A Cost-Utility Analysis of Three Alternatives Used to Diagnose

Obstructive Sleep Apnea Syndrome

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Acknowledgements

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Table of Acronyms

Acronym	Name	Definition
WTP or CV	Willingness-to Pay	Amount an individual desires to pay for a health improvement
CBA	Cost-Benefit Analysis	A form of economic evaluation where outcomes are measured as individual's willingness to pay
CUA	Cost-Utility Analysis	A form of economic evaluation where outcomes are measured as a von-Neumann Morgenstern utilities
CEA	Cost-Effectiveness Analysis	A form of economic evaluation where outcomes are measured as physical variables.
OSAS	Obstructive Sleep Apnea Syndrome	Syndrome in which upper airway collapse during sleep
CPAP	Continuous Positive Airway Pressure	Treatment for OSAS were air is pumped into airway to prevent its collapse
FN-PSG	Full Night Polysomnography	The "gold-standard" diagnostic sleep exam for sleep apnea which is conducted in a sleep lab
SN-PSG	Split-Night Polysomnography	Diagnostic sleep exam that resembles FN-PSG with the exception that patient is moved on to the titration step if a positive OSAS diagnosis is made within the first two hours of sleep
PSG-Titration	Polysomnography Titration	Exam used to determine CPAP pressure which is conducted in sleep lab
UHPSM	Unattended Partial Sleep Monitoring Exam	Diagnostic sleep exam administered by a machine the patient sets up in his/her own home
CPAP-Auto-Titration	CPAP-Auto-Titration	Exam, conducted in home, that sets optimal CPAP pressure
AHI	Apnea Hypopnea Index	Sum of apneas and hypopnea experienced by patient in an hour
C/U	Cost Utility Ratio	Ratio of expected costs to expected QALYs
SG	Standard Gamble	Technique used to determine utilities
TTO	Time-Trade-Off	Technique used to determine utilities
VAS	Visual Analogue Scale	Technique used to determine utilities
HRQOL	Health Related Quality of Life	General class of questionnaire that seek to measure health status
vNM	von Neumann-Morgenstern utility	A utility that is consistent with von Neumann-Morgenstern utility theory

Chapter 1

Motivation for Economic Evaluation in Healthcare

Figure 1 National Health Expenditure as a Share of Gross Domestic Product [93]
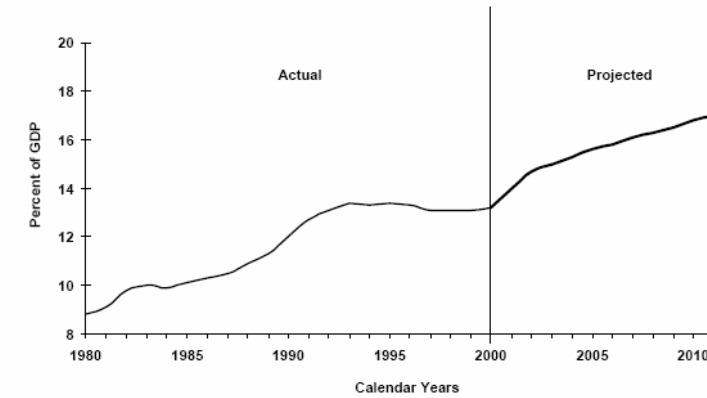
Source: CMS, Office of the Actuary, National Health Statistics Group.

The combination of rising healthcare costs and adverse demographic trends will present challenges for healthcare policymakers. Healthcare spending currently composes 12% of US GDP [Figure 1, 93]. Spending is conservatively forecasted to increase 1% faster than GDP for the next 10 years; by 2010, healthcare spending will account for 18% of GDP [Figure 2, Figure 1, 93].

Figure 2 Growth in National Health Expenditures [93]
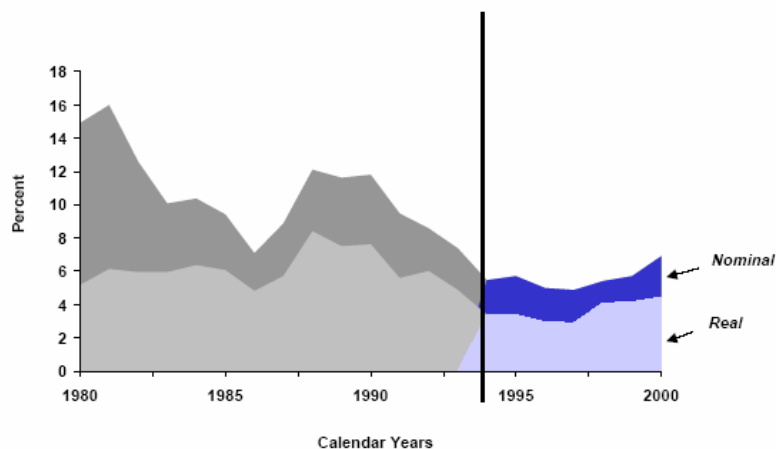
Note: Deflated using the GDP chain weighted price index. Nominal: values expressed in current dollar terms (not adjusted for inflation). Real: values adjusted for economy-wide inflation.

Source: CMS, Office of the Actuary, National Health Statistics Group.

The increase in aggregate healthcare spending comes from increases in healthcare prices and from higher healthcare utilization rates. Figure 3 suggests that price increases have played a larger role in increasing healthcare expenditure.

Figure 3 Growth in Personal Health Care Expenditures Per Capita [93]
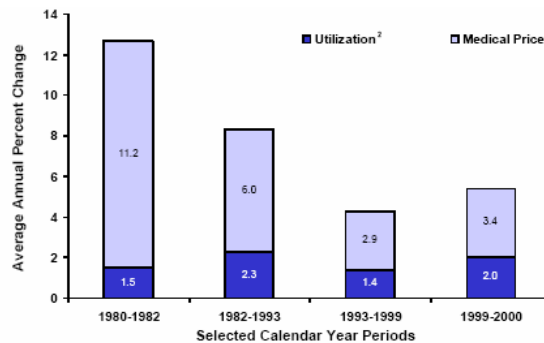
¹ Personal health care spending comprises therapeutic goods or services rendered to treat or prevent a specific disease or condition in a specific person.
² Utilization includes quantity, quality, and mix of services. As a residual, this factor also includes any errors in measuring prices or total spending.

Note: Medical prices are calculated using the personal health care chain-type index constructed from the producer price index for hospital care, nursing home input price index for nursing home care, and consumer price indexes specific to each of the remaining personal health care components.

Source: CMS, Office of the Actuary, National Health Statistics Group.

Government healthcare spending is predicted to grow rapidly as the "baby-boomer" generation reaches retirement age. Medicare and Medicaid programs constituted 2.6% of GDP in 2003; however, expenditures are estimated to increase to 3.4% of GDP by 2006 and 12.8% of GDP by 2078 [94]. Over the last fifty years, Federal tax receipts have only averaged 11% of GDP [94]. Policymakers are increasingly worried about Medicare's long-term solvency [94]. Medicare's financing deficit is expected to grow from 33% of expenditures (2003) to 45% of expenditures (2012) [94]. A recent report published by the Medicare Board of Trustees estimated that the Hospital Insurance Trust Fund "fails by a wide margin to meet the Trustees' long-rang test of close actuarial balance" and will see its assets decline from 125% of expenditures to default in the year 2019 [Figure 4, 94].

Figure 4 Hospital Insurance Trust Fund Balance as a Percentage of Annual Expenditure [94]
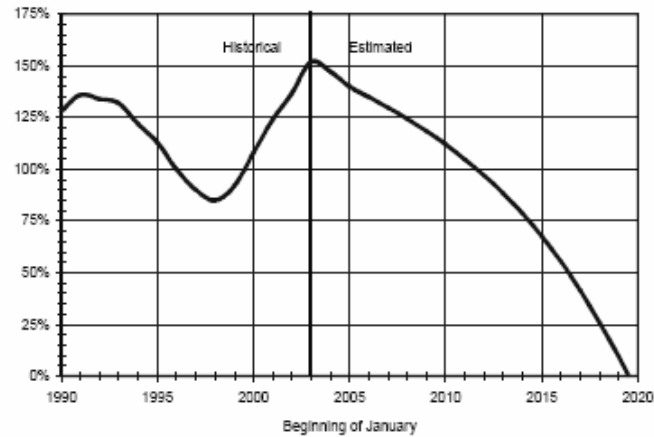
As Figure 5 indicates, taxes will need to dramatically increase to cover this shortfall [94].

Figure 5 Medicare Expenditures and Income as a Percentage of GDP [94]
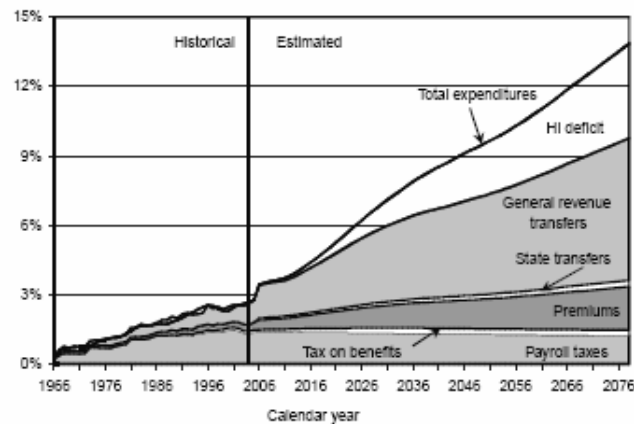
Given these troubling trends, it will be increasingly important to evaluate healthcare programs to ensure that society gets the greatest bang for its healthcare buck. Economics provides a systematic framework for conducting this analysis. Economics is both a prescriptive and descriptive discipline. The normative dimension of economics prescribes actions that help society redistribute resources in the most efficient way possible. The normative theory begins with the assumptions that

social utility[1] is *only* composed of individual utilities and those individuals are the best judges of their own utility. [65-65]. Efficiency is then defined as a state in which no member of society can be made better off without making another member worse-off[2].

Society's ability to reach an efficient equilibrium largely depends on its markets' characteristics. In perfectly competitive markets, natural forces drive the markets to efficient equilibriums. However, these perfectly competitive assume behavior that may not occur in the real-world. For example, it is assumed that: producers have "well-behaved" production functions and consumers have "well-behaved" preferences, goods are homogenous, firms can freely enter and exit the market, producers and consumers have perfect information, there are no externalities, and no one firm can influence price or demand. If any of these assumptions fails to hold, the market may not naturally reach an efficient equilibrium.

There is reason to believe that the healthcare market suffers from a variety of market failures. Figure 6 shows that insurance companies spend eighty cents out of every healthcare dollar.

Figure 6 Source of 2002 Healthcare Spending [93]

Other Public[1]
12%

Other Private[2]
6%

Medicaid and SCHIP
15%

CMS Programs
33%

Private Insurance
34%

Medicare
17%

Out-of-pocket
15%

Total National Health Spending = $1.3 Trillion

[1] Other public includes programs such as workers' compensation, public health activity, Department of Defense, Department of Veterans Affairs, Indian Health Service, and State and local hospital subsidies and school health.
[2] Other private includes industrial in-plant, privately funded construction, and non-patient revenues, including philanthropy.

Note: Numbers shown may not sum due to rounding.

Source: CMS, Office of the Actuary, National Health Statistics Group.

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[1] The definition of utility will be described in Chapter 4.
[2] The theory of welfare-economics is detailed in Chapter 2.

Large insurers may have oligopolistic power with which to price healthcare services. This may distort the price of healthcare services leading to inefficient production. Also, perfectly competitive markets assume atomistic consumers that make decisions based on perfect information. In the healthcare market, insurers largely make the decisions. Since healthcare decisions are made at the collective level, it is important that formal steps be used to evaluate different healthcare alternatives. Other market failures that plague the healthcare market include the positive externalities of healthcare goods, information-asymmetries caused by moral-hazard and adverse selection, and supplier-induced demand.

The existence of these market failures suggests that the healthcare market will not achieve an efficient equilibrium. Economic evaluation is a formal method for examining how to re-allocate resources in order to achieve a more efficient equilibrium. In my thesis, I use economic evaluation to determine how to most efficiently diagnose Obstructive Sleep Apnea Syndrome.

Chapter 2

Introduction to Welfare Economics

Welfare economics sets out to describe a definition of "the good" by which alternative resource allocations can be judged. The definition of social good comes from two assumptions. First, it is assumed that "individuals should be considered the best sources of information regarding their own utility," a principle known as "consumer sovereignty" [64]. The second assumption is that "social welfare should be made up from the welfare (or utilities) of each individual member of society" [64]. It is additionally "assumed that that resource allocation is preceded by the forces of a competitive market which is in equilibrium and that the pre-program income distribution is appropriate" [64].

Pareto used these assumptions to derive two principles with which to judge alternative resource allocations. A Pareto-improvement occurs if a re-allocation of resources increases the utility of *all* members of society [65]. As Figure 7 demonstrates, the Pareto-criteria makes unequivocal judgments regarding programs that make everyone better off and everyone worse off, but they have little to say about programs that make some better off and some worse off [65]. This is problematic since many real-world policy interventions have a mix of winners and losers [65].

Figure 7 Pareto Criteria
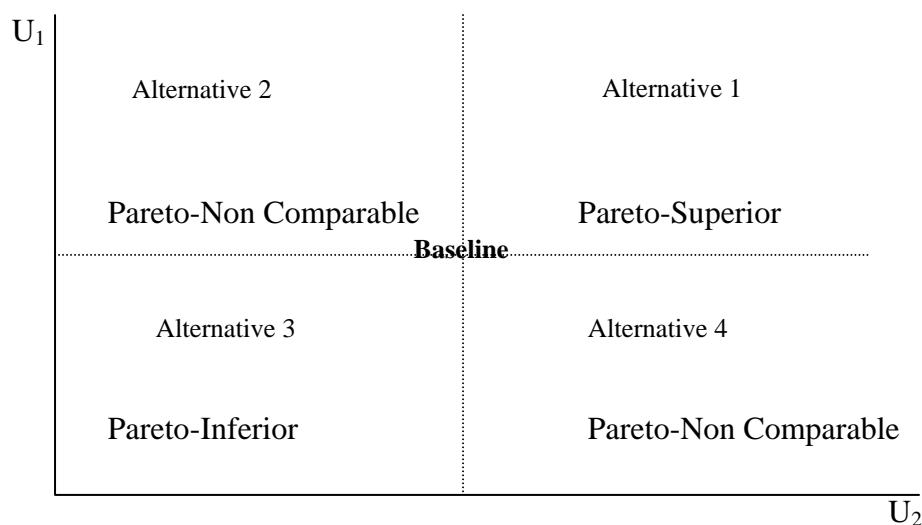
U_1 and U_2 denote the utilities of individual one and two respectively. Figure 7 specifies the normative Pareto value judgment of alternative resource allocations from the baseline, specified at the origin, and four alternatives [65].

Pareto-optimality is defined as a resources re-allocation that makes at least one individual better off and no individual worse off. In their famous paper, *Existence of Equilibrium for a Competitive Economy,* Arrow and Debreu find that given weak assumptions regarding consumer preferences and production functions, a Pareto-efficient equilibrium will be reached in a perfectly competitive economy [65]. This result leads to two theorems of welfare economics. The first theorem of welfare economics states that if a perfectly competitive equilibrium is attained, this equilibrium is also a Pareto-equilibrium [65]. The corollary of this theorem states that if a Pareto-optimum exists, this is also a competitive equilibrium [65].

Two damaging criticism are often leveled at Paretian welfare-economics [65]. First, critics note that the Pareto-criteria are compatible with a large set of potential allocations; some of these equilibriums could be judged to be highly inequitable [65]. Second, as demonstrated in Figure 7, the Pareto optimality critiera cannot rank states where some gain and some lose; evaluating these states would require some level of interpersonal comparison [65].

In 1939, Hicks proposed a solution to rank Pareto non-comparable states [65]. Assume that $u_i(y_a, z_a)$ represents individual i's utility under the circumstance 'a' with y_a defined as the consumer's income and z_a defined as a vector of health characteristics associated with the state 'a' [65]. Consider another state of the world, a_1, where the individual's health improves to z_h [65]. The compensating variation, CV, is defined as the amount of permanent income that must be taken from the consumer to make him/her indifferent between her current health state/income and the improved health state and reduced income [65].

$$u_i(y_{a_1} - CV, z_h) = u_i(y_a, z_a)$$

Hicks believed that Pareto non-comparable allocations could be judged by summing the compensating variation across all individuals [64,65] He reasoned that if the net compensating

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variation was positive, the winner must gain more from the re-allocation than the losers loses [64,65]. The winners could compensate the losers making all parties better off.

There are two problems with the Hicks-Kaldor criterion. First, the criterion implicitly assumes that all individuals place the same value on the marginal dollar regardless of their income [64,65]. Second, it can be shown that the Hicks-Kaldor criterion allows for preference-reversals; in other words, a re-allocation of resources can increase social welfare and a move back to the original allocation can also increases welfare [65].

While the potential-Pareto improvement criterion does not technically conform to the principles of welfare-economics, it forms the basis of cost-benefit analysis [65]. While cost-benefit analysis is the form of economic evaluation that is most closely aligned with the principles of welfare-economics, it has been criticized on several fronts. First, one must agree that individual's utility, as judged by the individual, is what should be maximized, and that consumers reveal their true preferences through their willingness-to-pay, even if compensation need not be actually paid [65]. Finally, one must be sensitive to the fact that programs condoned by the potential-Pareto criteria may lead to inequitable outcomes.

