.060	-6.500

Table L.42. Wilcoxon Signed Rank Test results for Mastectomy-Metastasis states. Wilcoxon Signed Rank Test: U6-DIFF

```
Test of median = 0.000000 versus median not = 0.000000

N
for Wilcoxon Estimated

N Test Statistic P Median

U6-DIFF 15 15 43.0 0.349 -7.000
```

```
Table L.43. Wilcoxon Signed Rank Test results for Lumpectomy-NED states. Wilcoxon Signed Rank Test: U7-DIFF
```

Test of median = 0.000000 versus median not = 0.000000 N for Wilcoxon Estimated N Test Statistic P Median U7-DIFF 15 12 61.0 0.092 1.500

```
Table L.44. Wilcoxon Signed Rank Test results for Lumpectomy-NEDI states. Wilcoxon Signed Rank Test: U8-DIFF
```

Test of median = 0.000000 versus median not = 0.000000

		N			
		for	Wilcoxon		Estimated
	Ν	Test	Statistic	P	Median
U8-DIFF	15	15	73.0	0.478	1.000

Table L.45. Wilcoxon Signed Rank Test results for Lumpectomy-NEDII states. **Wilcoxon Signed Rank Test: U9-DIFF** 

```
Test of median = 0.000000 versus median not = 0.000000

N for Wilcoxon Estimated

N Test Statistic P Median

U9-DIFF 15 14 42.0 0.530 -1.750
```

Table L.46. Wilcoxon Signed Rank Test results for Lumpectomy-Local Rec. states. **Wilcoxon Signed Rank Test: U10-DIFF** 

Test of median = 0.000000 versus median not = 0.000000 N for Wilcoxon Estimated N Test Statistic P Median U10-DIFF 15 15 64.5 0.820 2.000

Table L.47. Wilcoxon Signed Rank Test results for Lumpectomy-Salvaged states. Wilcoxon Signed Rank Test: U11-DIFF

Test of median = 0.000000 versus median not = 0.000000 N for Wilcoxon Estimated N Test Statistic P Median U11-DIFF 15 15 26.0 0.057 -7.000

# Table L.48. Wilcoxon Signed Rank Test results for Lumpectomy-Metastasis states. Wilcoxon Signed Rank Test: U12-DIFF

Test of median = 0.000000 versus median not = 0.000000 N for Wilcoxon Estimated N Test Statistic P Median U12-DIFF 15 15 45.0 0.410 -5.250

## **APPENDIX M**

## A SYNTHETIC MTMM (MULTI-TRAIT MULTI-METHOD) MATRIX



by permission.)

Figure M.1. Hypothetical Multitrait-Multimethod Matrix

## **APPENDIX N**

## K (RELATIVE IMPORTANCE WEIGHT) VALUES IN MULTIPLICATIVE UTILITY FUNCTION

		Hea	ılth	k		Hea	lth	k		Hea	ılth	k
Pa	rticipant	Sta	tes	Values	Participant	Sta	tes	Values	Participant	Sta	tes	Values
			1	0.0014			1	0.0025			1	0.0007
		Ma	2	0.0022		Ma	2	0.0056		Ma	2	0.0023
		ıste	3	0.0016		ıste	3	0.0220		ıste	3	0.0084
		cto	4	0.0017		cto	4	0.0228		cto	4	0.0090
		my	5	0.0056		my	5	0.0448		my	5	0.0217
	1		6	0.0271	2		6	0.1813	3		6	0.1231
	1	]	7	0.0001	2		7	0.0005	5		7	0.0006
		Lur	8	0.0011		Lur	8	0.0016		Lur	8	0.0009
		npe	9	0.0006		npe	9	0.0179		npe	9	0.0068
		ecte	10	0.0017		etc	10	0.0222		etc	10	0.0081
		nmy	11	0.0055		nmy	11	0.0426		my	11	0.0200
		1	12	0.0271		1	12	0.1813		1	12	0.1231
-		Неа	ılth	k		Hea	lth	k		Неа	ılth	k
Pa	rticipant	Hea Sta	ılth tes	k Values	Participant	Hea Sta	lth tes	k Values	Participant	Hea Sta	lth tes	k Values
Pa	rticipant	Hea Sta	ulth tes 1	k Values -0.0018	Participant	Hea Sta	lth tes 1	k Values 0.0008	Participant	Hea Sta	ulth tes 1	k Values 0.0010
Pa	rticipant	Hea Sta Ma	alth tes 1 2	k Values -0.0018 -0.0043	Participant	Hea Sta Ma	lth tes 1 2	k Values 0.0008 0.0012	Participant	Hea Sta Ma	ulth tes 1 2	k Values 0.0010 -0.0002
Pa	rticipant	Hea Sta Master	alth tes 1 2 3	k Values -0.0018 -0.0043 0.0034	Participant	Hea Sta Master	lth tes 1 2 3	k Values 0.0008 0.0012 0.0033	Participant	Hea Sta Maste	ulth tes 1 2 3	k Values 0.0010 -0.0002 0.0086
Pa	rticipant	Hea Sta Mastecto	1 1 2 3 4	k Values -0.0018 -0.0043 0.0034 0.0055	Participant	Hea Sta Mastecto	llth tes 1 2 3 4	k Values 0.0008 0.0012 0.0033 -0.0130	Participant	Hea Sta Mastecto	1 1 2 3 4	k Values 0.0010 -0.0002 0.0086 0.0160
Pa	rticipant	Hea Sta Mastectomy	1 1 2 3 4 5	k Values -0.0018 -0.0043 0.0034 0.0055 0.0213	Participant	Hea Sta Mastectomy	llth tes 1 2 3 4 5	k Values 0.0008 0.0012 0.0033 -0.0130 0.0131	Participant	Hea Sta Mastectomy	1 1 2 3 4 5	k Values 0.0010 -0.0002 0.0086 0.0160 0.0013
Pa	rticipant	Hea Sta Mastectomy	1 1 2 3 4 5 6	k Values -0.0018 -0.0043 0.0034 0.0055 0.0213 0.0771	Participant	Hea Sta Mastectomy	lth tes 1 2 3 4 5 6	k Values 0.0008 0.0012 0.0033 -0.0130 0.0131 0.0115	Participant	Hea Sta Mastectomy	1 1 2 3 4 5 6	k Values 0.0010 -0.0002 0.0086 0.0160 0.0013 -0.0815
Pa	rticipant	Hea Sta Mastectomy	1 1 2 3 4 5 6 7	k Values -0.0018 -0.0043 0.0034 0.0055 0.0213 0.0771 -0.0044	Participant	Hea Sta Mastectomy	lth tes 1 2 3 4 5 6 7	k Values 0.0008 0.0012 0.0033 -0.0130 0.0131 0.0115 0.0000	Participant 6	Hea Sta Mastectomy	1 1 2 3 4 5 6 7	k Values 0.0010 -0.0002 0.0086 0.0160 0.0013 -0.0815 -0.0026
Pa	rticipant	Hea ta Mastectomy Lur	1 1 2 3 4 5 6 7 8	k Values -0.0018 -0.0043 0.0034 0.0055 0.0213 0.0771 -0.0044 -0.0058	Participant	Hea Sta Mastectomy Lur	llth tes 1 2 3 4 5 6 7 8	k Values 0.0008 0.0012 0.0033 -0.0130 0.0131 0.0115 0.0000 -0.0005	Participant 6	Hea Sta Mastectomy Lur	1 1 2 3 4 5 6 7 8	k Values 0.0010 -0.0002 0.0086 0.0160 0.0013 -0.0815 -0.0026 -0.0002
Pa	rticipant	Hea ta Mastectomy Lumpe	1 1 2 3 4 5 6 7 8 9	k Values -0.0018 -0.0043 0.0034 0.0055 0.0213 0.0771 -0.0044 -0.0058 -0.0002	Participant	Hea Sta Mastectomy Lumpe	1       2       3       4       5       6       7       8       9	k Values 0.0008 0.0012 0.0033 -0.0130 0.0131 0.0115 0.0000 -0.0005 -0.0040	Participant	Hea ta Mastectomy Lumpe	llth tes 1 2 3 4 5 6 7 8 9	k Values 0.0010 -0.0002 0.0086 0.0160 0.0013 -0.0815 -0.0026 -0.0002 0.0055
Pa	rticipant	Hea Sta Mastectomy Lumpecto	alth tes 1 2 3 4 5 6 7 8 9 10	k Values -0.0018 -0.0043 0.0034 0.0055 0.0213 0.0771 -0.0044 -0.0058 -0.0002 0.0039	Participant	Hea ta Mastectomy Lumpecto	lth tes 1 2 3 4 5 6 7 8 9 10	k Values 0.0008 0.0012 0.0033 -0.0130 0.0131 0.0115 0.0000 -0.0005 -0.0040 -0.0096	Participant 6	Hea ta Mastectomy Lumpecto	1       2       3       4       5       6       7       8       9       10	k Values 0.0010 -0.0002 0.0086 0.0160 0.0013 -0.0815 -0.0026 -0.0002 0.0055 0.0112
Pa	rticipant 4	Heata Mastectomy Lumpectomy	Ith           1           2           3           4           5           6           7           8           9           10           11	k Values -0.0018 -0.0043 0.0034 0.0055 0.0213 0.0771 -0.0044 -0.0058 -0.0002 0.0039 0.0176	Participant	Hea ta Mastectomy Lumpectomy	Ith           1           2           3           4           5           6           7           8           9           10           11	k Values 0.0008 0.0012 0.0033 -0.0130 0.0131 0.0115 0.0000 -0.0005 -0.0040 -0.0096 0.0061	Participant 6	Heata Mastectomy Lumpectomy	1       2       3       4       5       6       7       8       9       10       11	k Values 0.0010 -0.0002 0.0086 0.0160 0.0013 -0.0815 -0.0026 -0.0002 0.0055 0.0112 -0.0008

