ASSESSING HEALTH STATE PREFERENCES AND THE DECISION TO MEDICATE IN OVERACTIVE BLADDER

DISSERTATION

Presented in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy in the Graduate School of The Ohio State University

by

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The Ohio State University
2004

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ABSTRACT

Overactive bladder is a condition that affects millions of Americans. While various studies exist to examine the cost-effectiveness of treatment alternatives, very few studies have examined the area of patient preferences. Once symptoms develop many individuals construct their preferences for treatment after considering the quality of life (QOL) effects of OAB and whether they possess prescription drug insurance. The purpose of this study was twofold: to examine the relative importance patients place on prescription drug coverage and QOL and to examine the effects of symptom severity and various demographic characteristics on patient quality of life.

The sample taken from a large clinic consisted of 133 patients with self-reported symptoms of OAB. To be included, participants were either male or female and were not taking medications to control their OAB symptoms. Data were obtained via self-administered questionnaire and telephone using trained interviewers. The QOL domains were those identified by the OAB-q instrument developed by Coyne et al.: coping, symptom concern, sleep disturbances, and problems with social interactions. All profile attributes had two levels—high / present or low / not present.

Using conjoint methodology, a questionnaire consisting of nine hypothetical profiles was used to elicit preferences. A linear fixed-effects model was used to analyze the results. The following coefficients were found for the five profile attributes:
insurance coverage, 34.36; sleep disturbances, 23.69; symptom concern, 19.73; social interaction problems, 19.44; and coping, 15.62. This suggests that prescription insurance coverage is the most important factor patients consider when considering medication therapy to control OAB symptoms.

The effects of demographic variables on QOL were examined using a linear regression model. After assembling the data on demographics and symptom severity, a model-building exercise was conducted to maximize the model $R^2$ value. The final model contained four variables: age, symptom severity, previous medication use, and medical insurance. After adjusting for outlying observations, the final model $R^2$ was 0.149. Since the concept of QOL is very large and encompasses many areas of an individual’s life, this value was acceptable.
This dissertation is dedicated with love to my grandparents.

Mrs. Marie Harpe
Mrs. Angeline Vance
Late Mr. Royce Vance

Your daily lives have served as an example for me.

“Make it your ambition to lead a quiet life, to mind your own business and to work with your hands just as we told you, so that your daily life may win the respect of outsiders and so that you will not be dependent on anybody.”

_1 Thessalonians 4:11_
ACKNOWLEDGMENTS

This dissertation, moreover my educational journey, has been influenced by many people.

I am deeply grateful to my adviser, Dr. Sheryl Szeinbach. She has gone above and beyond the call of duty as an academic adviser. From the early days talking with me at Ole Miss to making sure I was surviving my first Ohio winter to the hours spent talking about food from “back home”, she has been there for me at every step along the way. Her academic direction and practical guidance have proven to be helpful to me over the past few years and will help me well into the future.

Dr. Jeff Caswell has served double-duty for this project. In addition to being a member of my dissertation committee, he also served on my candidacy examination committee. His comments and insight have been invaluable throughout this process. A special note of appreciation goes to him for helping me combine my program in pharmacy with the MPH program in the School of Public Health.

A special thanks is in order for Dr. Ron Corey for helping with this project before it was even a project. His insight at the early stages of the project and continued guidance through the end are deeply appreciated.

I would like to thank Dr. Jim McAuley for serving on my committee. His insight helped me keep the “big picture” in mind while writing this dissertation.

This project could not have been completed without the help of the RRSF staff at UAB. To Dr. Mona Fouad, Dr. Charlotte Mayo, and Judy Smith, thank you so very much for your help and insight in developing and administering the questionnaire.

A very special thanks goes to Kathy Brooks and Judy Dawson, the graduate studies coordinators for the College of Pharmacy and School of Public Health, respectively. Their skills at helping graduate students safely navigate their graduate programs are truly amazing and greatly appreciated by all of us as confused graduate students.

To all the graduate students in pharmacy administration with whom I have shared an office—Dr. Suzanne Graden, Gregory Daniel, Margaret (Dowell) Scott, Dr. Prashant Nikam, Ronald Heitz, Satish Valluri, Dr. Joe Crea, and Katie Bellebaum; I thank you for your company and encouragement, for taking a moment to cheer me up when I was down...
(especially in the past few months when I was stressing over the dissertation), and for eating with me on the off chance that I was actually hungry.

For all of my friends who have helped me make it through these past few years, I am deeply indebted to you.

- To Martha Tzou, I appreciate your humor and support and encouragement throughout these past few years. Thanks even more for being my “public health buddy.” You’ll make a fabulous physician, so hang in there.
- To Ben Gruber, thanks for indulging my idiosyncrasies of speech and being a good reviewer.
- To Lori Wynkoop, for being my statistics buddy. Your help in making sure I had my “statistical mumbo jumbo” correct is deeply appreciated. Good luck in your writing. Make Abby proud!
- To Samantha (Carman) Clark, thank you for thinking about me and talking to me. It’s been difficult lately since I haven’t been too accessible. You know how special you are to me. Keep things straight in the ‘Burg. Plutonium rocks!
- To Jennifer Klerk, I apologize for the relationship you’ve had with my voice mail over the past few months. Things will get better I promise. Thanks for sticking with me. I hope I haven’t been in the bucket too many times. If I have, thanks for taking me out.
- To Andy Creamer and Dr. Leon Kok, thank you both for your friendship over the past few years. You’ve done so much for me, especially when my appendix became “grumpy.” Both of you mean a great deal to me.
- To Brian Rutledge, you know how special you are to me. Thank you for listening to me gripe and whine and for providing levelheaded advice when I couldn’t think straight. As my connection to the Motherland, you have kept me grounded. Our friendship is one of the things in life that I value most.
- To Josh Hobson and Duane Reynolds, thank you so much for everything you have done for me. You have always been there when I needed you. Always giving, never asking. I can’t begin to express how much you mean to me. I love you dearly.

Finally, a word of thanks from the very bottom of my heart is due my family. You have been there for me from the very beginning. Tracy, you’ve made me laugh and been the best little sister one could hope for. To my parents, I love you dearly. Thank you for always supporting me and never questioning the choices I’ve made in this educational journey. More than anything thank you for raising me in a Christian home. Rest assured that the things you taught me as a child will always be an important part of my life.

“He has showed you, O man, what is good. And what does the LORD require of you? To act justly and to love mercy and to walk humbly with your God.”

Micah 6:8
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2. King DS, Harpe SE. “An Update on the Management of Chronic Heart Failure.”

FIELDS OF STUDY

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Minor field: Public Health – Epidemiology
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CHAPTER 1

INTRODUCTION

The purpose of this dissertation is twofold: to examine the relative importance of quality of life and prescription insurance coverage on patient preferences for the pharmacotherapeutic management of overactive bladder and to examine the effects of symptom severity and various demographic characteristics on patient quality of life. This chapter provides a brief overview of overactive bladder disorder and its effects on quality of life. The significance of the study and statement of the problem will be set forth in this chapter. Following that, conceptual models for the study and relevant research objectives will be provided. The chapter concludes with an overview of the organization of this dissertation.
1.1 Overactive Bladder

1.1.1 Disease overview

Bladder control problems are a daily problem for millions of Americans. While many individuals may experience occasional bladder leakage, loss of bladder control that interferes with social functioning or results in poor hygiene is considered a medical problem. These problems may occur in any individual at any age but are more common in the elderly or in women following childbirth. However, bladder control problems are not considered “normal” at any age. Loss of bladder control, or urinary incontinence (UI), may be broken into two broad groups: transient incontinence and chronic bladder control problems. As the name implies, transient incontinence is generally short-lived and is often noted in acutely ill patients. Chronic bladder problems are often the result of a chronic medical condition, chronic medication use, or some underlying physiologic abnormality. Chronic bladder control problems are typically broken down into five classes: stress urinary incontinence, overactive bladder (OAB), overflow incontinence, functional incontinence, and mixed incontinence [1].

The key symptoms of OAB are urgency, frequency, and nocturia. Urge incontinence is frequently, but not always, noted in OAB patients [1]. Frequency is often defined as ≥ 8 micturitions per day [2]. OAB is generally believed to result from involuntary contractions of the detrusor muscle—the layer of smooth muscle within the bladder wall. Given the role of the central nervous system on bladder control, OAB may be classified as “unstable bladder” when there is no known neurogenic cause of symptoms or “hyperreflexive bladder” when a neurogenic cause (e.g., stroke, multiple sclerosis, spinal cord injury, etc.) can be identified [1].
Obtaining an accurate estimate of the prevalence of OAB in the United States has been difficult due to variations in definitions of the condition and symptom assessment. In 2002, the International Continence Society developed a definition of OAB: “urgency, with or without urge incontinence, usually with frequency and nocturia” in the absence of other physiologic factors that could explain the symptoms [3]. Prior to the development of this definition, research on bladder control problems focused primarily on UI since it included a broad range of bladder control problems. However, this definition does not include the two primary symptoms of OAB—frequency and urgency. Moreover, OAB does not always include incontinence. Thus, early studies on the prevalence of OAB may have underestimated the true prevalence [2]. Figure 1.1 provides a graphical representation of the relationship between UI and OAB. Note that only a portion of OAB includes incontinence. Also, urge incontinence does not consider the symptoms of frequency and urgency. This omission may have lead to underestimates of the true prevalence of OAB.

The National Overactive Bladder Evaluation (NOBLE) Program was started to obtain better estimates of the prevalence and burden of OAB in the US. In a nationwide random sample, the estimated overall prevalence was 16.5% in English-speaking adults aged 18 years and older. Interestingly, although symptom severity differed by sex, overall prevalence was only slightly different between men and women (16.0% vs. 16.9%, respectively) [4]. To put this number into perspective, consider the following prevalence estimates from the 1999 NHIS: 5.4% for diabetes in 1999, 19.2% for hypertension in 1999, and 8.5% for asthma in 1999 [6]. The prevalence of OAB increases with age. Although exact estimates are not known, the prevalence of OAB
Figure 1.1  Relationship between urinary incontinence and overactive bladder.  
(Source:  Ref. [5])

rises sharply after age 50, approaching 50% for community-dwelling individuals aged
50-59 [7] and possibly as high as 85% in institutionalized elderly individuals [2].

Diagnosis of OAB may often occur at primary care providers since these
practitioners, rather than specialists, are the first people that affected patients will see.
Diagnosis of urinary incontinence often begins with identifying medical causes or
conditions that contribute to transient incontinence (e.g., medications, infection, stool
impaction, delirium, etc.).  After transient causes are ruled out, it is necessary to
distinguish between stress incontinence and OAB.  Recognizing the presence of urgency
and frequency and the lack of urinary leakage during physical activity are key findings in
arriving at the diagnosis of OAB.  This distinction is necessary, as it may affect treatment
selection given the differing pathologic causes—bladder overactivity versus inadequate
urethral closure mechanisms (or both in the case of mixed incontinence). It is generally recommended that the initial patient evaluation include a review of the patient’s symptoms, physical examination, and urinalysis. Measurements of post-void residual may be useful in patients with suspected mixed incontinence. In cases where the diagnosis is unclear, urodynamic studies should be performed to clarify the diagnosis [8]. Recent research suggests that diagnosis of OAB based on symptomatology alone may result in underdiagnosis. For this reason, the more widespread use of urodynamic studies may be prudent [9]. The Agency for Health Care Policy and Research, now the Agency for Healthcare Research and Quality, developed evidence-based guidelines for the detection and management of urinary incontinence aimed at all types of physicians. However, the effectiveness of these guidelines has recently been called into question [10].

Treatment of OAB is focused on suppressing detrusor instability such that bladder capacity is improved and the time to voiding after the onset of urgency is increased. It may be useful to consider the following categories of treatment strategies for urinary incontinence: behavioral therapy and lifestyle changes, surgery, and pharmacologic therapy. The first category includes many options including bladder training, pelvic floor and/or vaginal muscle exercises, fluid management, biofeedback, and the use of incontinence products (e.g., absorptive products) [1]. Before a clinical diagnosis has been made, patients often begin lifestyle changes through the use of incontinence products or fluid management. Muscle exercises and bladder training have been shown to be effective in controlling incontinence episodes, especially in patients with mild to moderate symptoms. These exercises provide the most benefit when they are combined
with education programs to provide support structures for the patient [11-14]. Surgical treatments are typically reserved for those patients who do not respond well to pharmacologic therapy—either attributed to lack of effectiveness or poor compliance. Two commonly used surgical approaches include interruption of detrusor muscle innervation and bladder augmentation [8]. Sacral nerve stimulation is a relatively new treatment approach to correcting bladder overactivity and may be used more frequently in treatment refractory patients in the future [15].

The most common form of clinical therapy for OAB is pharmacologic therapy [2]. Pharmacologic management of OAB is challenging in that the medication must restore bladder function without significant adverse effects on other organ systems and suppress detrusor overactivity without interfering with normal micturition [8]. For these reasons, anticholinergic medications, specifically antimuscarinic agents, are the most commonly used medications among the spectrum of medical agents potentially useful in controlling OAB. The two most frequently used antimuscarinic agents are oxybutynin and tolterodine. Oxybutynin has long been used to treat symptoms of OAB. Unfortunately, it lacks selectivity for bladder muscarinic receptors and many patients experience anticholinergic side effects from the use of this agent [2]. These side effects may be so severe that compliance with therapy may be adversely affected [16]. In the geriatric population, these side effects may be particularly troublesome as oxybutynin may have adverse cognitive effects [17,18]. Tolterodine is the other antimuscarinic agent often used to treat OAB. It appears to exhibit somewhat higher selectivity for receptors in the bladder muscle than receptors elsewhere in the body. This is manifested clinically as a lower incidence of dry mouth. In addition, patients appeared to discontinue therapy
less frequently when compared to those on oxybutynin suggesting that tolterodine may be better tolerated than oxybutynin [19]. Tolterodine may be preferred for use in geriatric populations as it appears to possess fewer adverse cognitive effects but more evidence is needed to support this [7]. Extended-release preparations of both oxybutynin and tolterodine are currently available. When compared to their immediate-release counterparts, these formulations appear to possess comparable efficacy, but the improved delivery systems appear to increase patient tolerability [20-23]. A transdermal delivery system for oxybutynin is also available. This product offers comparable efficacy and safety when compared to extended-release tolterodine [24].

Other options include certain tricyclic antidepressants, calcium channel blockers, and estrogen, especially in post-menopausal women [1]. One innovative new treatment option is the use of botulinum-A toxin. When injected directly into the detrusor muscle, improved bladder function has been sustained for approximately nine months and anticholinergic medications may be reduced or stopped altogether as continence is restored in 95% of patients. However, the invasive nature of this treatment option and a lack of controlled clinical trials currently prevent this from being a widely used treatment option [25].

1.1.2 Health-related quality of life effects and economic burden

Urinary incontinence has been suggested to result in decreased levels of social and personal activities, increased levels of psychological stress, and a general reduction in quality of life [8]. Previous research has focused on the effect of urinary incontinence on QOL. Given the differences between OAB and general urinary incontinence, these studies may not accurately reflect the impact of OAB on QOL. To this end, recent
studies have been conducted using definitions of OAB specifically. For example, in one community-based survey, QOL was assessed using the Medical Outcomes Study Short-Form 20 (SF-20). In an analysis of all OAB patients, scores in the general health perception domain were 23.1% lower than community-based controls. Similar results were found when the OAB patients were stratified based on whether they exhibited urge incontinence [26]. Another study conducted in Italy found similar results when QOL was measured by the Medical Outcomes Study Short-Form 12 [27]. These studies used generic QOL instruments. Disease-specific QOL instruments have been developed for urinary incontinence. In addition, instruments specific to urge incontinence and OAB have been developed given the specific symptom subset that is unique to OAB and urge incontinence. The ability of these newer instruments to distinguish between frequency and urgency is important from a clinical perspective, as some patients with OAB may not experience urge incontinence [28]. These QOL issues will be discussed in more detail in Chapter Two.

In addition to the QOL effects of OAB, there is a significant economic burden associated with the condition. In one recent study, the estimated 2000 total costs of OAB were over $12 billion with costs being higher for women than men. The average yearly cost per community-dwelling person was $267 [29]. The largest portion of these costs was allocated to routine care and consequence costs [30]. In a medical claims analysis, OAB patients had higher total annual claims costs than patients without OAB ($5018 vs. $1767, respectively). These higher costs were thought to have been related to patient characteristics. After adjustment, OAB patients had claims costs that were 45% higher than non-OAB patients [31].
1.1.3 Patient preferences

Utility values can be derived from measures of preference or desirability for a given health state or health outcome. Measurement techniques that are an extension of decision theory include summated scales, indices, and profiles. These are used to determine preference weights for quality of life dimensions. Techniques based on economic decision theory are holistic approaches since the entire quality of life domain is considered by respondents to obtain utility estimates. Examples using this approach include visual analog scales, the standard gamble, and time trade-off methods [32]. Such techniques have been used to construct instruments that consider patient preferences when assessing outcomes in asthma [33] and to help determine the importance of pain in patients with rheumatoid arthritis [34].

Conjoint analysis offers another approach to assessing these preferences [35]. While conjoint analysis has been used for quite some time in marketing research and new product development, its use has only recently come to health care. Studies using conjoint methodology in health care research include a variety of diseases and conditions. Conjoint methods have been used to understand preference patterns in parents’ choice to initiate growth hormone therapy for their children [36], preferences for the processes and outcomes of liver transplantation [37], and preferences for magnetic resonance imaging in the treatment of knee injuries [38]. Conjoint methods have even been used to examine patient preferences for various attributes of the patient-provider relationship in health care [39,40]. Since the application of conjoint analysis is relatively new to health care, research is needed to assess the reliability and validity of these methods in health care. These topics have been studied for some time in marketing and operations research but
are only just beginning to be considered in health care [35]. Issues surrounding conjoint methodology, especially in relation to health care, will be discussed in more detail in Chapter Two.

1.2 Problem Statement

As discussed earlier, OAB exerts a significant adverse effect on patients’ QOL. Patients may be required to change their daily lives to accommodate the symptoms of OAB. At some point, patients will likely consider the prospect of medication therapy to control their symptoms of OAB. Before proceeding with seeking treatment, patients must consider the financial impact of initiating therapy and the impact of symptoms on their QOL. In this study conjoint methodology is employed with the purpose of examining the relative importance that patients place on QOL domains, as identified by the OAB-q [41], and prescription drug insurance with respect to the decision to manage their symptoms of OAB with prescription medications. As a secondary goal, this study seeks to examine the relationship between QOL and various demographic characteristics.