Economists have tried to work around the theoretical limitations of cost-benefit analysis in two ways. First, some economists have sought to formalize interpersonal comparison within the welfare criterion [86,63,65,85]. Other economists have attempt to use explicit welfare functions to aggregate individual preferences in order to address issues of resource distribution across individuals[65,86,85].

In traditional welfare-economics, individual utilities are the only arguments placed in society's welfare function [65]. Recently, some economists have argued that society's welfare function should be defined over a wider range of arguments [65]. These "extra-welfarists" believe that maximizing individual utility does not guarantee society's flourishing. For example, a society

that satiates individual utility by subsidizing heroin use may seed its own destruction. Many people would argue that health is an important prerequisite to societal flourishing. Thus, extra-welfarists seek to maximize society's health regardless of its link to utility.

Economists have developed a variant of cost-benefit analysis for evaluating healthcare interventions called cost-utility analysis (CUA). Instead of measuring benefits in monetary terms, CUA measures benefits with a cardinal preference scale. The most common preference scale is the Quality Adjusted Life Years (QALY) scale which measures patients' health-state preference in relation to their preference for a full year of healthy life. Under certain assumptions, QALYs are von-Neumann Morgenstern utilities. The advantages of CUA may include greater accuracy in measuring effectiveness and more equitable policy recommendations. Also, since the vast majority of healthcare evaluations use cost-utility analysis, performing a cost-utility analysis facilitates comparisons with other studies.

Chapter 3

Comparison of Cost-Effectiveness Analysis, Cost-Utility Analysis, Cost-Benefit Analysis in Healthcare Evaluation

Economic evaluation is increasingly used in forming healthcare policy. The United Kingdom relies upon economic evaluation for allocating the budget of its National Health Service [96,82,81,68,74]. The Canadian government currently requires that cost-utility studies accompany all pharmaceutical clinical trials, and the United States Federal Drug Administration requires that all drugs demonstrate cost-efficiency [67].

Three closely related methods are employed in evaluating healthcare interventions: cost-effectiveness analysis (CEA), cost-utility analysis (CUA), and cost-benefit analysis (CBA). Cost-utility analysis is overwhelmingly the method of choice in health-economic evaluation [95]. CUA is also the form of economic evaluation recommended by the Panel on Cost-Effectiveness in Health and Medicine, a panel of thirteen non-government scientists convened by the U.S. Public Health Service to standardize methods of economic evaluation in health [63,95]. Figure 8 demonstrates the rapid increase of cost-utility studies.

**Figure 8 Growth in Published Cost-Utility Analyses, 1976-2001 [95]**
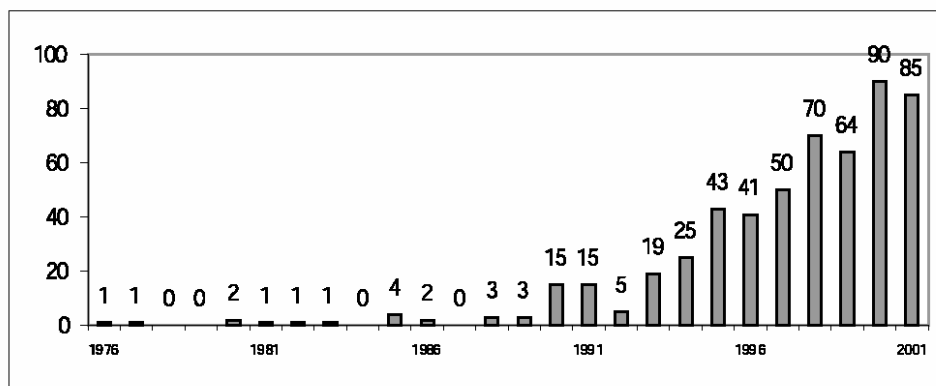
Source: CUA Registry, Harvard School of Public Health, 2003

Figure 9 demonstrates that studies have increasingly been conducted in accordance with the recommendations set by US Public Health Service's Panel [95]. This standardization of the cost-utility analysis methodology has greatly increased the comparability of studies [95].

Figure 9 Cost-Utility Analyses (1976-2001) Following Selected Recommendations of the US Public Health Service's Panel on Cost Effectiveness in Health and Medicine [95]
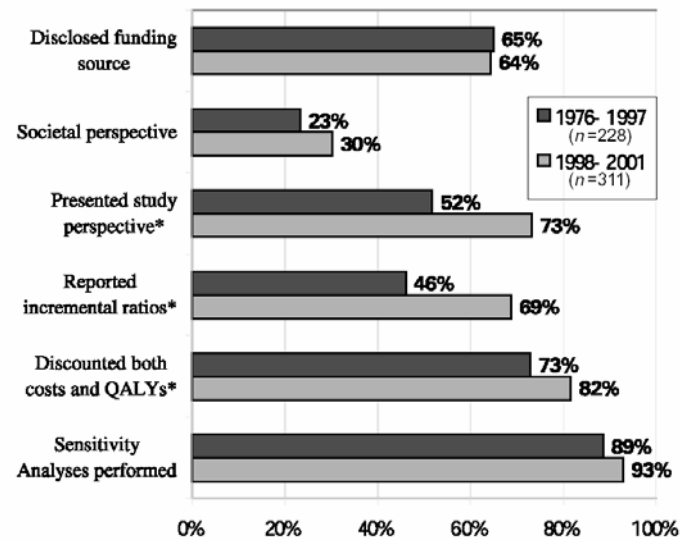
Source: CUA Registry, Harvard School of Public Health, 2003.

Policymakers are generally interested in answering three healthcare questions. First, policymakers try to determine the optimal procedure to treat a *specific* medical condition. Economic evaluation is also used to asses the relative value of treating *different* medical conditions. For example, policymakers may want to determine whether they should treat AIDS or breast cancer. In this context, CUA can be used to optimally allocate an exogenously determined healthcare budget [85]. In its broadest context, economic evaluation can be used to evaluate the desirability of spending money on healthcare versus spending money on all other goods [86]. In this context, economic evaluation can be useful for determining the optimal size of society's healthcare budget [63-65,86]. The appropriate methodology for a study largely depends on the questions it seeks to answer.

Economic methodologies should also be judged on their link to welfare economics, accuracy in measurements, and equity of their recommendations. Economic evaluation is ultimately used to prescribe an action. Economic methodologies that are closely linked to the prescriptive axioms of

welfare economic should yield policy recommendations that closely follow the concept of Pareto-efficiency. Methodologies should also be evaluated based upon the accuracy of their measurements. Finally, methodologies should be evaluated based upon the equity of their recommendations. In this section, I evaluate each methodology's performance based on these criteria.

Cost-Effectiveness Analysis (CEA)

Cost-effectiveness analysis (CEA) measures outcomes in terms of physical variables. For example, CEA studies may determine the amount of money spent per milligram of cholesterol reduced. The strength of CEA is its precision; measurements error can be controlled by increasing sample size in randomized clinical trials [63]. The drawback to CEA is its lack of applicability. CEA can only help determine the best procedure to treat a *specific* disease, and CEA does not conform to the axioms of welfare economics [63-65].

Cost-Utility-Analysis (CUA)

In cost-utility analysis (CUA) outcomes are measured as cardinal preferences for health states. The most popular preference measure is the Quality Adjusted Life Year (QALY). QALYs[3] are vNM utilities that are anchored on a scale that assigns death the utility of zero and perfect life the utility one.

CUA can compare alternative interventions by following the cost-utility algorithm. First, an expected cost-utility ratio (C/U) is calculated for each intervention by dividing the intervention's expected cost by its expected QALYs. As Figure 10 demonstrates, alternatives can fall within four quadrants relative to the baseline intervention.

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[3] Given certain assumptions which are detailed in Chapter Four.

Figure 10 Cost-Utility Plane

	Cost		
	Alternative 2		Alternative 1
	Dominated by Baseline	Baseline	Calculate Incremental C/U Ratio
	Alternative 3		Alternative 4
	Calculate Incremental C/U Ratio		Dominates Baseline
			Utility
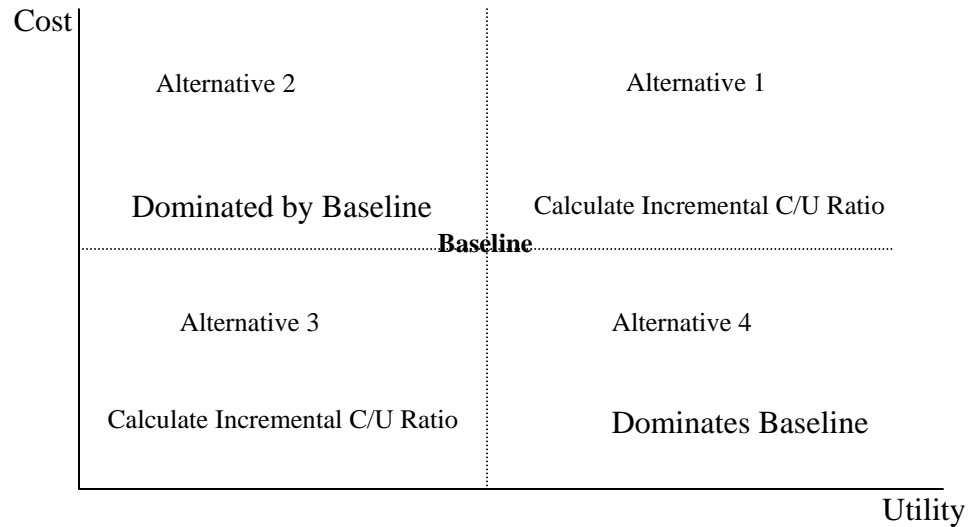
Outcomes in quadrant I are both more effective and more costly than the baseline intervention. In order to determine whether these "premium" interventions should be financed, an incremental C/U ratio should be computed by determining the intervention's incremental cost versus its incremental effectiveness [63]. This incremental C/U ratio should be compared against the incremental C/U ratio of alternative interventions that compete for the same budgetary resources and against society's maximum WTP for a year of healthy life. This maximum WTP value is highly controversial and is generally argued to be between $10,000/QALY -$200,000/QALY [63]. Alternatives that fall within quadrant II are more costly and less effective than the baseline alternative; thus, the baseline intervention should be strictly preferred over these alternatives [63]. Outcomes in quadrant III are both less costly and less effective than the baseline. An incremental C/U ratio should be calculated. If this value is greater than the socially determined maximum WTP, then the cheaper alternative in quadrant III should be used [63]. The alternative in quadrant IV is both more effective and less costly than the baseline; thus, this alternative should be strictly preferred to the baseline intervention [63].

Some economists argue that given the assumption that utilities: 1) are additively separable 2) individuals are willing to trade a constant proportion of their remaining life years to secure a better health state 3) individuals are risk-neutral, QALYs represent a well-behaved preference structure and thus reflect individuals' preferences for different health states[65]. These proponents believe that CUA is fully complaint with welfare economics and that CUA forms a complete prescription for social choice [85]. Other economists believe that CUA should only be considered an aid to decision making; thus, ranking interventions based on CUA is justified based on principles of optimization, an exogenously specified objective function (to maximize QALYs) and an exogenously specified resource constraint (society's healthcare budget) [85].

Since CUA measures all healthcare outcomes in the same units (QALYs), CUA can be used to compare interventions across diseases. This allows policymakers to use a simple algorithm to maximize health benefit from a fixed budget. First, the entire set of healthcare interventions should be ranked from the lowest to highest C/U ratio. Then, policy maker should add interventions until the healthcare budget has been exhausted. This algorithm will guarantee that: " (1) the resulting set of interventions will maximize the aggregate health effect achievable by the resources used, and (2) the resulting aggregate health effect will have been achieved at the lowest cost." [63].

Given some restrictive assumptions, CUA can determine the size of society's optimal healthcare budget. CUA measures the cost of producing one year of healthy life. If policymakers assume that all individuals place the same value on a year of healthy life, then they can monetize the value received from one QALY [63]. This converts CUA into cost-benefit analysis. If the monetary value gained from a year of perfect health exceeds the cost, then by the logic of the Potential-Pareto criterion, it is worth providing this service. Thus, CUA is closely linked to CBA, and it can be used to inform resource allocation.

CUA has traditionally been viewed as a more equitable form of economic evaluation than CBA [85]. CUA directly measures outcomes as utilities rather than as the amount individuals' would be willing to pay to for this utility. All forms of economic evaluation require some level of interpersonal comparison. CBA achieves this by summing over each individual's WTP. Since each individual is assumed to place the same marginal value on the dollar, WTP represents the net value of the intervention. The problem with CBA is that income inequality may prevent different individuals form placing the same value on each marginal dollar.

QALYs may provide a better means of interpersonal comparison. I would argue that there is likely to be more uniformity regarding how individuals value a year of perfect life in comparisons to how much they value the marginal dollar. This hypothesis is supported by the empirical evidence. Utility measures are found to correlate poorly with WTP, but they correlate well with WTP as a percentage of total income [91]. This suggests that budgetary constraints influence WTP measures. Consider a wealthy individual (with a net wealth of $1,000,000) and a poor individual (with net wealth of $1,000) that both value an improvement of health at .9 cardinal utility units[4]. Assume that the procedure costs $5,000. If each person is willing to pay 90% of their net wealth to purchase the improved health-state, CBA would suggest that it would make sense to treat the wealthy individual but not the poor individual since the poor person "values" the health improvement at only at $900.00.

Cost Benefit Analysis (CBA)

The difference between CBA and CUA is that outcome measures are monetized in cost-benefit analysis (CBA). CBA is the broadest form of economic evaluation, and CBA is also the form of analysis that is most consistent with welfare-economics. CBA is often criticized on equity grounds.

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[4] Assume the scales are the same so that the utility is directly comparable.

Overall, the method of economic evaluation used in a study depends on the questions the study seeks to answer and the characteristic demanded of the methodology. Figure 11 outlines each methodology's ability to answer the fundamental questions of economic evaluation.

Figure 11 What Fundamental Economic Questions Can Each Method of Economic Evaluation Answer?

Method	Which is the most cost-efficient intervention to treat a particular disease?	Is it more cost efficient to treat disease X or disease Y?	Is it justified to expand the healthcare budget to provide this intervention?
Cost Effectiveness Analysis	Yes	NO	NO
Cost-Utility Analysis	Yes	Yes	Possibly
Cost-Benefit Analysis	Yes	Yes	Yes

Figure 12 ranks each method on the domains of theoretical validity, precision and equity, with 1 being the best and 3 being the worst rank.

Figure 12 Economic Evaluation Methodology Rankings

Method	Theoretical Validity	Precision	Equity
Cost Effectiveness Analysis	3	1	NA
Cost-Utility Analysis	2	2	1
Cost-Benefit Analysis	1	3	2

There are several reasons that I chose to use the CUA methodology in my thesis. First, I believe utility is the most accurate measurement of effectiveness in health. Utility surveys are based on three decades of medical research developed to measure health functioning. Substantial progress has been made in this field, and these surveys have exhibited excellent levels of internal reliability, theoretical and empirical-validity, content-validity, face-validity, construct-validity, and responsiveness in the millions of patients to which they have been adminsterd.

Second, there is reason to believe that CUA is the most equitable form of economic evaluation in health. QALYs provide a fairer way to compare utilities across individuals. Since

QALYS are bounded on a cardinal scale from zero to one, everyone comes to the bargaining table with the same amount of utility resources.

The obvious goal of economic evaluation is to make timely and relevant policy recommendations. In order to make recommendations that can be practically interpreted, it is important to follow the conventions of similar studies. The final reason CUA was selected as the method of economic evaluation is that it follows the guidelines set forth by the US Department of Public Health's Panel on Cost-Effectiveness in Medicine [63]. By strictly conforming to the Panel's recommendations, this study enhances comparability with the thousands of other CUA studies carried out and recorded in the "National Registry of Cost-Effectiveness-Analysis" [95]. Economic evaluation is becoming increasingly important in allocating scarce healthcare resources. This study joins a series of other economic evaluations that have evaluated the cost-effectiveness of OSAS diagnosis and CPAP treatment. My choice to perform this study within the Panel's guidelines allows direct comparison with the results of these studies.

Chapter 4

Outcome Measurement in Economic Evaluation

The previously discussed methods of economic evaluation differ in the way they measure effectiveness. I begin this chapter by analyzing the difficulties encountered in measuring effectiveness with monetary values. I then describe how utilities are measured in CUA, and I compare the experimental evidence regarding WTP and vNM measures of health effectiveness.

Three different methods have been developed to measure the dollar value of health benefits in CBA 1) the human-capital approach 2) revealed-preference approach 3) contingent-valuation approach [63]. In the human-capital method, healthcare interventions are viewed as investments in a person's potential earning power; the value of the investment is simply the present value of future earnings [63]. Unfortunately, this technique is not consistent with welfare-economics. Economists have attempted to use revealed-preference studies to determine the monetary value of life. These studies examine the difference in wages for jobs that have different levels of risk [63]. Unfortunately, these estimates have been of little practical use since they are "wide-ranging and job-specific [63]."

Contingent-valuation studies are the most common form of monetary effectiveness measurement. There are a variety of theoretical difficulties in conducting WTP studies that attenuate the accuracy of their results. First, WTP studies differ widely in what they ask patients to value. Some studies only measure the WTP for the intangible benefits of health improvements; others include the future health care costs avoided and the increased productivity resulting from health improvements [65]. For example, consider the hypothetical decision regarding whether to buy a more effective cold medicine [63]. In this scenario, the consumers' WTP should be influenced by the health state improvement, increased productivity, and the decreased cost of having to purchase the less effective medicine [63]. However, many studies only value one of these dimensions.