|--|
	Hea	alth	k		Hea	alth	k		Hea	ılth	k
Participant	Sta	tes	Values	Participant	Sta	tes	Values	Participant	Sta	tes	Values
		1	0.0018			1	0.0022			1	0.0011
	Ma	2	0.0023		Ma	2	0.0020		Ma	2	-0.0013
	ıste	3	0.0015		ıste	3	0.0060		ıste	3	0.0018
	cto	4	0.0018		cto	4	0.0019		cto	4	-0.0061
	my	5	0.0068		my	5	0.0138		my	5	-0.0079
7		6	0.0115	<b>Q</b>		6	0.0703	0		6	-0.0330
/		7	-0.0005	0		7	-0.0003	9		7	0.0002
	Lur	8	-0.0002		Lur	8	0.0013		Lur	8	-0.0020
	npe	9	0.0009		npe	9	0.0065		npe	9	0.0033
	ecte	10	0.0007		ecte	10	0.0040		ecte	10	-0.0061
	my	11	0.0062		my	11	0.0120		ymy	11	-0.0080
		12	0.0110		~	12	0.0703		1	12	-0.0330
	Hea	alth	k		Hea	ılth	k		Hea	alth	k
Participant	Sta	tes	Values	Participant	Sta	tes	Values	Participant	Sta	tes	Values
		1	-0.0003			1	-0.0031			1	-0.0025
	Ma	2	-0.0003		Ma	2	-0.0046		Ma	2	-0.0013
	ste	3	-0.0119		ste	3	-0.0037		ste	3	0.0056
	cto	4	-0.0118		cto	4	-0.0062		cto	4	-0.0030
	my	5	0.0090		ny L	5	-0.0028	8 3 12	my	5	-0.0062
10		6	-0.0158	11		6	0.0051			6	-0.6207
10		7	-0.0003	11		7	-0.0013		Lur	7	-0.0009
	l	7 -0.0   8 0.00	0.0011		un	8	-0.0015			8	-0.0023
	Lumpe 9 -	-0.0123		npe	9	-0.0003		npe	9	0.0033	
	cto	10	-0.0119		cto	10	-0.0062		cto	10	-0.0033
	my	11	0.0174		my	11	0.0006		my	11	0.0085
	7	12	-0.0158		7	12	-0.0084		r	12	-0.6207
									-		
	Hea	alth	k		Hea	lth	k		Hea	alth	k
Participant	Sta	tes	Values	Participant	Sta	tes	Values	Participant	Sta	tes	Values
	-	1	0.0034			1	0.0050			1	0.0002
	Ma	2	0.0042		Ma	2	0.0040		Ma	2	-0.0002
	stec	3	0.0040		stec	3	-0.0050		stec	3	-0.0047
	tor	4	-0.0130		tor	4	-0.0034		tor	4	-0.0131
	$13 \qquad \boxed{\begin{array}{c} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 $	5	0.0014		ny	5	-0.0179		ny	5	0.0023
13		-0.2561	14		6	-0.1498	15		6	-0.0027	
15		7	0.0003	17	Н	7	-0.0029	15	Π	7	0.0001
	un	8	0.0003		'n	8	-0.0038	38	'n	8	0.0005
	8 0.0003 9 0.0007 10 -0.0138	0.0007		npe	9	-0.0093	93	npe	9	-0.0055	
			cto	10	-0.0036	36	cto	10	-0.0089		
	my	11	-0.0131		my	11	-0.0116		my	11	0.0015
	~	12	-0.2561		~	12	-0.1498		1	12	-0.0027

Table N. 1 (Continued). Constant k Values in Multiplicative Utility Function

## **APPENDIX O**

## A TEXT REPORTS OF SAMPLE SIMULATION RUNS

## Table O.1. Text Report of Mastectomy

Sample	Value	СТ	нт	IR	М	NT	s	Dist(u1)	Dist(u2)	Dist(u3)	Dist(u4)	Dist(u5)	Dist(u6)
1	699.574	0.768	1.875	0.195	1.552	5.171	0.039	97.268	89.933	68.026	52.567	41.748	25.693
2	665.236	0.720	1.849	0.194	1.491	5.285	0.035	88.518	88.569	70.768	60.751	41.316	26.182
3	648.878	0.744	1.770	0.189	1.575	5.371	0.029	93.643	70.281	57.420	50.932	41.198	26.352
4	676.362	0.748	1.825	0.200	1.693	5.135	0.051	96.291	83.011	68.764	67.147	43.162	22.459
5	688.248	0.763	1.907	0.222	1.618	4.990	0.019	101.315	84.733	58.404	57.730	39.308	25.463
6	608.583	0.748	2.017	0.200	1.650	5.026	0.019	80.369	83.658	63.813	49.191	39.721	24.469
7	588.605	0.751	1.835	0.176	1.515	5.242	0.025	84.360	64.878	59.918	49.867	43.211	25.633
8	607.486	0.746	1.864	0.204	1.644	5.062	0.027	83.315	79.214	65.882	48.751	39.083	25.871
9	602.749	0.728	1.914	0.157	1.555	5.195	0.028	82.388	77.935	60.784	57.574	43.061	22.976
10	658.860	0.771	1.987	0.197	1.584	4.990	0.025	92.344	88.134	63.911	36.330	42.805	23.255
11	614.541	0.743	1.929	0.219	1.569	5.082	0.056	80.092	83.597	68.005	67.138	40.164	26.554
12	650.607	0.739	1.794	0.181	1.623	5.134	0.025	92.638	74.847	78.085	67.244	41.946	25.510
13	668.752	0.744	1.789	0.214	1.775	5.011	0.024	95.875	87.154	65.271	52.606	42.498	25.176
14	660.616	0.766	1.798	0.167	1.481	5.332	0.040	91.530	78.373	64.051	74.293	39.076	27.535
15	676.089	0.727	1.946	0.210	1.513	5.020	0.033	97.773	82.062	64.510	61.632	39.988	26.193
16	607.186	0.761	1.915	0.196	1.538	5.152	0.024	85.291	70.494	65.157	50.223	42.650	25.279
17	647.970	0.770	1.764	0.182	1.461	5.158	0.028	90.969	89.684	56.427	53.972	41.623	24.958
18	620.984	0.759	1.786	0.212	1.675	5.083	0.039	87.460	82.285	56.207	55.306	43.450	24.590
19	667.236	0.735	1.917	0.207	1.679	5.000	0.046	95.614	81.455	70.221	66.077	39.357	23.466
20	635.568	0.740	1.773	0.208	1.612	5.117	0.054	88.868	86.817	53.680	71.090	41.028	24.366
21	676.320	0.741	1.840	0.202	1.571	5.204	0.039	93.824	83.339	73.371	65.188	38.939	24.607
22	613.687	0.727	1.824	0.202	1.454	5.263	0.052	83.158	75.275	69.847	73.389	42.530	24.740
23	650.713	0.773	1.694	0.197	1.709	4.999	0.025	97.182	81.955	60.523	63.130	39.230	23.265
24	653.530	0.735	1.874	0.207	1.593	4.925	0.030	98.936	77.027	59.934	67.625	40.630	24.066
25	631.048	0.760	1.891	0.164	1.533	5.323	0.026	81.138	88.562	62.161	70.083	39.280	23.832
26	670.832	0.742	1.873	0.217	1.601	5.114	0.039	93.733	86.468	59.778	60.598	42.612	26.841
27	661.616	0.757	1.836	0.173	1.520	5.225	0.028	89.185	87.569	62.611	78.833	39.535	28.158
28	618.598	0.785	1.855	0.196	1.451	5.115	0.036	82.031	84.782	68.387	66.389	43.823	25.915
29	609.062	0.754	1.845	0.192	1.588	5.172	0.026	86.073	76.380	51.912	62.715	39.998	24.087
30	660.231	0.752	1.783	0.183	1.607	5.292	0.014	92.950	82.740	59.167	58.898	38.665	23.291
31	658.559	0.743	1.938	0.188	1.512	5.275	0.022	91.197	78.077	63.792	54.830	41.961	26.077
32	619.678	0.753	1.999	0.184	1.546	5.028	0.026	88.238	73.683	62.033	55.928	40.868	25.538
33	658.798	0.748	1.830	0.155	1.398	5.524	0.015	91.393	75.450	59.869	57.363	44.379	24.820
34	652.461	0.738	1.860	0.202	1.583	5.202	0.029	95.407	72.890	55.861	66.869	40.752	24.668