1.3 Significance of the Study

Much research has been conducted on issues surrounding the QOL effects of OAB. As with other conditions, research into new treatment options and improvements on existing options is ongoing. Studies have been conducted to examine the cost-effectiveness of various treatment options [42-44]. Studies have also been conducted to examine QOL issues as they relate to patients with urge incontinence and/or OAB [28,45]. Such studies have lead to various condition-specific QOL instruments, such as the OAB-q [41]. However, very little research exists in examining patient preferences associated with OAB. This study seeks to add to the current body of literature associated
with OAB and patient preferences by examining the relative importance of QOL and prescription drug insurance coverage on patients’ decisions to use medications to treat symptoms of OAB.

1.4 Research Objectives and Hypotheses

This study consists of two general research objectives. The objectives and the related hypotheses are given here. All hypotheses are stated in terms of the relevant null hypothesis.

**Research Objective 1:** To examine the relative importance of QOL domains and prescription insurance coverage on patients’ preferences for medication therapy of OAB.

Testing whether the following coefficients, or part worths, are equal to zero (i.e., the variable has no effect on patient preference):

Hypothesis 1.1: Coping
Hypothesis 1.2: Symptom concern
Hypothesis 1.3: Problems with social interactions
Hypothesis 1.4: Sleep disturbances
Hypothesis 1.5: Prescription insurance coverage

**Research Objective 2:** To determine if various demographic variables and OAB symptom severity affect quality of life.

Testing whether the following coefficients are equal to zero (i.e., the variable has no effect on QOL):

Hypothesis 2.1: Age
Hypothesis 2.2: Gender
Hypothesis 2.3: Length of symptoms
Hypothesis 2.4: Previous OAB medication use
Hypothesis 2.5.1: Discussion of symptoms with family/friends
Hypothesis 2.5.2: Value of discussions with family/friends
Hypothesis 2.6.1: Discussion of symptoms with health care professionals
Hypothesis 2.6.2: Value of discussions with health care professionals
Hypothesis 2.7: Income
Hypothesis 2.8: Education
Hypothesis 2.9: Medical insurance coverage
Hypothesis 2.10: Prescription drug coverage
Hypothesis 2.11: Type of prescription drug coverage
Hypothesis 2.12: OAB symptom severity

1.5 Conceptual Models

To fulfill the research objectives for this study, two separate linear models are constructed. The two models are provided below with brief explanations.

1.5.1 Model I

Research Objective 1 is accomplished through the use of conjoint methodology. A series of profiles are presented to the respondents. Each profile contains five attributes corresponding to the four QOL domains—coping, concern about symptoms, sleep disturbances, problems with social interactions—and prescription insurance coverage. All attributes are represented as having two levels. A series of 8 orthogonal profiles are selected using a one-fourth fractional factorial subset of all possible attribute combinations. A ninth profile is included as a holdout for validation purposes. Analysis
is conducted using a general linear model for longitudinal data in which the dependent variable is the participant’s estimate of the percentage of patients from each profile preferring drug therapy. The profile attributes are the five independent variables. The model can be written as Equation 1.1.

\[ Y_{ij} = \sum_{k=1}^{5} \beta_k X_k + \epsilon_{ij} \]  

(Eq. 1.1)

In this model, \( Y_{ij} \) is the \( i \)th person’s response for the \( j \)th profile, \( X_k \) is an indicator variable for the \( k \)th profile attribute, and \( \beta_k \) is the regression coefficient for the \( k \)th attribute. The model takes into consideration the correlation between responses from the same subject through the use of the correlated error term (\( \epsilon_{ij} \)). This model is considered a decompositional model since it serves to “decompose” the participants’ responses thereby providing the relative importance that is placed on each of the five profile attributes.

1.5.2 Model II

To accomplish Research Objective 2, the relationship between demographic variables, OAB symptom severity, and QOL are examined using ordinary least squares regression. The model for this regression can be written as Equation 1.2.

\[ Y_i = \sum_{j=1}^{p} \beta_j X_j + \epsilon_i \]  

(Eq. 1.2)

In this model, \( Y_i \) is the QOL score for the \( i \)th person and \( X_j \) is the \( j \)th demographic variable with \( \beta_j \) being the relevant regression coefficient. Although this model may look like the same model as presented for Model I, it is conceptually different. Unlike the first model, Model II is compositional since the goal is to develop a model by selecting those demographic variables that best predict QOL scores. In compositional models, the model
components are not specified before the analysis is conducted; rather, the model components are selected according to some model-building rule. In the decompositional approach, the structure, or components, of the model are defined \textit{a priori}.

1.6 Scope of the Study

Patients are recruited for the study through the Recruitment and Retention Shared Facility (RRSF) at the University of Alabama at Birmingham. During initial recruitment by RRSF staff, patients are asked a number of questions. One of these questions deals with urinary incontinence. Potential participants are selected from the RRSF database if they mentioned having had symptoms of urinary incontinence on their initial recruitment interview. The study is limited to those patients aged 40 and older who are not current users of bladder control medications. All patients in the study are from Alabama.

1.7 Organization of the Study

The remainder of this dissertation is organized into four chapters. Chapter Two contains a review of the literature relevant to this study. The two areas of focus for that chapter are health-related quality of life as it relates to OAB and conjoint methodology with special attention given to its applications in health care research. A description of the data collection and analytic methods is provided in Chapter Three. The results of the two models under study are provided in Chapter Four. Chapter Five concludes this dissertation with a discussion of the results, limitations of the current study, possible applications of the findings, and potential areas for future research.
1.8 References


CHAPTER 2

REVIEW OF RELATED LITERATURE

The first section of this literature review provides background information pertaining to quality of life, health-related quality of life, and instruments used to assess quality of life in patients with overactive bladder. In the second section, conjoint analysis deserves considerable attention because this methodology was used to investigate the relationships between health-related quality of life, prescription insurance coverage, and patient preferences for medication therapy.
2.1 Quality of Life

2.1.1 Quality of life overview

Although health is usually viewed from the medical standpoint, it actually represents a much broader concept. As defined by the World Health Organization, “health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity” [1]. Given this definition, it is easy to understand that health can affect almost every aspect of a person’s life. Although WHO might not have explicitly considered quality of life (QOL) when developing their definition of health, it is certainly a very important concept today. While QOL was once considered a “soft outcome,” it is now the source of rigorous methodological research and may even be an independent predictor of health outcomes beyond the typical physiological indicators [2].

In the broadest sense of the term, “quality of life” can be viewed as an overall measure of general well-being as observed through objective and subjective evaluations of various life domains. The evaluations of these domains are then “weighted” according to an individual’s (or society’s) set of values and then combined to arrive at quality of life [3]. A graphic conceptualization of quality of life is provided in Figure 2.1. Some find it beneficial to view QOL in terms of “life satisfaction” or general well-being as discussed in Campbell’s book The Quality of American Life [4]. QOL was made popular in the political arena in the 1960s. At that time, the concept of quality of life consisted primarily of social indicators, such as housing, employment, standard of living, and marriage [4-6]. The term “quality of life” was introduced as a medical subject heading, or MeSH, in 1977 by the National Library of Medicine accompanied by the following definition: “a generic concept reflecting concern with the modification and
Figure 2.1  Graphical conceptualization of general quality of life (Adapted from Ref. [3] and [8])
enhancement of life attributes, e.g., physical, political, moral and social environment; the overall condition of a human life” [7]. Despite the various definitions, there are four widely accepted domains associated with quality of life: physical status/functional abilities, psychological status/well being, social interactions, and economic/vocational status and factors [8].

Quality of life can be divided into two general areas: health-related quality of life and non-health-related quality of life. However, these two distinctions are not completely independent as part of one may directly or indirectly affect parts of the other [8]. The difficulty in separately defining QOL and health-related QOL is related to the relative lack of a clear definition for QOL [9]. Health care researchers have sometimes used the term “health-related quality of life” (HRQOL) to set their research apart from general QOL research [10]. Unfortunately, many health care researchers fail to provide a clear definition of their conceptualization of HRQOL. Some QOL frameworks are based solely on ideas generated by the researchers while others seek patient input in developing their QOL models [5,6].

To further complicate matters, the term “health status” is often used interchangeably with HRQOL. While HRQOL is a relatively poorly defined term, health status has been discussed in the literature and provides the foundation for various measurement instruments. Health status is concerned with various aspects of health (e.g., functional capacity, mental condition, physiologic condition, etc.) and how they affect one another, but not necessarily how they relate to other aspects of a person’s life (e.g., quality) [5,11]. On the other hand, HRQOL is concerned with a patient’s beliefs, expectations, and perceptions of their health status. Therefore, HRQOL might be
considered to have two dimensions. One would be a patient’s health status, and the other would be the patient’s “perceptions” of his or her health status [12].

2.1.2 Quality of life effects in overactive bladder

The disruptions in bladder function caused by urinary incontinence can interfere with an individual’s daily life and adversely affect the many aspects of quality of life [13]. The degree to which bladder dysfunction adversely affects QOL depends to a great extent on the individual patient. Some patients may perceive the symptoms as a minimal nuisance while others may experience extreme hardship associated with their symptoms. Patients may often experience such psychological effects as embarrassment or depression as a result of their bladder dysfunction [14]. Dugan et al. found a statistically significant relationship between depressive symptoms and urinary incontinence [15]. In addition to the psychological effects, individuals may experience disruptions in their work, social lives, and/or sleep patterns due to coping activities (e.g., frequent breaks to use the restroom) [16,17]. Some individuals may even avoid sexual activity due to the fear of urine leakage associated with their dysfunction [16,18]. In the elderly population, bladder dysfunction may also pose a relatively important risk factor for falls and resultant fractures [19]. Wagner et al. supported this fracture-related finding in their study on patients with OAB. The odds of an OAB patient being injured in a fall were over twice that of a patient without OAB. Although not significant, they also found that OAB patients had higher risks of bone fracture. OAB patients also reported more physician visits and more urinary tract infections than non-OAB controls [20].

While several studies report the QOL effects of urinary incontinence, relatively few studies have documented the effects of OAB, with or without incontinence. This
distinction may seem like a relatively minor difference in definitions, but it does ignore an important subset of the population and the relevant QOL effects. One possible reason for this omission in QOL studies is the lack of standard diagnostic criteria [21].

Literature reports have suggested that patients with OAB exhibit significantly lower QOL scores, using the Short Form (SF) 36, than age-matched population controls. In one survey, almost two-thirds of patients with OAB reported that their symptoms exerted an adverse effect on their lives. Moreover, some 60% of the respondents found their symptoms provided sufficient cause for worry that they sought medical attention [22]. Wagner et al. reported that patients with OAB had lower self-reported health status than those patients without OAB symptoms [20].

To further quantify the QOL effects of OAB symptoms on individuals, Liberman et al. divided their study group into OAB patients with incontinence and OAB patients without incontinence. QOL scores were then obtained using the SF-20. After adjustment for age, sex, and physician visits, OAB patients had significantly lower QOL scores than community controls in all SF domains except social functioning. The continent OAB group had significantly lower QOL scores in the mental health, health perception, and bodily pain domains of the SF-20. The incontinent OAB group had significantly lower QOL scores in all six domains measured. These results suggest that OAB patients, regardless of continence status, may have poorer QOL than non-OAB patients [21].

Chiaffarino et al. performed a similar study in Italian women. Overall, cases (defined as the presence of any incontinence) had significantly lower QOL scores than controls. As a subgroup, OAB patients had significantly lower scores than controls. Interestingly, OAB patients had significantly higher scores than those patients with urge or mixed urinary
incontinence. However, it was unclear as to how the authors classified OAB patients who also experienced urge incontinence. This could have resulted in biased results [23].

As discussed in Chapter One, there are various pharmacologic options for treating symptoms of OAB. It is important to determine whether these treatments have any effect on QOL in patients. To this end, various studies have been conducted to examine this topic. The two medications primarily used to treat OAB are oxybutynin and tolterodine. Therefore, these two agents are discussed.

In a short-term (12-week) study, Kelleher, Reese, et al. examined the effects of extended-release tolterodine on QOL as measured by the King’s Health Questionnaire (KHQ) and the SF-36. Significant improvements were noted in the following domains of the KHQ: incontinence impact, role limitations, physical limitations, sleep and energy, coping measures, and symptom severity. No significant differences were detected by the SF-36 [24]. In a long-term (one year) study of extended-release tolterodine, Kelleher, Kreder, et al. noted significant improvements in all domains of the KHQ except general health perceptions. These differences were evident at both the 3-month and 12-month measurement points. As with the short-term study, no differences were noted using the SF-36 instrument [25].

QOL effects of extended-release oxybutynin were examined in a long-term safety trial published by Diokno et al. Various measures were used to evaluate QOL: Individual Incontinence Impact Questionnaire (I-IIQ), Sleep Impact Questionnaire, and the General Health and Bother Scale. All measures were given at baseline, end of dosage adjustment, 3 months, and study end (12 months). In addition, the General Health and Bother Scale was repeated at 9 months. Significant improvements were noted on all measures at all
measurement points. Thus, long-term users of extended-release oxybutynin may experience improvement in QOL in addition to any clinical improvements [26].

2.1.3 Measuring quality of life in overactive bladder

In order to examine the QOL effects that a given treatment has on a patient or population, one must first be able to measure QOL. Today, a myriad of instruments exist for this purpose. Each instrument has its own purpose and specific attributes that make it more or less appropriate for a given situation. The instruments available can be divided into two general categories: general measures and specific measures. While this classification seems simple, the practical application in clinical studies seems to be less straightforward.

As the name implies, general QOL measures are designed to provide a measurement of the whole of an individual’s quality of life. Often, these measures are divided into various domains. For example, the Short Form 36 (SF-36) measures the following eight domains: physical functioning, role limitations (physical problems), social functioning, bodily pain, general mental health, role limitations (emotional problems), vitality, and general health perceptions [27]. Since these general measures are not anchored to any one disease, they may be used to compare the QOL effects of various diseases [17]. For example, Komaroff et al. examined patients with chronic fatigue syndrome and patients with other diseases. Their use of the SF-36, a general QOL measure, allowed them to make these comparisons [28]. Unfortunately, general measures may lack the sensitivity needed to detect QOL changes in some diseases. This is especially true in diseases or conditions where the patient reports fairly high overall health, such as OAB [17,24-25]. General QOL measures may be as simple as a single
question asking the individual to rate their QOL. However, this is rarely the case in most studies. General QOL measures may be developed to perform one of two general functions: to measure all important facets of QOL or to measure the utility associated with QOL and health states. The former is useful in the cross-disease comparison mentioned earlier. The latter is important because it incorporates patient preferences and provides information necessary for cost-utility analyses. In general, utility measures require a given health state to be rated on a continuum bounded by perfect health at one end and death at the other [8]. However, states worse than death are being considered and may be used in some situations [29-31].

Specific QOL measures were developed under the premise that general measures might not provide sufficient sensitivity, or responsiveness, to detect changes in patients under study. These specific measures may contain only those aspects of QOL that are important to the study group. The characteristic of these specific measures that may be confusing to some is that they may be specific to disease, condition, function, or patient population [8]. Specific measurement exist for numerous conditions, including asthma, depression, and rhinitis [10]. Those measures specific to OAB will be discussed shortly. By using condition specific measures, researchers hope to increase their chances of detecting changes in domains of interest. However, there may be a trade-off between generalizability to other conditions or populations and responsiveness within a specific area [17]. Some authors have suggested using both generic and specific measures in combination to obtain the greatest amount of information [32,33]. This practice has sparked considerable debate in the literature [34-38].
Regardless of the scope of the chosen instrument, several psychometric properties must be present in order to be clinically useful. Instruments must demonstrate both reliability and validity. Reliability is concerned with the repeatability and consistency of a given measure. Cronbach’s coefficient alpha is commonly used as a measure of scale internal consistency. The kappa coefficient may be used to assess test-retest reliability, or the repeatability of a measure. Validity generally refers to whether the instrument is measuring what it actually purports to measure. There are three types of validity: content validity, construct validity, and criterion validity. Content validity relates to how well a given concept is actually captured by the scale items developed to measure that concept. This type of validity is determined by comparing the scale under study to some definitional standard to ensure that all aspects of that definition are contained in the scale items. Construct validity is concerned with how well an instrument can detect logical differences or similarities as shown by other measures across patient groups (e.g., age, sex, disease). Convergent validity and discriminant validity are two special types of construct validity. Criterion validity refers to how well an instrument correlates to a “gold standard.” Since there are no “gold standards” in QOL, new instruments are often compared to well-validated existing instruments [39]. For example, many instruments are compared to the SF-36 as it has been well validated in numerous patient populations [10].

Various methods are available for the measurement of QOL in the OAB condition. Some researchers have used the Medical Outcomes Study Short Form instrument in varying lengths. These might be considered the “general” instruments. Other researchers have developed new instruments for the measurement of QOL in OAB
patients—the specific instruments. It is important at this point to note that some of the specific instruments previously used in OAB QOL research were not necessarily developed for use in OAB. In fact, many of the early methods used instruments originally developed for urinary incontinence or urge incontinence. This may lead to some confusion since some researchers refer to the instruments for use in urinary incontinence as “general measures” and those for specific subsets of incontinence as “specific measures” (see the 2003 review published by Symonds [40]). One should understand that these distinctions are solely for the purpose of distinguishing instruments within the area of urinary incontinence and do not necessarily reflect the actual scope of the instrument with respect to overall QOL.

The various Medical Outcomes Study Short Form (SF) instruments—SF-36, SF-20, SF-12—have demonstrated reliability and validity elsewhere [27,41,42]. Table 2.1 provides a summary of studies using SF measures to assess QOL in OAB patients. As mentioned earlier, some researchers felt that these general methods were not able to detect the QOL changes present due to the specific symptomology of OAB, notably frequency and urgency. This lack of responsiveness is likely due to the fact that most of the other QOL instruments used were developed for use in urinary incontinence; thus, they may not detect QOL changes in continent OAB patients [43]. To detect these changes, various specific methods have been developed. Generally, the condition-specific QOL measures used in OAB can be divided into two categories: those developed for use with urinary incontinence in general and those developed for use with urge incontinence and/or OAB. For the sake of clarity and brevity, stress incontinence measures will not be discussed.
<table>
<thead>
<tr>
<th>Authors (Year)</th>
<th>Instrument</th>
<th>Domains with differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kobelt (1997) [44]</td>
<td>SF-36</td>
<td>Physical functioning, physical role, general health, vitality, social function, emotional role</td>
</tr>
<tr>
<td>Kobelt et al. (1999) [45]</td>
<td>SF-36</td>
<td>Physical function, physical role, bodily pain, general health, vitality, social function, emotional role</td>
</tr>
<tr>
<td>Liberman et al. (2001) [21]</td>
<td>SF-20</td>
<td>Continent OAB patients: mental health, health perception, and bodily pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Incontinent OAB patients: physical functioning, role functioning, social functioning, mental health, health perception, bodily pain</td>
</tr>
<tr>
<td>Kelleher, Kreder, et al. (2002) [25]*</td>
<td>SF-36</td>
<td>SF-36 results not explicitly reported</td>
</tr>
<tr>
<td>Kelleher, Reese, et al. (2002) [24]*</td>
<td>SF-36</td>
<td>No differences. (Specific domains not used because summary measures for physical and mental health were used.)</td>
</tr>
<tr>
<td>Chiaffarino et al. (2003) [23]</td>
<td>SF-12</td>
<td>Physical health and mental health</td>
</tr>
</tbody>
</table>

*Trial involving therapeutic intervention(s)

Table 2.1 Selected quality of life studies in overactive bladder using Short Form instruments

The Incontinence Impact Questionnaire (IIQ) was developed to assess how urinary incontinence affected various aspects of the daily lives of women. The domains covered are physical functioning, emotional functioning, social functioning, and travel and mobility. The IIQ consists of 30 items rated on a four-point Likert scale. A second part was added to the IIQ to assess symptom “bother”: the Urological Distress Inventory. A total of 19 two-part items are included in the UDI. An individual provides whether or not a symptom is present and the degree of bother the individual experiences as a result of that symptom. A shorter 13-item IIQ/UDI has also been developed [46,47].