Willingness-to-pay studies differ considerably in the variables they seek to measure. Some studies examine the WTP for improvements in health under conditions of certainty; other studies examine the WTP for uncertain health improvements, and some studies value the WTP for an

insurance policy [63]. These methods differ widely in their theoretical validity and their empirical results. Consider the results of a study conducted by Neumann and Johannesson that examined the *ex-post* and *ex-ante* WTP for in-vitro fertilization [63]. In the *ex-post* case, respondents were told that they were infertile and wanted children; the WTP for in-vitro fertilization that was assumed to have a 10% chance of success was $ 17,730.00 suggesting the WTP for a statistical child was $177,300 [63]. However, in the *ex-ante* case where respondents were told to assume that there was a 10% chance of being infertile and that in-vitro fertilization had a 10% chance of success, respondents were willing to pay $865 for insurance coverage suggesting the implied WTP for a statistical child was $1.8 million dollars [63].

The survey methods used in WTP studies may bias results. Close-ended WTP questionnaires use bidding games to determine a patient's WTP. Research suggests that these measures are often biased since WTP becomes anchored to the experimenter's initial bid [63]. Open-ended WTP questionnaires avoid this bias. However, they are often imprecise and have impractical standard errors due to patient's inability to think about the maximum they are willing to pay [63].

Ideally, economists would like to test the external validity of WTP studies. The 'gold standard' test of validity would be to compare the predicted WTP values against consumer's actual expenditure [63]. However, this is seldom possible since a market does not exist for programs evaluated with CBA.

Measuring Utility in Cost-Utility Analysis

This section introduces the theoretical properties of Quality Adjusted Life Years (QALYs). A cardinal measure of preference is needed to calculate QALYs; these preferences should be measured on an interval scale that has no natural zero and that is unique under a positive linear transformation [63]. The terms 'utility', 'value' and 'preference' are often used interchangeably; however, each term has a unique meaning [63]. Preference is the umbrella term [63]. Values

represent cardinal preferences measured under conditions of certainty; utilities signify vNM utilities [64].

QALYs are the commensurate measure of patient's preference for given health states. QALY theory assumes that patient preferences are a function of quantity and quality of life. The health profile of a patient can be described by a graph as shown in Figure 13.

Figure 13 Graphical Representation of Quality Adjusted Life Years
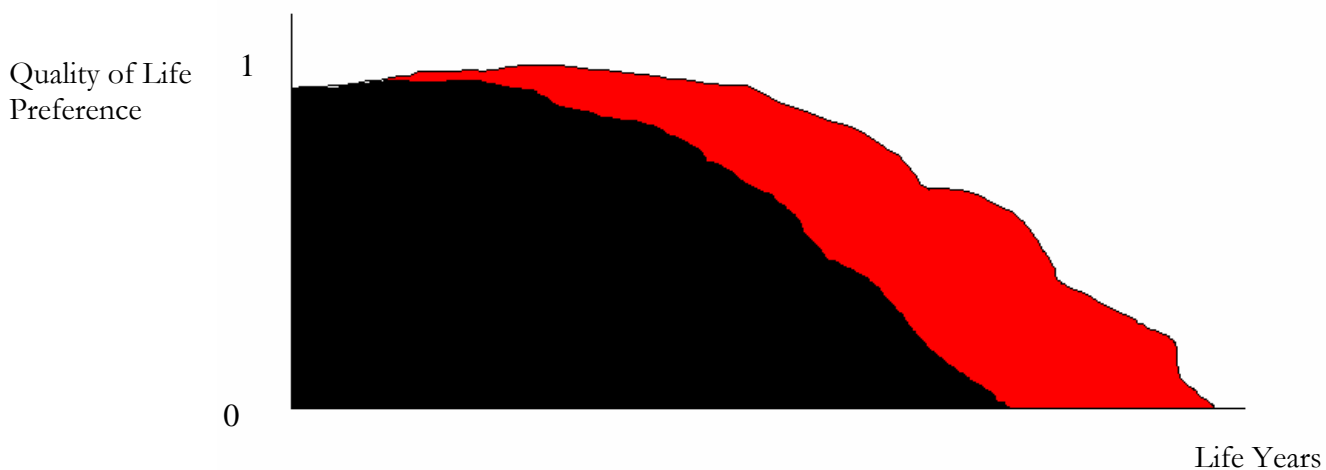
The QALY is simply the integral under this curve. The red area represents the incremental QALYs from a transition in health profiles. The quality of life at a given point in time is measured as a vNM. It is convenient to anchor the interval scale used to measure this utility at zero for death and one for perfect life; this allows the interpretation of QALYs as the number of life years lived in perfect health [63]. It is recommended that QALYs are discounted since individuals are found to prefer health gains earlier in their lives [63].

Under certain assumptions, QALYs can be interpreted as a vNM utilities [63-65,86]. First, the attributes of quality and quantity of life must be mutually utility independent (preferences for gambles on the one attribute are independent of the amount of the other attribute); the trade-off of

quantity for quantity must exhibit the constant proportion trade-off property (the proportion of remaining life that one would trade off for a specified quality improvement is independent of the amount of life remaining) and the single attribute utility function for additional life years must be linear with respect to time implying risk neutrality [64].

These conditions are formalized in Broome's analysis of QALYs [68]. People maximize discounted QALYs if and only if their preferences can be represented by the following value function which is additively separable [68]:

$$V(q_1, q_2, \ldots q_y) = v(q_1) + r_2 v(q_2) + \ldots + r_y v(q_y).$$

where $r_1 \ldots \ldots r_y$ represent discount weights and $q_1 \ldots q_y$ represented one year of life at health state q_x until time y and v(x) represents the subvalue function, on a cardinal scale of 0-1, of health state q_x [68].

For additive seperability to hold, preferences must be strongly separable [68]. In other words, the preference for a health state at a point of time must be independent of the preference for health states at all other points in time. It can be shown that this definition of QALY maximization determines V and v uniquely up to increasing linear transformations [68]. The zero on the scale is not arbitrary. It is defined as the health state, q^0, in which a person would just assume not live. Formally, this can be expressed as [68]:

$$(q_1, q_2, \ldots q_y, q^0) \approx ((q_1), (q_2), \ldots (q_y). \text{ for all values y and } q_1, q_2, \ldots q_y,$$

Also, it is customary to assign the best imaginable health state the value of one such that $v(h) = 1$ [68]. This definition of QALYs suggests several methods to determine patient's utility weights. If the policy maker knew the patient's discount weights, he could econometrically fit their utility function [68]. However, this would require more information than is generally available. On the other hand, consider the case when a person does not discount preferences such that all

discount weights are 1 [68]. Now, assume the person is indifferent between living for t years in the best imaginable state of health and k[5] years of life at state q [68]. Then the discounted QALY equation guarantees that kv(q)=tv(h) [68].

This suggests a method for measuring utilities. The analyst can determine the number of healthy years the patient would be willing to trade for k years of life in their impaired health state [68]. Their response divided by k gives a cardinal measure of their preference for their current health state. This preference is a value rather than a utility since it does not embody the patients' risk preference [63-65,68]. The technique is known as the time-trade off method (TTO).

Now, let's transfer from a value function to a utility function defined as: $u(V(q_1,q_2,.....q_y))$. For a person to maximize discounted QALYs, their preferences amongst gambles can be represented by the expected utility function [68]:

$$E(u(V(q_1,q_2,.....q_y))) = E(u(v(q_1) + r_2 v(q_2) + ... + r_y v(q_y))).$$

where E is the expectation operator and u is an increasing transformation of discounted QALYs [68]. A person is risk neutral if and only if u is linear [68]. In this case, the patient always prefers gambles that offer the greater expectation of discounted QALYs. Consider the case when the person is indifferent between living k years at quality q and having a chance, p, of k years in perfect health and (1-p) chance of dying immediately. Allow R to be $(1+r_1+ r_2+...+ r_k)$ [68]. Then:

$$u(Rv(q)) = pu(Rv(h)) + (1 - p)u(0) = pu(R) + (1 - p)u(0)$$

If the person is risk neutral so that u is linear, then p=v(q) [68]. This gives another method to solicit utility values called the standard-gamble (SG) [68]. Patients are asked to determine the probability that would make them indifferent between their current health state and the gamble between perfect health for k years and immediate death [68].

---

[5] Such that k>t

Properties of Health State Measurements

When choosing how to solicit health-state utilities, one should evaluate the practicality, internal-consistency, reliability, theoretical-validity, experimental-validity, content-validity, construct-validity, and responsiveness of the different health-related quality of life (HRQOL) instruments [92]. Practicality refers to the acceptability of the questionnaire to the patient, physician and ethics committee [92]. Internal-consistency refers to the extent to which respondent's valuation corresponds with the known logical ordering of health states [92]. Reliability refers to the questionnaires' ability to reproduce results over repeated measurements on an unchanged population with the minimum amount of random error [92]. Measurements should have high reliability over time (test-retest reliability) and have high agreement among raters (inter-rater reliability) [92]. Ideally, tests would show an agreement between scores taken in different locations.

Validity is defined as the extent to which an instrument measures what it is intended to measure. In economic evaluation, the gold standard test of validity is the questionnaire's ability to predict preferences revealed from actual decisions [92]. However, revealed preference methods are not used due to market failures in healthcare. "Revealed preference methods require the consumer to be sovereign, but in healthcare, the consumer is often ignorant of the outcomes of care. Furthermore, the doctor can act as the patient's agent in the consumption of healthcare, but the level of ignorance is such that the patient cannot be sure his/her doctor is benign as a perfect agent. Thus, it cannot be assumed that the health services provided would have been the consumer's preferences [92]." In order to examine validity, economists focus on evaluating the methods theoretical, experimental, content, construct, and convergent validity [92].

Theoretical validity refers to a questionnaires theoretical link to vNM utility theory [92]. To examine experimental validity, economists evaluate the health state utility ranking versus rankings devised from voting algorithms [92, 82-84,89]. Content validity refers to the extent to which the

questionnaire includes the arguments of the utility function that are most relevant to health [92]. Construct validity measure how a test correlates with other hypothesized indicators of health [92]. Convergent validity seeks to determine how tests correlate with other measures of the same concept [92]. Responsiveness refers to the tests ability to measure clinically significant changes in health. In economic evaluation, it is hard to tell whether tests are not responsive or whether patients do not value these health changes [92]. Reliability is statistically assessed using the 'effect size' where the mean change in score is divided by either the standard deviation at the baseline or by the standard deviation of the health change [92].

Techniques of Health State Measurements

In clinical medicine, it is extremely important to measure changes in health functioning. A significant amount of research has been conducted over the last forty years to determine how to best measure these changes. Thousands of different surveys have been developed to measure changes in health. When examining these surveys, it is informative to make two distinctions. One distinction is whether the health questionnaire is generic or disease-specific. Generic questionnaires, such as the SF-36, can be used to measure health status for all diseases; disease-specific questionnaires only measure health changes for one disease. Also, it is informative to distinguish between preference-based and non-preference based questionnaires. Preference based questionnaires measure patient's preferences for different health states. Non-preference based questionnaires measure and index of health functioning regardless of how patients value this level of functioning. Figure 14 demonstrates common questionnaires within each domain of questionnaire. These questionnaires can be examined in Appendix V-VI.

Figure 14 Types of Health Questionnaires

	Non Preference Weighted	Preference Weighted
Generic	SF-36	Health Utilities Index EuroQol Sf-6D
Disease Specific	FOSQ SAQLI	Standard Gamble VAS Time Trade Off

In order to determine QALYs, one must use a preference weighted instrument. There are three specific techniques that are used to determine a patient's utility for a specific disease. The visual analogue scale consists of a thermometer diagram. Patients are told to mark their state of health relative to the endpoints of the perfect health and death. These preferences are revealed under conditions of certainty so that a power transform is used to simulate the risk preference of the general population.

Figure 15 Reliability of Standard Gamble (SG) Time-Trade-off (TTO) and Value [92]

Test-Retest Reliability	SG	TTO	VAS
1 week or less	.80	.87	.77
4 weeks	.82	.81	.62/.89
3-6 weeks		.5-.75	
6 weeks		.63-.80	
10 weeks		.73	.78
6-16 weeks	.63	.83	
1 year	.53	.62	

In the time-trade off procedure (TTO), patients are interviewed and asked to determine how much impaired life they would trade for a specified amount of perfect health. Various props are used to help patients visualize the trade-off [92]. The TTO technique shows good experimental validity. One study found that the TTO showed "a considerable degree of consistency between the ordinal ranking and the rank ordering of the TTO values [92]."

The standard gamble (SG) is a technique that asks patients to determine the probability that would make them indifferent between a gamble that could either yield perfect health or instant death versus their current health state with certainty. A probability wheel is used to help patients visualize the gamble [92]. The SG is considered to have the best theoretical-validity of any measure. Figure 15 shows the SG has decent test-retest reliability and another study finds a inter-rater reliability of 0.77 [92]. The SG appears to have acceptable experimental validity as several studies have found "empirical evidence relating to the consistency of SG responses with expected rankings [92]."

Several generic, preference-weighted, questionnaires have been developed to determine health-related-quality-of-life. The advantage of these questionnaires is that an interview process is not needed to complete them. The EuroQol 5-D and SF-6D questionnaires rely on econometrics to derive utility states. These questionnaires were developed in three steps. First, questions were designed to measure a patient's level of functioning in each health domain. Second, a sample of health states was selected and the general population was asked to evaluate these health states based on the standard-gamble technique. Third, the value of other health states was determined econometrically.

The Health Utilities Index is a generic, preference-weighted, HRQOL questionnaire that parameterizes society's health-state utility function. This was achieved in two steps. First, individual domains were ranked on a cardinal value scale. Second, the relationships between domains were determined. This allowed for development of a multiplicative, multi-attribute utility function [67,69-70].

A thorough review of the practicality, internal-consistency, reliability, theoretical-validity, experimental-validity, content-validity, construct-validity, and responsiveness of these generic, preference-weighted, HRQOL would require several hundred pages and is beyond the scope of this thesis. John Brazier's, A Review of the Use of Health Status Measures in Economic Evaluation,

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provides an excellent overview on the measurement properties of these instruments [92]. Overall, these questionnaires perform acceptably in most domains.

Relationship of TTO to WTP

A recent study by Richard Smith examined the relationship between WTP and TTO utility values [91]. Smith finds that the TTO "appeared to perform better in differentiating significantly between different levels of health within each dimension, but not so well in differentiating between different dimensions of health at the same nominal 'level' of health status; WTP, compared with TTO, appeared to perform far less well in differentiating significantly between different dimensions of health at the same nominal level of health status, but performs *slightly* better at differentiating between different levels of health within each dimension [91]." The main reason the WTP is more sensitive for identifying health states within a domain is can measure small changes in health. In other words, patients are not willing to trade life years for small health improvements, but they are willing to pay for these improvements.

The WTP data showed large differences between the mean and median values and large standard errors [91]. The data suggested that a few high WTP outliers generated a higher mean value for each question [91]. In addition, there was little dispersion in valuing relatively healthy states; however, there was tremendous dispersion in valuing highly impaired health states [91]. This suggests that at high levels of impairment, some respondents' budget constraints limit their valuations. When WTP was expressed as a proportion of total income, the mean WTP was closer to the median value and the standard errors declined [91]. In most cases, the mean and median TTO values were nearly identical suggesting a much less skewed distribution [91].

Regression analysis did not reveal a significant correlation between the TTO and WTP data; however, it showed a significant negative correlation between TTO and WTP as a percentage of income [91]. These results further underscore the equity problems in WTP measurements.

Chapter 5

Introduction to Obstructive Sleep Apnea Syndrome

Dr. William Dement vividly describes Obstructive Sleep Apnea Syndrome in *The Promise of Sleep*:

"Every night more than 50 million Americans stop breathing. In a stunning evolutionary failure, nature endowed us with throats that tend to collapse during sleep and stop air flow but did not endow our sleeping brains with the ability to start breathing again calmly. At this breathless moment, the immediate future holds only two possibilities: death or waking up to breath. In the worst cases, no air enters the lungs for 40,50,60 seconds, or longer. The muscles of the diaphragm struggle harder and harder against the blocked throat, without success. Carbon dioxide builds up in the bloodstream and the level of life giving oxygen falls precipitously. After a minute or more, the brain is panicking, suffocating, screaming out for oxygen. The skin and lips turn blue. Just when death seems imminent, the sleeper suddenly struggles awake and the tongue and throat muscles tighten, allowing oxygen to flood into the lungs in a series of gasping, snorting, breaths. Oxygen is restored to the blood, and the fatal course is reversed. Instead of being alarmed and staying awake, the victim is immediately asleep again. After a few seconds, snoring begins—the cycle starts again, repeating hundreds and hundreds of times a night… It never ceases to amaze me that sleep apnea victims can awaken hundreds of times in a single night and remember nothing of that torment. It's hard to measure how much sleep such patients lose, but it's at least a third of their time in bed. And when sleep is interrupted this many times, it has little value erasing sleep debt [66]"

Obstructive sleep apnea syndrome (OSAS) is "characterized by periodic, complete, or partial upper airway obstruction during sleep, causing intermittent cessations of breathing (apneas) or reductions in airflow (hypopneas) despite ongoing respiratory effort" [2,1]. Apneas are technically defined "as a cessation of airflow for 10 or more seconds"; hypopneas are "defined as a thirty percent reduction in airflow associated with a four percent decrease in oxygen saturation"[2,1].OSAS is commonly divided into three levels of severity: mild (5< AHI[6] <15 events per hour); moderate (AHI=15-30 events per hour); and severe (AHI>30 events per hour) [2,1,3,5,7].