35	669.387	0.758	1.744	0.197	1.602	5.069	0.035	95.421	85.608	69.610	66.354	40.725	26.618
36	604.556	0.756	1.838	0.184	1.498	5.344	0.022	81.299	74.645	62.779	62.497	42.069	24.948
37	589.838	0.747	1.806	0.188	1.716	5.135	0.045	79.056	78.589	62.652	65.905	40.399	24.656
38	613.951	0.733	1.845	0.212	1.504	5.177	0.036	79.647	84.436	71.311	69.448	43.430	26.177
39	600.535	0.734	1.951	0.176	1.452	5.181	0.033	83.201	76.119	60.553	42.905	41.468	22.607
40	651.911	0.749	1.876	0.199	1.478	5.301	0.031	86.271	90.183	67.409	46.567	40.883	22.048
41	600.313	0.742	1.869	0.190	1.575	5.264	0.023	79.409	79.755	57.033	64.921	42.294	25.604
42	688.348	0.743	1.846	0.212	1.584	5.214	0.046	99.831	80.307	59.796	55.473	39.934	25.164
43	635.709	0.739	1.945	0.184	1.502	5.208	0.020	84.285	88.638	55.174	64.593	40.023	24.932
44	615.806	0.747	1.890	0.211	1.601	5.075	0.038	85.506	82.152	56.470	51.321	42.138	23.771
45	614.486	0.718	1.786	0.171	1.625	5.304	0.034	81.974	80.141	67.087	61.656	38.614	25.310
46	647.449	0.753	1.739	0.189	1.596	5.147	0.023	91.732	80.801	75.558	48.954	43.319	24.242
47	702.051	0.754	1.796	0.200	1.645	5.104	0.021	102.936	84.325	62.080	67.995	42.046	25.943
48	594.871	0.723	1.802	0.170	1.574	5.279	0.043	79.142	79.594	59.074	68.195	42.656	25.308
49	663.585	0.753	1.802	0.198	1.554	5.150	0.018	97.682	78.334	56.479	75.119	42.117	23.905
50	623.045	0.749	1.835	0.193	1.620	5.330	0.026	83.952	79.317	54.423	57.511	38.610	27.041
51	625.585	0.736	1.804	0.194	1.420	5.290	0.034	81.407	86.091	71.588	66.337	44.984	25.697
52	638.494	0.750	1.778	0.209	1.638	5.141	0.038	89.441	84.492	57.029	58.356	43.586	25.064
53	612.760	0.757	1.793	0.199	1.602	5.085	0.021	87.442	76.316	58.606	62.970	39.656	25.646
54	607.932	0.784	1.622	0.210	1.652	5.217	0.021	86.301	76.245	63.636	49.944	39.823	23.777
55	620.039	0.745	1.753	0.206	1.565	5.099	0.029	86.191	83.331	60.700	61.248	39.194	26.967
56	620,468	0.763	1.850	0.176	1.602	5.102	0.030	82.106	93.333	51.071	60.893	40.049	26.155
57	654 853	0 763	1 718	0 199	1 784	5 149	0.022	92 214	83 863	63 118	68 208	37 641	24 943
58	664.617	0.746	1.831	0.180	1.444	5.338	0.023	92.208	79.578	67.041	65.459	41.855	25.353
59	642 023	0 741	1 791	0 208	1 635	5 106	0.030	89 396	84 406	65 874	59 182	44 268	25 331
60	637 123	0.755	1.870	0.220	1 531	5 193	0.038	88 495	80 141	65.073	47 021	42 302	23 360
61	625.067	0.760	1.070	0.165	1.535	5 309	0.037	85 063	81 287	62 311	53 860	40 511	24 461
62	621 679	0.751	1.700	0 178	1.574	5 175	0.023	86 843	74 017	68 938	58 595	42 877	26.376
63	645 101	0 764	1 750	0 206	1.528	5 278	0.021	85 282	87 871	76 122	52 922	41 485	24 656
64	620 972	0.734	1.700	0.206	1.624	5 198	0.036	84 955	81 466	61 133	60 439	39 352	24 402
65	573 464	0.761	1.011	0.201	1.684	5 144	0.058	80 891	64 458	63 751	62 301	42 004	25 029
66	675 607	0 734	1.865	0 184	1.396	5 378	0.023	91 054	83 989	64 772	78 908	39 975	27 790
67	685 820	0.778	1.856	0 176	1 457	5 366	0.020	89 343	93 037	69 786	59 870	43 014	26 674
68	619 957	0 777	1 637	0 215	1 636	5 242	0.031	83 156	85 227	65 625	62 751	37 520	26 715
69	663 403	0.768	1 770	0 191	1.607	5 157	0.026	92 830	88 498	64 158	64 664	40 554	23 072
70	637 079	0.760	1.837	0.196	1 4 3 7	5 229	0.027	88 093	78 179	69 697	61 260	41 144	25 722
70	609 103	0.738	1.852	0.215	1 4 9 9	5 331	0.026	79 444	82 472	61 136	60 798	38 728	24 250
72	658 613	0.757	1.827	0.216	1.560	5 171	0.020	01 451	84 177	58 452	66 470	42 035	27 410
73	601 380	0.761	1.027	0.210	1.606	5 240	0.047	77 626	80.830	70 631	58 944	38 971	28 722
74	644 742	0.764	1.770	0.132	1 481	5 502	0.047	85 153	78 703	70.001	72 772	38 184	23 376
75	677 237	0.764	1.906	0.193	1.551	5 288	0.024	94 216	79 105	65 381	65 326	42 550	26 269
76	696 576	0.740	1.807	0.100	1.001	5 4 0 9	0.024	97 612	83 303	59 223	45 972	40 982	28 209
70	608 430	0.745	1.007	0.202	1 4 9 4	5 341	0.020	97.012	82 277	71 371	56 465	39 535	28 346
78	667 486	0.760	1.006	0.100	1.570	5 104	0.010	00 033	74 058	60 734	57 736	11 962	25.092
70	667.087	0.752	1.900	0.156	1.575	5 272	0.030	04 720	92 212	54 394	56 072	41.022	25.032
79 90	647 795	0.752	1.000	0.100	1.400	5.272	0.022	94.729	74 752	04.304 61 596	52 569	41.055	25.475
91	659 150	0.760	1 704	0.131	1 404	5 201	0.010	06 756	79 976	101.000	45 900	41.204	27.041
01 02	606 950	0.752	1.724	0.1/9	1.494	4 0 27	0.010	90.700	10.010	40.940	40.090	41.900	21.000
02 93	620 106	0.760	1.042	0.202	1.002	4.921 5 315	0.020	04.22U	70 622	68 400	51 925	43.240	20.009
03 94	620.025	0.759	1.022	0.172	1.019	5 200	0.021	02.070 90.011	19.000	10 750	04.020 66.270	41.700	23.900
04 95	620 747	0.731	1.002	0.100	1.491	J.∠dU	0.019	00.011	30.335	49./09	00.3/8	41.007	20.204
86	624 250	0.740	1.712	0.197	1.554	5.310 5.320	0.040	00.021	79 061	09.0/3	52 569	40.501	20.991
00	024.302	0.750	1.722	0.190	1.550	5.229	0.031	00.173	10.001	72.092	62.000	40.091	23.113
07	0/4./40	U.153	1.095	U. 192	1.591	3.154	0.045	90.441	09.090	12.002	03.059	<b>JO.305</b>	20.171