The King’s Health Questionnaire is another general incontinence QOL measure. This
21-item instrument covers eight domains: general health, incontinence impact, role limitations, physical and social limitations, personal limitations, emotional problems, sleep/energy disturbance, and symptom severity measures [48]. The Bristol Female Lower Urinary Tract symptoms questionnaire (BFLUT) is an instrument that assesses symptom bother with 20 items, QOL with nine items, and sexual function with four items. The patients also rate how much each item is a “bother” to them when responding to the questionnaire. The items concerning symptom bother cover bladder filling, urinary voiding, and incontinence [49]. The Incontinence Quality of Life Instrument (I-QOL) is a 22-item general incontinence instrument developed from interviews conducted with patients suffering from stress, urge, and mixed urinary incontinence. Although originally rated on a four-point Likert scale, the updated version is rated on a five-point Likert scale. Although the I-QOL developers chose not to construct distinct domains within their instrument, the topics covered are similar to those used in the other instruments [50,51]. The York Incontinence Perceptions Scale (YIPS) is slightly different than the previous instruments mentioned. Rather than examining particular symptoms, it assesses an individual’s overall psychosocial adjustment to living with incontinence. It consists of eight items that measure self-perception of continence and health. Individuals provide information on how they feel about, cope with, and control incontinence; how well their condition has been accepted; and how much the condition has affected their life and family [52].

While these general incontinence measures can be used in OAB patients, using these measures or some general QOL measure (e.g., SF-12) may not fully capture the effects of OAB on an individual’s QOL. This may be due, in part, to the complexity of
the OAB symptom set and the fact that patients often develop coping methods after symptoms develop. The role of incontinence in OAB patients further complicates QOL assessment since all OAB patients are not incontinent by definition. (See Liberman et al. [21].) To remedy this problem, new instruments have been developed and existing instruments have been validated with the unique characteristics of OAB in mind.

Reese et al. recently conducted the validation of the KHQ in patients with OAB. This was conducted as part of a randomized clinical trial of tolterodine for management of OAB symptoms. This analysis provided a multinational validation for the KHQ. The results suggested that the KHQ was valid and reliable in the OAB population. However, the applicability could be called into question. As part of the inclusion criteria, patients were required to have at least five episodes of urge incontinence per week. Therefore, it is conceivable that continent OAB patients were not part of this study potentially limiting the usefulness in those patients [53]. In an earlier study by Kobelt et al., the KHQ was used in a group of OAB patients with satisfactory psychometric performance so the practical implications of the lack of continent OAB patients in the Reese et al. study remain to be fully elucidated [45].

Like the KHQ, the IIQ/UDI has been adapted to include items pertaining to urge incontinence. The Urge-Incontinence Impact Questionnaire, or U-IIQ, consists of 32 items rated on a six-point scale. The following six domains are covered: travel, activities, physical activities, feelings, relationships, and sexual function. Two additional items have been included to assess nighttime bladder control and treatment satisfaction. The U-UDI contains nine items and measures which symptoms bother the patient and the extent to which they bother the patient. Two summary measures are provided by the
The OAB-q was developed specifically for use with OAB patients, regardless of their continence status. One of the objectives in developing this measure was to create an instrument that would be useful in evaluating both the continent and incontinent symptoms of OAB and their resultant effects on QOL. The OAB-q was developed through a patient-focused approach using focus groups and discussions aimed at symptoms of particular importance to OAB: frequency, urgency, and nocturia. The OAB-q covers five areas: symptom bother (symptom severity), coping behaviors, symptom concern/worry, social interactions, and sleep. The actual questionnaire is divided into two parts: a symptom severity section (eight items) and a QOL section (25 items over four domains). The OAB-q demonstrated satisfactory psychometric performance and is a reliable and valid instrument for use in OAB patient of either gender regardless of their continence status [43].

Two other instruments deserve mention. The Incontinence Quality of Life Index (IQoLI) is an instrument that measures social, emotional, and physical impact of urge incontinence symptoms. This 25-item instrument appears to exhibit satisfactory psychometric performance. However, it was developed for use in urge urinary incontinence in women. Therefore, it may not be useful in OAB patients without incontinence or men. Unfortunately, evidence is lacking in this area [55]. The Urge Impact Scale (URIS-24) is an instrument developed for use in the elderly population. Items were constructed through focus groups and interviews. The 24-item scale covers
three domains: psychological burden, personal control, and self-concept. Although the instrument possess satisfactory psychometric properties, it was not tested in OAB patients [56].

In summary, instruments are available to assess the extent that OAB symptoms affect patient quality of life. However, the degree of importance that patients place on symptoms with respect to decisions to seek therapy is not known. If symptoms continue to be bothersome, patients may eventually consider such options as lifestyle changes, surgery, or pharmacotherapy. Although psychological considerations and financial resources, including insurance coverage, may affect treatment decisions, it is the intention of this research to determine how much importance patients place on quality of life dimensions with respect to treatment preferences.

2.2 Conjoint Analysis

2.2.1 Theoretical background

The term “conjoint analysis” (CA) was made popular by Green and Srinivasan in their 1978 paper “Conjoint Analysis in Consumer Research.” In this paper, they define CA as “any decompositional method that estimates the structure of a consumer’s preferences (e.g., part worths, importance weights, ideal points) given his/her overall evaluations of a set of alternatives that are prespecified in terms of levels of different attributes” [57]. Basically, researchers are able to derive a measurement “scale” that represents an individual’s preferences by comparing that individual’s judgments about alternatives for which the differences of the attributes are known or fixed [58,59]. This helps explain why CA has proven to be a valuable tool in analyzing product preference data and in simulating consumer choice [60]. By providing individuals with a set of
multiattribute alternatives from which to choose, conclusions about their value systems based on behavior rather than self-reports can be derived [61].

Simultaneous conjoint measurement, the foundation for CA, was described by Luce, a mathematical psychologist, and Tukey, a statistician, in 1964 [62]. From this work, Luce and Tukey were able to demonstrate mathematically that individual choice behaviors or responses, in general, follow transitive and additive properties [63]. Further developments, such as Kruskal’s work on monotone transformations for the analysis of factorial experiments [64], provided more theoretical support for CA [57]. When coupled with the increased power and availability of computers, the use of CA in practice increased throughout the 1980s [65].

Through the use of conjoint measurement, researchers are able to measure the trade-offs that individuals make when constructing their preferences for various alternatives. In addition, researchers may be able to derive the utility of the alternatives based on the analysis of the conjoint measurement data. In considering CA studies, it is important to remember that “conjoint” actually refers to the measurement process—the process of measuring the relative values of characteristics considered jointly that might not be measurable when considered individually [61]. The actual data collected during the conjoint measurement process can be of various levels: continuous (or metric) ratings, ranks of preferences, or discrete choices. These various response modes have been the source of confusion for some. Some thought leaders sought to clarify the field of conjoint analysis by drawing a distinction between judgment-based ratings and choice-based ratings. Louviere has been the primary force behind this movement. In his 1988 paper, judgment data was defined as “evaluative rankings or ratings of a set of
multiattribute alternatives” where the measurement was at least at the ordinal level. Choice data was defined as the situation where the individual selected only one option out of a set of designed alternatives, thus the individual’s choice. Louviere also provided the theoretical justifications for the distinction between these two paradigms [66]. Louviere has further explained stated preference discrete choice modeling, as it has come to be called, in other places [67,68].

When the data from a conjoint analysis have been collected, the researcher must decide the level at which the analysis will be conducted—individual or aggregate. Conjoint analysis has traditionally been used to estimate individual level preferences. In this method, a separate set of part worth utilities is estimated for every individual in the sample. While these individual level models provide very good predictive ability, their value to administrators may be limited since a multitude of preferences is provided. From the administrative standpoint, a single set of preferences might be more useful. With aggregate level results, one could say that “on average” the group prefers X over Y. While this is arguably more useful, this pooled analysis can lead to incorrect predictions due to group heterogeneity, known as the “majority fallacy.” A third option is to group the participants into segments based on various characteristics. This segmentation approach is an intermediate approach and demonstrates the advantages of both individual and group level analyses. In segmentation methods, a relatively small number of utility functions are estimated (one for each segment) but the predictive ability rivals that of individual level analysis [69]. An alternative method has been developed to model preferences in situations where the decision is made by a group of individuals (e.g., roommates seeking a new apartment, a family considering a new automobile, etc.). It is
possible that in these situations neither aggregate nor individual levels accurately reflect the preferences of the group as a whole. In this method, the group is asked to complete a conjoint exercise together by discussing the questions and arriving at a consensus. In doing this, the group decision-making process is reflected in the results. Molin et al. developed and tested this alternative model. Their results suggested that the group exercise exhibited better predictive ability than the individual level analysis [70].

Since conjoint analysis is both a widely accepted and widely used method in marketing research, various studies have been conducted to document the reliability and validity of conjoint methodology. While conjoint has typically presumed to be more reliable and valid than self-explicated weights, Leigh et al. demonstrated that preference weights estimated using conjoint analysis are very similar to self-explicated weights [71]. The reliability of conjoint measurement has been demonstrated with respect to time (i.e., temporal reliability) and with respect to changes in the attributes in the model (i.e., structural reliability) [72]. Internal validity has been further assessed by examining whether estimation methods (e.g., OLS vs. logistic regression) affect the preference weights. Jain et al. demonstrated that that the different methods produced comparable results [73]. Interestingly, evidence suggests that the format of the response—rating, ranking, or discrete choice—may affect the preference rated; however, this is mainly a concern when rating or ranking data are recoded into a choice [74]. It is important to remember that reliability and validity are not fixed concepts; rather, they depend on the context and the population under study. To this end, research has been conducted to examine these issues within health care. Ryan et al. demonstrated internal validity and internal consistency and failed to note any effects related to the ordering of the profiles.
Interestingly, this study suggested that elicited preferences were found to be related to prior experiences [75]. A high degree of temporal reliability has been demonstrated [76]; however, the evidence supporting structural reliability is mixed [77].

In conducting the actual data analysis, researchers have used various methods to estimate the preference parameters. These have included such methods as MONANOVA, least squares regression, and logistic regression [65]. Various methods have been used to increase the predictive ability of CA analyses. Factor analysis and cluster regression analysis are two such methods [78]. With increases in desktop computing power, other methods that were previously unavailable are currently under study. Mixed effect models are one such method [79-81].

When presenting the alternatives to individuals, researchers are faced with important choices. When the number of attributes is small, say six or fewer, using the full profile method for presentation typically works well. A “profile” is one of many combinations of the particular attributes under study when performing CA. In the full profile method, the number of theoretical profiles is the product of the number of levels of each attribute. For example, if an experiment were concerned with four attributes at two levels each, the number of possible profiles would be $2 \times 2 \times 2 \times 2$ (i.e., $2^4$), or 16. As one can see, the number of potential profiles increases quickly as the number of attributes increases. Even with six attributes at only two levels each, using all the profiles would require an individual providing 64 (or $2^6$) responses. In situations with more than two attribute levels, the number of profiles increases even more quickly. Respondent fatigue might certainly become an issue in situations with a large number of attributes. To avoid this problem, fractional factorial methods have been used to reduce the number of
profiles required. The profiles may be chosen in such a way that all resulting combinations are orthogonal, that is no interactions are present. Alternatively, certain interactions may be built into the design and selection of the profiles. Other ways to reduce the number of profiles needed include such recent developments as adaptive conjoint analysis (ACA) and hybrid approaches [65]. More recently, research has been conducted to determine the impact of increased overlap of attributes in conjoint profiles. The results of this research are inconclusive, thus more evidence is needed determine whether this overlap is useful and, if useful, what is the optimal amount of overlap [82].

From a practical standpoint, CA is a very useful tool for researchers. In 1982, Cattin and Wittink surveyed commercial research firms on their use of CA. Their paper provided a sort of “state of the industry” with respect to the use of CA throughout the 1970s. In their survey of 17 firms, they found that CA was most frequently used on analyses concerned with consumer goods, especially new product or new concept identification. In terms of the development of attributes for consideration, the three most frequently used methods for development were the expert judgment of clients, group interviews, and direct questioning of individual subjects. The most frequent response modes were rank order and rating scales with “preference” or “intention to buy” used as the definition of the response variable. The actual methods used for data analysis, or parameter estimation, were MONANOVA, regression (OLS and logistic), and ANOVA. Sample sizes for studies varied widely from 138 to over 2000 with a median value of 466. Cattin and Wittink also asked respondents about potential problems that were worthy of attention in the future. These included such topics as establishing the validity of the results, handling large numbers of attributes (and levels), and accounting for
nonlinearity and interactions in the models [83]. This survey was updated in 1989. Results from the 1989 study were similar to those found in 1982. An increase in the use of least squares methods for analysis was noted as well as a slight increase in full profile methods. The authors included a question about data collection methods in their update. Almost two-thirds of respondents noted the use of personal interviews to collect data for conjoint studies [84].

2.2.2 Applications to health care

While CA has been widely used in such diverse areas as marketing research, new product development [85], food service planning [86], and environmental economics [87], its widespread use in health care is a relatively recent phenomenon. Early papers focused primarily on health care marketing. For example, a 1982 article by Malhotra and Jain described an approach to marketing and planning within health care using a conjoint approach [88]. A 1983 paper by Akaah et al. used conjoint segmentation to demonstrate the development of consumer-oriented planning in health maintenance organization (HMO) programs [89]. In 1985, Rosko et al. published a study demonstrating the use of CA in the determination of the most appropriate marketing mix for a health maintenance organization that was entering into a new market [90]. Outside of the realm of strategic marketing in health care, CA has been used to model university students’ choices of health plans [91], to determine the demand for patient-oriented pharmacy services [92], to assess the variables that affect pharmacists’ willingness to accept prescription contracts [93], and to examine pharmaceutical manufacturers’ use of value-added services in building customer loyalty [94].
Another interesting, and more recent, use of CA in health care is its use in evaluating patient, or consumer, preferences in various situations. One very important result of measuring patient or consumer preferences in health care is the consideration of patient and community input in health care decision making [95]. Methods previously used to assess patient preferences have included the standard gamble, time trade-off, rating scales (e.g., visual analog scale), and magnitude estimation [96]. CA is particularly useful in assessing patient preferences since it forces the patient to consider a variety of characteristics simultaneously, rather than separately. CA also has a number of other advantages in patient preference assessment. First, all attribute levels are measured on common utility scale in which one level of one attribute serves as the anchor point. Second, the overall effects for each attribute can be estimated separately from other scale values. For example, it is possible to estimate the contribution of each quality of life dimension with respect to patient preference. Besides its ability to determine which health state patients prefer, CA can be used to examine the contribution of various non-health attributes (e.g., insurance coverage, waiting times, etc.). This aspect of conjoint analysis has important implications for economic decisions concerning resource allocation and individual decisions concerning level of care. Selected studies using CA to evaluate patient preferences in health care are provided in Table 2.2.
<table>
<thead>
<tr>
<th>Authors (Year)</th>
<th>Method</th>
<th>Objective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chinburapa and Larson (1988) [97]</td>
<td>Rating</td>
<td>Assess drug attribute importance on prescription prescribing intentions</td>
</tr>
<tr>
<td>Reardon and Pathak (1990) [98]</td>
<td>Rating</td>
<td>Examine patient preferences for product attributes of antihistamines and determine whether segments exist</td>
</tr>
<tr>
<td>Szeinbach, Mason, et al. (1990) [93]</td>
<td>Rating</td>
<td>Examine the relative importance of factors on community pharmacists’ willingness to accept third-party prescription contracts</td>
</tr>
<tr>
<td>Chakraborty, Gaeth, et al. (1993) [99]</td>
<td>Rating</td>
<td>Assess consumers’ preferences for dental services</td>
</tr>
<tr>
<td>Chakraborty, Ettenson, and Gaeth (1994) [100]</td>
<td>Discrete choice</td>
<td>Identify attributes affecting consumer choice of health plans and the relative importance of those attributes</td>
</tr>
<tr>
<td>Ryan and Hughes (1997) [101]</td>
<td>Discrete choice</td>
<td>Assess women’s preferences for management of miscarriages</td>
</tr>
<tr>
<td>Szeinbach, Barnes, and Garner (1997) [94]</td>
<td>Discrete choice</td>
<td>Determine which value-added services used by pharmaceutical manufacturers are liked the most by hospital pharmacy directors</td>
</tr>
<tr>
<td>Freeman et al. (1998) [103]</td>
<td>Discrete choice</td>
<td>Assess university students’ preferences for student health services</td>
</tr>
<tr>
<td>Singh et al. (1998) [104]</td>
<td>Ranking</td>
<td>Understand preferences for growth hormone therapy; determine whether patients utilize multiple attributes in decision making; determine whether patient treatment patterns show heterogeneity and/or disparate patterns</td>
</tr>
<tr>
<td>Hakim and Pathak (1999) [105]</td>
<td>Discrete choice</td>
<td>Examine various strategies to model EuroQOL data</td>
</tr>
<tr>
<td>Ratcliffe and Buxton (1999) [96]</td>
<td>Discrete choice</td>
<td>Assess the relative importance of health outcome versus various process-related attributes (e.g., waiting time, continuity of contact, etc.) in patients who had received liver transplants</td>
</tr>
<tr>
<td>Ryan (1999) [106]</td>
<td>Discrete choice</td>
<td>Assess patient preferences for in vitro fertilization and consider the effects various non-health factors on those preferences</td>
</tr>
</tbody>
</table>