OSAS prevalence differs by age, gender and level of severity [2,1]. Dr. Dement estimates that forty percent of the population has some sleep apnea; half of these cases are "clinically relevant"[66]. Other studies find that nine percent of women and twenty four percent of men have mild to severe OSAS [2,1,7]; women's susceptibility to OSAS approaches that of men after menopause. It is estimated that roughly two percent of women and four percent of men have OSAS that needs to be immediately managed [1,2]. OSAS begins to appear in men and women in their thirties, forties, and fifties, and the incidence of sleep apnea appears to increase with age. In the community-dwelling

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[6] AHI denotes the "Apnea Hypopnea Index" which is calculated as the sum of apneas and hypopneas.

elderly over sixty five years of age, the prevalence of OSAS has been reported to be as high as sixty-two percent [2].

<p style="text-align:center">*Pathophysiology of OSAS*</p>

OSAS results from competing engineering demands on the human throat. The throat must be capable of breathing, eating, and speaking [66]. In order to speak, humans need a flexible tongue, throat, and upper airway [66]. To breath, human need to have stiff upper airway [66]. The rigidity of the pharynx is maintained by a complex web of muscles that form rings around the throat [2,1]. The brain controls the contraction of these muscles through three pathways. Part of the control is packaged with the "breathing reflex" [2]. In addition, upper airway sensors provide proprioceptive feedback on the state of the airway [2]. Finally, chemical pathways increase activation of the pharyngeal muscles when oxygen saturation is low [2].

The pathways that control the throat's tension turn off during sleep, leaving the throat soft and limp [66]. During inspiration, the diaphragm expands causing a "vacuum" of negative pressure to develop within the respiratory tract [66]. This vacuum causes the throat muscles to pull inward, rebound, and pull inward again causing rapid snoring vibrations. In patients with OSAS, the snoring cycle results in the airway's collapse which causes blood oxygen levels fall precipitously [66]. In response, the diaphragm "makes a tremendous and futile increasing effort to pull air in, and then relaxes and lets a little air out in effect ratcheting out all the remaining air in the lungs" [66].

OSAS patients generally have an upper airway abnormality that makes their airways more susceptible to collapse during sleep [62]. For many OSAS patients, especially those who are overweight, this abnormality is composed of extra throat tissue. Other common abnormalities include having a large tongue, large tonsils, large lymph nodes or having a narrow palate [2].

The cycle that leads to the airway's collapse is shown in Figure 16-18.

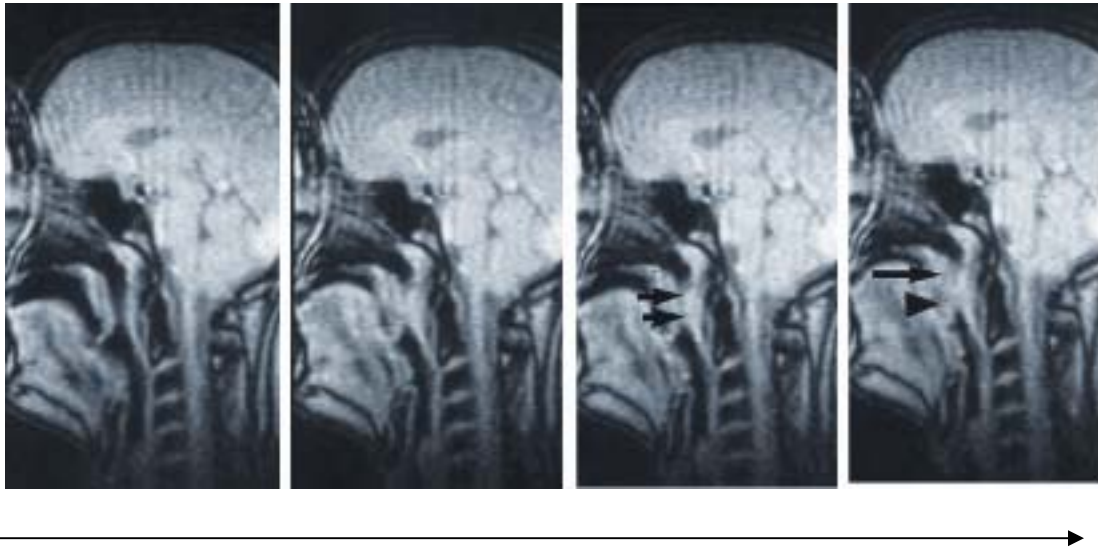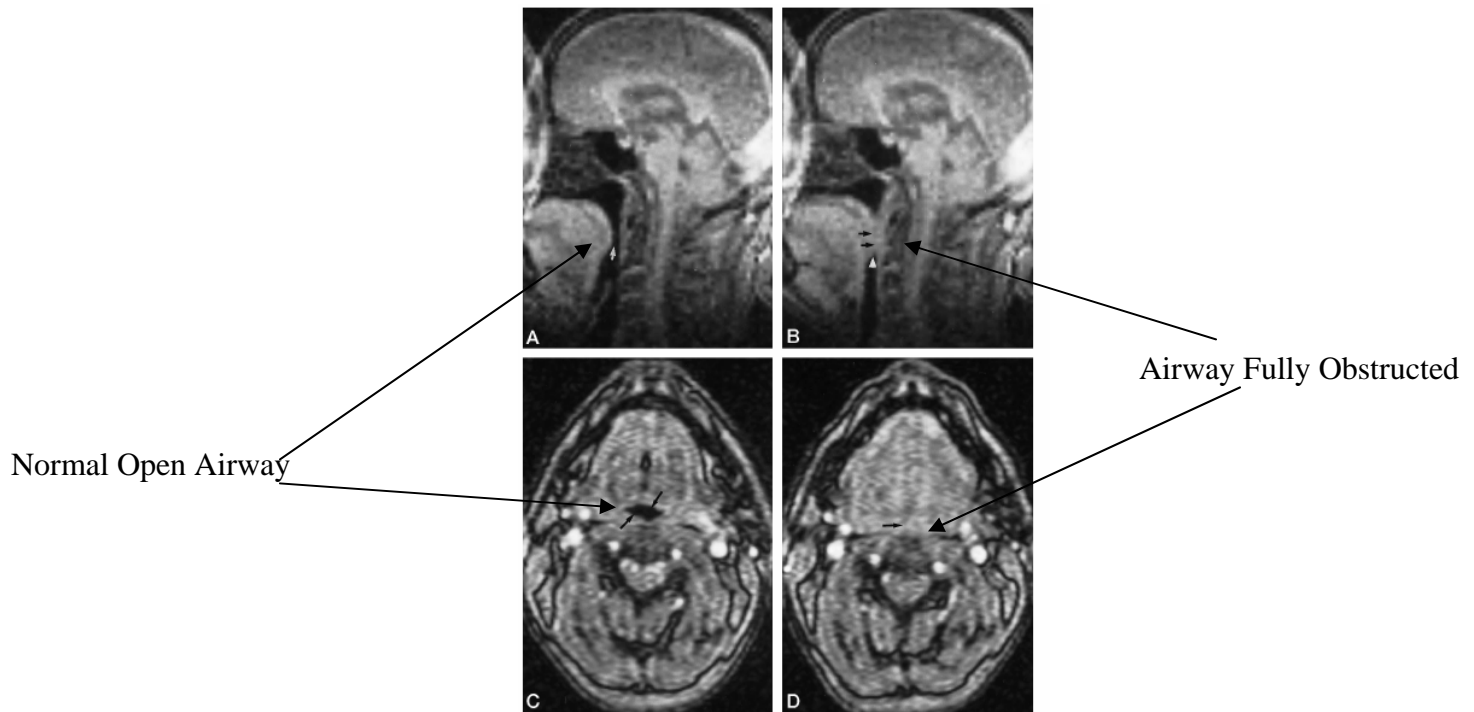**Figure 16 Collapse of the Airway During Inspiration [96]**

Figure 17 High Resolution MRI of Normal Airway (A) and Obstructed Upper Airway (B)

Normal Patent Airway

Fully Obstructed Airway

Figure 18 Sagital and Axial View of Airway Collapse of Patient with OSAS [96]

Normal Open Airway

Airway Fully Obstructed

Symptoms of OSA

The three most common symptoms of OSAS include snoring, daytime fatigue and daytime

drowsiness [66]. Sleep deprivation often results in personality changes such as increased irritability,

aggressiveness, and anxiety [66]. Other physiological symptoms include esophageal reflux, frequent

nocturnal urination, heavy nighttime sweating, morning headaches, raspy throat, loss of hearing, and

male impotence [2,66]. In addition to these symptoms, some anatomic findings are predicative of

OSAS including: large neck circumference, obesity, dental overbite, low hanging soft palate, narrow

mandible, narrow maxilla, and nasal septal deviation [2]. Other risk factors include: family history of

OSAS, race (African American, Pacific Islander, and Mexican American), down syndrome, marfan

disease, Pierre-robin disease, alcohol ingestion before bedtime, respiratory allergies, nasal congestion,

and underling hypertension [2]. A study by Hoffstein and Szali found that diagnosis based on

subjective impression of the patient's clinical features has a sensitivity of 60% and a specificity of 63% [2].

<p style="text-align:center">Clinical Consequences of OSA</p>

The most common consequences of OSAS include excessive daytime somnolence, depression, and neurocognitive defects from sleep deprivation [11,14,2, 14-22]. A recent study found that OSAS patients exhibited neurocognitive impairment equivalent to fifty percent of the effect of administering a sedative hypnotic or up to five years of additional age [2]. Sleep deprivation caused by OSAS seriously impairs patients' quality-of-life [3-6]. Preference weighted quality of life studies show that OSAS patients have a quality-of-life equivalent to the quality of life of stroke patients [14-22].

Several studies have found OSAS patients are more likely to be involved in motor vehicle accidents [2,5,6]. One study finds that OSAS patients have a thirty-three percent greater chance of being in an automobile accident and a two-hundred percent greater chance of being in repeated accidents than a matched control group [5]. Another study finds that OSAS patients had an accident rate of .07 crashes per year per driver as opposed to .01 crashes per driver per year for the general population; after CPAP treatment, OSAS patients' crash rate decreased to 0.0 [2].

The stress created by repeated airway collapse exacerbates other medical conditions. Approximately forty percent of patients with OSAS have hypertension [2,4-8]. Three recent clinical trials indicated that the presence of OSAS was associated with a one and a half to three fold increase in the risk of getting hypertension [2]. The National Commission on Sleep Disorders Research estimated that OSAS contributed to 38,000 heart attacks and strokes in the United States every year [66]. Another recent study found that thirty-seven percent of patients with OSAS reported cardiovascular disease as opposed to only seven percent of patients in the general population [2]. Over seven years of follow-up, fifty-seven percent of inadequately treated OSAS patients developed

new cardiovascular disease as compared to seven percent of adequately treated patients [2]. Since

OSAS compromises blood flow to the brain, patients with OSAS are eight times more likely to

suffer a stroke than the general population [2].

Untreated OSAS is an economic liability to the healthcare system. One study found that

patients with untreated OSAS were more likely to be admitted to the hospital and used $750.00

more in annual health care resources than a matched control group [8]. Given the high prevalence of

OSAS, the syndrome could cost the health system nine billion dollars a year.

Treatment of OSAS

OSAS can be treated in three ways. The cheapest, most effective, and most utilized

treatment option is nasal Continuous Positive Airway Pressure (CPAP). Figure 19 shows a CPAP

machine and a person wearing a CPAP mask.

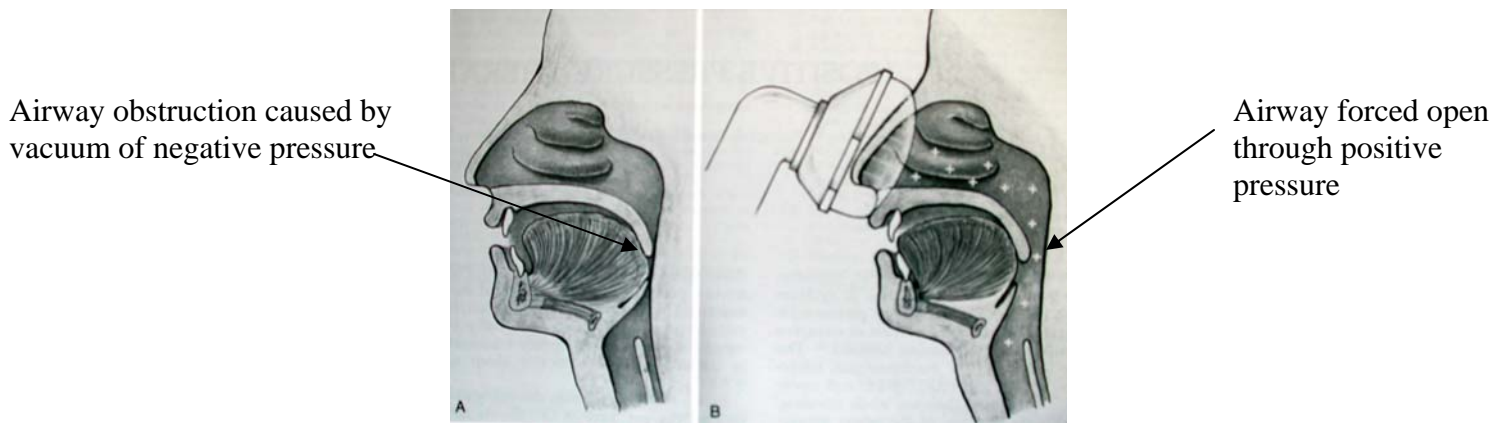**Figure 19 CPAP Machine (A) and Mask Hookup (B)**

A

B

Nasal CPAP therapy works by pumping air into the upper airway which creates positive air-

pressure that cancels the negative air-pressure caused by the expansion of the diaphragm. Figure 20

demonstrates how the CPAP machine prevents upper airway collapse by pumping positive air-pressure into the airway.

Figure 20 Demonstration of CPAP Functionality

Airway obstruction caused by vacuum of negative pressure

Airway forced open through positive pressure

Numerous placebo controlled CPAP studies have found that CPAP is effective in increasing patient's s neurological functioning and quality-of-life [2,1,12,13,45] . CPAP compliance rates vary between sixty-five and ninety percent [2,1,12,18,19]. The most commonly cited reasons for CPAP non-compliance include: nasal congestion, nasal dryness, and mask intolerance [2,1,13,45,19].

Other available treatments for OSAS include oral devices and surgical treatment [2]. Oral devices work by mechanically applying pressure on the tongue and jaw[2]. Only three clinical trials have been conducted on these oral devices[2]. These trials have shown that even in patients with "mild OSAS, CPAP therapy produced better results with greater improvements in AHI and sleepiness than observed with oral devices [2]." The final option for patients is surgery. Surgeons can increase the size of the upper airway by cutting away excess fatty tissue or by reshaping the jaw and mandible [2]. Surgery is substantially more expensive than CPAP and can lead to complications that include: "bleeding, infections, upper airway obstruction caused by surgical swelling[2]." Limited research in these surgical procedures suggests that they are less effective than CPAP [2].

There are three common techniques used to diagnose OSAS. Full-night polysomnography (FN-PSG) is as the "gold-standard" diagnostic pathway [22,23]. FN-PSG is conducted in a dedicated sleep lab and requires a sleep technician to monitor the patient throughout the night [Figure 21].

Figure 21 Sleep Technician Monitoring (A) Sleep Lab Setup (B)

In order to identify REM sleep, EEG leads are attached to the temples, EOG leads are attached to the eyes and EMG sensors are attached to the chin and lower leg [23].

Figure 22 Attachment of EEG, EOG, and EMG Sensors
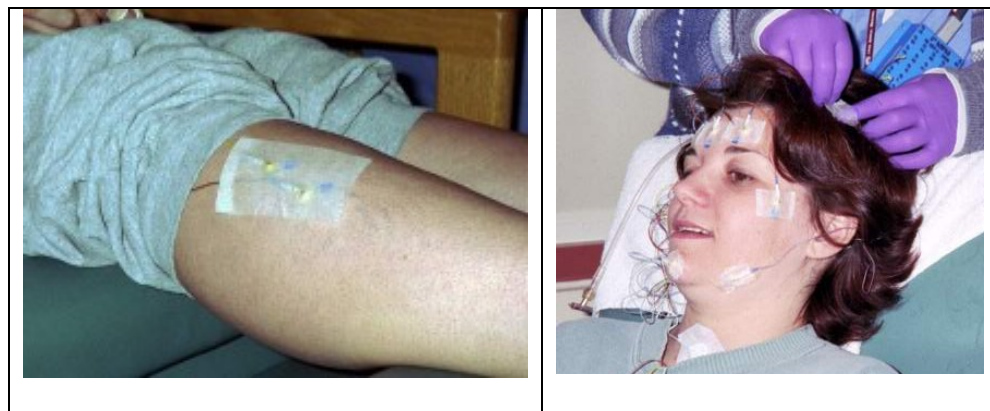
Belts are attached to the patient's abdomen and chest to test for breathing effort. An airflow lead is inserted into the nose to measure air volume passed through the upper airway [23]. An EKG lead is placed on the chest to measure heart activity [23]. A pulse-ox lead is attached to the finger in order to measure oxygen saturation [23]. Finally, a "position lead" is attached to determine if the patient is supine, prone, or on their side [23]. Figure 23 shows instrument setup while Figure 24 shows a sleep study in progress.