88	650.046	0.747	1.863	0.203	1.550	5.327	0.040	84.741	87.887	68.711	55.411	39.507	24.269
89	649.283	0.719	1.914	0.173	1.500	5.318	0.014	89.912	76.560	66.040	74.897	41.631	23.062
90	642.967	0.758	1.818	0.182	1.775	4.953	0.023	91.909	85.221	65.602	49.462	42.128	24.221
91	636.108	0.769	1.752	0.212	1.545	5.175	0.024	88.314	85.419	59.367	67.145	41.550	24.196
92	661.388	0.729	2.001	0.185	1.514	5.235	0.027	88.603	88.494	57.893	52.940	41.616	24.895
93	702.365	0.755	1.851	0.198	1.556	5.180	0.027	101.431	87.261	54.330	51.406	42.130	26.915
94	626.714	0.744	1.862	0.187	1.593	5.058	0.054	89.422	79.294	59.869	66.059	43.080	22.955
95	645.101	0.782	1.748	0.189	1.447	5.375	0.034	91.285	75.750	58.904	56.257	40.941	24.755
96	704.094	0.751	1.753	0.188	1.481	5.280	0.016	101.704	86.988	59.674	61.428	40.576	24.592
97	612.841	0.750	1.828	0.187	1.614	5.338	0.022	75.032	91.822	62.098	75.210	43.286	26.435
98	648.004	0.761	1.761	0.213	1.641	5.161	0.017	91.869	82.041	55.983	68.128	43.632	25.970
99	627.409	0.748	1.873	0.170	1.558	5.279	0.021	83.495	85.395	57.854	71.662	41.179	23.266
100	666.691	0.730	1.854	0.192	1.591	5.033	0.032	93.055	94.058	57.783	64.437	41.415	24.975
101	627.140	0.750	1.820	0.215	1.556	5.249	0.033	88.321	69.026	73.281	61.867	39.504	23.940
102	633.199	0.777	1.868	0.187	1.575	5.265	0.022	85.575	77.655	64.773	60.604	42.256	27.456
103	714.410	0.724	1.878	0.201	1.479	5.246	0.024	100.210	88.103	71.709	67.398	41.133	23.464
104	672.420	0.759	1.798	0.201	1.546	5.210	0.021	94.237	86.315	68.513	51.417	42.900	23.536
105	592.743	0.747	1.757	0.184	1.592	5.286	0.024	81.625	73.024	61.175	73.179	42.862	23.238
106	605.263	0.739	1.831	0.207	1.523	5.142	0.028	84.578	77.741	58.083	49.523	41.583	25.981
107	687.088	0.760	1.813	0.185	1.565	5.095	0.025	100.507	83.217	69.240	60.312	39.997	23.638
108	714.726	0.763	1.889	0.196	1.473	5.367	0.017	96.543	90.552	70.511	60.675	41.027	23.952
109	655.159	0.743	1.885	0.188	1.607	5.004	0.036	91.153	86.307	70.006	67.085	39.225	25.160
110	687.445	0.739	1.757	0.234	1.525	5.134	0.035	96.354	94.769	64.870	54.495	41.351	25.059
111	598,128	0.756	1.765	0.178	1.667	5.136	0.021	79.605	86.568	58.959	51,289	40.761	26.326
112	657 577	0 736	1 798	0 195	1 527	5 212	0.030	94 578	82 499	61 320	57 126	38 515	21 130
113	640 673	0 757	1 738	0.209	1 686	5 170	0.028	90 451	76 917	71 739	64 723	37 703	24 054
114	633 968	0.739	1.825	0.195	1.522	5 235	0.016	83 851	88 460	63 385	63 338	41 424	25 974
115	681 180	0 777	1.882	0 164	1 497	5 262	0.026	95 535	80 701	67 713	70 746	40 810	24 069
116	653.245	0.750	1.756	0.167	1.542	5.309	0.022	90.532	80.308	67.243	64.310	40.455	26.307
117	680.598	0.760	1.929	0.201	1.577	5.078	0.031	93.902	85.680	73.715	56.815	39.344	27.151
118	668.732	0.768	1.703	0.194	1.585	5.230	0.033	92.730	86.253	72.555	69.054	43.562	24.039
119	619.576	0.767	1.771	0.194	1.610	5.216	0.025	85.485	83.480	56.228	56.555	44.066	23.090
120	624.794	0.742	1.998	0.190	1.679	5.135	0.015	80.503	87.977	62.876	69.581	37.405	23.020
121	683.818	0.768	1.801	0.174	1.458	5.336	0.033	101.461	75.471	54.288	57.711	39.183	23.005
122	637.841	0.757	1.675	0.183	1.604	5.330	0.019	88.413	78.773	63.310	80.875	40.288	25.179
123	621,799	0.752	1.805	0.201	1.539	5.200	0.039	88.077	74.883	58.017	67.126	42,114	25.126
124	672.313	0.781	1.820	0.200	1.604	5.242	0.031	90.404	90.330	65.386	57.808	42.705	25.528
125	675.187	0.760	1.765	0.207	1.583	5.268	0.026	91.946	91.438	67.680	55.185	41.643	23.459
126	621.046	0.750	1.821	0.200	1.513	5.149	0.020	87.499	77.534	61.228	66.715	42.366	24.720
127	611.068	0.762	1.860	0.185	1.478	5.205	0.031	82.885	83.523	55.862	50.099	41.871	24.458
128	598.410	0.777	1.744	0.193	1.618	5.345	0.024	81.249	75.176	59.211	50.579	43.071	24.992
129	627.338	0.773	1.751	0.174	1.598	5.124	0.035	90.930	75.927	58.467	64.184	42.219	25.516
130	610.995	0.749	1.813	0.184	1.487	5.351	0.033	83.696	70.259	69.120	63.353	41.400	25.096
131	631.712	0.731	1.883	0.178	1.561	5.257	0.024	90.406	68.853	63.630	57.759	39.312	25.663
132	594.055	0.747	1.875	0.188	1.565	4.986	0.025	83.823	75.336	62.860	64.675	41.126	25.136
133	676.366	0.748	1.858	0.205	1.606	5.058	0.051	95.947	85.412	65.790	54.954	40.474	27.519
134	617.625	0.748	1.824	0.226	1.553	5.138	0.035	90.216	75.876	49.238	49.150	40.695	23.048
135	673,102	0.736	1.973	0.185	1.568	5.105	0.042	90.364	90.730	65.498	67.737	40.794	26.349
136	669.437	0.755	1.745	0.200	1.564	5.169	0.023	100.236	73.399	61.019	66.699	41.313	25.990
137	633,559	0.758	1.839	0.208	1.553	5.260	0.031	84.487	86.158	58,226	62,861	39.816	24.879
138	736,960	0.766	1.729	0.188	1.471	5.507	0.017	100.508	92.264	69.494	73.527	39,598	24.270
139	651.236	0.751	1.793	0.190	1.560	5.081	0.020	93.863	83.421	57.944	64.573	40.007	25.914
140	687.497	0.745	1.840	0.186	1.518	5.238	0.035	93.861	96.412	50.715	52.054	42.164	28.257