Table 2.2  Studies in health care using conjoint analysis methodology to assess patient preferences
<table>
<thead>
<tr>
<th>Study Reference</th>
<th>Methodology</th>
<th>Study Objective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bouldin et al. (2000) [108]</td>
<td>Rating</td>
<td>Examine preferences for label information in purchasing herbal supplements</td>
</tr>
<tr>
<td>Carman (2000) [109]</td>
<td>Ranking</td>
<td>Evaluate the relative importance patients give to the attributes for quality of care for acute care hospital services</td>
</tr>
<tr>
<td>Farrar et al. (2000) [110]</td>
<td>Discrete choice</td>
<td>Examine discrete choice modeling as a method for priority setting within health care organizations</td>
</tr>
<tr>
<td>Gates et al. (2000) [111]</td>
<td>Discrete choice</td>
<td>Measure preferences in consumers’ choice of health plans</td>
</tr>
<tr>
<td>Johnson et al. (2000) [112]</td>
<td>Discrete choice</td>
<td>Measure patient willingness to pay for reductions in acute episodes of respiratory and cardiovascular ill health</td>
</tr>
<tr>
<td>Ratcliffe (2000) [113]</td>
<td>Resource allocation</td>
<td>Measure individuals’ preferences in the allocation of donor liver grafts</td>
</tr>
<tr>
<td>Ryan and Farrar (2000) [85]</td>
<td>Ranking</td>
<td>Examine the trade-offs individuals were willing to make between location of treatment and waiting time for the provision of orthodontic services</td>
</tr>
<tr>
<td>Tilley and Chambers (2000) [114]</td>
<td>Discrete choice</td>
<td>Estimate the relative importance of attributes of day hospital care</td>
</tr>
<tr>
<td>Bingham et al. (2001) [115]</td>
<td>Discrete choice</td>
<td>Examine consumer preferences on selection of new pharmaceutical products</td>
</tr>
<tr>
<td>Leung et al. (2001) [95]</td>
<td>Ranking</td>
<td>Examine patient preferences for emergency departments and alternate settings for non-emergent cases</td>
</tr>
<tr>
<td>Longworth et al. (2001) [116]</td>
<td>Discrete choice</td>
<td>Estimate the relative importance of various process-related characteristics of intrapartum care for women who chose home birth vs. those who chose hospital birth</td>
</tr>
<tr>
<td>McKenzie et al. (2001) [117]</td>
<td>Discrete choice</td>
<td>Measure patient preferences over asthma symptoms</td>
</tr>
<tr>
<td>Ryan, Bate, et al. (2001) [118]</td>
<td>Discrete choice</td>
<td>Examine patient preferences for potential benefits from a change in organization of service delivery in the setting of an outpatient rheumatology clinic</td>
</tr>
<tr>
<td>Shackley et al. (2001) [119]</td>
<td>Discrete choice</td>
<td>Investigate whether and the extent to which vascular patients are willing to trade expected health outcomes for improvements in non-health benefits</td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Study</th>
<th>Methodology</th>
<th>Research Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aristides et al. (2002) [120]</td>
<td>Discrete</td>
<td>Examine preferences for a new chemotherapy agent (over standard therapy) and determine willingness to pay for a particular treatment</td>
</tr>
<tr>
<td>Gyrd-Hansen and Slothuus (2002) [122]</td>
<td>Discrete</td>
<td>Examine the Danish taxpayer’s preferences for health care services in the presence of opportunity costs</td>
</tr>
<tr>
<td>Heiberg and Kvien (2002) [123]</td>
<td>Rating</td>
<td>Compare the relative values of various influenza treatment strategies</td>
</tr>
<tr>
<td>Moayyedi et al. (2002) [125]</td>
<td>Discrete</td>
<td>Measure patient preferences for time allocation in the reorganization of a gastroenterology clinic</td>
</tr>
<tr>
<td>Ratcliffe, Van Haselen, et al. (2002) [126]</td>
<td>Discrete</td>
<td>Examine asthma patients’ preferences for treatment attributes and determine whether preferences varied across subgroups</td>
</tr>
<tr>
<td>Schmier et al. (2002) [127]</td>
<td>Discrete</td>
<td>Assess preferences for pain treatment outcomes in cancer and non-cancer patients with chronic pain</td>
</tr>
<tr>
<td>Slothuus et al. (2002) [128]</td>
<td>Contingent</td>
<td>Determine preferences and willingness to pay for alleviation of rheumatoid arthritis symptoms</td>
</tr>
<tr>
<td>Townend and Shackley (2002) [129]</td>
<td>Rating</td>
<td>Examine the preferences of service users of psychiatric day hospital services</td>
</tr>
<tr>
<td>Ross, et al. (2003) [130]</td>
<td>Ranking</td>
<td>Examine the relative importance that the elderly attach to various factors when making theoretical choices about cataract surgery</td>
</tr>
<tr>
<td>Schwappach (2003) [81]</td>
<td>Resource allocation</td>
<td>Examine public preferences for budget allocation and compare to decisions based on the health maximization principle</td>
</tr>
</tbody>
</table>

MRI = magnetic resonance imagine; QOL = quality of life
2.3 References


35. Guyatt G. Commentary on Jack Dowie, "Decision validity should determine whether a generic or condition-specific HRQOL measure is used in health care decisions". *Health Economics* 2002; 11(1): 9-12.
36. Feeny D. Commentary on Jack Dowie, "Decision validity should determine whether a generic or condition-specific HRQOL measure is used in health care decisions". *Health Economics* 2002; 11(1): 13-16.


CHAPTER 3

METHODS

This chapter begins with an explanation of the pilot study for the initial development and testing of the study instrument, including a summary of selected descriptive statistics from the pilot study. This is followed by details of the development of the final study instrument, as well as a discussion of the sampling plan, sample size determination, and implementation of the main study, including data collection methods. The chapter also includes a brief explanation of the assessment of the performance of the final study instrument and concludes with a description of the statistical methods used to fulfill the Research Objectives set forth in Chapter One.
3.1 Pilot Study

In conducting a study using conjoint methodology, special care is needed in developing the study instrument. For this reason, the first part of this chapter is devoted to explaining how the study questionnaire was developed and tested. While many articles exist detailing the steps necessary to conduct a conjoint analysis study, the five steps detailed by Ryan and Farrar are loosely followed here. These steps are identifying the characteristics for study, assigning levels to the chosen characteristics, choosing the scenarios for presentation, establishing preferences (or profile presentation), and data analysis [1]

3.1.1 Scope of the pilot study

The pilot study was conducted in patients with symptoms of OAB who were at least 40 years of age or older and were not current users of any bladder control medications. Thirty patients were selected by the Recruitment and Retention Shared Facility (RRSF) at the University of Alabama at Birmingham (UAB). These patients completed the pilot version of the study questionnaire. The purpose was to determine whether any changes needed to be made to the design, wording, or formatting of the questionnaire in order to increase the understandability or readability of the instrument. In addition to completing the questionnaire, respondents were asked to provide any comments on the wording or design of the instrument and whether any changes might improve the questionnaire.

3.1.2 Selection of QOL attributes

In selecting attributes to represent the area of QOL within OAB, it was necessary to choose areas that captured the variety of effects that OAB patients might experience.
With this focus, general QOL instruments based on the Short Form would likely not be sensitive enough to changes related to OAB. The decision was made to use an disease-specific QOL measure. As noted in Chapter Two, a variety of disease-specific measures are available. Given the rather specific symptoms associated with OAB (frequency, urgency, and nocturia), only those instruments validated in OAB patients were considered. Thus, the King’s Health Questionnaire (KHQ), the Incontinence Impact Questionnaire/Urological Distress Inventory (IIQ/UDI), and the OAB-q were considered. While the IIQ/UDI has been adapted for urge urinary incontinence, the validation study did not consider continent OAB patients since all patients were said to be incontinent [2]. The KHQ was recently validated in the OAB population [3]. However, the KHQ was developed to consider urinary incontinence in general. Moreover, the KHQ covers nine domains. Despite the reliability and validity in OAB, using the KHQ would have resulted in a large number of profiles required for participant consideration increasing the likelihood of respondent fatigue. The OAB-q was developed specifically for use in the OAB population, regardless of continence status. Its development was based on a patient-focused approach, thus increasing the likelihood that it is directly applicable to OAB patients. Also, the OAB-q covers only four QOL domains: coping behaviors, symptom concern/worry, social interactions, and sleep [4]. By reducing the number of QOL domains to four, rather than nine, the number of potential profiles is greatly reduced.

3.1.3 Instrument design

Part I of the instrument consisted of the hypothetical patient profiles. Each profile consisted of the four QOL attributes described above and an attribute relating to
prescription drug insurance coverage. Once the attributes were selected, each was
assigned two levels. A dichotomous “present/absent” (or many/few) approach was taken
in assigning attribute levels. Using the sleep domain as an example, the two possible
levels for this attribute are “many problems with sleep patterns” and “few problems with
sleep patterns.” Restricting the attributes to two levels each maintained profile simplicity
and reduced the number of potential profiles. In the case of prescription insurance
coverage, “no coverage” versus “full coverage” was not completely realistic since
relatively few patients possess full prescription drug coverage (i.e., no out of pocket
costs). It was decided that some monetary value should be associated with the levels of
prescription drug coverage to aid the participants in providing their responses. For the
“full coverage” level, the participants were instructed to assume that they would be
required to pay $20 per month or less for the medication. In the situation of “no
coverage,” participants were to assume that they would be responsible for the full amount
of the medication, or $80 per month or higher. The value chosen for the prescription
coverage level was based on the average copay from the 2002 Employer Health Benefits
Survey conducted by the Kaiser Family Foundation and the Health Research and
Educational Trust [5]. The 2003 edition of this report showed a small increase in the
copay amounts, but not so great as to render the value chosen for this study as too low
[6]. The monetary value for “no coverage” was chosen as price representative of the cash
price for a one-month supply of the one of the brand name products used to treat OAB
[7]. After levels were assigned to attributes, profiles were selected using a fractional
factorial method described later in this chapter. The participants provided an estimate of
the percentage of patients similar to those presented in the hypothetical profiles that
would prefer drug therapy to treat their OAB symptoms versus doing nothing about their symptoms. This estimate was the dependent variable for Model I.

Part II of the instrument consisted of eight health status items based on the four QOL domains selected for Part I. Two items were included for each domain. The items selected were those two items with the highest factor loadings within their respective domains as reported in the OAB-q validation study published by Coyne et al. [4]. The items were rated using a visual analog scale. For each of the eight items, participants provided a rating of an individual’s overall health status. The scale ranged from 0 (Worst possible state) to 100 (Best possible state).

The third part of the instrument consisted of two general areas: symptom severity and overall QOL. Within each area, patients provided responses to two items. One item asked the individuals to compare themselves to patients with OAB symptoms, and the other asked the individuals to compare themselves to patients without OAB symptoms. Responses were rated on a six-point ordinal scale. For symptom severity, “1” represented “mild” symptoms and “6” represented “severe symptoms.” For overall QOL, “1” represented “poor” and “6” represented “excellent.”

The fourth, and final, section of the questionnaire consisted of demographic information about the respondent. The respondent’s age, gender, and length of OAB symptoms were requested. Questions relating to whether symptoms had been discussed with friends and/or health care providers, as well as the value associated with that discussion, were included. Information on education, average annual household income, and insurance coverage were also captured. An item asking the respondent about their
use of medications to treat OAB symptoms was included to check the validity of the screening process.

After the initial pilot questionnaire was assembled, the content validity was assessed by members of the dissertation committee and RRSF staff. To test the face validity of the initial questionnaire, staff members of the Riverside Methodist Hospital inpatient pharmacy who had experienced bladder control problems in the past were asked to review the instrument and provide input. Based on the input from these reviews, changes were made to improve clarity. After approval from the dissertation committee, the initial questionnaire was sent to UAB for the pilot study.

3.1.4 Profile selection

In some situations, the number of attributes under study may result in a large number of profiles required for consideration by the respondent. For example, in this study there are five attributes (four for QOL and one for insurance coverage) at two levels each resulting in $2^5$, or 32, potential profiles. As a side note, if the KHQ had been used to identify QOL domains, there would have been a total of $2^{10}$, or 1024, potential profiles since there are nine QOL domains identified by the KHQ. This would most certainly overwhelm even the most dedicated participant, not to mention the researchers attempting the analysis. Methods available for reducing the number of profiles required for consideration by the respondent include fractional factorial designs, adaptive conjoint, and various hybrid methods [8].

Fractional factorial designs are used to select a set of alternatives based on a particular mathematical algorithm. Using these methods, it is possible to construct a set of alternatives containing the minimum number of profiles required to estimate the
desired effects. For this study, a one-fourth, or \(2^{k-2}\), fractional factorial design was used to select profiles included in the questionnaire. The result of this method was a set of orthogonal alternatives. This orthogonal selection was desirable since only main effects were of interest [9]. While the choice of an orthogonal design may prohibit the estimation of interactions, practice has indicated that main effects typically account for 70 to 90 percent of explained variance in linear models. Interactions of the second order account for only 5 to 15 percent of variance, and higher order interactions account for the remainder [10]. Estimation of main effects results in a minimum number of profiles thereby reducing the potential of respondent fatigue without sacrificing significant explanatory power.

3.1.5 Initial instrument administration and results

The pilot study consisted of 30 patients taken from UAB. Half of the patients completed the questionnaire via self-administration. RRSF interviewers administered the questionnaire via telephone to the other half of the sample. The RRSF staff also collected any comments that participants may have had concerning their experience with the questionnaire. In addition to testing the response to the instrument, the pilot study also sought to assess the comparability of the two modes of administration. This was done by comparing the results from the telephone-administration group and the self-administration group. Descriptive results from the pilot study are provided in Table 3.1.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall (n=24)</th>
<th>Telephone (n=11)</th>
<th>Self (n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.3 (10.2)</td>
<td>57.8 (13.4)</td>
<td>64.6 (5.6)</td>
</tr>
<tr>
<td>Gender (% female)</td>
<td>88.0</td>
<td>91.7</td>
<td>84.6</td>
</tr>
<tr>
<td>Education (% per category)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than HS</td>
<td>12.0</td>
<td>8.3</td>
<td>15.4</td>
</tr>
<tr>
<td>Some HS</td>
<td>4.0</td>
<td>0</td>
<td>7.7</td>
</tr>
<tr>
<td>HS graduate</td>
<td>36.0</td>
<td>25.0</td>
<td>46.2</td>
</tr>
<tr>
<td>Some college</td>
<td>12.0</td>
<td>16.7</td>
<td>7.7</td>
</tr>
<tr>
<td>College graduate</td>
<td>28.0</td>
<td>50.0</td>
<td>7.7</td>
</tr>
<tr>
<td>Graduate or professional degree</td>
<td>8.0</td>
<td>0</td>
<td>15.4</td>
</tr>
<tr>
<td>Income (% per category)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; $10,000</td>
<td>24.0</td>
<td>8.3</td>
<td>38.5</td>
</tr>
<tr>
<td>$10,000 to $17,999</td>
<td>8.0</td>
<td>0</td>
<td>15.4</td>
</tr>
<tr>
<td>$18,000 to $24,999</td>
<td>16.0</td>
<td>25.0</td>
<td>7.7</td>
</tr>
<tr>
<td>$25,000 to $34,999</td>
<td>8.0</td>
<td>8.3</td>
<td>7.7</td>
</tr>
<tr>
<td>$35,000 to $49,999</td>
<td>8.0</td>
<td>8.3</td>
<td>7.7</td>
</tr>
<tr>
<td>$50,000 to $69,999</td>
<td>20.0</td>
<td>16.7</td>
<td>23.0</td>
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<td>$70,000 to $99,999</td>
<td>8.0</td>
<td>16.7</td>
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<td>$100,000 to $124,999</td>
<td>8.0</td>
<td>16.7</td>
<td>0</td>
</tr>
<tr>
<td>≥ $125,000</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% with medical coverage</td>
<td>96.0</td>
<td>91.7</td>
<td>100.0</td>
</tr>
<tr>
<td>% with prescription coverage</td>
<td>73.9</td>
<td>90.0</td>
<td>61.5</td>
</tr>
<tr>
<td>Duration of OAB symptoms (years)</td>
<td>19.1 (27.5)</td>
<td>17.6 (28.3)</td>
<td>20.4 (27.8)</td>
</tr>
<tr>
<td>Health status item means</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coping</td>
<td>45.9 (30.6)</td>
<td>45.5 (24.6)</td>
<td>46.2 (36.2)</td>
</tr>
<tr>
<td>Concern</td>
<td>47.0 (26.8)</td>
<td>44.7 (24.2)</td>
<td>49.2 (29.8)</td>
</tr>
<tr>
<td>Sleep</td>
<td>39.6 (31.1)</td>
<td>42.9 (29.5)</td>
<td>36.5 (33.4)</td>
</tr>
<tr>
<td>Social interactions</td>
<td>38.4 (29.1)</td>
<td>44.7 (22.8)</td>
<td>32.6 (33.8)</td>
</tr>
</tbody>
</table>

Values provided are means (std. dev.) except where noted; HS = high school

Table 3.1  Descriptive statistics from the pilot study
Table 3.2 Mean profile responses and attribute levels from the pilot study

3.2 Main Study

3.2.1 Scope of the main study

The main study was conducted in patients from Alabama who were recruited by the RRSF at UAB. To be included, these patients had to be 40 years of age or older, be experiencing OAB symptoms, and could not be currently taking any bladder management medications. Careful attention was taken to improve the design, formatting, and understandability of the final instrument based on the suggestions provided by the pilot study participants and the experience of the RRSF interviewers.
The data collection for main study proceeded in a similar manner as during the pilot study. Rather than allocating one-half of the sample to each type of instrument administration, only 15 more individuals were asked to complete the questionnaire by self-administration. The remainder of sample completed the questionnaire via telephone interview. This was done because the researchers also wanted to assess the comparability of telephone-administration and self-administration of the instrument.

3.2.2 Instrument design

The attention provided during the early stages of instrument development suggested the need for relatively few revisions to the final instrument. These changes included minor rewording to increase readability by both the participants and the interviewers and a reformatting of the original introduction of the study. At the suggestion of the RRSF staff, the description of the profile attributes was included in both the introduction and in the instructions for Part I to aid the participants in providing their responses to the patient profiles in Part I. No significant changes were made from the pilot instrument in developing the final instrument. A copy of the final questionnaire can be found in Appendix A.

3.2.3 Sampling plan and sample size determination

While some form of random sampling, or some probability sampling method, is usually the preferred sampling plan, it is not practical, or even feasible, in every situation [11]. In these situations, various non-probability sampling methods may be employed. In order to use probability sampling methods, it is often necessary to have a list of the entire population before selecting individuals [12]. Unfortunately, there is no readily available list of patients with OAB. For this reason, a convenience sampling plan was
used to select patients for participation in the study. Patients with OAB were screened for the study until a sufficient number of eligible patients was available to meet the desired sample size. The Recruitment and Retention Shared Facility conducted recruitment and enrollment of all participants.