Figure 23 Attachment of Belts, EKG lead, and Airflow Lead

Figure 24 Sleep Study in Progress

If FN-PSG yields a positive result, the patient is required to return to the sleep lab for

Polysomnography titration (PSG-titration) [23]. Titration allows the sleep technician to determine

the optimal positive pressure setting for the CPAP machine. The PSG-titration setup is almost

identical to the FN-PSG setup [23]. The only change is that the patient is fitted with a CPAP mask

and another lead is added to measure the positive pressure passed through the mask [23].   During

the titration, the sleep technician increases the positive pressure until the number of arousals and

apneas are minimized and the 0_2 saturation levels are maximized. Figure 25 shows the PSG-titration

setup.

Figure 25 Picture of Titration Setup

FN-PSG followed by a full PSG-titration can cost up to $2,000 [Figure 29] Two cheaper

approaches have been devised to diagnose OSAS [24-28,29-40]. Split-night polysomnography (SN-

PSG) is a variation on the two night FN-PSG/ PSG-titration [24-28]. The difference between SN-PSG and FN-PSG is that if the patient is diagnosed OSAS positive within the first two hours, SN-PSG continues with PSG-titration on the same night [24-28]. If the patient is not diagnosed within the first two hours, FN-PSG is continued for the remainder of the night [24-28]. If this continued monitoring leads to a positive OSAS diagnosis, the patient is required to return to the lab for a full night of PSG-titration [24-28]. Thus, if sufficiently accurate, the SN-PSG pathway provides a way to diagnose OSAS with half the expense of the current FN- PSG pathway [24-28].

The third technique commonly used in OSAS diagnosis is the unattended home partial sleep monitoring study (UHPSM) [28-40]. In the UHPSM study, patients are given a machine that includes a breathing effort lead, a tidal volume lead, and a pulse-oximeter lead [28-40]. The patient returns the UHPSM machine to their physician who interprets the data stored on the machine [28-40]. While diagnosis via UHPSM is significantly cheaper than diagnosis via FN-PSG, there are some drawbacks to the UHPSM study [28-40]. First, patients may not set up the machine properly. Thus, there is the chance of nonexistent, incomplete, or lost data [28-40]. Second, the home study machines are susceptible to theft or damage [30]. Third, the UHPSM are less accurate. This occurs since the UHPSM machines do not record EEG, EOG, EMG, or EKG tracings; thus, there is less data available with which to make a diagnosis [28-40].

CPAP-auto-titration has been introduced as a more effective method to determine CPAP pressure settings [34-40]. Unlike PSG-titration which must be conducted in a sleep-lab, CPAP-auto-titration is conducted in a patient's home. This CPAP-auto-titration machine is similar to the UHPSM machine, but it includes a CPAP mask to measure CPAP airflow pressure [34-40]. While less expensive, CPAP auto-titration is less accurate in determining optimal fixed pressure readings.

# Chapter 6

Introduction and Methods

It is estimated that eighty-four percent of patients with severe OSAS are undiagnosed [66]. This thesis performs a cost-utility analysis (CUA) to determine the optimal strategy to diagnose OSAS. I view this thesis as the most realistic economic evaluation of OSAS diagnostic pathways conducted to date. One particular novelty of my thesis is its modeling of the SN-PSG pathway. The merit of SN-PSG has been the subject of much debate; the results of this thesis should informatively add to that debate.

This paper is aimed at three audiences. First, this report aspires to assist practitioners recommend the most appropriate method of OSAS diagnosis to their patients. Second, this report hopes to help insurers assess OSAS diagnostic methods. Third, this analysis should help policy-makers evaluate the merit of diagnosing OSAS versus other medical conditions.

Literature Review

A study by Ronald Chervin compared the cost-effectiveness of FN-PSG and UHPSM to the baseline alternative of treating all symptomatic patients with CPAP [45]. The study found that FN-PSG provided the most cost-effective means of diagnosing OSAS [45]. This study hopes to improve upon Chervin's study in several ways. First, this study hopes to more realistically model clinical pathways; some of Chervin's pathways bare no resemblance to clinical practice [45, Figure 26]. Secondly, my model includes the recently developed SN-PSG pathway which may help address a timely questions regarding SN-PSG's cost-effectiveness relative to FN-PSG and UHPSM [45].

Figure 26 Chervin's Model [36].
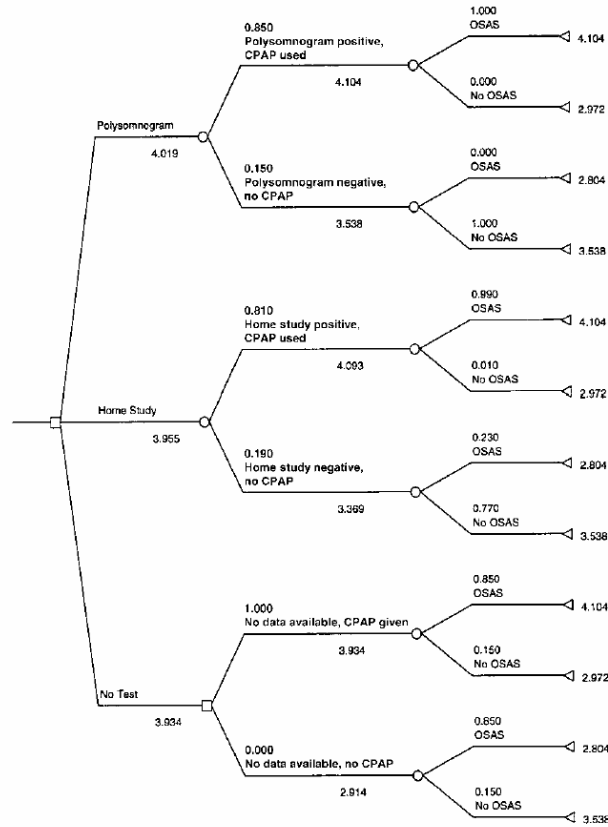
Methods

A decision tree was created to model the steps involved in each diagnostic pathway [97]. In order to operationalize the model, it was necessary to begin with a hypothetical cohort of patients. I chose a cohort that is highly at risk for OSAS; specifically, the cohort consisted of patients aged 30 to 60 years who experienced two or more of the following symptoms: persistent snoring, excessive daytime somnolence, or witnessed apneas during sleep.

The tree begins with a square decision node that leads to three possible pathways: 1) full-night Polysomnography (FN-PSG); 2) split-night Polysomnography (SN-PSG); and 3) home sleep study (UHPSM). Along each pathway, circular chance nodes represent the probability a patient will traverse that respective branch. The triangular terminal nodes represent the final outcome of the each pathway. This model allows for four possible outcomes: 1) the patient could be diagnosed

50

OSAS negative; 2) the patient could be diagnosed OSAS positive and accept CPAP treatment 3) the patient could be diagnosed OSAS positive but refuse CPAP treatment; 4) the patient drops out of the study without a diagnosis (and is either OSAS positive or OSAS negative).

Figure 27 Baseline Decision Tree
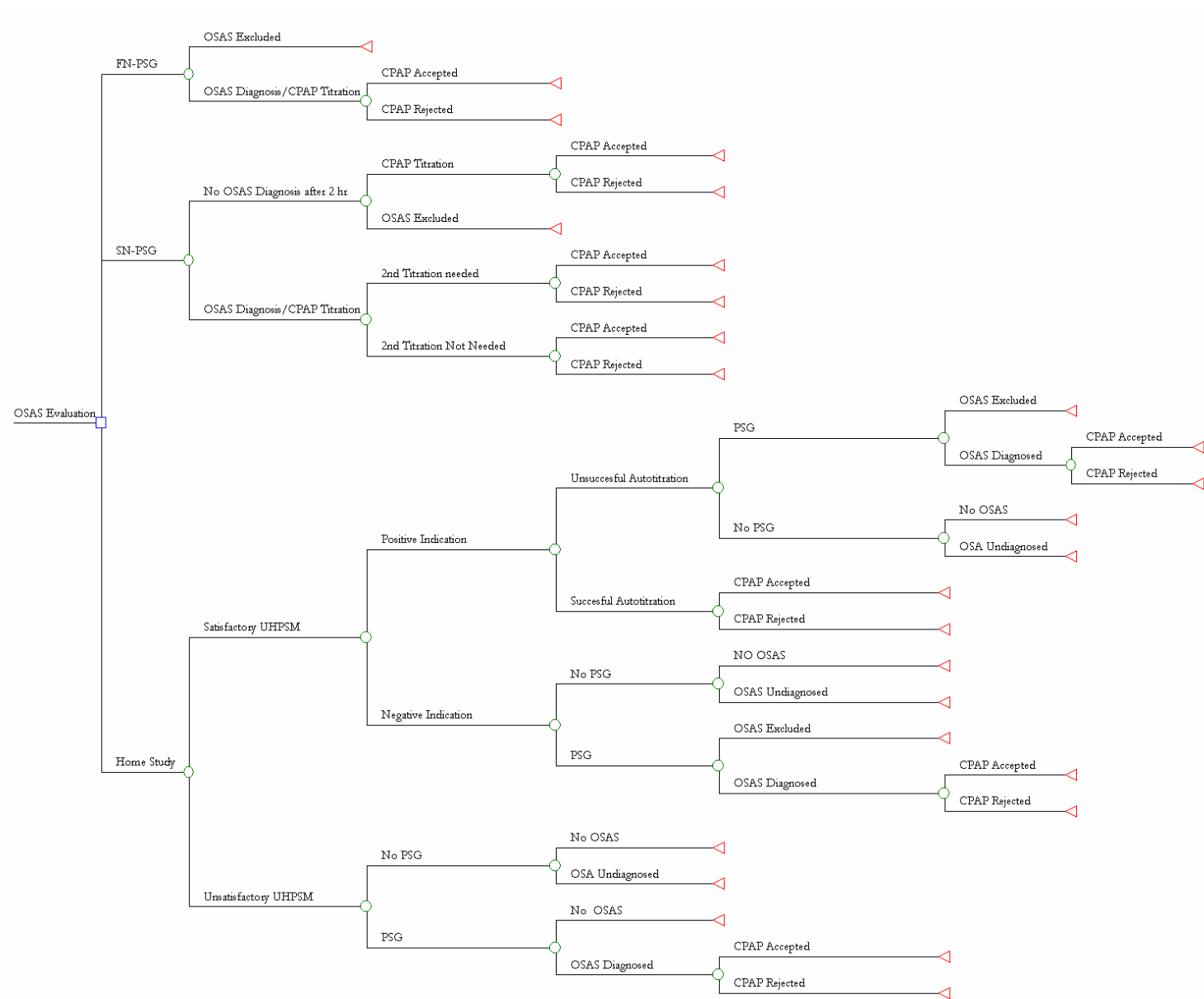
FN-PSG is the current "gold-standard" for the diagnosis or exclusion of OSAS [22]. In this pathway, located at the top of the decision tree, patients receive diagnostic FN-PSG at the first probability node. If the diagnosis excludes OSAS, the patient traverses to the "OSAS excluded" state. If FN-PSG yields a positive diagnosis, the patient goes on to receive PSG-titration and either accepts or rejects CPAP therapy.

In the SN-PSG pathway, shown in the middle of the tree, patients begin FN-PSG. However, if a positive OSAS diagnosis is made within the first two hours of the study, the patient traverses the "OSAS-Diagnosis/CPAP Titration" branch. A potential difficulty with the SN-PSG study is that it seeks to diagnose OSAS and titrate for CPAP in the same night; however, there may not be enough time remaining to complete both studies. If a successful titration is achieved during the first night, the patient traverses along the "2nd Titration Not Needed" pathway, and the patient begins CPAP therapy. If there is not enough time to fully titrate the patient during the SN-PSG study, the patient traverses the "2nd Titration Needed" branch; after a successful second titration, the patient can either accept or reject CPAP treatment.

On the other hand, if a positive OSAS diagnosis is not reached within the first two hours of the study, the patient traverses along the upper branch labeled "No OSAS Diagnosis after 2 hrs." The SN-PSG's baseline sensitivity within the first two hours is .90, so it will yield some false-negatives [24-48]. If the patient is OSAS negative, s/he traverses down the OSAS excluded branch to the terminal state of " No OSAS." If the patient is OSAS positive, the patient receives a second night of PSG-titration. The patient starts CPAP therapy and either traverses to the "CPAP Accepted" or "CPAP Rejected" branches.

The bottom branch of the tree details the steps of the UHPSM/ CPAP auto-titration pathway (28-34). In the first node of the UHPSM pathway, patients either set up the machine

correctly to receive a "Satisfactory Diagnosis," or they do not set up the machine correctly and receive an "Unsatisfactory Diagnosis." Patients who experience an unsatisfactory diagnosis are prescribed FN-PSG. However, some patients never report back to the lab and dropout of the study as indicated by the "No-PSG" branch. It is assumed that the probability of receiving a satisfactory UHPSM result is independent of the probability of a patient having OSAS. In addition, the probability that a patient pursues FN-PSG is assumed to be independent of the chance that the patient is OSAS positive. This allowed me to separate the FN-PSG drop-outs in the "NO PSG" branch into those who are OSAS positive but remain undiagnosed and those that drop-out of the study and never had OSAS. Patients that continue with FN-PSG after an indeterminate UHPSM either have "OSAS excluded" or have "OSAS diagnosed" followed by CPAP therapy.

Patients that have a successful UHPSM either received a positive or negative OSAS diagnosis. UHPSM is subject to significant error so the probability of a positive diagnosis does not coincide with the pretest probability. The chance of a positive diagnosis was calculated using the UHPSM's sensitivity and specificity as measured in several clinical trials [28-34]. The American Sleep Association advises that the UHPSM should not be used to exclude OSAS due to the high false-negative rate [29]. Thus, patients that received a negative OSAS diagnosis are prescribed FN-PSG. Some patients drop out of the study and end up in the terminal states "Undiagnosed OSAS" or "No OSAS" while others continue with FN-PSG and end up either accepting or rejecting CPAP.

Patients that are diagnosed positive via UHPSM continue on with CPAP-auto-titration to determine optimal CPAP pressure. CPAP-auto-titration is not one-hundred percent accurate for two reasons [34-40]. First, the machine may not be sensitive enough to correctly give an accurate pressure reading [34-40]. Second, some of the patients diagnosed positive by the UHPSM machine are actually false positive; it is assumed that all of these false-positive patients will fail CPAP-auto-

titration while thirteen percent[7] of OSAS positive patients will fail CPAP auto-titration [36]. If the

auto-titration is successful, the patient begins CPAP therapy. If auto-titration fails, the patient is

prescribed FN-PSG followed by PSG-titration. This costly step is necessary to identify the false-

positives. Some patients drop out of the study before FN-PSG and remain untreated.

Time Horizon

The time horizon for this study was restricted to five years. This increased the precision of

the data and facilitated comparison with other studies.

Probability and Test Characteristics

There are two classes of probability values that are stored in the chance nodes of the

decision tree. Some probabilities are taken directly from the medical literature. In such cases, values

from studies with cohorts most similar to the hypothetical cohort were used. In cases where the

probability varied among different studies that used similar cohorts, a mean value was used for the

baseline parameter and a sensitivity analysis was performed over the range of values reported in the

study. Probabilities concerning the diagnostic tests naturally depend on the pretest probability of the

cohort. FN-PSG is assumed to be completely accurate in diagnosing OSAS. The probability of a

positive diagnosis for the other chance nodes was calculated using the test's sensitivity and

specificity as estimated from the medical literature. Figure 28 shows the chance node probabilities

used in the study and the parameter ranges used in the sensitivity analysis.

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[7] This estimate is subject to extensive sensitivity analysis. See Table 28 and Table 41.

Figure 28 Chance Node Probabilities

Pathway	Event	Probability (Range)	References
FN-PSG, Home Studies	OSAS documented by7 FN-PSG	0.82 (0.45 - 0.95)	15,36,40
FN-PSG, SN-PSG, Home Studies	CPAP accepted after PSG titration	0.86 (0.70 – 0.95)	41-44
SN-PSG	Sensitivity within first 2 hrs	0.90 (0.80 – 0.95)	15
SN-PSG	Second night needed for CPAP titration after OSAS documented in first 2 hr	0.18 (0.09 – 0.25)	16,18,30,33
Home Studies	Satisfactory UHPSM	0.80 (0.65 – 0.90)	23-26,45
Home Studies	Dropout Rate After Unsuccessful UHPSM or CPAP-Auto-titration	0.23 (0.05 - 0.5)	23,26,28,30
Home Studies	UHPSM sensitivity	0.95 (0.90 – 1.00)	22,24,25,36
Home Studies	UHPSM specificity	0.73 (0.70 – 0.84)	22,24,25,36
Home Studies	CPAP auto-titration unsuccessful for patient with OSAS	0.13 (0.05 – 0.20)	29
Home Studies	Sensitivity of Diagnosis From Symptoms	.60 (.30-1)	21
Home Studies	Sensitivity of Diagnosis From Symptoms	.63 (.30-1)	21

Costs

This study is performed from the perspective of a healthcare delivery system. As such,

only healthcare costs or savings were considered. Non-healthcare costs, such as those associated

with travel, economic-productivity, or the environment, were excluded. Considering the time

horizon used in this study, these costs are immaterial and can be excluded according to the "reference case" guidelines [63]. The costs of diagnosis and treatment were computed in US dollars at each terminal node and included the cost of OSAS diagnosis, titration, CPAP costs, and the cost of office visits.