141	586.203	0.758	1.839	0.178	1.625	5.166	0.018	77.652	75.143	68.983	70.031	39.016	25.890
142	572.031	0.747	1.832	0.202	1.693	4.977	0.041	75.565	79.809	69.187	72.400	44.635	23.426
143	682.893	0.755	1.824	0.164	1.535	5.349	0.029	92.262	90.543	65.042	67.408	41.950	23.200
144	646.918	0.766	1.749	0.193	1.707	5.112	0.014	90.345	89.941	56.534	59.991	42.796	24.524
145	649.554	0.736	1.869	0.165	1.513	5.403	0.013	85.429	84.869	64.652	55.982	41.677	26.469
146	569.451	0.759	1.812	0.174	1.522	5.353	0.025	65.958	89.555	71.940	53.754	38.644	27.735
147	583.108	0.739	1.808	0.197	1.658	5.070	0.018	78.841	74.272	78.339	53.526	41.580	24.439
148	650.922	0.764	1.826	0.168	1.464	5.326	0.030	86.660	93.903	55.054	49.316	42.281	24.086
149	617.198	0.736	1.809	0.182	1.526	5.463	0.025	80.333	82.383	55.809	59.283	42.714	26.432
150	711.556	0.786	1.793	0.200	1.677	5.129	0.027	104.319	82.442	67.512	58.806	40.371	25.489
151	661.004	0.739	1.765	0.166	1.557	5.333	0.015	88.056	94.885	66.993	56.368	39.142	21.507
152	651.020	0.745	1.758	0.189	1.552	5.242	0.014	92.936	79.875	58.970	50.190	39.174	27.127
153	619.577	0.782	1.717	0.176	1.584	5.274	0.043	87.830	79.488	50.030	60.187	39.452	23.408
154	576.504	0.749	1.754	0.172	1.565	5.330	0.021	75.286	76.772	62.267	72.490	43.250	25.442
155	606.771	0.764	1.918	0.221	1.663	5.010	0.020	82.676	78.533	67.037	61.785	41.745	24.159
156	594.682	0.754	1.840	0.173	1.580	5.232	0.019	82.246	73.439	56.818	64.101	41.269	24.418
157	602.857	0.756	1.846	0.224	1.638	5.197	0.037	76.925	84.242	68.187	71.064	41.968	23.700
158	643.342	0.761	1.799	0.193	1.558	5.167	0.033	90.115	78.002	67.403	70.741	43.557	26.264
159	610.789	0.748	1.893	0.241	1.602	5.042	0.045	85.333	73.296	66.823	58.778	35.757	26.230
160	601.467	0.755	1.739	0.192	1.525	5.369	0.034	79.470	80.916	55.373	55.953	37.492	28.430
161	635.020	0.769	1.840	0.210	1.583	5.086	0.027	79.539	97.137	76.259	62.274	41.947	25.705
162	651.209	0.748	1.904	0.191	1.604	4.938	0.029	93.018	86.036	57.604	72.595	37.589	25.554
163	608.269	0.736	1.892	0.205	1.557	5.097	0.035	85.441	75.810	57.176	58.865	40.242	25.821
164	654.429	0.751	1.849	0.178	1.729	5.054	0.026	92.552	80.582	63.304	63.720	41.182	28.759
165	637.732	0.755	1.750	0.206	1.628	5.122	0.021	88.460	87.934	63.438	56.207	41.314	23.557
166	611.386	0.754	1.854	0.225	1.515	5.118	0.016	83.010	81.640	66.736	45.386	41.295	25.403
167	636.451	0.759	1.936	0.202	1.511	5.053	0.038	90.618	77.126	66.232	58.958	42.841	23.552
168	655.140	0.749	1.874	0.203	1.501	5.149	0.018	90.760	84.896	61.984	79.950	42.346	23.867
169	641.788	0.750	1.807	0.199	1.569	5.285	0.045	85.470	89.141	58.603	57.571	43.774	24.645
170	565.061	0.751	1.879	0.202	1.585	5.061	0.010	71.776	84.686	66.761	58.936	38.098	22.758
171	625.739	0.794	1.861	0.171	1.646	5.114	0.025	91.687	70.823	52.764	60.362	42.452	26.428
172	654.390	0.726	1.936	0.180	1.503	5.288	0.021	87.325	84.659	68.422	49.664	43.079	25.234
173	645.255	0.754	1.903	0.177	1.474	5.252	0.029	91.480	72.573	61.341	79.915	35.823	25.284
174	631.934	0.752	1.977	0.167	1.532	5.144	0.044	91.499	69.370	60.510	74.471	43.120	23.498
175	662.481	0.758	1.801	0.200	1.549	5.281	0.032	92.635	81.465	63.714	59.207	42.299	24.104
176	661.883	0.752	1.895	0.200	1.585	5.075	0.029	94.813	84.778	55.865	56.920	41.223	24.508
177	610.487	0.747	1.771	0.184	1.482	5.277	0.038	83.833	75.737	63.694	70.342	42.208	25.462
178	635.264	0.747	1.883	0.199	1.493	5.253	0.033	83.382	86.841	64.102	59.262	41.664	25.782
179	637.470	0.754	1.847	0.191	1.507	5.186	0.042	83.258	90.245	71.476	54.319	43.793	25.305
180	597.767	0.762	1.867	0.187	1.544	5.080	0.021	77.029	91.644	58.739	60.304	42.035	24.993
181	633.919	0.748	1.877	0.219	1.734	4.913	0.026	89.543	80.995	66.734	56.275	38.687	27.180
182	646.073	0.744	1.719	0.209	1.566	5.383	0.021	92.663	70.207	66.461	59.267	39.729	23.265
183	676.845	0.744	1.748	0.196	1.556	5.381	0.033	96.056	78.113	63.403	55.852	39.240	25.360
184	709.626	0.763	1.841	0.200	1.452	5.370	0.048	101.511	80.022	62.477	64.011	41.852	23.875
185	648.986	0.739	1.890	0.212	1.642	5.012	0.047	94.214	76.706	61.622	69.791	44.003	25.651
186	711.054	0.769	1.868	0.196	1.425	5.266	0.035	98.297	88.727	75.324	64.341	43.466	22.915
187	642.522	0.747	1.767	0.207	1.532	5.257	0.017	93.776	67.336	65.302	62.852	42.931	26.796
188	595.998	0.777	1.860	0.200	1.574	5.090	0.030	78.688	80.844	69.166	58.177	39.895	25.335
189	607.139	0.741	1.751	0.187	1.629	5.209	0.026	83.855	74.376	69.397	55.692	44.608	25.734
190	641.321	0.785	1.874	0.172	1.460	5.199	0.033	91.623	78.557	50.694	68.310	41.871	25.119
191	637.866	0.761	1.924	0.223	1.519	5.175	0.046	84.500	88.074	60.533	62.082	43.730	23.005
192	647.717	0.760	1.848	0.210	1.504	5.263	0.032	86.591	85.474	67.489	66.860	42.237	23.412
193	631.198	0.739	1.958	0.214	1.618	5.138	0.036	80.721	88.806	70.612	67.625	38.931	23.390

194	617.200	0.771	1.732	0.202	1.572	5.160	0.052	88.785	74.445	59.709	61.390	38.841	24.555
195	605.530	0.744	1.810	0.206	1.592	5.134	0.024	83.284	76.664	69.068	64.497	40.728	24.289
196	650.033	0.758	1.808	0.208	1.542	5.211	0.050	91.737	79.560	67.893	50.126	40.021	23.167
197	669.728	0.753	1.931	0.176	1.522	5.312	0.025	87.986	92.024	65.503	54.110	40.422	22.737
198	656.640	0.734	1.799	0.211	1.741	5.000	0.029	95.239	80.560	68.324	61.686	40.834	25.282
199	734.930	0.750	1.794	0.189	1.542	5.294	0.022	108.266	82.858	61.177	65.263	40.114	24.991
200	587.731	0.756	1.805	0.205	1.639	5.158	0.010	77.915	85.366	53.249	65.683	41.283	23.198