In recruiting patients for the study, the RRSF utilized three methods: telephone recruitment, clinic recruitment, and campus recruitment. In telephone recruitment, a list of individuals was drawn from the RRSF database who had previously completed an RRSF supplemental survey indicating that they would like to be contacted about additional research studies. The individuals selected had answered “yes” to a health question concerning incontinence on the initial RRSF screening questionnaire. Trained research interviewers contacted each potential participant via telephone to determine eligibility. Recruitment flyers (see Appendix B) were distributed to patients in waiting areas at various clinics and at various community events. If an individual showed interest in participating in the study, the trained RRSF staff member present determined the eligibility of the individual. If the inclusion criteria were met, the individual was provided with a questionnaire to complete and return to the RRSF staff member. The recruitment flyers were also posted at various sites around UAB. Interested individuals were invited to call a telephone number to determine their eligibility for participation in the study. Since OAB was the focus of the study, it was important to ensure that those with other forms of bladder control problems were not included. During the screening process, potential participants were asked whether they regularly experienced bladder loss on physical exertion (i.e., stress incontinence). These individuals were not allowed to participate in the study. Patients were also asked whether they experienced symptoms
of urgency, frequency, and/or nocturia regularly during the past month or if their physician had told them that they had OAB. Individuals answering positively to either of these questions were allowed to participate provided they met the other inclusion criteria previously described.

In calculating the sample size, it was important to take into consideration that each participant provided multiple responses to Part I. These repeated measurements reduced the number of individuals needed for an adequate sample size. At the same time, it was important to consider the number of potential explanatory variables that would enter into Model II. According to work by Harrell et al., approximately 10 observations for each potential explanatory variable will produce a sufficient sample size in most regression situations [13]. Using that suggestion, approximately 140 individuals would be needed since there were 14 potential explanatory variables in Model II. A sample size calculation was performed based on Model I to ensure that an adequate sample size was obtained. In this calculation, a basic sample size equation was modified (Equation 3.1) to take into account the number of repeated measurements and the within-subject correlation as suggested by Diggle et al. [14].

\[
 n = \frac{2\sigma^2(Z_{\alpha/2} + Z_{\beta})^2(1 - \rho)}{\delta^2m} 
\]  

(Eq. 3.1)

In this equation, \( \rho \) represents the within-subject correlation. Assuming no correlation, or \( \rho = 0 \), produces a conservative sample size estimate since all observations are considered independent. The number of repeated measures is accounted for by \( m \). The variance \( (\sigma^2) \) can be estimated by dividing the range of the response variable by six as suggested by Kish [15]. Using Equation 3.1, the approximate sample size needed was 122. This is
similar to the sample size estimated using Model II. It was assumed that approximately 10% of the questionnaires would not be useable due to incomplete responses; therefore, the required sample size was rounded to 150.

3.3 Study Implementation

The study was completed in cooperation with the RRSF at UAB. Questionnaire administration and all data collection took place at UAB. Since the actual data collection was not being conducted at The Ohio State University, the Office of Responsible Research Practices determined that the study was exempt from full review by the Institutional Review Board (IRB) at OSU since a review was being conducted at UAB. The IRB at UAB granted approval for the conduct of this research project. Material related to the approval process for this project is provided in Appendix C.

3.4 Data Collection and Data Entry

The data were collected with the help of the RRSF at UAB. RRSF staff completed patient recruitment and initial screening to determine whether inclusion criteria were met. Data collection was completed in one of two modes: self-administration or telephone interview. Self-administration took place in the clinics at UAB. Trained interviewers from the RRSF conducted the telephone interviews.

Questionnaires were reviewed for completeness and entered into a spreadsheet. A respondent’s questionnaire was considered complete if he/she provided complete responses to Parts I, II, and III (Patient Profiles, Health Status, and Quality of Life, respectively) and provided responses to at least 50% of the items in Part IV (Demographics). Each participant’s responses were evaluated to ensure that the responses provided were usable. For example, if a respondent marked 100% on every
profile and 0% on every health status item, it was highly likely that he/she did not understand the questions or did not truly care to participate, therefore these responses were excused from the analysis. The profile attributes were coded using indicator variables where “1” denoted that the attribute/condition was present and “0” denoted that the attribute/condition was not present. For example, in a profile where prescription drug coverage was available, the variable for prescription drug coverage was given a value of 1. A set of indicator variables was constructed for each of the nine hypothetical profiles using these coding method. Items with multiple response categories (e.g., income, education, etc.) were coded numerically but treated as indicator variables in all statistical analyses. All other items were entered as the actual response provided by the participant. The codebook for the study is provided in Appendix D.

3.5 Instrument Performance

3.5.1 Reliability

In this study, new measurement scales were not developed. Therefore, measures of internal consistency, such as Cronbach’s $\alpha$, were not applicable. Measures of test-retest reliability were not applicable since each participant completed the questionnaire only once. However, reliability was assessed from a descriptive standpoint. By observing the results from the study, it was possible to determine whether the results were “stable” (i.e., standard deviations that were not exceedingly large given their respective means).

Using concepts from the multitrait-multimethod work by Campbell and Fiske, it was possible to show reliability and validity by using different methods to measure the various attributes under study [16]. In this study, two administration modes were used:
telephone interviews and self-administration. By examining any statistical differences in profile responses by administration mode, it was possible to determine the reliability of the questionnaire. This was similar to methods used by other researchers using multiple modes of administration [17].

3.5.2 Validity

Two methods were used to assess the validity of the conjoint analysis portion of the questionnaire. The first involved the use of a holdout profile. While the first eight profiles in the instrument were identified using the fractional factorial method, the ninth profile was selected for validation purposes. This profile was purposefully constructed so that the attribute levels were neither consistently low nor consistently high (e.g., all attributes were “present”). Using the holdout profile is similar to the cross-validation method described by Mosier [18]. In cross-validation, a model is estimated using a subset of the sample, or the training set. That model is then used to predict the responses for the rest of the sample, or the validation set. The correlation between the actual and predicted values from the validation subset is used to determine validity. High correlation suggests high validity. In the case of conjoint analysis, the model is estimated without the holdout profile. Then, the model is used to predict the response to the holdout. If the measurement is valid, then the predicted and observed responses to the holdout profile should be very similar. The use of holdout profiles is common in conjoint studies and has been suggested to be a “demanding prediction task” for conjoint models [19]. Although the objective of this study was not prediction, the holdout profile still provided a useful validation method.
The second validation method used in this study was the use of the visual analog scale (VAS) ratings from the health status items in Part II of the questionnaire. This method used concepts from Campbell and Fiske [16]. By using a second method to measure preferences, two sets of rankings would be available for comparison. If the rankings from the conjoint portion and the VAS portion were the same, or very similar, then the questionnaire could be considered valid. While Part II did not include an item on insurance coverage, the rankings for the four QOL domains was considered to be sufficient for validation purposes.

3.6 Data Analysis

In this section, the data analysis methods are described. In addition to Models I and II, descriptive statistics were also calculated and are provided in the Results section of this dissertation (Chapter Four). All statistical analyses were conducted with Stata/SE version 8 [20].

3.6.1 Model I

Research Objective 1 used conjoint methodology to examine the relative importance of QOL domains and insurance coverage on patients’ preferences for pharmacotherapeutic management of OAB. In conducting a conjoint analysis, certain assumptions were necessary [21,22]:

a) Products are bundles of tangible and intangible attributes, and these attributes adequately describe the product

b) Each individual possesses a unique utility, or value, for each attribute level

c) An individual’s utility for a given attribute level is independent of the levels of the other attributes present
d) Total utility, or preference, for a given product is a function of individual attribute utilities

The term “product” in the above assumptions can be replaced with the relevant term in health care. For example, the “product” described may be some new pharmaceutical product or a new health benefit structure. It is also assumed that individual choice behaviors and responses generally demonstrate additive and transitive properties [23].

In analyzing the data for Model I, a general linear model (GLM) was used to decompose the responses into the part worths. These part worths represented the relative importance that the respondents placed on the attributes under study. The data collected in this study required special consideration for data analysis. Participants provided a response to each of the nine profiles in Part I. Using typical ordinary least squares (OLS) regression techniques, the correlation between responses from the same subject would be ignored, thereby providing cause for concern. While the estimates of the regression coefficients would still be unbiased, the typical properties of these estimates would no longer apply. Two important problems resulting from this method are underestimated standard errors and incorrect t- and Z-values [24]. Various methods could be used to account for this correlation. The use of a linear fixed effects model was the approach taken for this study to take into account the repeated measures on each subject. Equation 1.1 can be expanded and rewritten as Equation 3.2 to include random effects ($b_i$).

$$ Y_{ij} = \sum_{k=1}^{5} \beta_k X_k + \sum_{k=1}^{5} b_{ik} Z_k + \epsilon_i \quad \text{(Eq 3.2)} $$

In this equation $Y_{ij}$ is the response from the $i^{th}$ participant to the $j^{th}$ profile. $\beta_k$ and $b_{ik}$ are the fixed (or group-level) and random (or individual-level) effects, respectively.
In a general linear model for longitudinal data, the assumption of independent error terms from OLS regression is relaxed. Although the errors within subjects are allowed to be correlated, it is assumed that the between-subject errors are independent. Therefore, the assumptions from traditional OLS regression can be modified to provide the assumptions for a general linear model for longitudinal data:

a) \( \mathbb{E}(Y) = X\beta \)

b) \( Y \sim \text{MVN}\left(X\beta, \sigma^2V\right) \); \( Y_i \) (but not \( Y_{ij} \)) are independent

c) \( V(Y_i) = Z_i\Sigma_bZ'_i + V_i \)

d) \( b_i \sim \text{N}(0, \Sigma_b) \) and \( \varepsilon_i \sim \text{N}(0, V_i) \)

As shown above, the general linear model for longitudinal data can be expanded to incorporate random effects by further partitioning the correlated error term (\( \varepsilon_{ij} \)) to estimate a second set of regression coefficients (i.e., the random effects for each subject, or \( b_i \)) [14]. Since individual-level predictions were not an objective of this study, only the fixed effects (or group effects) were of interest; therefore, the random effects (\( b_i \)) were not estimated.

3.6.2 Model II

The second objective of the study was to determine if various demographic variables and OAB symptom severity affect quality of life. To fulfill this objective, a second linear model was constructed. In this case, OLS regression was appropriate since each subject provided only one QOL measure. The assumptions for OLS regression are as follows…

a) \( \mathbb{E}(\varepsilon_i) = 0 \), or \( Y_i = \sum_{j=1}^{p} \beta_j X_j + \varepsilon_i \)
b) $\varepsilon_i$ are independent, or $Y_i$ are independent

c) $V(\varepsilon_i) = \sigma^2$, or $Y_i$ have a common variance $\sigma^2$

d) $\varepsilon_i$ are normally distributed, or $Y_i$ are normally distributed

These assumptions can be stated briefly as Equation 3.3, which will serve as the working equation for Model II [25].

$$Y_i = \sum_{j=1}^{p} \beta_j X_j + \varepsilon_i \quad \text{where} \quad \varepsilon_i \sim N(0, \sigma^2) \quad \text{(Eq. 3.3)}$$

In this study, $Y_i$ is the QOL measure for the $i^{th}$ participant, $X_j$ is value for the $j^{th}$ demographic variable, and $\beta_j$ is the relevant regression coefficient.

Since there were multiple demographic variables to examine, the model was built using a forward stepwise approach under the control of the researcher. First, all variables were examined univariately. The variable resulting in the largest $R^2$ value for the model was retained. The remaining values were added individually. After each variable was entered into the model, a generalized $F$-test was conducted to see if the new variable resulted in a significant increase in the $R^2$ value for the model. This $F$-test is provided in Equation 3.4.

$$F^* = \left( \frac{R^2_F - R^2_R}{df_R - df_F} \right) \div \left( \frac{1 - R^2_F}{df_F} \right) \quad \text{(Eq 3.4)}$$

The $F$ and $R$ subscripts refer to the full and reduced models, respectively; and $df$ refers to the degrees of freedom associated with the error sums of squares. The test statistic, $F^*$, is compared to an $F(1-\alpha; df_R - df_F, df_F)$ distribution [25]. The variable resulting in the most significant $F^*$ statistic was retained. This process was completed until the addition of new variables did not result in significant increases in the $R^2$ value for the model. Once
the final model was complete, regression diagnostics were performed to assess the performance of the model.
3.7 References


CHAPTER 4

RESULTS

In this chapter, the results of the current study are presented. First, the results of the conjoint exercise from the pilot study are reviewed. Following this review, a summary of the descriptive statistics from the main study are presented. The remainder of the chapter contains a description of the analyses used to fulfill the two Research Objectives for this study.
### 4.1 Pilot Study Results

The purpose of the pilot study was outlined in Chapter 3. The descriptive statistics from that study are provided in Table 3.1. An analysis to examine Part I of the questionnaire was also conducted to assess whether the participants understood the exercise. A comparison of the descriptive statistics for the two groups failed to note statistically significant differences between questionnaire administration modes. Based on this finding, the responses from the telephone-administration group and the self-administration group were pooled for further analysis. Table 4.1 provides the results from the linear model to analyze the conjoint exercise. From these results, it appears that the most important attribute to the participants was prescription drug coverage. The QOL domains followed prescription coverage in this order: sleep disturbances, concern/worry about symptoms, coping mechanisms, and problems with social interactions.

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Coefficient [95% CI]</th>
<th>Standard Error</th>
<th>Z-score</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coping</td>
<td>14.99 [7.67, 22.31]</td>
<td>3.73</td>
<td>4.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Symptom Concern</td>
<td>18.59 [11.27, 25.91]</td>
<td>3.73</td>
<td>4.98</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sleep disturbances</td>
<td>21.99 [14.67, 29.31]</td>
<td>3.73</td>
<td>5.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Problems with social interactions</td>
<td>14.53 [7.21, 21.85]</td>
<td>3.73</td>
<td>3.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prescription insurance coverage</td>
<td>25.41 [18.09, 32.73]</td>
<td>3.73</td>
<td>6.80</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

No. of observations = 200; No. of subjects = 25; $\chi^2(5) = 659.04, p < 0.001$

CI = confidence interval

Table 4.1 Conjoint exercise results from the pilot study
4.2 Main Study Descriptive Statistics

The data collection for the main study took place during August and September 2003. As discussed in the Methods section, an additional 15 participants were recruited for self-administration of the questionnaire. The remainder of the sample completed the questionnaire via telephone-interview. After data collection was complete, the responses were assessed for completeness. A total of 133 useable questionnaires, or 88.7% of the sample, were available for analysis. This sample size was sufficient to perform the analysis for both Model I and Model II [1,2]. A comparison of the pilot and main study groups was performed to determine whether the pilot responses could be pooled with the main study responses. Since substantive changes to the instrument were not made after the pilot study, the decision to pool the responses from the pilot study and the main study was based on the comparability of the demographics of the two samples. A significance level of 0.01 was used to assess differences in the two groups. Based on the descriptive statistics, only one variable (average QOL compared to those individuals with OAB symptoms) was significant at the 0.01 level, thus the pilot responses were combined with the main study responses for further analysis. Table 4.2 provides descriptive statistics.

On average, respondents were 66.5 years of age. Women formed the majority of the sample (82.8%). Over 84% of the participants has a high school diploma or higher. Approximately 20% of the participants were college graduates. The average annual household income was $25,000 or more for almost one-half of the participants. Using the results from the NOBLE study, the patients in the current study were slightly older. The average income in the NOBLE study was higher than that for the current study. Educational levels were fairly similar. The current study also contained considerably
more women than did the NOBLE study. It is important to remember that the NOBLE study sample was constructed to be representative of US population estimates at the time the study was completed; therefore, the demographics of this study may not be similar on all variables since a convenience sampling method was used [3]. The majority of the sample (94%) was covered by medical insurance for the six months prior to the administration of the survey and almost two-thirds of those had prescription drug coverage. The profiles with the highest and lowest responses were Profile 8 and Profile 2, respectively. Figure 4.1 provides a series of box plots for the profile responses.

Figure 4.1  Box plots for profile responses from Part I
<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall (n=133)</th>
<th>Main (n=109)</th>
<th>Pilot (n=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age*</td>
<td>66.5 (8.5)</td>
<td>67.5 (8.0)</td>
<td>62.3 (10.2)</td>
</tr>
<tr>
<td>Gender (% female)</td>
<td>82.8</td>
<td>81.7</td>
<td>88.0</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than HS</td>
<td>8.2</td>
<td>7.3</td>
<td>12.0</td>
</tr>
<tr>
<td>Some HS</td>
<td>7.5</td>
<td>8.3</td>
<td>4.0</td>
</tr>
<tr>
<td>HS graduate</td>
<td>33.6</td>
<td>33.0</td>
<td>36.0</td>
</tr>
<tr>
<td>Some college</td>
<td>30.6</td>
<td>34.9</td>
<td>12.0</td>
</tr>
<tr>
<td>College graduate</td>
<td>14.9</td>
<td>11.9</td>
<td>28.0</td>
</tr>
<tr>
<td>Graduate or professional degree</td>
<td>5.2</td>
<td>4.6</td>
<td>8.0</td>
</tr>
<tr>
<td>Income (n = 116)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; $10,000</td>
<td>16.4</td>
<td>14.3</td>
<td>24.0</td>
</tr>
<tr>
<td>$10,000 to $17,999</td>
<td>20.7</td>
<td>24.2</td>
<td>8.0</td>
</tr>
<tr>
<td>$18,000 to $24,999</td>
<td>16.4</td>
<td>16.5</td>
<td>16.0</td>
</tr>
<tr>
<td>$25,000 to $34,999</td>
<td>19.0</td>
<td>22.0</td>
<td>8.0</td>
</tr>
<tr>
<td>$35,000 to $49,999</td>
<td>11.2</td>
<td>12.0</td>
<td>8.0</td>
</tr>
<tr>
<td>$50,000 to $69,999</td>
<td>8.6</td>
<td>5.5</td>
<td>8.0</td>
</tr>
<tr>
<td>$70,000 to $99,999</td>
<td>5.2</td>
<td>4.4</td>
<td>8.0</td>
</tr>
<tr>
<td>$100,000 to $124,999</td>
<td>2.6</td>
<td>1.1</td>
<td>8.0</td>
</tr>
<tr>
<td>≥ $125,000</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Insurance</td>
<td>94.0</td>
<td>93.5</td>
<td>96.0</td>
</tr>
<tr>
<td>% with medical coverage</td>
<td>63.3</td>
<td>61.0</td>
<td>73.9</td>
</tr>
<tr>
<td>% with prescription coverage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insurance type (%)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>71.3</td>
<td>72.0</td>
<td>68.4</td>
</tr>
<tr>
<td>Public/Government</td>
<td>26.7</td>
<td>26.8</td>
<td>26.3</td>
</tr>
<tr>
<td>Other</td>
<td>2.0</td>
<td>1.2</td>
<td>5.3</td>
</tr>
<tr>
<td>Duration of OAB symptoms</td>
<td>12.2 (17.2)</td>
<td>10.7 (13.5)</td>
<td>19.0 (27.5)</td>
</tr>
<tr>
<td>OAB medication use (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never used</td>
<td>72.0</td>
<td>73.2</td>
<td>66.7</td>
</tr>
<tr>
<td>Not within past 6 months</td>
<td>28.0</td>
<td>26.9</td>
<td>33.3</td>
</tr>
<tr>
<td>Current user</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Health status item means</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coping</td>
<td>47.8 (26.7)</td>
<td>48.2 (25.9)</td>
<td>45.9 (30.6)</td>
</tr>
<tr>
<td>Concern</td>
<td>48.4 (25.3)</td>
<td>48.8 (25.1)</td>
<td>47.0 (26.8)</td>
</tr>
<tr>
<td>Sleep</td>
<td>43.2 (27.2)</td>
<td>44.1 (26.3)</td>
<td>39.6 (31.1)</td>
</tr>
<tr>
<td>Social interactions</td>
<td>46.2 (26.2)</td>
<td>40.8 (25.3)</td>
<td>38.4 (29.1)</td>
</tr>
<tr>
<td>Avg. symptom severity compared to:*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Those with symptoms</td>
<td>2.9 (1.5)</td>
<td>3.0 (1.5)</td>
<td>2.6 (1.1)</td>
</tr>
<tr>
<td>Those without symptoms</td>
<td>3.8 (1.7)</td>
<td>4.8 (1.7)</td>
<td>3.1 (1.7)</td>
</tr>
</tbody>
</table>

(continued)
## Table 4.2 continued

<table>
<thead>
<tr>
<th>Patient profile</th>
<th>Attributes</th>
<th>Coping</th>
<th>Concern</th>
<th>Sleep</th>
<th>Social</th>
<th>Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>66.4 (29.6)</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td>39.7 (29.3)</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>66.5 (28.8)</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td>55.8 (28.0)</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>55.6 (30.0)</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>74.6 (23.2)</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>56.0 (28.4)</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>86.9 (18.2)</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>59.4 (27.1)</td>
</tr>
</tbody>
</table>

✓ = Attribute is present; Telephone = telephone administration; Self = self-administration

Values provided are mean (std. dev.). Differences were significant at 0.05 level.