Figure 29 Cost Estimates for OSAS Diagnostic Evaluation and CPAP Treatment

Component Reimbursement	FN-PSG	SN-PSG	Home Sleep Studies
FN-PSG: CPT 95810	$783.30	[$783.30]†	[$783.30]†
Polysomnographic CPAP titration: CPT 95811	$807.81	[$807.81]†	[$807.81]†
SN-PSG: CPT 95811		$807.81	
UHPSM: CPT 95806			$223.66
CPAP Autotitration: CPT 95806			$223.66
CPAP Rental + Accessories: Yr 1	$1660	$1660	$1660
CPAP Rental + Accessories: Yr 2	$821	$821	$821
CPAP Rental + Accessories: Yr 3-5	$700	$700	$700
Office Visits: CPT 99214	$86.31 (11 visits)	$86.31(11visits)	$86.31 (14 visits)
Additional Medical Costs of OSAS positive patients not Treated with CPAP	$750.00	$750.00	$750.00

Published methodology for a standardized approach to the calculation of costs of OSAS diagnosis, CPAP titration and CPAP treatment is currently lacking. Therefore, 2003 Medicare reimbursement rates were used in determining costs [Figure 29].

CPAP Distribution Assumptions

Previous studies took an all or nothing approach to CPAP usage [45]. In order to more accurately calculate the true cost and benefits associated with CPAP, a distribution of CPAP usage was assumed. The CPAP distribution was derived from literature estimates of CPAP usage at three months, one year and five years [40]. The cumulative probability of these three estimates summed up to ninety-seven percent; it was assumed that the remaining probability would be equally dispersed among the remaining three intervals [40].

Figure 30 Point Estimates of Probability [40]

CPAP Duration (Years)	Probability
0≤.CPAP Usage≤.25	.195
.25<CPAP Usage≤1	.065
1<CPAP Usage≤2	.01
2<CPAP Usage≤3	.01
3<CPAP Usage≤4	.01
4<CPAP Usage≤5	.71

Office Visits Costs

Costs for office visits were based on 2003 Medicare reimbursement rates for follow-up specialist visits. Patients who were found to have no OSAS, who were diagnosed but refused CPAP, or who remained undiagnosed were assumed to have one post-evaluation office visit. The American Academy of Sleep Medicine (AASM) guidelines suggest a different schedule of office visits depending on the method in which a patient is diagnosed [29]. Specifically, since CPAP auto-titration is not as accurate in determining optimal fixed pressure levels, it is recommended that CPAP-auto-titration patients receive more frequent office visits. Patients who accepted

CPAP after PSG titration had one post-evaluation office and bi-annual office visits while they continued with treatment [29]. For patients who accepted CPAP after CPAP-auto-titration, the following schedule of visits was assumed:

1. 1x office visit /month for the first 3 months

2. 1 x office visit/ 3 months for the next 9 months

3. 2 x office visit a year for the duration of the treatment

CPAP Costs

The costs of CPAP include the cost of equipment purchases and maintenance [Figure 29]. The costs of CPAP decline dramatically after the first year reflecting the fixed costs of the CPAP machine. Patients that discontinued CPAP after three months were assumed to incur twenty five percent of yearly CPAP treatment costs. Costs incurred before six months were not discounted.

Extra Healthcare Costs

Ideally, the indirect costs for additional long-term health services due to untreated OSAS should be included in cost-utility analysis. Although it has been established that patients with OSAS consume more health services than the general population, the costs due to OSAS that are independent of co-morbid conditions have not been measured. Estimates of additional costs up to $750 per year for untreated OSAS have been reported [8]. Chervin excluded this cost from his baseline analysis, but he included the cost in a sensitivity analysis [45]. I chose to use long-term healthcare costs in my baseline model since this better fits with the theoretical guidelines specified by the Panel on Cost-Effectives in Medicine [63]. However, I also performed calculations without these costs to enhance comparability with other CUA studies.

Discounting

Cost and QALYs were discounted at a rate of 1.5% biannually, consistent with the recommendations of the Panel on Cost Effectiveness in Health and Medicine [63]. While

discounting over the reduced time horizon makes little difference in this study, discounting was performed to enhance comparability with other CUA studies.

<center>*Outcome Measures*</center>

The diagnostic pathways can result in three possible health states. The first state, *OSAS untreated,* occurs if an OSAS positive patient is never diagnosed with OSAS because of study dropout or if the patient is diagnosed with OSAS but cannot comply with CPAP therapy. The second state, *OSAS treated*, occurs if the patient accepts CPAP after diagnosis. This node leads to the distribution of CPAP usage, and the node ultimately represents the expected value of QALYs gained. The final outcome state, *No OSAS*, occurs when the patient is correctly diagnosed OSAS negative.

Utilities for treated and untreated OSAS were determined from a number of studies. One commonly cited utility study was conducted by Tousignant and consisted of retrospective interviews of sixteen Canadian patients [14]. In Tousignant's study, patients had already been treated with CPAP, and they were asked to assess their utility before they began CPAP using the standard gamble technique [14] . Since the study interviewed Canadian patients, the utilities should be valid for the North American population. Tousignant and colleagues did not assess symptomatic patients with no OSAS. These patients were assigned a utility value midway between the utility for treated and untreated OSAS. This method was also used by Chervin, the rationale being that symptomatic patients who do not have OSAS often remain untreated or receive less efficacious alternative therapies [45]. QALYs over the five year horizon were calculated for each health-state. This study followed Chervin's example and assumed that patients with untreated OSAS would have reduced five year survival rates based on previously published studies [4-6].   Since the mean survival of 4.7 years has not been confirmed in a large population, this value was subject to a large sensitivity analysis. Figure 3 shows utility data based on Tousignant's study [14].

<center>60</center>

Figure 31 Utilities, Mean Survival and QALYs Based on Tousignant's Utilities [14]

Health State	Utility	Mean Survival over the 5 Year Period	Possible QALYs over the 5 Year Period
OSAS Untreated	0.63	4.7 years	2.743
OSAS Treated: All patients for 5 years	0.87	5.0 years	4.012
No OSAS Diagnosed	0.75	5.0 years	3.458

The model was also programmed with health utilities from Chakravorty's recent study of seventy one patients with OSAS [15]. Chakravorty's study may be superior in several respects. First, the sample size is significantly larger [15]. Also, instead of being retrospective, Chakravorty study was conducted as a clinical trial [15]. In addition, Chakravorty used regression analysis to control for the morbidity of each sample [15]. Chakravorty recorded standard-gamble and EuroQol 5-D utilities before CPAP treatment and three months after treatment [15, Figure 32].

Figure 32 Utilities Based on Chakravorty's Study Using Standard Gamble and EuroQol 5-D [15]

Health State	Standard Gamble Utility (s.e)	EuroQol 5-D Utility (s.e)
OSAS Untreated	0.33 (.17)	0.73 (.18)
OSAS Treated	0.55 (.26)	0.77 (.26)
No OSAS Diagnosed	0.41 (.2)	0.75(.2)

While the baseline values measured by Tousignant and Chakravorty were significantly different, the difference between their measured values was almost identical. This is reassuring since the model's results depend on difference in utility between health states.

Utility data was also collected by giving utility questionnaires to OSAS positive patients in Los Angeles and by giving questionnaires to physicians that specialize in treating sleep disorders. Physicians were asked to rate each of the three health states used in the study as well as well as the health state experienced by a patient that has been diagnosed with OSAS but cannot tolerate CPAP. Having physician evaluate the states "CPAP Rejected" and "No OSAS" allowed me to more critically evaluate my assumption that these states were near the midpoint of OSAS Untreated and OSAS Treated.

Physicians were given a battery of tests the including the Visual Analogue Scale (VAS), the Time Trade-Off (TTO), Standard Gamble (SG), Health Utilities Index Mark 3 (HUI III), and the SF-6D [Appendix I]. The tests given to patients included the Health Utilities Index HUI and the SF-6D questionnaires [Appendix II]. The solicitation of utilities from patients was approved by an Institutional Review Board [Appendix VII]. The Visual Analogue Scale and Time Trade-Off questionnaires elicit health values under conditions of certainty. These value measurements were transformed into utilities using the general power relationship, $u = v^{1.6}$ [67].

Figure 34 Physician Estimated Utility Data

	OSAS Treated	CPAP Rejected	No OSAS	OSAS Untreated
VAS	.8 (.15)	.565 (.19)	.543 (.16)	.367 (.11)
VAS Utility	.73(.22)	.42 (.26)	.39 (.21)	.21 (.10)
TTO	.97 (.03)	.83 (.09)	.88 (.07)	.81 (.12)
TTO Utility	.951 (.06)	.745 (.13)	.821 (.11)	.728 (.19)
SG	.94 (.04)	.82 (.05)	.85 (.10)	.81 (.11)
HUI (III)	.959 (.06)	.5615 (.21)	.597 (.15)	.470 (.25)
SF-6D	.925 (.09)	.635 (.07)	.656 (.077)	.605 (.08)

Figure 35 Utility Values Solicited From Patients OSAS Positive Patients

Test Administered	OSAS Untreated
HUI (III)	.49 (.30)
SF-6D	.65 (.10)

Figure 35 demonstrates the results of the utility questionnaires given to OSAS patients. This represents the first time that utility values from the Health Utilities Index and SF-6D surveys have been reported for patients with OSAS. The results of the patient based surveys suggest that these questionnaires are appropriate for measuring the utility of patients with OSAS.

Overall, these utility measures provide a consistent picture of OSAS patient utility. Patient's measurement of the "OSAS Untreated" state with the HUI (III) and SF-6D corresponded quite well to physicians' assessment of these states. Also, physician's standard-gamble assessments of the OSAS Treated and OSAS Untreated states were generally consistent with the utility measured by Chakravorty and Tousignant. Physicians, on the whole, assigned higher utility values to these states. Physicians' higher utility estimates may reflect a more risk adverse attitude than that of the general population. This observation is supported by the fact that physician's HUI III and SF-6D utility estimates better matched patients' responses; in these surveys, risk preference has been adjust to reflect the risk preference of the general population. Overall, the difference between OSAS treated and untreated health states, as measured by the standard gamble, were consistent with that measured by patients to within the level of accuracy of the surveys. In addition, the physician's data suggest that the states "No OSAS" and "CPAP Rejected' remain somewhere near the midpoint of the"OSAS Untreated" and "OSAS Treated" states. This result supports my estimation of these states.

Overall, the utility data used in this study appears to be sufficiently robust. My analysis heavily depends on the difference in utility between the treated and untreated OSAS health states which is relatively constant among surveys. Another key assumption in the model is that the utility

for the "No OSAS" and 'CPAP rejected" health states is near the midpoint of the treated and

untreated OSAS values. This assumption seems to be well supported by the physician utility study.

Chapter 7

Model Results

I present two sets of results in this section. First, I present results that I believe are parameterized with the best cost and utility data. Specifically, I use Chakravorty's utility values and I include the extra costs associated with untreated OSAS [15,8]. In order to facilitate comparison with other studies, I present results that use Tousignant's utility values and that exclude the extra costs of untreated OSAS [14]. I then experiment with permutations of extra cost and utility variables in order to determine the affect each series has on the model's results.

Figure 38 Expected Costs, QALYs, and Cost-Utility Ratios for the Baseline Pathway[8]

Pathway	Expected Cost	Incremental Cost	QALYs over 5 Year Period	Incremental QALYs[9]	Cost-Utility Ratio	Incremental Cost-Utility Ratio[4]
FN-PSG	$5,910.10	$508.30	2.6229	0.0796	$1,979/QALY	Dominated
SN-PSG	$4,681.80	$94.4	2.6229	0.0796	$1,785/QALY	$1,186/QALY Gained
UHPSM	$4,587.40	__	2.5433	__	$1,804/QALY	__

Over the five year time horizon used in this study, the QALYs for the FN-PSG and SN-PSG pathways (2.62) exceeded those for the UHPSM pathway (2.54). Because of the lower five year

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[8] Calculated with utility values measured by Chakravorty and includes extra medical costs associated with untreated OSAS.

[9] Expected costs of diagnosis and expected QALYs for the 5 year time horizon for each of the three diagnostic pathways were calculated using DATA 4.0. Incremental QALYs were determined as the difference in expected QALYs between the two pathways. Cost-utility ratios for each of the pathways was computed as the quotient of the 5 year expected total costs for the pathway divided by the expected QALYs. Incremental cost utility ratios were calculated with the numerator being the difference in expected costs between pathways and the denominator, the difference in expected QALYs over the 5 year period. Incremental C/U ratio are reported in reference to the UHPSM study pathway.

expected costs ($4,681.80 versus $5,910.10) and identical QALYs, the SN-PSG pathway dominated

the FN-PSG pathway. Therefore, comparison of the incremental QALYs and C/U ratios is limited

to the SN-PSG and UHPSM studies. The five year C/U ratios for the SN-PSG and UHPSM studies

were $1,785 and $1,804 respectively. While the SN-PSG pathway is more expensive than the FN-

PSG pathway, the SN-PSG has the lowest C/U ratio suggesting that it yields the greatest healthcare

benefit. The incremental C/U ratio between the SN-PSG pathway and UHPSM pathway is $1,186.

Figure 39 Expected Costs, QALYs, and Cost-Utility Ratios Calculated
With Tousignant Utilities and the Exclusion of Extra Costs

Pathway	Expected Cost	Incremental Cost	QALYs over 5 Year Period	Incremental QALYs	Cost-Utility Ratio	Incremental Cost-Utility Ratio
Full-night PSG	$4,251.40	$470.80	3.541	0.051	$1,201/QALY	Dominated
Split-night PSG	$3,780.60	$456.20	3.541	0.051	$1,068/QALY	$5,190/QALY Gained
Home Study	$3,516.30	—	3.490	—	$1,008/QALY	—

In order to facilitate comparison with other CUA studies, the results were recalculated with

Tousignant's utility values and with the costs of untreated OSAS excluded from the model [Figure

39]. With these changes, the expected cost of each diagnostic alternative decreased since the extra

costs were excluded. Also, the expected effectiveness of each diagnostic alternative increased since

the utilities measured by Tousignant were higher than those measured by Chakravorty. The incremental cost between the UHPSM and the SN-PSG study increased with this specification. In the UHPSM study, some patients dropout of the study. Thus, in the UHPSM study, a larger fraction of the OSAS positive patients are not treated with CPAP and incur extra medical costs. When these extra medical costs are excluded, the UHPSM appears cheaper relative to the SN-PSG study. The incremental utility values between the UHPSM and FN-PSG/SN-PSG pathway decreased with this model specification since Tousignant measured a smaller difference in utility between the treated and untreated OSAS health states. Finally, in the second specification, the UHPSM study has a lower C/U ratio ($1,008) than the UHPSM ($1,068) which suggests that the UHPSM yields the greatest per dollar health benefit.

Several permutations of utility and extra cost data were conducted. One interesting result is that the model's predictions were not sensitive to the utility series. The affect of adding the extra costs of untreated OSAS was more subtle. In all cases, the SN-PSG was found to have a larger expected cost than the UHPSM study. However, the relative magnitude of the C/U ratio depended on the inclusion or exclusion of extra costs. If the extra-costs of untreated OSAS were included, SN-PSG generally had a lower C/U ratio than the UHPSN study. If the extra costs were excluded, the UHPSM study would have a lower C/U ratio. In almost all cases, the incremental C/U ratio generally remained below $10,000/QALY.

The results of my study are comparable to the results reported by Chervin as shown in Figure 40 [45].

Figure 40 Comparison of Thesis and Chervin's Results [45]

Thesis Results (2004)				Chervin's Results [45]			
Pathway	Expected Cost	Expected QALY	Cost-Utility Ratio	Pathway	Expected Cost	Expected QALY	Cost-Utility Ratio
FN-PSG	$4,251.40	3.541	$1,201/QALY	FN-PSG	$4,210.00	4.019	$1,047.52/QALY
SN-PSG	$3,780.60	3.541	$1,068/QALY	UHPSM	$3,460.00	3.955	$874.85/QALY
UHPSM	$3,516.30	3.490	$1,008/QALY	No Diagnosis	$3,020.00	3.934	$767.67/QALY

The expected cost of the FN-PSG and UHPSM pathways were similar to those calculated in Chervin's model [45]. The expected utility values differed since different utility states were used in the two studies [45]. For example, some patients in Chervin's model ended up being negative for OSAS but were still placed on CPAP. Thus, Chervin had to estimate the utility of patients who were placed on CPAP but received no benefit from the therapy. In reality, this health state is unlikely to exist in the real world as patients that receive no benefit from CPAP are will dropout of treatment. Overall, I believe that the QALYs reported in my study are more accurate since the terminal health states are more realistic.

Chapter 8

Sensitivity Analysis and Discussion

A univariate sensitivity analysis was conducted for several reasons. First, the analysis allowed me to assess the robustness of the model. Second, examining how parameter changes affected the model's results helped me to develop an intuitive understanding of the model. Finally, the results of the sensitivity analysis helped me to determine alternative pathways that may be more effective in diagnosing OSAS.

Understanding the model's results largely depends on understanding how study dropout affects the UHPSM pathway. The FN-PSG and SN-PSG studies will have identical expected QALYs since both pathways' dropout rates are zero. Dropout does occur in the UHPSM pathway because some patients refuse to continue with FN-PSG after an unsuccessful UHPSM/CPAP auto-titration. These patients never get a diagnosis and never begin CPAP. For dropout rates greater than zero, the UHPSM will have a lower expected utility than the FN-PSG/SN-PSG pathways. The magnitude of the incremental effectiveness is simply a function of the size of the dropout rate and the difference between the OSAS untreated and OSAS treated states. The size of the dropout rate also affects the expected cost of the UHPSM pathway since it alters the number of patients that begin expensive CPAP therapy. The change in the incremental C/U ratio between the SN-PSG study and the UHPSM study is a result of the interaction of these two factors. If, as the dropout rate decreases, the increases in the costs of CPAP outweigh the increases in utility, the incremental C/U will decrease.