Sample	Value	СТ	HT	LR	М	NT	S	Dist(u1)	Dist(u2)	Dist(u3)	Dist(u4)	Dist(u5)	Dist(u6)
1	752.440	0.749	1.866	0.197	1.563	5.177	0.027	101.324	95.776	73.357	78.930	46.779	36.685
2	679.703	0.750	1.835	0.192	1.536	5.221	0.028	96.636	89.821	66.110	72.489	63.101	12.882
3	686.981	0.747	1.845	0.189	1.551	5.179	0.034	91.767	87.680	70.533	65.060	44.256	35.901
4	713.902	0.752	1.844	0.194	1.517	5.293	0.031	97.005	96.496	70.591	55.771	20.235	22.401
5	688.523	0.753	1.849	0.192	1.515	5.241	0.028	92.473	93.071	62.358	64.457	31.405	29.236
6	688.328	0.750	1.842	0.196	1.550	5.174	0.033	96.288	96.424	62.321	61.252	34.375	17.412
7	685.688	0.752	1.844	0.189	1.545	5.180	0.030	96.972	89.900	66.774	64.015	39.253	18.885
8	732.246	0.750	1.856	0.191	1.587	5.166	0.027	98.591	92.450	73.178	62.258	38.952	38.504
9	659.941	0.745	1.836	0.189	1.550	5.243	0.025	94.328	92.068	66.197	55.131	51.120	4.897
10	664.313	0.753	1.820	0.187	1.561	5.195	0.031	91.921	96.422	58.907	59.159	56.036	16.128
11	695.039	0.755	1.819	0.197	1.584	5.147	0.032	91.690	99.008	69.762	72.756	25.714	29.523
12	691.379	0.751	1.826	0.194	1.532	5.267	0.025	94.065	95.589	64.795	56.261	29.071	22.526
13	680.564	0.745	1.831	0.195	1.514	5.242	0.027	97.679	90.821	59.102	51.083	18.686	15.484
14	672.882	0.758	1.830	0.191	1.589	5.138	0.037	88.784	90.658	76.558	78.041	50.355	28.602
15	751.142	0.745	1.846	0.196	1.529	5.226	0.031	104.130	96.696	66.205	68.694	43.796	29.964
16	714.481	0.746	1.832	0.197	1.571	5.184	0.033	100.595	94.060	81.638	68.531	48.754	14.032
17	679.395	0.751	1.801	0.188	1.541	5.263	0.026	91.770	95.266	66.898	44.101	33.875	24.226
18	679.942	0.746	1.808	0.200	1.534	5.282	0.033	94.261	89.829	68.138	47.301	48.410	20.374
19	694.347	0.745	1.835	0.206	1.544	5.174	0.033	95.025	96.012	68.541	65.843	49.940	22.011
20	702.414	0.746	1.832	0.197	1.554	5.208	0.035	96.597	90.934	86.698	54.769	29.207	20.079
21	699.897	0.756	1.783	0.197	1.581	5.209	0.030	95.416	89.934	72.556	66.407	23.275	30.603
22	705.487	0.747	1.852	0.202	1.560	5.206	0.032	91.925	98.412	77.311	62.129	36.569	29.070
23	739.771	0.751	1.808	0.196	1.532	5.241	0.028	101.342	96.154	60.789	59.416	58.189	36.289
24	658.907	0.757	1.808	0.195	1.546	5.268	0.022	88.485	86.835	63.615	61.673	58.661	28.382
25	709.812	0.749	1.855	0.192	1.544	5.238	0.023	97.935	88.478	82.885	62.991	48.960	21.888
26	723.648	0.754	1.849	0.203	1.561	5.183	0.035	96.536	94.349	76.079	67.112	43.215	33.413
27	769.356	0.754	1.835	0.198	1.575	5.181	0.029	107.162	87.903	86.177	68.343	41.310	36.199
28	698.313	0.754	1.848	0.196	1.543	5.193	0.028	95.325	91.734	58.754	62.435	49.812	32.960
29	677.461	0.751	1.833	0.190	1.548	5.197	0.028	90.008	96.209	71.315	62.576	30.720	24.019
30	652.150	0.749	1.811	0.197	1.566	5.215	0.032	86.717	99.357	63.062	66.730	41.838	16.262
31	705.121	0.754	1.809	0.193	1.533	5.237	0.034	96.945	87.377	68.703	54.562	46.045	33.700
32	665.380	0.748	1.815	0.200	1.573	5.180	0.033	92.676	93.016	69.127	56.352	47.128	14.893
33	635.671	0.749	1.836	0.198	1.545	5.189	0.029	88.784	86.586	62.154	65.694	41.095	15.512
34	718.714	0.746	1.839	0.194	1.532	5.215	0.028	97.609	94.233	54.636	56.945	34.607	39.593
35	745.569	0.750	1.842	0.191	1.569	5.159	0.028	105.022	87.993	70.576	56.885	44.562	37.552
36	748.406	0.749	1.857	0.196	1.531	5.242	0.029	100.782	99.948	65.834	65.492	56.542	32.619
37	646.785	0.752	1.852	0.178	1.531	5.228	0.029	92.852	85.777	57.155	44.352	40.182	14.557
38	707.438	0.751	1.851	0.184	1.555	5.193	0.034	97.272	95.903	62.300	53.227	49.090	27.420
39	712.815	0.757	1.834	0.201	1.590	5.180	0.027	105.634	91.611	56.597	52.465	38.762	15.381
40	720.531	0.746	1.834	0.194	1.540	5.225	0.026	99.139	95.082	75.620	67.244	58.614	22.340
41	705.784	0.751	1.816	0.185	1.529	5.274	0.031	97.527	94.252	64.656	57.935	22.259	23.835
42	706.699	0.745	1.834	0.187	1.543	5.235	0.023	100.425	86.898	66.131	71.793	56.018	23.320
43	729.560	0.745	1.809	0.197	1.587	5.195	0.033	101.444	94.859	62.942	66.163	47.327	30.707
44	695.971	0.752	1.859	0.190	1.562	5.199	0.027	92.353	93.249	75.841	72.298	63.733	27.140
45	693.413	0.746	1.842	0.194	1.546	5.201	0.029	97.775	90.620	64.345	62.485	41.699	21.127
46	644.192	0.748	1.828	0.193	1.549	5.203	0.033	84.850	90.933	74.154	62.778	45.050	21.644
47	699.949	0.752	1.787	0.190	1.525	5.237	0.024	95.065	95.744	62.055	72.430	32.423	29.017
48	726.878	0.753	1.866	0.199	1.541	5.214	0.033	102.552	94.539	58.401	58.715	18.059	25.625
49	723.523	0.751	1.842	0.191	1.516	5.263	0.032	96.419	97.568	56.426	64.251	54.526	37.178
50	643.117	0.757	1.781	0.197	1.571	5.196	0.027	84.359	93.894	63.163	55.149	36.808	27.871