**Table 4.3** Mean profile responses and attribute levels for the main study

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4.3 **Research Objective 1**

The first research objective of this study was to examine the relative importance of QOL domains and insurance coverage on patients’ preferences for pharmaco-therapeutic management of OAB. This was accomplished through the use of conjoint methodology. The data were analyzed using a linear fixed effects model (Eq. 3.2)

4.3.1 **Hypotheses**

Five hypotheses were developed for Research Objective 1. The hypotheses are stated below in terms of the relevant null hypothesis.

Testing whether the following coefficients, or part worths, are equal to zero (i.e., the attribute has no effect on patient preference):

Hypothesis 1.1: Coping
Hypothesis 1.2: Symptom concern
Hypothesis 1.3: Problems with social interactions
Hypothesis 1.4: Sleep disturbances
Hypothesis 1.5: Prescription insurance coverage

4.3.2 **Model I**

In estimating Model I, only the first eight profile responses were used. The ninth response was a holdout profile to aid in predictive validation of the model. Since only the group (or fixed) effects were of interest, the random effects \( (b_i) \) in Equation 3.2 were not estimated. The model was estimated using Stata’s command for panel-data models using feasible generalized least squares (\( \texttt{xtgls} \)) [4]. Equation 4.1 provides the estimated regression function.
\[ \hat{Y}_j = (15.62) \text{Cope}_j + (19.73) \text{Concern}_j + (23.69) \text{Sleep}_j + (19.44) \text{Social}_j + (34.36) \text{Coverage}_j \]  
(Eq. 4.1)

In this model \( \hat{Y}_j \) is the predicted response for the \( j \)th hypothetical profile. The subscripts for each profile attribute correspond to Table 4.3. If a check mark (✓) is in the column for a given attribute in a profile, then that value is 1; otherwise, it is 0. For example, in Profile 3 check marks are under “Concern” and “Coverage”; therefore, these two variables would become 1 in Equation 4.1. The others would be 0 and fall out of the equation. The overall model was significant at the 0.05 level. According to the results, the most important component of the group’s preference for medication therapy was the presence of prescription drug coverage. This can be seen through the estimated coefficient for the prescription drug coverage attribute. The coefficient for drug coverage had the highest value of the five attributes tested (\( \beta = 34.36, p < 0.001 \)). In order of decreasing importance, the remaining attributes were sleep disturbances, concern about symptoms, problems with social interactions, and coping. A graphical comparison of the part worths for the profile attributes are provided in Figure 4.2. With these results, all of the null hypotheses for Research Objective 1 (Hypotheses 1.1 – 1.5) were rejected since all attributes were significant at the 0.05 level. The full results of Model I are provided in Table 4.4.
Figure 4.2 Graphical comparison of attribute coefficients from Model I

Table 4.4 Results from the conjoint exercise (Model I)

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Coefficient [95% CI]</th>
<th>Standard Error</th>
<th>Z-score</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coping</td>
<td>15.62 [12.20, 19.04]</td>
<td>1.75</td>
<td>8.95</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Symptom concern</td>
<td>19.73 [16.30, 23.15]</td>
<td>1.75</td>
<td>11.30</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sleep disturbances</td>
<td>23.69 [20.26, 27.11]</td>
<td>1.75</td>
<td>13.57</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Social interaction problems</td>
<td>19.44 [16.02, 22.87]</td>
<td>1.75</td>
<td>11.14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prescription coverage</td>
<td>34.36 [30.94, 37.78]</td>
<td>1.75</td>
<td>19.69</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

No. of observations = 1064; No. of subjects = 133; $\chi^2_{(s)} = 4235.74$, $p < 0.001$
4.3.3 Validation

Two methods were used to validate the results of Model I—the use of a holdout profile and alternate rating method using the visual analog scale. The holdout profile was used to evaluate the predictive validity of the model. To accomplish this, the model was estimated using only the first eight profiles. That model was then used to predict the value for the holdout profile. The relation between the observed response for Profile 9 and the predicted response was then examined [5]. Figure 4.3 provides a qualitative comparison of the observed and predicted values for the profile responses. The predicted holdout is represented by a large plus sign (+). Notice that the predicted value for the holdout profile is very close to the observed value. From Table 4.3, the average response for Profile 9 was 59.4 with a standard deviation of 27.3. Using the estimated model (Eq. 4.1), the predicted response for Profile 9 was calculated by choosing the appropriate attributes present in that profile: coping, symptom concern, and sleep disturbances (see Appendix B). The predicted response for the ninth profile is simply the sum of the three relevant coefficients, or $15.62 + 19.73 + 23.69 = 59.04$. This value and the relevant standard errors were obtained using Stata’s linear combination command (\texttt{lincom}). Table 4.5 provides a comparison of the predicted and observed values of the holdout profile. From a qualitative standpoint, the predicted mean value falls within the 95% confidence interval of the observed mean value. This suggests that the observed and predicted values are close. To formally compare the predicted versus observed responses for the holdout profile, Hotelling’s $T^2$ test was performed. This is the multivariate analog to the common $t$-test. The $p$-value for this test was 0.882 suggesting that the observed and predicted values were not significantly different. If this predicted
Figure 4.3  Comparison of observed and predicted responses for profiles from the conjoint exercise

<table>
<thead>
<tr>
<th>Observed response</th>
<th>Standard error</th>
<th>95% CI</th>
<th>Predicted response</th>
</tr>
</thead>
<tbody>
<tr>
<td>59.39</td>
<td>2.35</td>
<td>[54.74, 64.03]</td>
<td>59.04</td>
</tr>
</tbody>
</table>

Hotelling’s $T^2 = 0.0221$ [$F(1, 264)$], $p = 0.8820$; CI = confidence interval

Table 4.5  Comparison of observed holdout response to predicted holdout response
value were significantly different from the observed value, then the model might have been misspecified or the participants could have had trouble completing the conjoint exercise. Since the test was not significant, evidence was provided that the model was valid.

The second validation method was the use of the alternate method to examine the ranking of the QOL attributes. This was done through the eight items ranked using a visual analog scale (VAS) in Part II of the questionnaire. Participants provided responses to eight items—two from each QOL domain. Responses were provided on a scale from “0” (Worst possible state) to “100” (Best possible state). A mean VAS score for each of the four QOL domains was calculated. The domain means were ranked from lowest (or worst rated state) to the highest (or best rated state). The lowest mean score represented the domain that was the “worst possible state.” It was assumed that the lowest rated domain would be the “most important.” These rankings were compared to the attribute rankings for the QOL domains from the conjoint exercise (Model I). Table 4.6 provides a comparison of the rankings of the QOL attributes from the two methods (conjoint and VAS). Sleep disturbances was the most highly ranked QOL domain from both methods. Beyond that, the rankings differed. The exact reason for this is unknown, but possible explanations will be discussed in the next chapter of this dissertation.
### Table 4.6 Comparison of quality of life attribute rankings

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Ranks from Conjoint (Part I)</th>
<th>Ranks from VAS* (Part II)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep disturbances</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Symptom concern</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Problems with social interactions</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Coping</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

VAS = visual analog scale

*In Part II, the scale ranged from 0 (Worst possible state) to 100 (Best possible state).

#### 4.4 Research Objective 2

The second objective of this study was to determine if various demographic variables and OAB symptom severity affect quality of life (QOL). To accomplish this objective, a multiple linear regression model was constructed to determine which factors affected quality of life. Unlike Model I, the method of ordinary least squares was used.

#### 4.4.1 Hypotheses

The hypotheses for Research Objective 2 related to the various demographic factors obtained by the study instrument and OAB symptom severity. These hypotheses are stated below. Each hypothesis is stated in terms of the null.

Testing whether the following coefficients are equal to zero (i.e., the variable has no effect on QOL):

- **Hypothesis 2.1**: Age
- **Hypothesis 2.2**: Gender
- **Hypothesis 2.3**: Length of symptoms
- **Hypothesis 2.4**: Previous OAB medication use
Hypothesis 2.5.1: Discussion of symptoms with family/friends
Hypothesis 2.5.2: Value of discussions with family/friends
Hypothesis 2.6.1: Discussion of symptoms with health care professionals
Hypothesis 2.6.2: Value of discussions with health care professionals
Hypothesis 2.7: Income
Hypothesis 2.8: Education
Hypothesis 2.9: Medical insurance coverage
Hypothesis 2.10: Prescription drug coverage
Hypothesis 2.11: Type of prescription drug coverage
Hypothesis 2.12: OAB symptom severity

4.4.2 Model II

To begin model estimation, each demographic variable was entered into a separate univariate linear regression model with QOL as the dependent variable. QOL was calculated as the mean of the specific and general QOL measures provided in Part III. QOL increased as the score increased. A similar method was used to calculate a mean symptom severity score for each participant. Symptom severity increased as the score increased, so higher scores denote worsening symptom severity. This mean symptom severity score was also examined as a potential predictor of QOL. For continuous variables (e.g., length of symptoms, symptom severity, etc.), each variable was examined in its continuous form as well as in various categories. Age as a continuous variable was the best option of those categorizations considered. Length of symptoms failed to produce a significant p-value in any category. Symptom severity was
<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>Model p-value</th>
<th>Model $R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom severity (continuous)</td>
<td>$-0.197$</td>
<td>$0.022$</td>
<td>$0.032$</td>
</tr>
<tr>
<td>Symptom severity (high/low)</td>
<td>$-0.452$</td>
<td>$0.067$</td>
<td>$0.018$</td>
</tr>
<tr>
<td>Age (continuous)</td>
<td>$0.037$</td>
<td>$0.009$</td>
<td>$0.044$</td>
</tr>
<tr>
<td>Length of symptoms (continuous)</td>
<td>$-0.006$</td>
<td>$0.515$</td>
<td>$0.003$</td>
</tr>
<tr>
<td>Length of symptoms (median-split)</td>
<td>$0.096$</td>
<td>$0.691$</td>
<td>$0.001$</td>
</tr>
<tr>
<td>Length of symptoms (quartiles)</td>
<td>$0.200, 0.321, 0.079$</td>
<td>$0.805$</td>
<td>$0.008$</td>
</tr>
<tr>
<td>Gender</td>
<td>$0.03$</td>
<td>$0.935$</td>
<td>$0.0001$</td>
</tr>
<tr>
<td>Previous medication use</td>
<td>$-0.418$</td>
<td>$0.126$</td>
<td>$0.018$</td>
</tr>
<tr>
<td>Discussed symptoms with family/friends</td>
<td>$-0.312$</td>
<td>$0.252$</td>
<td>$0.010$</td>
</tr>
<tr>
<td>Discussed symptoms with a health care professional</td>
<td>$0.028$</td>
<td>$0.919$</td>
<td>$0.0001$</td>
</tr>
<tr>
<td>Income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$&lt; 10,000$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$10,000 to $17,999$</td>
<td>$0.217$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$18,000 to $24,999$</td>
<td>$0.123$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$25,000 to $34,999$</td>
<td>$-0.074$</td>
<td>$0.015$</td>
<td></td>
</tr>
<tr>
<td>$35,000 to $49,999$</td>
<td>$0.289$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$50,000 to $69,999$</td>
<td>$-0.261$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$70,000 to $99,999$</td>
<td>$0.373$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$100,000 to $124,999$</td>
<td>$-0.044$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td>$0.500$</td>
<td></td>
</tr>
<tr>
<td>Less than HS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some HS</td>
<td>$-0.105$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HS graduate</td>
<td>$0.403$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some college</td>
<td>$0.582$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>College graduate</td>
<td>$0.145$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graduate or professional degree</td>
<td>$0.903$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical insurance</td>
<td>$-1.26$</td>
<td>$0.012$</td>
<td>$0.047$</td>
</tr>
<tr>
<td>Prescription insurance</td>
<td>$-0.173$</td>
<td>$0.506$</td>
<td>$0.004$</td>
</tr>
<tr>
<td>Prescription insurance type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>$0.387$</td>
<td></td>
<td>$0.934$</td>
</tr>
<tr>
<td>Public / Government</td>
<td>$0.417$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Reference groups are denoted by a “—”

Table 4.7  Univariate regression results for Model II
used as dichotomous (high/low) and continuous; the continuous form was the best option. The results of the univariate regression models are provided in Table 4.7. The model-building process involved selecting those variables resulting in the most significant increases in the $R^2$ value of the model. The end result was a model with the highest possible predictive ability. The variables selected for the model were age, medical insurance coverage, symptom severity, and previous medication use. Medical insurance coverage and previous medication use were both dichotomous variables. Age was entered as a continuous variable. With an $R^2$ value of 0.1050, just over 10% of the variance in QOL was explained by including the four variables in the equation. Relating the results to the original research hypotheses, only Hypotheses 2.1, 2.4, 2.9, and 2.12 were rejected. For the others, insufficient evidence existed to reject the relevant null hypotheses. The results for the final regression model (Model II) are provided in Table 4.8

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient [95% CI]</th>
<th>Std. Error</th>
<th>t-score</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>0.713</td>
<td>1.12</td>
<td>0.64</td>
<td>0.525</td>
</tr>
<tr>
<td>Age</td>
<td>0.0313 [0.0047, 0.0579]</td>
<td>0.013</td>
<td>2.33</td>
<td>0.022</td>
</tr>
<tr>
<td>Medical insurance</td>
<td>1.28 [0.307, 2.26]</td>
<td>0.492</td>
<td>2.60</td>
<td>0.010</td>
</tr>
<tr>
<td>Symptom severity*</td>
<td>−0.134 [−0.308, 0.036]</td>
<td>0.086</td>
<td>−1.56</td>
<td>0.121</td>
</tr>
<tr>
<td>Previous medication use</td>
<td>0.378 [−0.160, 0.916]</td>
<td>0.272</td>
<td>1.39</td>
<td>0.167</td>
</tr>
</tbody>
</table>

$F(4, 126) = 4.81, p = 0.0012$; Adjusted $R^2 = 0.1050$; CI = confidence interval
*Higher symptom severity scores indicate worsening severity

Table 4.8 Final regression results for Model II
4.4.3 Regression diagnostics

After a linear regression model is estimated, it is necessary to perform various regression diagnostics to ensure that the assumptions of linear regression were not violated. Many of these measures are concerned with residuals from the regression model. Other methods examine the potential effect of extreme observations and the potential effects of multicollinearity [6]. For this study, the normality and variance of the residuals were examined. Diagnostic measures for the potential effect of outlying observations and the effects of multicollinearity are also provided.

Various residual plots, such as residuals versus predictor variables, are commonly constructed when assessing the fit of a linear regression model. In a multiple linear regression model, it is not useful to plot the residuals against each explanatory variable individually. Instead, the residuals are plotted against the fitted values. Ideally, the points in the graph should form a level, horizontal band. There should be no shape to the cloud of residuals (i.e., funnel-shaped or curved). Figure 4.4 provides the residual versus fitted value plot for Model II. There is no significant clustering of values. The plot does lack the level nature of the ideal plot. With a few exceptions, the spread of the points in the graph is fairly constant along the x-axis. The residual versus fitted values plot is a qualitative assessment the assumption of homoskedasticity, or common variance. Formal tests of homoskedasticity (e.g., Breusch-Pagan Test and White’s Test) can be performed. Each test was performed on the data, and there was insufficient evidence to reject the null hypothesis of homoskedasticity.
Normality plots can be constructed to assess the assumption of normality of the residuals. Three plots are presented here: a density plot, a normal probability plot, and a normal quantile plot. The density plot of the residuals (Figure 4.5) suggests that the distribution is fairly normal. While the distribution could be smoother, this is not unacceptable given the rather ordinal nature of the outcome variable. The probability plots of the residuals suggest that the residuals (and the outcome variable) are almost normally distributed. On the normal probability plot (Figure 4.6), the residuals fall very close to the reference line. A similar finding can be seen in the normal quantile plot (Figure 4.7). In the quantile plot, there is some deviation at the tails, but this is likely due to a few large residuals. Also, the normal quantile plot tends to be more sensitive to
extreme values than the normal probability plot, but it may provide a better assessment of deviations from normality in the “middle” of the data. The results of the Shapiro-Wilk test for normality provided insufficient evidence to suggest that the residuals were not normally distributed ($p = 0.111$). This same test was performed on the dependent variable (mean QOL score) and similar results were found ($p = 0.640$) providing further evidence that the dependent variable was normally distributed.