Figure 41 demonstrates the results of a detailed sensitivity analysis. Variables were varied simultaneously if there was a statistical relationship between the variables.

Figure 41 Results of Univariate Sensitivity Analyses

Variable	Baseline Estimate	Range Tested	Incremental QALYs[10]	Incremental Cost-Utility [6] ($/QALY gained)
Pre-test OSAS Probability	0.82	0.45 – 0.95	0.044 – 0.092	230– 1,344
Probability of Satisfactory UHPSM	0.80	0.65 – 0.90	0.110 – 0.059	404 – 2,148

UHPSM
  Sensitivity
  Specificity
	0.95
	0.73
		0.90 – 1.00
		0.70 – 0.84
			0.088 – 0.071
			0.0796
				908 – 1,531
				1,174 – 1,231

S/N PSG Sensitivity	.90	.85-.95	.0796	1,279-1,093
Probability of Unsuccessful CPAP Auto-titration for Patient with OSAS	0.12	0.05 – 0.20	0.067 – 0.094	1,907 – 602
Dropout after Unsuccessful UHPSM or CPAP-Auto-titration	0.23	0.05 – 0.5	0.173 – (.017)	1,950 –Dominated (Threshold 0.875)
Probability of Second Titration after SN-PSG	0.18	0.09 – 0.25	0.0796	512-1,711
Probability of CPAP Accepted	0.86	0.70 – 0.95	0.065 – 0.088	882 – 1,321
Probability of CPAP Used at 5 years	0.71	0.50 – 0.85	0.059 – 0.063	1,439 – 1,079

Study Reimbursement Rate
  FN-PSG[11]
  Polysomnographic CPAP Titration[7]
  SN-PSG[7]
  UHPSM[12]
  CPAP Autotitration[8]
	
	$783.30
	$807.81
	$807.81
	$223.66
	$223.66
		
		$665.81 –
		$1018.29
		$686.64 –
		$1050.15
		$686.64 –
		$1050.15
		$150.00 -
		$400.00
		$150.00 -
		$400.00
			
			0.0796
			0.0796
			0.0796
			0.0796
			0.0796
				180 – 3,198
				180 – 3,198
				180 – 3,198
				2,725 -Dominated
				7,594 -Dominated
				(Threshold $285.93)

Office Visit Reimbursement Rate	$80.00	$65.00 –$100.00	0.0796	1,365 – 948

CPAP Reimbursement Rate
  Year 1
  Year 2
  Year 3-5
	
	$1660
	$821
	$700
		
		$950.00 –
		$2160.00
		$300.00 –
		$1321.00
		$300.00 -
		$1200.00
			
			0.0796
			0.0796
			0.0796
				
				290 – 1,634
				290 – 1,634
				290 – 1,634

Indirect Costs for Untreated OSAS	$750	$0 -$1,000	0.0796	3,322 – 474

Utilities
  Uncorrelated
    Undiagnosed or Untreated OSAS
    Treated OSAS
    No OSAS
  Simultaneously Varied
	
	0.33
	0.55
	0.41
		
		0.13 – 0.53
		0.35 – 0.75
		0.21 – 0.61
			
			0.05 – 0.00
			0.073 – 0.126
			0.080
			0.041 – 0.049
				
				2,005-37,851
				1,289 – 748
				1,186
				2,317 – 1,920

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[10] Measured in relation to the UHPSM pathway

[11] FN-PSG was varied simultaneously with the cost of PSG- titration cost and the cost of SN-PSG.

[12] The cost of the UHPSM study was varied simultaneously with the cost of CPAP auto-titration.

I performed a sensitivity analysis to investigate several model properties. Since the SN-PSG dominates the FN-PSG study, I was primarily interested in comparing the relative cost-effectiveness of the SN-PSG versus the UHPSM study. The results of the baseline analysis suggest that the SN-PSG pathway is both more effective and more expensive than the FN-PSG test; thus, the SN-PSG falls within the second quadrant of the cost/utility plane[13]. I wanted to see if the SN-PSG remained in this quadrant as I changed parameter values. Also, I wanted to examine how changes in parameter values affected the relative cost and effectiveness of the SN-PSG exam relative to the UHPSM. The incremental C/U ratio is a statistic that measures this relationship.

The results of the model did not change much in response to parameter changes. SN-PSG remained in the second quadrant of the C/U plane under most parameter assumptions. However, the SN-PSG dominated the UHPSM when the dropout rate was very low or when the UHPSM/CPAP auto-titration costs were high.

Sensitivity of the Model to Probabilities and Test Characteristics

Within the ranges tested, few variations of the probabilities resulted in substantial differences in incremental QALYs or C/U ratios from the baseline case. Increasing the pretest probability resulted in a higher incremental C/U ratios for the SN-PSG. This occurs because many patients remain untreated in the UHPSM study due to dropout. For high pretest probabilities, nearly all of the patients undergo expensive CPAP therapy in the SN-PSG pathway. However, in the UHPSM, many of the OSAS positive patients dropout and do not incur CPAP costs. While this saves the health system money in the short-run, it ultimately fails its purpose in diagnosing patients as efficiently as possible.

Probabilities that favored satisfactory or positive UHPSM studies and successful CPAP auto-titration were preferential toward the UHPSM pathway since they resulted in lower incremental

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[13] The cost-utility plane is discussed in Chapter 2.

QALYs and higher incremental C/U ratios over the SN-PSG pathway. Increasing the sensitivity of the UHPSM resulted in lower false-negatives so that more patients entered the lower cost CPAP auto-titration route, which resulted in slightly lower incremental QALYs and higher incremental cost-utility ratios for the SN-PSG pathway versus the UHPSM pathway. Changes in specificity had little effect on the incremental C/U ratios. These results are partially surprising since increasing the accuracy of the UHPSM should increase the expected costs of CPAP. Costs do not rise since increasing the accuracy of the UHPSM decreases the cost of duplicate FN-PSG testing.

Dropout is a serious problem with the UHPSM [28-34]. Dropout occurs in the model after patients elect not to continue with PSG after a failed UHPSM or CPAP-auto-titration and traverse the "NO PSG" to the states "OSAS Undiagnosed" and "OSAS Untreated" [See Figure 27]. As the dropout rate decreases, the UHPSM treats more patients with CPAP resulting in increased costs and increased effectiveness. Costs of CPAP increase faster than utility, causing the incremental C/U between the SN-PSG and UHPSM pathways to decrease. Above a threshold value of a five percent dropout rate, the SN-PSG pathway dominates the UHPSM study.

With increasing probability that CPAP was accepted and used at five years there were increasing incremental QALYs and decreasing cost per QALY gained for the SN-PSG pathway versus the UHPSM pathway. Once the diagnosis of OSAS was made, acceptance of CPAP resulted in an increase in QALYs relative to the cost of CPAP treatment. Continued use of CPAP over the five year time period resulted in continued high QALYs with lower marginal costs for CPAP treatment.

Overall, this analysis yields several intuitive conclusions. Increasing the morbidity of the sample advantages the UHPSM, albeit in a perverse way. This occurs because the UHPSM pathway is less effective at diagnosing patients and incurs smaller CPAP treatment costs. However, increasing the accuracy of the UHPSM study advantages the UHPSM relative to the SN-PSG pathway even

though this results in higher treatment costs. As the UHPSM becomes more accurate, it substitutes duplicate diagnostic costs for CPAP treatment costs. Thus, increasing the accuracy of the UHPSM allows the pathway to increase utility for free.

The primary reason the UHPSM study is less costly and less effective than the UHPSM study is that the UHPSM diagnoses and treats fewer patients with CPAP. If the UHPSM study's dropout rate was set to zero so each pathway was equally effective, the SN-PSG would dominate the UHPSM study. Thus, the real question to ask is: is treating patients with CPAP cost-effective in the first place? Three C/U studies of CPAP therapy all agree that CPAP is cost-effective [12,13,45]. If we assume that CPAP therapy is cost-effective, than the results of this sensitivity analysis clearly suggests that the SN-PSG pathway is the optimal pathway.

Sensitivity of the Model to Costs

The affect of varying test costs was amplified since there was a strong correlation between these costs. Changes in these variables were observed to be additive in the pathways in which they were present together. This phenomenon was particularly pronounced for the UHPSM and CPAP auto-titration reimbursement rates since these costs only affected the UHPSM pathway. After a threshold of $382.70 per UHPSM study, the SN-PSG dominated the UHPSM pathway.

Office visit and CPAP reimbursement rates also had noteworthy effects on incremental C/U ratios. Variation of office-visit rates had a greater effect on the UPSM pathway because of the greater number of visits during the first year after OSAS diagnosis [29]. Variation of CPAP reimbursement rates had a greater impact on SN-PSG cost-utility because of the greater proportion of patients who were diagnosed with OSAS and treated with CPAP.

Sensitivity of the Model to Outcome Measures

Varying the utility of no OSAS had no affect on the incremental C/U ratio since this

outcome occurred with equal frequency in all pathways. Lower utilities for untreated OSAS and

higher utilities for treated OSAS resulted in substantial reductions in the cost per QALY gained for

the SN-PSG pathway due to the lower rate of OSAS diagnosis and treatment than in the UHPSM

pathway. Increasing survival of undiagnosed or untreated OSAS patients over the five year time

horizon resulted in higher incremental C/U ratios for the SN-PSG versus the UHPSM pathway due

to a greater proportion of undiagnosed and untreated patients in the UHPSM pathway.

Monte-Carlo Simulation Results

A Monte Carlo simulation was conducted to test the model's sensitivity to simultaneous

parameter changes. Probability and utility variables were transformed into logit-normal distributions

so that the mean of the new distribution was equal to the baseline probability/utility value reported

in Figure 28 [84]. Cost variables were assumed to follow a triangular distribution. The cost shown in

Figure 29 was assumed to be the most likely value of the distribution and the sensitivity analysis

range formed the base of the triangle. The results of the Monte-Carlo experiment are shown in

Figure 42.

Figure 42 Expected Cost, QALYs and Cost Utility Ratio

Pathway	Expected Cost (S.E)	QALYs over 5 Year Period (S.E)	Cost Utility Ratio $/QALY (S.E)
FN-PSG	$5,080 (649)	2.625 (.51)	$2036 (595)
SN-PSG	$4,582 (601)	2.625 (.51)	$1,836 (539)
UHPSM	$4,414 (582)	2.54 (.492)	$1, 821 (499)

One of the most important functions of CUA is to compare a baseline treatment against an alternative treatment. Chapter 3 provided a decision algorithm for making this choice. Since the SN-PSG pathway is generally more costly and more effective than the UHPSM pathway, the algorithm suggests that the incremental C/U ratio should be compared against other interventions competing for the same funds, and it should be compared against society's maximum WTP[14]. While this WTP value is controversial, I choose a conservative $10,000/QALY for this study. In order to examine if the SN-PSG pathway was likely to be under $10,000/QALY, I wanted to use a Monte-Carlo simulation to devise a confidence interval for the incremental C/U ratio. Since the ratio of two normal distributions has neither a finite mean nor a finite variance, the best way to calculate this confidence interval has been the subject of some debate [65]. In Van Hout's method, it is assumed that the costs and effects follow a joint normal distribution, and the resulting cost and effect density function is elliptical in shape [65]. This allows for the calculation of an elliptical confidence interval that covers ninety-five percent of the integrated probability. The incremental C/U ratio's confidence interval can then be found by drawing rays from the origin of the cost-utility plane that are tangent to the ellipse [65]. Figure 43a shows an isocontour map of the SN-PSG treatment over the cost/utility plane while Figure 43b shows the ninety-five percent confidence ellipse.

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[14] This is effectively the shadow price of one year of perfectly healthy life.

Figure 43 Isocontour Map of Incremental C/U ratio (A) and Ninety Five Percent Confidence Ellipse for Incremental C/U Ratio (B).
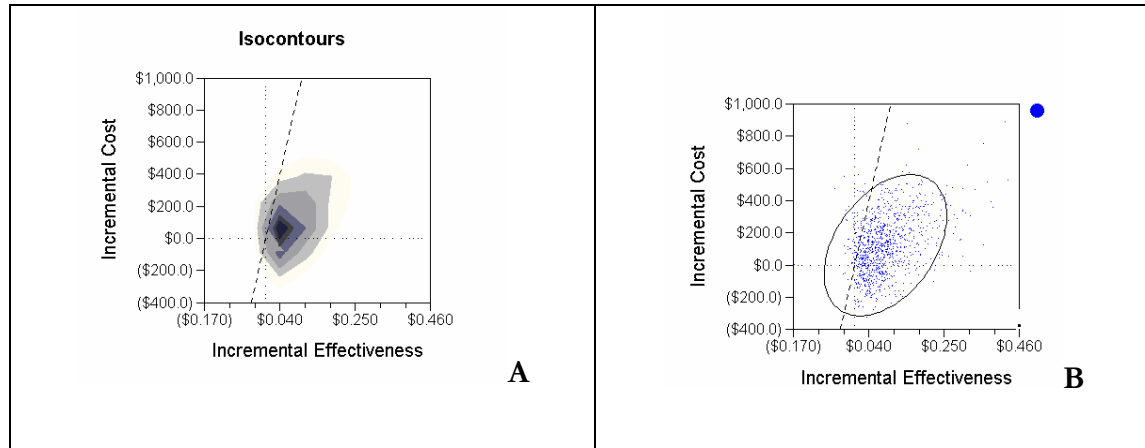
In both graphs, the dotted lines represent the cost-utility axis while the dashed line represents the maximum incremental C/U ratio. The isocontour graph shows the joint Cost/QALY density function where darker areas represent a higher density of C/U ratios. The graph suggests that the incremental C/U ratio falls in the first quadrant of the cost-utility plane where the expected cost of the treatment exceeds the expected utility of the treatment. It appears that the incremental cost-utility ratio generally resides below the maximum $10,000/QALY. Occasionally, the incremental C/U ratio resides in the fourth quadrant where the SN-PSG dominates the UHPSM study.

Ideally, I would like to use Figure 43b to calculate the incremental C/U ratio by drawing lines from the origin tangent to the confidence ellipse. Unfortunately, a ninety-five percent confidence interval cannot be created for this incremental C/U ratio. This occurs because the SN-PSG study is not significantly more costly and significantly more effective than the UHPSM. In other words, there is uncertainty regarding the quadrant in which the incremental C/U ratio falls.

Since this approach does not work for my data, I have used other bootstrapping methods to gauge the acceptability of the incremental C/U ratio. One way to examine the acceptability is to record how many times the C/U falls within the acceptable parts of the cost-utility plane. Figure 44 shows the frequency with which the incremental C/U ratio falls within a specified part of the C/U plane.

Figure 44 Probability Increment C/U Ratio in Select Part of the Cost-Utility Plane

Descriptioin	Probability
SN-PSG Dominant	23.6%
SN-PSG more effective, more expensive and Incremental C/U ratio less than $10,000	67.8%
SN-PSG more effective, more expensive and Incremental C/U ratio is greater than $10,000	3.9%
SN-PSG dominated	2.8%

The table shows that SN-PSG is either dominate or below in maximum WTP 91.4% of the time. Another way to gauge the acceptability of the incremental C/U ratio is to draw an acceptability curve as a function of the maximum WTP [65].

Figure 45 Acceptability of SN-PSG as Function of Maximum WTP
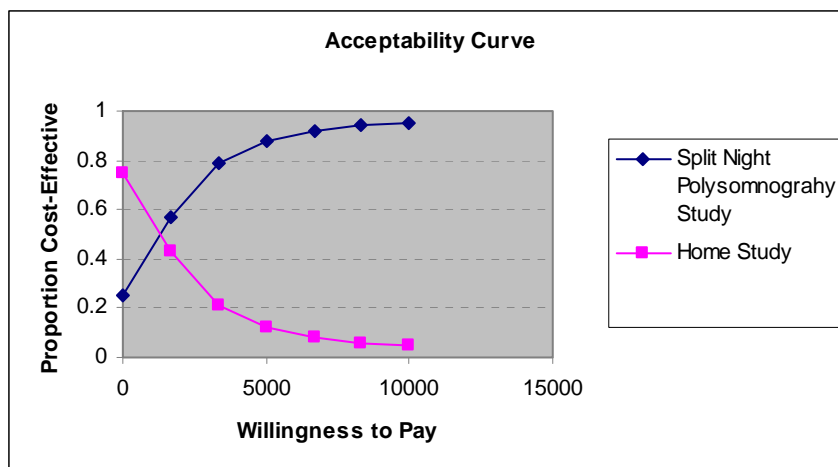
The results of this Monte-Carlo simulation are highly favorable toward the SN-PSG pathway. The results suggest that the SN-PSG pathway either dominates the UHPSM pathway or is below the maximum WTP over 95% of the time. Thus, there is strong evidence to support the cost-effectiveness of the SN-PSG pathway.

In the results section, two model specifications were discussed. In the second model specification, Tousingant's utilities replaced Chakavorty's utilities and the extra costs of untreated OSAS were dropped from the model. As a result, both SN-PSG's C/U ratio and incremental C/U ratio increased relative to that of the UHPSM. I wanted to conduct a Monte-Carlo simulation on this model specification in order to guarantee that the SN-PSG' incremental C/U ratio remained acceptable even with these adverse parameter changes.