Table O.2. Text Report of Lumpectomy

51 678.992	0.752	1.825	0.185	1.582	5.179	0.027	95.315	92.692	67.996	60.676	36.047	16.757
52 682.273	3 0.751	1.843	0.202	1.573	5.165	0.030	94.523	87.110	52.933	77.022	27.900	32.794
53 725.174	1 0.747	1.873	0.194	1.535	5.182	0.029	102.961	96.308	66.951	54.558	55.836	18.678
54 717.062	2 0.752	1.824	0.194	1.549	5.199	0.031	100.752	96.971	59.033	54.344	42.274	24.904
55 731.320	0.751	1.802	0.198	1.552	5.233	0.032	104.908	87.976	76.867	48.521	28.879	23.819
56 710.28	0.746	1.824	0.197	1.533	5.221	0.031	99.597	90.970	70.155	64.132	21.564	23.602
57 662.23	3 0.754	1.799	0.200	1.543	5.250	0.027	89.744	90.758	77.829	53.685	50.595	17.347
58 701.31	1 0 741	1 850	0 198	1 536	5 221	0.027	96 802	89 310	62 571	57 753	48 777	30 897
59 680.78	0.749	1.857	0.191	1.565	5.163	0.032	94.447	90.759	57.027	49.542	39.137	28.652
60 744.14	0.756	1.809	0.199	1.539	5.229	0.035	100.021	99.453	84.480	68.920	38.081	26.225
61 714.53	5 0.752	1.827	0.192	1.532	5.243	0.027	95.677	96.494	73.035	64.191	38.544	28.210
62 736.19	5 0.754	1.829	0.205	1.552	5.222	0.029	103.385	94.894	65.772	62.946	40.825	25.501
63 728.20 <sup>.</sup>	0.746	1.835	0.195	1.547	5.208	0.028	99.977	96.051	66.257	59.072	20.910	30.899
64 702.55	0.757	1.835	0.198	1.562	5.223	0.032	96.119	93.733	68.552	46.972	41.934	26.399
65 725.40	7 0.749	1.842	0.198	1.538	5.209	0.032	104.092	92.532	62.722	59.575	50.225	21.652
66 686.892	2 0.749	1.844	0.192	1.504	5.264	0.030	87.493	98.042	65.262	49.134	42.886	36,710
67 711 35	3 0 753	1 813	0 194	1 565	5 174	0.035	100 583	85 861	73 157	54 463	58 714	29 392
68 695.14	0.752	1.841	0.200	1.559	5.194	0.026	96.564	96.581	56.789	49.075	41.248	23.973
69 681.80	7 0 751	1 865	0 198	1 558	5 123	0.026	97 022	95 067	68 106	64 280	51 354	10 448
70 694 120	3 0 745	1 839	0 191	1 547	5 199	0.030	93 562	93 363	61 724	63 076	44 182	32 401
71 708.13	0.747	1.817	0.198	1.583	5.196	0.027	95.948	88.961	52.869	66.807	53.262	44.124
72 719 75	7 0 752	1 861	0 198	1 586	5 171	0.024	97 461	98 608	72 345	60 563	49 164	25 500
73 703 19	3 0 754	1 836	0 190	1 566	5 182	0.031	92 045	99 289	63 248	71 676	21 445	34 701
74 741 42	0 753	1 880	0 203	1 561	5 186	0.027	102 630	97 527	66 959	72 516	44 766	25 285
75 679 45	1 0 747	1 860	0.200	1 542	5 177	0.035	94 099	99.056	52 448	62 679	43 214	17 943
76 673.37	3 0 745	1 856	0.189	1.548	5 158	0.030	94 670	87 863	67 215	48 613	32 710	22 762
77 739 859	0 743	1 844	0.206	1.590	5 122	0.031	101 009	86 395	74 671	61 142	53 386	45 942
78 746.930	0 742	1 861	0 195	1.533	5 213	0.028	101.026	93 155	71 814	82 635	45 087	36 460
79 704 79	7 0 752	1 823	0 194	1 583	5 212	0.027	96 977	95 218	63 308	62 992	49 958	25 432
80 702 64	5 0 749	1 841	0 200	1.528	5 199	0.028	94 029	102 668	57 469	70 230	35 797	26 237
81 665.920	6 0.746	1.856	0.200	1.556	5.191	0.036	93.022	96.201	51.982	61.745	44.125	15.140
82 739.61	3 0.754	1.829	0.190	1.539	5.226	0.028	105.311	90.391	78,464	61.088	45.508	21.826
83 702.68	0.745	1.825	0.199	1.571	5.169	0.026	95.852	92.088	74.772	58.349	40.009	28.963
84 720.624	1 0.748	1.862	0.195	1.533	5.212	0.030	101.353	93.669	59.132	62.071	55.407	25.525
85 684.71	0.751	1.841	0.195	1.507	5.238	0.030	98.332	83,109	63.242	58.976	46.045	21.781
86 709 994	1 0 742	1 849	0 191	1 568	5 184	0.030	97 216	99 736	71 175	52 797	33 892	21 154
87 660.564	0.752	1.816	0.192	1.554	5.220	0.031	89.105	90.115	65.557	49.980	29.197	26.867
88 691.11	5 0.753	1.832	0.190	1.542	5.196	0.025	94,399	94.096	59,166	55.311	30.778	29.969
89 724.05	0.758	1.809	0.189	1.534	5.236	0.022	95,403	98.141	75.768	82.978	46.934	31,140
90 692.76	3 0.749	1.815	0.195	1.562	5.169	0.027	96.853	86.844	71.075	44.381	45.777	30.049
91 711.16	3 0.750	1.860	0.206	1.524	5.234	0.030	101.360	82.047	66.788	74.787	32.534	26.845
92 658 262	0 755	1 830	0 191	1 532	5 274	0.028	89 290	89 641	55 805	51 792	49 449	26 173
93 695.069	0.752	1.876	0.196	1.542	5.188	0.029	97.410	99.533	61.757	49.506	41.246	13.529
94 717 790	0 754	1 835	0 194	1 555	5 2 1 8	0.027	103 365	94 618	55 637	71 964	52 201	17 568
95 672 12	0 752	1 853	0 193	1 524	5 234	0.028	86 751	97 097	70 308	69 940	47 571	25 234
96 709.87	0 755	1 817	0 200	1 562	5 229	0.030	95 086	87 409	71 948	59 830	32 394	39 492
97 734 62	0 757	1 815	0 191	1 504	5 239	0.028	102 044	91 093	58 837	64 697	29 238	38 240
98 692 170	0 745	1 864	0 199	1 544	5 2 1 5	0.029	93 458	95 156	70 907	63 926	24 994	22 077
99 712 150	0 750	1 832	0 192	1 539	5 241	0.030	97 871	92 963	62 652	69 817	42 932	28 502
100 737 53	5 0 755	1 823	0 197	1 557	5 202	0.028	105 240	93 141	56 534	56 165	60 330	30 189
101 733 71	1 0 750	1 841	0.200	1 558	5 191	0.030	100.030	96 263	81 749	52 275	53 321	26 780
102 751 97	0.756	1.820	0.196	1.533	5.213	0.029	101 717	94,121	76 479	67 835	35 245	38 029
			2		2.2.10	2.020						10.020

1	1		1		1	1		1	1		1	1	
104	751.252	0.757	1.819	0.192	1.542	5.229	0.022	102.445	102.068	69.182	63.213	40.093	29.040
105	681.466	0.750	1.849	0.193	1.544	5.240	0.026	93.151	89.810	64.512	51.274	39.272	26.582
106	683.041	0.750	1.824	0.195	1.556	5.177	0.028	93.890	95.783	59.337	62.823	35.934	24.044
107	708.073	0.756	1.808	0.188	1.577	5.186	0.030	99.292	85.494	58.189	57.661	38.013	38.442
108	721.255	0.743	1.901	0.196	1.546	5.162	0.035	96.036	95.502	61.029	66.107	51.015	38.619
109	704.871	0.754	1.866	0.197	1.584	5.155	0.029	99.678	92.983	60.655	69.981	51.349	21.393
110	694.288	0.749	1.857	0.199	1.569	5.161	0.020	93.817	94.916	71.375	64.462	31.530	25.436
111	696.013	0.745	1.853	0.191	1.543	5.203	0.027	89.761	98.432	75.344	61.774	40.102	31.308
112	693.888	0.753	1.806	0.200	1.571	5.201	0.025	95.605	92.709	75.597	73.019	20.297	19.936
113	670.628	0.744	1.833	0.191	1.532	5.255	0.025	97.616	90.677	74.412	63.365	42.161	-1.664
114	691.377	0.754	1.828	0.205	1.569	5.153	0.030	90.920	100.702	56.486	66.426	45.601	33.477
115	661.421	0.755	1.839	0.200	1.541	5.232	0.026	96.538	86.959	70.720	56.030	51.816	2.870
116	691.949	0.745	1.827	0.189	1.531	5.219	0.027	99.093	93.125	72.238	80.257	55.312	6.706
117	680.116	0.760	1.813	0.198	1.548	5.175	0.038	99.366	84.112	73.118	56.880	34.614	14.035
118	698.579	0.755	1.793	0.200	1.629	5.151	0.024	95.433	97.249	72.236	61.283	28.021	23.964
119	714.313	0.752	1.840	0.190	1.517	5.225	0.032	103.730	86.415	60.166	61.218	49.270	23.466
120	696.756	0.745	1.852	0.188	1.549	5.206	0.027	99.198	90.702	76.962	60.754	46.380	12.148
121	690.708	0.758	1.824	0.192	1.520	5.225	0.024	95.762	92.105	55.737	58.009	32.384	28.307
122	696.044	0.756	1.832	0.199	1.570	5.142	0.030	99.386	92.472	65.449	74.565	30.348	17.247
123	682.639	0.750	1.837	0.189	1.538	5.204	0.032	99.617	90.061	55.004	62.165	45.469	13.749
124	716.299	0.747	1.825	0.188	1.556	5.247	0.027	98.675	96.674	48.644	66.093	39.716	32.009
125	707.470	0.748	1.876	0.195	1.538	5.184	0.029	96.430	92.676	63.065	69.567	55.435	30.601
126	692.298	0.747	1.870	0.184	1.511	5.250	0.032	96.450	92.745	69.487	68.950	44.087	14.143
127	698.442	0.749	1.764	0.191	1.562	5.232	0.030	96.423	96.929	70.622	55.794	41.376	21.104
128	736.173	0.753	1.815	0.192	1.564	5.219	0.033	101.611	91.797	67.371	69.193	46.611	34.260
129	703.517	0.746	1.858	0.194	1.544	5.223	0.029	96.499	98.045	58.468	59.537	43.209	23.472
130	709.868	0.750	1.839	0.196	1.532	5.235	0.026	101.474	89.467	55.974	54.913	35.948	25.904
131	700.894	0.756	1.800	0.199	1.585	5.193	0.031	96.097	92.776	49.810	61.125	37.926	37.469
132	701.584	0.756	1.814	0.191	1.527	5.218	0.027	94.887	87.972	79.020	70.047	65.141	30.325
133	685.448	0.750	1.811	0.201	1.553	5.226	0.027	96.682	88.389	57.577	67.859	33.302	24.270
134	733.804	0.758	1.814	0.198	1.580	5.186	0.029	103.722	92.482	76.263	60.254	45.179	23.870
135	703.979	0.753	1.862	0.193	1.523	5.221	0.029	93.617	100.113	62.616	53.679	30.597	28.828
136	715.249	0.750	1.811	0.192	1.548	5.200	0.030	93.036	94.215	65.801	58.908	57.047	46.791
137	682.842	0.753	1.852	0.183	1.552	5.195	0.026	94.101	94.624	66.522	54.183	36.462	19.900
138	722.044	0.751	1.846	0.203	1.581	5.118	0.029	98.406	88.495	78.720	55.807	46.115	38.077
139	630.445	0.755	1.811	0.202	1.500	5.215	0.032	86.378	87.364	56.570	57.738	39.487	22.315
140	711.994	0.748	1.834	0.184	1.531	5.216	0.034	99.871	94.894	77.628	64.754	50.697	14.796
141	692.582	0.753	1.807	0.189	1.557	5.193	0.029	94.179	93.923	70.824	66.385	53.300	25.564
142	715.393	0.749	1.835	0.196	1.577	5.185	0.024	95.860	96.049	60.051	69.495	35.310	36.874
143	690.647	0.745	1.833	0.195	1.547	5.207	0.030	91.067	97.735	66.779	53.892	62.663	30.112
144	657.250	0.740	1.861	0.194	1.576	5.146	0.031	98.635	94.501	57.963	46.661	30.550	-2.868
145	707.056	0.750	1.806	0.190	1.558	5.230	0.029	98.436	87.801	74.812	58.493	39.159	27.076
146	677.194	0.752	1.842	0.189	1.521	5.204	0.032	94.847	85.367	63.275	52.466	34.872	27.533
147	729.465	0.748	1.834	0.192	1.581	5.199	0.029	99.467	94.971	72.261	55.880	52.302	31.639
148	688.035	0.750	1.792	0.195	1.559	5.286	0.028	97.231	85.350	65.020	64.478	33.735	22.262
149	715.791	0.755	1.827	0.194	1.547	5.215	0.025	96.799	97.351	64.783	67.048	51.860	29.565
150	713.753	0.751	1.827	0.197	1.530	5.201	0.029	97.284	86.843	73.106	75.317	45.968	35.747
151	733.344	0.750	1.855	0.189	1.527	5.225	0.028	99.374	101.853	66.523	66.397	58.486	25.440
152	694.780	0.751	1.816	0.198	1.538	5.230	0.027	92.326	94.765	67.254	55.693	51.484	32.125
153	658.846	0.755	1.840	0.182	1.485	5.289	0.030	89.521	89.314	49.634	56.124	48.399	28.566
154	688.348	0.756	1.821	0.197	1.562	5.235	0.028	99.484	86.500	60.584	53.470	47.462	18.857
155	708.205	0.750	1.823	0.195	1.563	5.199	0.028	96.922	99.248	59.454	57.615	46.566	26.708
156	717.678	0.746	1.823	0.190	1.536	5.283	0.031	96.770	94.183	66.270	59.929	39.234	31.816