Figure 4.5  Density plot for the residuals from Model II
Figure 4.6 Normal probability plot of the residuals from Model II

Figure 4.7 Normal quantile plot of the residuals from Model II
Another area for investigation after estimating a regression model is the assessment of potential outliers. An individual with a large residual may or may not be an outlier. It is necessary to examine that individual’s influence on the regression model. This can be done manually by dropping those suspect individuals and re-estimating the model or it can be done by calculating various statistics, such as leverage or Cook’s distance. Plotting the leverage values against the squared residuals (Figure 4.8) provides a way to examine the relative effects of leverage and residuals. Those observations with both high leverage values and high residuals should be investigated further. Plotting the residuals against the leverage statistics using Cook’s distance as the size of the points in the plot combines several methods to assess influence (Figure 4.9). Those observations with big circles that are far from the main “cluster” might suggest highly influential observations.

Figure 4.8 Plot of the leverage values versus squared residuals for Model II
Various observations were examined for their influence on the regression model. The following participants (by patient identification number) were determined to exert the greatest effect on the model: 1902, 2802, 2803, 2810. Although the $R^2$ for the model increased to 0.149 (versus 0.105 before), the increase was not statistically significant at the 0.05 level [$F(1,122) = 1.99, p = 0.161$].

A final issue that is important to consider in multiple linear regression is multicollinearity. In some situations, correlation between explanatory variables exists. While moderate degrees of correlation are not problematic, high degrees of correlation can be. In the case of a high level of correlation (or multicollinearity), the regression model becomes mathematically unstable. This may be seen as extremely large standard
error estimates. Examining the variance inflation factors, or VIF, and tolerance are two methods of assessing multicollinearity. While no strict rules exist for the assessment of multicollinearity, one rule of thumb suggests that VIFs greater than 20 (or tolerances smaller than 0.05) provide cause for concern [7]. From Table 4.7, multicollinearity does not appear to be an issue in this model as all the VIF values are less than 20 (and tolerances larger than 0.05).

Overall, the regression model estimated for Research Objective 2 appears to be a well-fit model. Given the methods used to construct the model, the variables selected appear to be those variables representing the greatest predictive value. After deleting four cases, the predictive capacity of the model increased to almost 15%; however, this increase was not statistically significant.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model II</th>
<th>Model II (four observations deleted)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VIF</td>
<td>Tolerance</td>
</tr>
<tr>
<td>Previous medication use</td>
<td>1.12</td>
<td>0.892</td>
</tr>
<tr>
<td>Symptom severity</td>
<td>1.10</td>
<td>0.907</td>
</tr>
<tr>
<td>Medical insurance</td>
<td>1.04</td>
<td>0.962</td>
</tr>
<tr>
<td>Age</td>
<td>1.01</td>
<td>0.991</td>
</tr>
<tr>
<td>Mean VIF</td>
<td>1.07</td>
<td></td>
</tr>
</tbody>
</table>

VIF = variance inflation factor; Tolerance = 1 / VIF

Table 4.9 Multicollinearity diagnostics for Model II
4.5 References


CHAPTER 5

DISCUSSION, CONCLUSIONS, AND RECOMMENDATIONS

This chapter opens with a summary of the purpose and implementation of the study. Next, the research findings are discussed with respect to the two objectives for the study. The third section examines the limitations of the current study. This chapter concludes with suggestions for future research.
5.1 Study Overview

5.1.1 Background

With an estimated prevalence of 16.5%, overactive bladder (OAB) is a condition that affects millions of Americans. Although OAB is traditionally considered a problem affecting primarily women, the NOBLE study demonstrated that the prevalence of OAB in men and women was very similar [1]. OAB is characterized by urgency to urinate, increased frequency of urination, and nocturia. OAB may or may not involve incontinence [2]. Unlike other forms of urinary incontinence, OAB does not typically involve urinary leakage on physical activity [3].

The symptoms of OAB exert a significant adverse effect on patient quality of life (QOL). Reduced QOL has been measured by both Short Form instruments, such as the SF-36 [4,5], and various specific instruments, such as the King’s Health Questionnaire [6] and the OAB-q [7]. For the current study, the OAB-q was chosen because it was developed specifically for use in OAB patients, regardless of continence status.

In addition to the QOL aspects of OAB, there are also important economic impacts related to the condition. The estimated 2000 annual costs for OAB were $12 billion, or an average of $267 per community-dwelling person per year with the majority of costs related to routine medical care and consequence costs [8,9]. From the health plan perspective, patients with OAB have higher total annual claim costs when compared to those without OAB [10].

As the patient’s role in health care has become an increasingly important concept, methods to examine patient preferences are becoming more popular. Preference evaluation methods include those that are an extension of decision theory—summated
scales, indices, and profile presentation methods—and those that are based on economic
decision theory—standard gamble, visual analog scale, and time trade-off [11]. Conjoint
analysis is another technique useful in preference
measurement [12].

Due to the symptoms associated with OAB, individuals with OAB are sometimes
required to change their lifestyles to accommodate their symptoms. Patients often
consider medication therapy to control their symptoms [13]. While various studies have
been conducted to examine the cost-effectiveness of pharmacologic treatments for OAB
[14-16], very little research has been conducted to examine the preferences patients have
for pharmacotherapeutic management of OAB symptoms. More specifically, little
research exists to explore how patients consider the financial impact of medication
therapy. The current study has two objectives. First, the relative importance that patients
place on QOL domains, as identified by the OAB-q [7], and insurance with respect to the
decision to manage their symptoms of OAB with prescription medications is examined
using conjoint methodology. Second, the relationship between QOL and various
demographic characteristics is examined.

5.1.2 Study implementation

The study was carried out with the help of the Recruitment and Retention Shared
Facility (RRSF) at the University of Alabama at Birmingham. The RRSF recruited
patients who had symptoms of OAB but were not currently taking medications to control
their symptoms. The initial study questionnaire was sent to the RRSF for pilot testing.
After the results of the pilot test were analyzed, the final instrument was updated; and
data collection for the main study proceeded. Participants completed the questionnaire by telephone interview or self-administration in the clinics at UAB.

Of the 150 patients who completed the questionnaire, 133 provided valid responses for the analysis representing a useable response rate of approximately 89%. The obtained sample was mostly female (82.8%). The mean age was 66.5 years. While almost all (94%) of the participants had medical insurance coverage, just under two-thirds of those with insurance coverage had prescription drug coverage.

5.2 Discussion of Results

5.2.1 Research Objective 1

Conjoint methodology is a useful tool in examining an individual’s or a group’s preferences for a set of characteristics. While it has been used in many places, the widespread use of conjoint in health care is a relatively new phenomenon [17]. In Research Objective 1, a conjoint exercise was constructed to examine the relative importance of QOL domains and prescription insurance coverage on patients’ preferences for pharmacotherapeutic management of OAB symptoms. Since there were 5 attributes of interest—prescription insurance coverage and the four domains for QOL—a fractional factorial design was used to reduce the number of profiles required [18,19]. This analysis was interested in examining the group-level preferences, so a linear fixed-effects model was used to estimate these preferences.

In each profile, respondents were presented with a hypothetical patient with a certain set of QOL and prescription insurance coverage characteristics. The respondent was then asked what percentage of people like this patient would prefer drug therapy for
<table>
<thead>
<tr>
<th>Patient profile</th>
<th>Attributes</th>
<th>Overall</th>
<th>n=133</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coping</td>
<td>Concern</td>
<td>Sleep</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>2</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>✔</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>6</td>
<td>✔</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>8</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>9</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>

✓ = Attribute is present; Values provided are mean (std. dev.).

Table 5.1 Mean profile responses and attribute levels for the main study

OAB symptom control versus doing nothing. By eliciting responses as a percentage (from 0 to 100), the data were of an interval nature, thereby avoiding some of the difficulties in modeling ordinal data [20,21]. From Table 5.1, the profile with the highest percentage of patients preferring medication therapy was Profile 8. In this profile, problems existed in all four QOL areas and prescription insurance coverage was available. It makes sense that this would be the profile with the highest response given the nature of the profile. Profile 2 was given the least percentage. In Profile 2, coping was the only area that was causing problems for the hypothetical patient. In addition,
prescription drug coverage was not available. Since coping mechanisms are a part of
daily life for many OAB patients [22], it is logical that this would be the least preferred
profile.

The results of the conjoint analysis revealed that the most important attribute was
prescription drug coverage ($\beta = 34.36$). The descriptive results reflect this. Profiles 1, 3,
6, and 8 represented situations where prescription drug coverage was present. These are
the four profiles with the highest responses (all 66% or higher). The next most important
attribute was sleep disturbances ($\beta = 23.69$). Symptom concern and problems with social
interactions had similar part worths ($\beta = 19.73$ and 19.44, respectively). While a formal
test was not performed, it is likely that these two values are not significantly different
from each other. Indeed, the 95% confidence intervals for these two coefficients almost
completely overlap suggesting that patients give approximately equal importance to these
two areas when considering prescription drug therapy. The attribute with the lowest
importance was coping ($\beta = 15.62$). Since coping behaviors are often some of the first
things that individuals with OAB do to accommodate their symptoms [23,24], it follows
that coping would have the lowest importance when patients are considering medication
therapy. It is should be noted that the effect of prescription insurance coverage was
almost overwhelming when the magnitude of the other coefficients is considered. While
it is unlikely that a reversal in the order of the QOL attributes would have occurred had
prescription coverage not been included in the profile, it is possible that there may have
been a better distinction between the four QOL attributes.

The model performed quite well in predicting the holdout profile response. The
observed response for Profile 9 (the holdout profile) was 59.4% and the predicted value
was 59.0%. The predicted value fell well within the 95% confidence interval of the observed value. In validating the model using the holdout profile method, the model is constructed without the holdout profile. This cross-validation method is very useful in determining the validity of a model since they use one set of data to derive the model and a second set of data to test the model [25,26]. This cross-validation is similar to the use of a “training cohort” or “training datasets” in comorbidity studies [27-29].

The second validation method used was the visual analog scale (VAS) rating section (Part II). Participants provided ratings of how good or bad their health status would be given a certain condition (e.g., lack of sleep due to overactive bladder). Using these ratings, the QOL attributes were ranked from lowest (worst health state) to highest (best health state). These rankings were then compared to the QOL attribute rankings from the conjoint analysis. The ranking for sleep disturbances was the same from both the conjoint analysis and the VAS rankings. Beyond that, the rankings differed. There are a few possible explanations for this difference. Looking at the coefficients for coping, symptom concern, and social interactions, it can be seen that these are relatively close, especially in the case of symptom concern and social interactions. By presenting each item individually, rather than together as in the conjoint exercise, it is conceivable that the rankings could be different. Indeed, one of the strengths of conjoint analysis is that it enables researchers to measure the value of a set of attributes rather than measuring each attribute individually [30]. It is also possible that the nature of the VAS exercise was slightly different than that of the goal of Part II. While it was possible to generate rankings from the VAS responses, an alternate approach could have involved asking the participants to rank the importance of the four QOL attributes.
5.2.2 Research Objective 2

A linear regression model was constructed to determine whether various demographic variables and OAB symptom severity affected quality of life. A variety of demographic variables were considered for inclusion in the model (see Appendix A). In selecting the variables, a researcher-controlled forward stepwise method was use. While the major statistical software packages have stepwise selection procedures, these methods are based on entry and removal probabilities to which the computer strictly adheres. It is often more useful for the researcher to consider the merits of each variable entered into the model, including those not selected for inclusion by the software package [31]. Using this method, the final model contained four variables: age, medical insurance coverage, symptom severity, and previous medication use (see Table 4.7). The final $R^2$ value of the model was 0.105. This may seem rather low, but given the nature of QOL, it is not inconceivable that these four variables only account for 10% of the variability in QOL in these patients. There are certainly many other aspects to these participants’ QOL beyond the effects of their OAB symptoms. These other variables might include occupation, measures of coping ability, or social involvement, to name a few [32].

To assess the fit of Model II, various regression diagnostics were performed. While the normality and variance of the residuals were not of great concern, several potential outliers were identified. These observations were omitted, and the model was re-estimated. After a series of combinations, four observations were identified as being potentially beneficial to omit from the analysis for Model II. After model re-estimation, the $R^2$ of the revised model increased to 0.149. While this represented almost a five percentage point increase, this change was not statistically significant.
Two points of interest for Model II concern symptom severity and previous medication use. At first glance, it might seem counterintuitive that the coefficient for symptom severity is negative. It is important to remember that symptom severity was measured on a scale from “1” (Mild) to “6” (Severe). Keeping this in mind it follows naturally that QOL would decrease as the severity of symptoms worsened (or the symptom severity score increased). Also, note that the coefficients for both symptom severity and previous medication use are not statistically significant at the 0.05 level. This is most likely due to the method in which the model was constructed. Rather than basing the model solely on \( p \)-values, the change in \( R^2 \) was used as the determining factor in selecting variables. If only \( p \)-values were used or the computer had total control over the variable selection process, these two variables would not have been in the model. Consequently, the \( R^2 \) value for the model would have also been lower (\( R^2 = 0.076 \)).

5.3 Study Limitations

Although the models constructed in this study appeared to be valid, it is important to consider the limitations of the current study. The primary focus of these limitations has to do with the generalizability of the results from this study. First, the study sample was selected from Birmingham, Alabama and the surrounding areas. Without conducting similar studies in other areas, or a nationwide sample, it is unclear as to whether these results are indicative of preference patterns elsewhere in the US.

The sampling method used in this study was a non-random; therefore, it is difficult to generalize the results beyond the confines of the sample. For example, the NOBLE study used a nationwide random sample to collect data. This allowed the researchers to provide estimates of the nationwide prevalence and burden of OAB [1]. If
the sample in this study had been representative of the population, it might have been slightly easier to relate the results outside the sample [33]. Even in this case, participants from other geographical areas would be needed to suggest that preference patterns did not vary by geographic region. Unfortunately, a nationwide-random sample of OAB patients difficult to accomplish since no list of OAB patients exists. A great deal of time and effort would be required to identify OAB patients. For the purposes of this study a nationwide sample would have been cost-prohibitive.

In light of the demographics of this sample, it is easy to see that women were rather overrepresented. Given the gender distribution in the sample, it might be difficult to effectively generalize the results to men with OAB. While it seems unlikely that gender differences exist in preference patterns for medication therapy for OAB, these differences were not explicitly considered in constructing Model I. Furthermore, differences based on other demographic variables (e.g., age, income, education, race) were not explored. All of the participants in the study were not current users of medications to control OAB symptoms. As with gender, it is unclear whether this would have affected the preference patterns revealed during the conjoint exercise.

A final limitation of the current study is in the validation of Model I. The holdout method is effective in assessing the predictive ability of a conjoint model and is commonly used in many conjoint analyses [26]. Unfortunately, this method does not compare the predicted preference to what the participant actually does. Some would argue that preferences do not always reflect choices [34,35]. Choice-based experiments (e.g., discrete choice or choice-based conjoint) may be more realistic in imitating actual consumer/patient behavior [36]. The ultimate validation tool would be to examine
whether the participants actually sought drug therapy to control their OAB symptoms. Unfortunately, budgetary constraints on this project prevented this method of validation. Also, access to prescription records would have been necessary to whether patients’ acquired the medication; however, these records were not available to the researchers.

Due to the manner in which the profiles were chosen, interactions between attributes could not be examined. The fractional factorial method produced orthogonal profiles, which are desirable for main effects designs. In traditional OLS regression models, interaction terms can be constructed *post hoc* and examined. This is partly due to the fact that these models are compositional. In this decompositional method, all aspects of the model were specified at the beginning, and the profiles were constructed accordingly. In order to consider interactions, they would need to have been specified when the profiles were constructed. However, the impact of these interactions is generally thought to be relatively small (i.e., \( \leq 10\% \) of the variability in the responses) [37] so their omission would probably not change the conclusions of Model I.

### 5.4 Areas for Future Research

As discussed above, one area for future research would be to examine whether differences in preference patterns exist based on demographic variables. The patient preference literature does not sufficiently address demographic differences. Examining whether these differences exist and the extent of these differences could improve the applicability of existing patient preference studies.

Another potential for future research would be to repeat this study as a discrete choice experiment. This study is based on what Louviere refers to as “judgment data” since it involves evaluations of alternatives [21]. A discrete choice study may also more
closely reflect actual patient intentions with respect to medication therapy [36,38]. Discrete choice studies are often concerned with various products as alternatives, so adapting the current study to a discrete choice design might be challenging. Under the discrete choice method, the patient’s would be whether he or she would prefer drug therapy to doing nothing at all. Analysis would then be performed using a logit or probit model; however, the results would still provide a measure of the relative importance that patients placed on the various attributes.

Examining whether patients actually sought medication therapy would be a potential area for external validation of this study. This could be done relatively easily with the use of member prescription claims from a health plan. As an example, OAB patients could be selected based on their prescription records. An instrument containing a conjoint exercise and a QOL assessment would be provided to a sample of the patients. Using their QOL scores and the overall conjoint results, the predicted preferences could be obtained. Those patients who are currently taking OAB medications might be expected to have high preferences for medication therapy.

Although medication therapy for OAB is the most commonly used treatment [13], other treatments do exist. Various effective surgical treatments are available [3], as well as newer neuromodulation procedures [39]. Non-medical treatments include various muscle exercises [40-42] and the use of incontinence products[22]. It might be potentially beneficial to examine patients’ preferences for the various treatment options, both pharmacologic and nonpharmacologic, given their QOL and insurance coverage.

One area for future research that may be of particular interest to pharmacy benefit managers is the derivation of willingness to pay (WTP). Various studies have combined
WTP methods with conjoint exercises [43-46]. By incorporating more levels of the insurance coverage, it would be possible to determine how much financial responsibility OAB patients would be willing to assume in reducing the effects of their symptoms on their QOL. Market researchers sometimes use this to determine the price for a new product (e.g., a new drug product for a disease). This could be beneficial to benefits designers in this day of increasing drug costs [47]. However, this approach could prove to be troublesome since the prescription insurance coverage had an overwhelming affect on patient preferences.

From a comparative standpoint, it might be interesting to examine the effect of QOL changes and insurance coverage on other disease states. For example, in a disease state, such as hypertension, where the treatment may not significantly affect quality of life [48], it is quite possible that similar results would be seen (i.e., insurance coverage or “cost” would be the most important factor). In other situations where treatment represents a seemingly life or death dichotomy (e.g., diabetes or cancer) [49,50], it is conceivable that a cost variable might not be the most important factor that patients.

5.5 Conclusion

From the results of the study, prescription insurance coverage appears to be the most important factor patients consider when constructing their preferences for pharmacotherapeutic management of their symptoms of overactive bladder. Sleep disturbances represent the most important quality of life factor that patients consider; however, this is still less important than the presence of prescription insurance coverage. When examining the ability to explain the variability of QOL, four variables appeared to be important: age, symptom severity, medical insurance coverage, and previous OAB
medication use. While these explained the greatest amount of variability in QOL, the $R^2$ value for the final model was only 0.149. The limitations of the study deal primarily with the generalizability of the results due to the nature of the sample. Despite these limitations, this study adds to the body of literature surrounding patient preferences, especially in the area of overactive bladder.
5.6 References


APPENDIX A

FINAL STUDY QUESTIONNAIRE
Assessing Health State Preferences
and the Decision to Medicate in Overactive Bladder

Part I. Profiles

We are trying to learn more about the importance of quality of life and prescription drug coverage on your decision to seek drug therapy to control symptoms of OAB. You will be asked to listen to a series of patient profiles describing the experience of persons with OAB, and then tell us what you think the patients would do. To help you understand the way these profiles will work, we have a simple example about buying a car.

Suppose we think about people who are shopping for a car. We will describe a profile of the characteristics of a particular car. After considering the characteristics included in the profile, please give us your estimate of the percentage (from 0% to 100%) of people shopping for cars that you believe would decide to buy this car.

Example Using the Purchase of a Car

1. Small size car
2. Dislike the color
3. Like the styling
4. High practical use
5. No rebate incentive from dealer

What percentage of car shoppers (from 0% to 100%) would purchase this car? ___

Now a series of 9 patient profiles will be presented for you to consider. Please provide an estimate of the percentage of patients similar to those described who would prefer drug therapy to control their symptoms of overactive bladder versus doing nothing about their symptoms. In providing your responses, remember to think about the relative importance you would put on each of the five areas described in each profile.
Patient 1

1. Few changes required to cope with the condition
2. Symptoms cause little concern
3. Few problems with sleep patterns
4. Many problems with social interactions
5. Full prescription drug coverage

If symptoms could be controlled with drug therapy during the next 6 months, what percentage (from 0% to 100%) of people like Patient 1 would prefer drug therapy compared to doing nothing? _____

Patient 2

1. Many changes required to cope with the condition
2. Symptoms cause little concern
3. Few problems with sleep patterns
4. Few problems with social interactions
5. No prescription drug coverage

If symptoms could be controlled with drug therapy during the next 6 months, what percentage (from 0% to 100%) of people like Patient 2 would prefer drug therapy compared to doing nothing? _____

Patient 3

1. Few changes required to cope with the condition
2. Symptoms cause a great deal of concern
3. Few problems with sleep patterns
4. Few problems with social interactions
5. Full prescription drug coverage

If symptoms could be controlled with drug therapy during the next 6 months, what percentage (from 0% to 100%) of people like Patient 3 would prefer drug therapy compared to doing nothing? _____
Patient 4

1. Many changes required to cope with the condition
2. Symptoms cause a great deal of concern
3. Few problems with sleep patterns
4. Many problems with social interactions
5. No prescription drug coverage

If symptoms could be controlled with drug therapy during the next 6 months, what percentage (from 0% to 100%) of people like Patient 4 would prefer drug therapy compared to doing nothing? ____

Patient 5

1. Few changes required to cope with the condition
2. Symptoms cause little concern
3. Many problems with sleep patterns
4. Many problems with social interactions
5. No prescription drug coverage

If symptoms could be controlled with drug therapy during the next 6 months, what percentage (from 0% to 100%) of people like Patient 5 would prefer drug therapy compared to doing nothing? ____

Patient 6

1. Many changes required to cope with the condition
2. Symptoms cause little concern
3. Many problems with sleep patterns
4. Few problems with social interactions
5. Full prescription drug coverage

If symptoms could be controlled with drug therapy during the next 6 months, what percentage (from 0% to 100%) of people like Patient 6 would prefer drug therapy compared to doing nothing? ____
Patient 7

1. Few changes required to cope with the condition
2. Symptoms cause a great deal of concern
3. Many problems with sleep patterns
4. Few problems with social interactions
5. No prescription drug coverage

If symptoms could be controlled with drug therapy during the next 6 months, what percentage (from 0% to 100%) of people like Patient 7 would prefer drug therapy compared to doing nothing? _____

Patient 8

1. Many changes required to cope with the condition
2. Symptoms cause a great deal of concern
3. Many problems with sleep patterns
4. Many problems with social interactions
5. Full prescription drug coverage

If symptoms could be controlled with drug therapy during the next 6 months, what percentage (from 0% to 100%) of people like Patient 8 would prefer drug therapy compared to doing nothing? _____

Patient 9

1. Many changes required to cope with the condition
2. Symptoms cause a great deal of concern
3. Many problems with sleep patterns
4. Few problems with social interactions
5. No prescription drug coverage

If symptoms could be controlled with drug therapy during the next 6 months, what percentage (from 0% to 100%) of people like Patient 9 would prefer drug therapy compared to doing nothing? _____
Part II. Health Status

To help assess the impact of overactive bladder symptoms on health status, imagine a scale that resembles a thermometer. On this scale, Best Possible State is marked as 100 (most desirable), and Worst Possible State is marked as 0 (least desirable).

Please indicate on this scale (from 0 to 100) how bad or good a person’s overall health status would be if he or she were experiencing each of the following states or conditions over a six-month period.

**Worst Possible State**

<table>
<thead>
<tr>
<th>Must adjust travel plans to always be near a restroom</th>
<th>Best Possible State</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

**Worst Possible State**

<table>
<thead>
<tr>
<th>Concern due to overactive bladder</th>
<th>Best Possible State</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

**Worst Possible State**

<table>
<thead>
<tr>
<th>Lack of sleep due to overactive bladder</th>
<th>Best Possible State</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

**Worst Possible State**

<table>
<thead>
<tr>
<th>Friends or family express concern due to overactive bladder</th>
<th>Best Possible State</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Problem Description</td>
<td>Worst Possible State (Least Desirable)</td>
</tr>
<tr>
<td>---------------------</td>
<td>---------------------------------------</td>
</tr>
<tr>
<td>Advance planning needed due to overactive bladder</td>
<td>0</td>
</tr>
<tr>
<td>Personal frustration or anxiety due to overactive bladder</td>
<td>0</td>
</tr>
<tr>
<td>Constantly feeling tired due to overactive bladder</td>
<td>0</td>
</tr>
<tr>
<td>Problems exist in relationships with friends or family due to overactive bladder</td>
<td>0</td>
</tr>
</tbody>
</table>
Part III. Quality of Life

The following two questions refer to the severity of your symptoms of overactive bladder. Each question is rated on a scale from 1 (Mild) to 6 (Severe). To aid you in providing an accurate answer, please consider the time period covering only the past six months.

Compared to other people with symptoms of overactive bladder, how would you rate the severity of your symptoms over the past six months?

<table>
<thead>
<tr>
<th>Mild</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

Compared to people without symptoms of overactive bladder, how would you rate the severity of your symptoms over the past six months?

<table>
<thead>
<tr>
<th>Mild</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

The next two questions refer to your overall quality of life. Each question is rated on a scale from 1 (Poor) to 6 (Excellent). To aid you in providing an accurate answer, please consider the time period covering only the past six months.

Compared to other people with symptoms of overactive bladder, how would you rate your overall quality of life over the past six months?

<table>
<thead>
<tr>
<th>Poor</th>
<th>Excellent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

Compared to people without symptoms of overactive bladder, how would you rate your overall quality of life over the past six months?

<table>
<thead>
<tr>
<th>Poor</th>
<th>Excellent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>
Part IV. Demographics

What is your age in years? _____

What is your gender? Male Female

Approximately how long have you had symptoms of OAB? _____ years _____ months

Which category best describes your use of medications for OAB symptom control?

___ Never used ___ Not used within the past six months ___ Currently using

Have you discussed your symptoms before with friends and/or family? YES NO

If YES, how valuable was that discussion to you?

<table>
<thead>
<tr>
<th>Not at all Valuable</th>
<th>Extremely Valuable</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

Have you discussed your symptoms with a health care provider? YES NO
(Health care providers may include nurses, pharmacists, and physicians)

If YES, how valuable was this discussion to you?

<table>
<thead>
<tr>
<th>Not at all Valuable</th>
<th>Extremely Valuable</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

What is your average annual household income (select the appropriate category)?

___ Less than $10,000 ___ $50,000 to $69,999
___ $10,000 to $17,999 ___ $70,000 to $99,999
___ $18,000 to $24,999 ___ $100,000 to $124,999
___ $25,000 to $34,999 ___ $125,000 or greater
___ $35,000 to $49,999

What is the highest level of education you have completed?

___ Less than high school
___ Some high school
___ High school graduate / GED
___ Some college
___ College graduate (BA, BS, etc.)
___ Graduate or professional degree (MS, MA, MPH, MD, PhD, JD, etc.)

During the six months before today, were you continuously covered by health insurance? YES NO

Did that insurance coverage have any type of prescription drug coverage? YES NO

If YES, what was the primary source of prescription drug coverage? Private
___ (Blue Cross/Blue Shield, AdvancePCS, Aetna, etc.)
___ Public / Government-based
___ (Medicaid, VA, military, etc.)
___ Other or Not sure
APPENDIX B

PATIENT RECRUITMENT FLYERS
The purpose of the "Overactive Bladder and Quality of Life Study" study is to learn more about how difficulties with overactive bladder, sometimes called incontinence, affect people's quality of life. The researchers at UAB and OSU hope to use this information to design better programs, medications, or assistive devices to help people manage or reduce their bladder symptoms. This study does not involve any sort of medical tests or medical treatments. We would only like for you to complete a survey questionnaire in person or over the phone. It will take approximately 20-30 minutes of your time. Participation in this study is completely voluntary and all information will be kept strictly confidential and will be used only for research purposes.

You may be eligible to participate if you are age 40 or older and you experience symptoms such as:

- Frequently needing to urinate during the daytime hours
- Needing to get up at night to urinate
- Accidental loss of small amounts of urine
- An uncomfortable or sudden urge to urinate

For more information please see our friendly representative stationed in your waiting room, or call Luevenia Barnes at 205-934-6850. You may also call Ms. Barnes if you would like to make arrangements to complete the questionnaire by telephone interview.
The purpose of the “Overactive Bladder and Quality of Life Study” study is to learn more about how difficulties with overactive bladder, sometimes called incontinence, affect people’s quality of life. The researchers at UAB and OSU hope to use this information to design better programs, medications, or assistive devices to help people manage or reduce their bladder symptoms. This study does not involve any sort of medical tests or medical treatments. We would only like for you to complete a survey questionnaire in person or over the phone. It will take approximately 20-30 minutes of your time. Participation in this study is completely voluntary and all information will be kept strictly confidential and will be used only for research purposes.

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For more information please see our friendly representative stationed in your waiting room, or call Laevenia Barnes at 205-934-6850. You may also call Ms. Barnes if you would like to make arrangements to complete the questionnaire by telephone interview.
APPENDIX C

STUDY APPROVAL MATERIAL
Form 4: IRB Approval Form
Identification and Certification of Research
Projects Involving Human Subjects

The Institutional Review Board for Human Use (IRB) has an approved Multiple Project Assurance with the Department of Health and Human Services and is in compliance with 21 CFR parts 50 and 56 and ICH GCP Guidelines. The Assurance became effective on January 1, 1999 and the approval period is for five years. The Assurance number is M-1149.

Principal Investigator: MAYO, CHARLOTTE
Co-Investigator(s):  
Protocol Number: X020816602
Protocol Title: Quality of Life Study in Patients with Overactive Bladder

The IRB reviewed and approved the above annual project on 9-5-03. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services. This Project will be subject to Annual continuing review as provided in that Assurance.

This project received EXPEDITED review.
IRB Approval Date: 9-5-03
Date IRB Approval Issued: 9-9-03

HIPAA Waiver Approved? No

Marilyn Sosa, M.A.
Vice Chair of the Institutional Review Board for Human Use (IRB)

Investigators please note:

The IRB approved consent form used in the study must contain the IRB approval date and expiration date.

IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.

Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.

Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.
FORM 4: IRB Approval Form
Identification and Certification of Research Projects Involving Human Subjects

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Protocol Number: X020816002
Protocol Title: Quality of Life Study in Patients with Overactive Bladder

The IRB reviewed and approved the above named project on 2-28-02. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services. This Project will be subject to Annual continuing review as provided in that Assurance.

This project received EXPEDITED review.
IRB Approval Date: 2-28-02
Date IRB Approval Issued: 2-28-02

Marilyn Doee, M.A.
Vice Chair of the Institutional Review Board for Human Use (IRB)

Investigators please note:

The IRB approved consent form used in the study must contain the IRB approval date and expiration date.

IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.

Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.

Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.
APPENDIX D

STUDY CODEBOOK
<table>
<thead>
<tr>
<th>Variable name</th>
<th>Variable label</th>
<th>Description</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>id</td>
<td>ID</td>
<td>Respondent ID number</td>
<td></td>
</tr>
<tr>
<td>profile</td>
<td>Profile</td>
<td>Conjoint profile number</td>
<td>1 – 9</td>
</tr>
<tr>
<td>coping</td>
<td>Coping</td>
<td>Coping with OAB symptoms</td>
<td>0 = low 1 = high</td>
</tr>
<tr>
<td>concern</td>
<td>Concern</td>
<td>Concern over OAB symptoms</td>
<td>0 = low 1 = high</td>
</tr>
<tr>
<td>sleep</td>
<td>Sleep</td>
<td>Sleep interference of OAB symptoms</td>
<td>0 = low 1 = high</td>
</tr>
<tr>
<td>social</td>
<td>Social</td>
<td>Affects of OAB symptoms on social interactions</td>
<td>0 = low 1 = high</td>
</tr>
<tr>
<td>coverage</td>
<td>Prescription drug coverage</td>
<td>Level of prescription drug coverage</td>
<td>0 = none (&gt; $80/month) 1= full (≤$20/month)</td>
</tr>
<tr>
<td>choice</td>
<td>Choice</td>
<td>Patient’s choice</td>
<td>0 – 100</td>
</tr>
</tbody>
</table>

**Model I – Validation with VAS**

| cop1          | Coping 1       | VAS score for coping item #1 | 0 – 100 |
| cop2          | Coping 2       | VAS score for coping item #2 | 0 – 100 |
| copemean      | Coping mean    | Mean VAS score for coping    | 0 – 100 |
| con1          | Concern 1      | VAS score for concern item #1 | 0 – 100 |
| con2          | Concern 2      | VAS score for concern item #2 | 0 – 100 |
| concernmean   | Concern mean   | Mean VAS score for concern   | 0 – 100 |
| slp1          | Sleep 1        | VAS score for sleep item #1  | 0 – 100 |
| slp2          | Sleep 2        | VAS score for sleep item #2  | 0 – 100 |

(continued)
[Codesheet continued]

<table>
<thead>
<tr>
<th>sleepmean</th>
<th>Sleep mean</th>
<th>Mean VAS score for sleep</th>
<th>0 – 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>soc1</td>
<td>Social 1</td>
<td>VAS score for social interactions item #1</td>
<td>0 – 100</td>
</tr>
<tr>
<td>soc2</td>
<td>Social 2</td>
<td>VAS score for social interactions item #2</td>
<td>0 – 100</td>
</tr>
<tr>
<td>socialmean</td>
<td>Social mean</td>
<td>Mean VAS score for social</td>
<td>0 – 100</td>
</tr>
</tbody>
</table>

Model II – Linear Regression: QOL vs. Demographics and symptom severity

<table>
<thead>
<tr>
<th>sxsevs</th>
<th>Global symptom severity 1</th>
<th>Symptom severity relative to others with symptoms</th>
<th>1 – 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>sxsevg</td>
<td>Global symptom severity 2</td>
<td>Symptom severity relative to perfectly health people</td>
<td>1 – 6</td>
</tr>
<tr>
<td>sxsev</td>
<td>Global symptom severity score</td>
<td>Mean score of global symptom severity items 1 and 2</td>
<td>1 – 6</td>
</tr>
<tr>
<td>qols</td>
<td>Global QOL 1</td>
<td>QOL relative to others with symptoms</td>
<td>1 – 6</td>
</tr>
<tr>
<td>qolg</td>
<td>Global QOL 2</td>
<td>QOL relative to perfectly health people</td>
<td>1 – 6</td>
</tr>
<tr>
<td>qol</td>
<td>Global QOL score</td>
<td>Mean score of global QOL items 1 and 2</td>
<td>1 – 6</td>
</tr>
<tr>
<td>age</td>
<td>Age</td>
<td>Age in years</td>
<td>0 – 99</td>
</tr>
</tbody>
</table>
| gender    | Gender                   | Gender | 0 = male  
                         |         | 1 = female |
| sxlength  | Length of symptoms       | Length of symptoms in months | 0 – 99 |
| prevmeds  | Use of previous medications | Respondent previously used medications for OAB symptoms | 0 = no  
                         |         | 1 = yes |
| discussfam| Discussion of symptoms with family and/or friends | Respondent discussed symptoms with family and or friends | 0 = no  
                         |         | 1 = yes |

(continued)
| Codesheet continued |
|---------------------|-----------------|-----------------------|
| **famvalue**        | Value of        | Patient rated value   | 1 – 6                  |
|                     | discussion      | of discussion on scale|                       |
|                     | with family     | from 1 (little value) |                       |
|                     | and/or friends  | to 6 (great value)   |                       |
| **discusshc**       | Discussion of   | Respondent discussed  | 0 = no                |
|                     | symptoms with   | symptoms with health  | 1 = yes               |
|                     | health          | care providers (RN,    |                       |
|                     | care providers  | RPh, MD, etc.)       |                       |
| **hcvalue**         | Value of        | Patient rated value   | 1 – 6                  |
|                     | discussion      | of discussion on scale|                       |
|                     | with health     | from 1 (little value) |                       |
|                     | care providers  | to 6 (great value)   |                       |
| **income**          | Income          | Average annual        | 1 = <$10000           |
|                     |                 | family income         | 2 = $10000 to $17999  |
|                     |                 |                       | 3 = $18000 to $24999  |
|                     | **education**   | Highest level of      | 4 = $25000 to $34999  |
|                     |                | education completed   | 5 = $35000 to $49999  |
|                     |                 |                       | 6 = $50000 to $69999  |
|                     | **medins**      | Respondent had        | 7 = $70000 to $99999  |
|                     | Medical         | medical insurance in  | 8 = $100000 to $124999|
|                     | insurance       | the past six months   | 9 = >$125000          |
| **rxins**           | Prescription     | Respondent had        | 0 = no                |
|                     | drug coverage   | prescription drug      | 1 = yes               |
|                     |                 | coverage in the past   |                       |
|                     |                 | six months             |                       |
| **rxtype**          | Prescription     | Source of the         | 1 = private           |
|                     | drug coverage   | prescription drug      | 2 = public            |
|                     | type            | benefit                | 3 = other / don’t know|
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