157	736.304	0.753	1.832	0.189	1.559	5.216	0.028	94.851	98.667	79.250	47.579	46.776	42.366
158	682.764	0.750	1.844	0.198	1.515	5.212	0.030	95.723	89.724	55.727	56.403	44.582	25.685
159	707.407	0.750	1.831	0.194	1.538	5.237	0.031	97.414	95.516	64.978	69.442	46.894	22.518
160	708.968	0.750	1.831	0.202	1.546	5.202	0.029	97.785	83.131	76.321	50.772	46.460	36.356
161	704.822	0.751	1.850	0.196	1.576	5.170	0.030	95.986	97.158	69.701	55.402	34.832	24.952
162	677.714	0.753	1.808	0.199	1.550	5.215	0.031	90.952	92.676	68.649	64.926	65.119	25.998
163	684.498	0.752	1.865	0.199	1.569	5.133	0.028	98.495	93.713	48.416	50.959	51.662	20.632
164	683.958	0.752	1.806	0.195	1.543	5.227	0.027	95.828	98.270	64.561	54.555	38.421	12.521
165	702.247	0.748	1.835	0.187	1.549	5.211	0.028	97.208	95.160	60.905	61.410	40.176	25.059
166	677.846	0.756	1.832	0.196	1.561	5.182	0.032	94.491	94.335	66.804	54.929	37.066	16.637
167	664.018	0.749	1.833	0.191	1.542	5.232	0.025	92.996	83.056	55.895	67.248	37.051	27.495
168	688.921	0.753	1.819	0.187	1.555	5.293	0.025	91.386	88.662	76.663	53.082	48.076	30.346
169	667.819	0.746	1.886	0.199	1.562	5.173	0.024	93.071	94.547	65.052	75.938	49.481	9.499
170	722.767	0.751	1.857	0.191	1.566	5.147	0.028	104.873	87.388	63.734	60.180	55.362	26.216
171	697.942	0.750	1.856	0.195	1.568	5.184	0.033	94.376	91.695	61.520	75.171	30.619	32.491
172	666.901	0.743	1.841	0.195	1.531	5.262	0.036	92.002	97.081	60.678	56.232	44.178	11.651
173	699.881	0.747	1.839	0.198	1.544	5.158	0.027	100.529	91.572	62.129	54.650	54.359	20.686
174	667.760	0.751	1.805	0.199	1.582	5.181	0.030	89.759	91.676	64.595	73.954	61.288	26.634
175	714.028	0.743	1.860	0.194	1.577	5.191	0.030	98.884	89.614	75.106	67.596	37.942	26.153
176	684.208	0.746	1.843	0.196	1.561	5.190	0.029	94.509	80.218	63.070	65.123	49.673	37.835
177	692.110	0.750	1.823	0.186	1.521	5.223	0.028	100.220	90.310	64.435	55.522	37.589	14.310
178	753.185	0.753	1.839	0.194	1.547	5.218	0.027	105.286	96.533	75.605	60.487	35.374	24.905
179	671.918	0.749	1.886	0.194	1.535	5.189	0.031	92.205	92.166	52.130	74.551	50.938	23.758
180	698.623	0.756	1.823	0.188	1.559	5.178	0.030	95.691	90.780	64.269	42.174	44.078	35.168
181	673.093	0.749	1.829	0.196	1.541	5.256	0.027	92.304	94.381	71.485	66.501	36.786	12.509
182	695.607	0.748	1.808	0.201	1.578	5.183	0.039	95.656	90.274	76.585	53.399	46.968	26.063
183	711.404	0.744	1.838	0.196	1.545	5.238	0.027	96.940	91.890	67.879	55.143	45.174	31.281
184	649.858	0.750	1.840	0.199	1.553	5.181	0.027	90.439	86.597	61.158	59.301	30.146	21.756
185	694.832	0.755	1.849	0.195	1.545	5.170	0.031	98.164	98.304	59.501	63.063	48.491	14.526
186	678.580	0.746	1.795	0.187	1.538	5.212	0.037	96.494	89.902	65.409	53.579	49.420	18.324
187	673.094	0.757	1.794	0.199	1.581	5.170	0.033	92.901	90.293	72.733	61.677	50.306	21.296
188	682.729	0.753	1.836	0.194	1.532	5.200	0.028	91.347	94.700	57.833	70.898	43.588	30.769
189	734.320	0.756	1.839	0.196	1.539	5.213	0.029	100.457	93.629	92.230	66.494	49.469	21.093
190	700.978	0.744	1.868	0.195	1.517	5.259	0.026	92.834	92.032	75.433	41.059	54.979	32.009
191	712.312	0.748	1.839	0.199	1.597	5.127	0.030	96.020	90.871	80.174	47.203	48.762	35.779
192	640.187	0.754	1.813	0.196	1.567	5.183	0.028	87.669	81.718	68.850	57.679	36.568	26.700
193	685.961	0.747	1.793	0.200	1.568	5.251	0.025	93.089	91.673	62.470	66.145	52.699	28.300
194	702.336	0.749	1.863	0.188	1.508	5.260	0.035	95.773	92.978	78.518	67.564	40.306	18.085
195	680.191	0.749	1.825	0.202	1.570	5.172	0.030	98.371	90.473	64.314	66.821	35.908	12.163
196	714.342	0.748	1.853	0.191	1.551	5.199	0.030	94.723	100.439	62.746	67.611	46.778	31.534
197	721.932	0.745	1.830	0.198	1.542	5.198	0.026	101.182	91.493	75.463	49.880	21.243	26.322
198	702.277	0.748	1.854	0.190	1.544	5.218	0.029	94.035	95.900	92.711	59.552	43.935	16.039
199	657.386	0.746	1.856	0.195	1.558	5.183	0.026	91.478	98.990	64.264	62.349	23.838	5.559
200	738.949	0.745	1.851	0.191	1.534	5.226	0.031	102.581	91.060	77.138	57.292	37.020	29.357