Figure 46 Isocontour Map (A) and Ninety-Five Percent Confidence Interval (B) of Model Parameterized with Tousignant Utilities and Extra Costs of Untreated OSAS Excluded
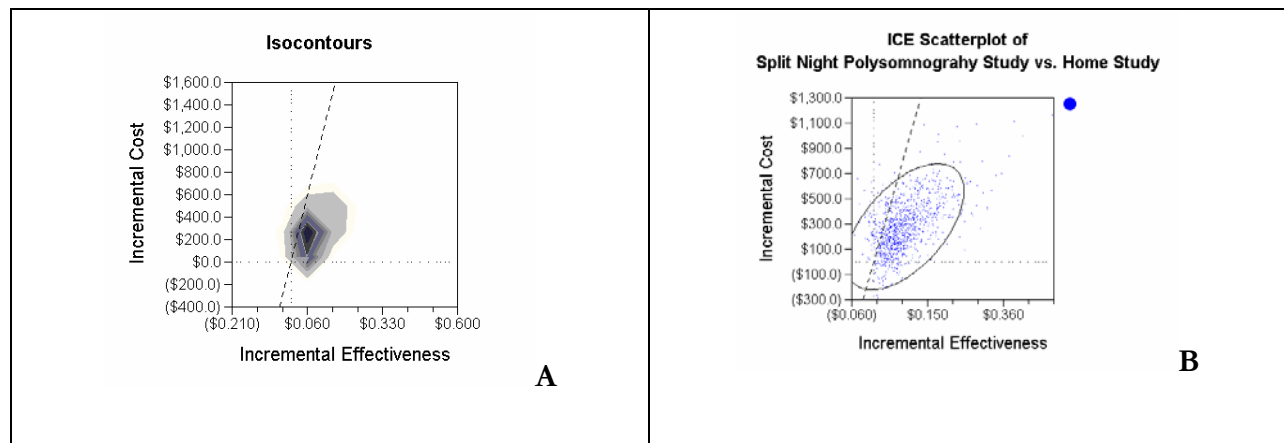
The isocontour graph shows that the cost-utility density function has shifted upward [Figure 46a]. The incremental cost-utility scatter plot shows that a ninety –five percent confidence interval still cannot be created since the confidence ellipse is not completely within the first quadrant. Thus,

to assess the acceptability of the incremental C/U ratio, bootstrapping method were repeated. Figure 48 shows the percentage of time the incremental C/U ratio falls within each of the three regions.

Figure 48 Probability Increment C/U Ratio in Select Part of the Cost-Utility Plane Given The Second Model Specification

Descriptioin	Probability
SN-PSG Dominant	6.6%
SN-PSG more effective, more expensive and Incremental C/U ratio less than $10,000	82.6%
SN-PSG more effective, more expensive and Incremental C/U ratio is greater than $10,000	7.3%
SN-PSG dominated	3.6%

While the bootstrapping results are expectantly more disadvantageous to the SN-PSG, the results still suggest a high degree of acceptability. In order to gauge the acceptability of the incremental C/U ratio as a function of maximum WTP, an acceptability curve was drawn [Figure 49].

Figure 49 Acceptability of SN-PSG as Function of Maximum WTP Under Model Two's Specification
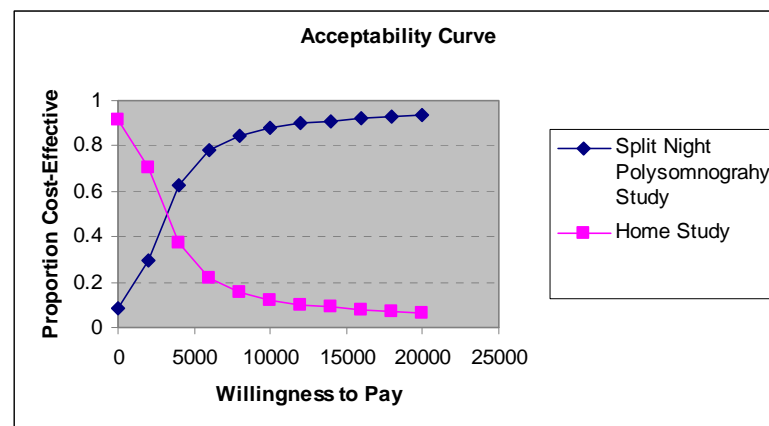
This acceptability curve shows that the SN-PSG is the optimal strategy at least 90% of the time.

Overall, both model specifications support use of the SN-PSG pathway.

The results of the sensitivity analysis highlight pathway bottlenecks and suggest mechanism to improve the pathways. The univariate sensitivity analysis showed that the UHPSM can increase its cost-effectiveness by increasing its sensitivity, specificity, or increasing the chance that patients will have a successful UHPSM study. The obvious recommendation for improving the UHPSM is to increase the accuracy of the test. Most patients fail to have successful tests because they set up the machine incorrectly. To increase the chance that patients have successful tests, nurses could drive to patients' homes to help them set up the UHPSM machine [30-35]. However, this will require expenditures that may cancel out the benefit of increasing test accuracy.

I hypothesized that the cost-effectiveness of the UHPSM could be improved by adding a screening step before the UHPSM [49]. The reason I believed that this would increase cost-effectiveness is that the UHPSM cannot be used to exclude OSAS; thus, giving OSAS negative patients the UHPSM study is a waste of money. In the screening step, physicians are told to make a diagnosis of OSAS based on physical features and patient history. It was assumed that physicians could screen patients with a sensitivity of .6 and specificity of .63 [2,29]. Figure 50 shows the proposed screening pathway.
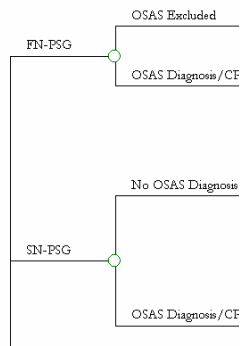
Model

FN-PSG

OSAS Excluded

OSAS Diagnosis/CP

SN-PSG

No OSAS Diagnosis

OSAS Diagnosis/CP

Figure 51 Expected Costs, QALYs, and Cost-Utility Ratios for the Screening Pathway using Chakravorty Utilities and Extra Costs Data

Pathway	Expected Cost	Incremental Cost	QALYs over 5 Year Period	Incremental QALYs	Cost-Utility Ratio	Incremental Cost-Utility Ratio
Full-night PSG	$5,910.10	$508.30	2.623	0.0796	$1,973/QALY	Dominated
Split-night PSG	$4,681.80	__	2.623	0.0796	$1,785/QALY	___
UHPSM	$5,172.00	$491.40	2.456	__	$2,106/QALY	Dominated

The screening pathway results show that my hypothesis was not correct. Attempting to screen out OSAS positive patients tremendously disadvantaged the UHPSM study. This occurred for several reasons. First, the screening procedure was not that accurate so that a significant proportion of the cohort underwent expensive FN-PSG. Sensitivity analysis confirmed that the UHPSM was not dominated given very high sensitivities and specificities[15]. The other problem with this screening pathway is that it reduced the dropout rate. In the screening pathway, a larger proportion of patients are recommended FN-PSG at the beginning of the tree and a larger percentage of patients receive a diagnosis. However, the pool of patients that begin with FN-PSG is saturated with patients that are OSAS negative. These patients incur the cost of expensive FN-PSG,

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[15] Sensitivity and Specificity had to be nearly 1.0 for this to occur.

but they never receive any benefit from treatment. Thus, the screening pathway should not be implemented.

CPAP Auto-Titration Pathway

I wanted examine a hypothetical pathway that substitutes PSG-titration with CPAP auto-titration. The FN-PSG and SN-PSG pathways use expensive PSG-titration. CPAP auto-titration costs half as much as FN-PSG. I wanted to examine how this substitution affected two of the model's results. First, SN-PSG always dominated FN-PSG in the baseline pathway. I hypothesized that the substitution of CPAP-auto-titration may make the FN-PSG less expensive than SN-PSG since FN-PSG use PSG-titration more intensively. Also, I wanted to examine the affect the substitution had on expected QALYs for the FN-PSG and SN-PSG pathways since the addition of CPAP-auto-titration would result in some study dropout.

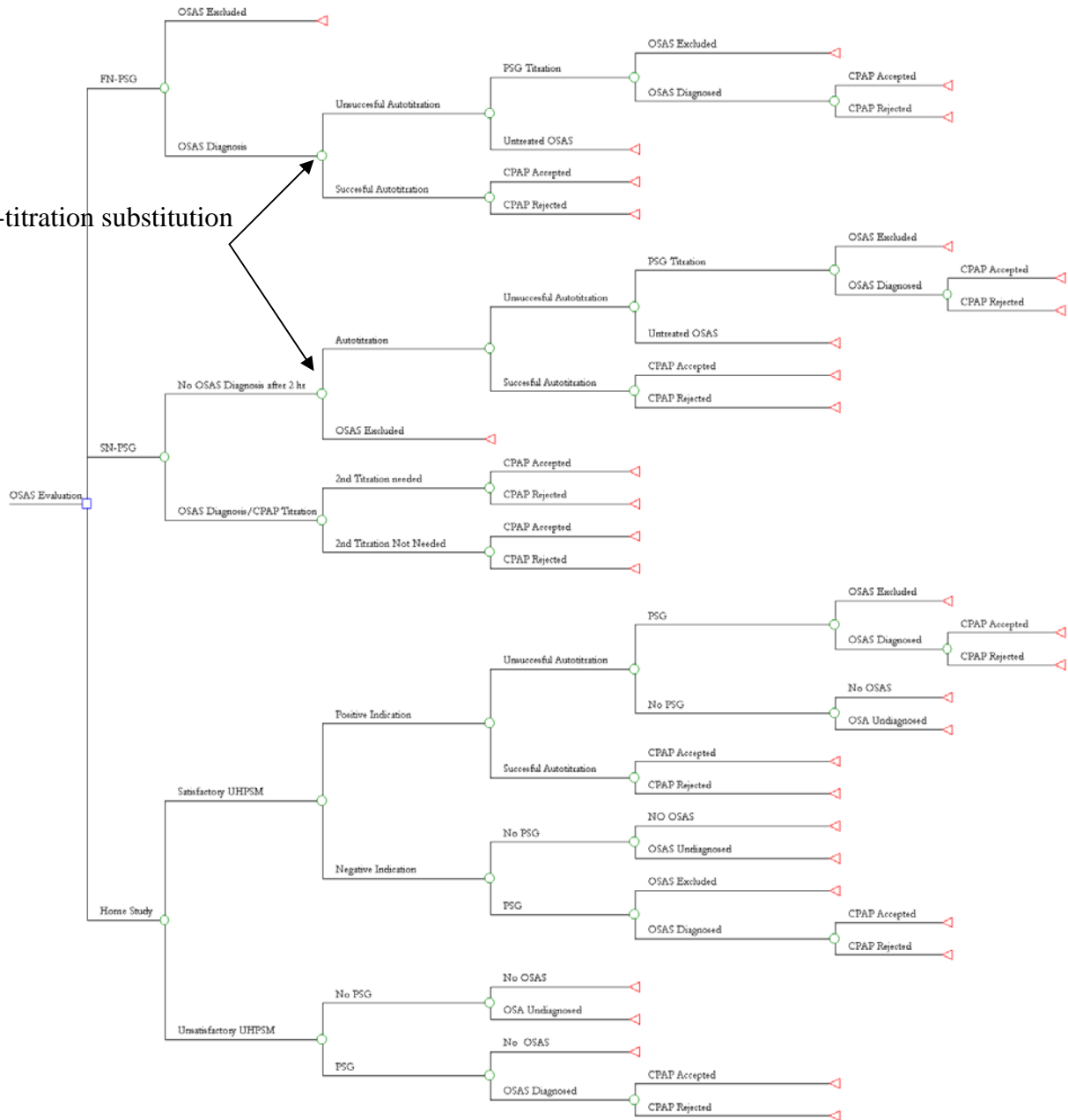**Figure 52 CPAP-Auto-Titration Pathway**

CPAP auto-titration substitution

Figure 53 Expected Costs, QALYs, and Cost-Utility Ratios for the CPAP Auto-Titraion Pathway with Chakravorty Utilities and Extra Costs Included

Pathway	Expected Cost	Incremental Cost	QALYs over 5 Year Period	Incremental QALYs	Cost-Utility Ratio	Incremental Cost-Utility Ratio
FN- PSG	$4,745.0	$107.70	2.5941	----	$1,829/QALY	Dominated
SN-PSG	$4,673.40	$86.00	2.6200	0.0797	$1,770/QALY	$ 652.00
UHPSM	$4,587.40	__	2.5433	__	$2,106/QALY	___

The results suggest that the CPAP-auto-titration pathway may be a viable alternative to the SN-PSG pathway. The substitution of CPAP-auto-titration for PSG-titration reduced the expected costs of FN-PSG significantly from $5,190 to $4,745. However, this cost decrease was associated with an increase in patient dropout which caused QALYs to decrease from 2.63 to 2.59. The CPAP auto-titration substitution also caused the expected cost of SN-PSG to decrease form $4,681 to $4,673 without an appreciable decrease in QALYs. This caused the incremental C/U ratio between the SN-PSG and UHPSM pathways to decrease to half its baseline value

The decrease in the incremental C/U ratio suggests that SN-PSG/CPAP-auto-titration may be competitive with the SN-PSG/PSG-titration pathway. The CPAP-auto-titration pathway adds several branches to the tree and increases the variability of the results. In order to test the stability of

the incremental C/U ratio, a Monte-Carlo simulation was performed. The results of the Monte

Carlo Simulation are presented in Figure 54 and Figure 55.

Figure 54 Iscontour Map of Incremental C/U Ratio (A) and Ninety Five Percent Confidence Ellipse for Incremental C/U Ratio (B) for CPAP-Auto-Titration Pathway
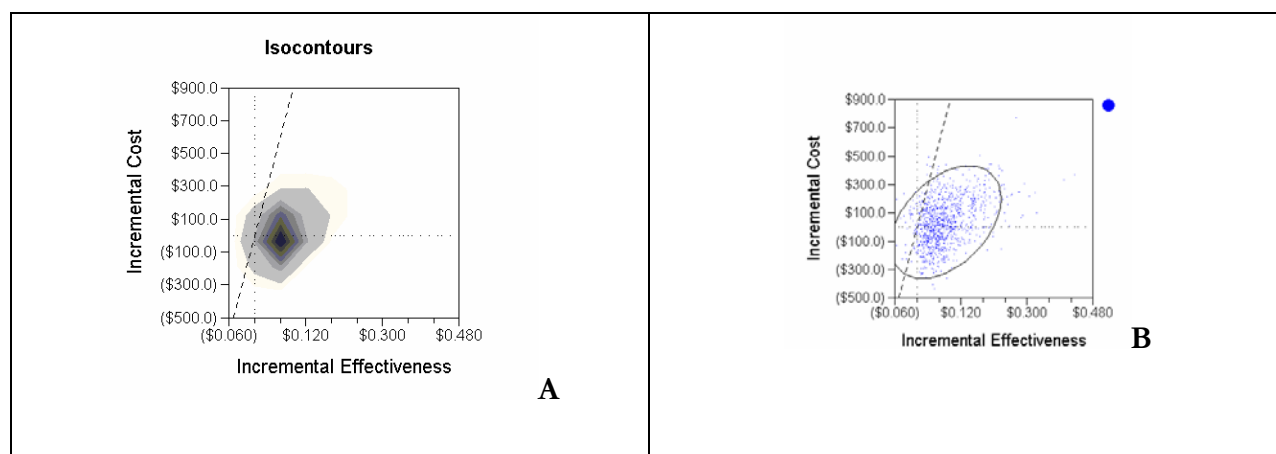

Figure 55 Isocontour Map of Incremental C/U ratio (A) and Ninety Five Percent Confidence Ellipse for Incremental C/U Ratio (B)

Area on C/U Plane	Probability
SN-PSG Dominant	41%
SN-PSG more effective, more expensive and Incremental C/U ratio less than 10,000	53.4%
SN-PSG more effective, more expensive and Incremental C/U ratio is greater than 10,000	1.5%
SN-PSG dominated	2.3%

The results of the Monte-Carlo simulation are very similar to the baseline pathway's results.

The incremental C/U ratio in the CPAP auto-titration pathway appears to be $500/QALY less than

the incremental C/U ratio of the baseline pathway. Clinical trials should be conducted on this SN-

PSG/CPAP auto-titration pathway to confirm parameter values [36]. One limitation to my results is

that that I assume that CPAP compliance rates are identical for patients titrated with PSG-titration and with CPAP-auto-titration. Compliance rates are probably lower for CPAP auto-titration patients since this test is less accurate in determining CPAP pressure [36,38-42].

Chapter 9

Conclusions

The forecasted healthcare funding shortfall will force policymakers to carefully evaluate the cost-effectiveness of medical interventions. Cost-utility analysis is the preferred form of economic evaluation in healthcare. This thesis uses cost-utility analysis to determine the optimal pathway with which to diagnose Obstructive Sleep Apnea Syndrome (OSAS).

This thesis finds that SN-PSG is the best procedure with which to diagnose OSAS. SN-PSG had the lowest C/U ratio of any intervention suggesting that it yields the greatest health benefit per dollar. SN-PSG is more costly and more effective than the UHPSM pathway since SN-PSG diagnoses and treats more patients. However, SN-PSG's extra cost is acceptable under a wide variety of assumptions. Univraite and bivaraite sensitivity analyses affirmed the model's robustness. A Monte-Carlo simulation found that the SN-PSG's incremental C/U ratio remained under $10,000/ QALY in over ninety percent of all trials. This incremental C/U ratio compares favorably with the incremental C/U ratio of interventions that compete for the same resources and against society's maximum WTP.

Some differences in methodology, study design, and assumptions limit detailed comparison with other CUAs of OSAS diagnostic pathways. For example, the study by Reuveni used a two-level decision tree, micro-costing, and compared overall process costs rather than incremental cost-utility ratios for PSG versus UHPSM [46]. Chervin's model was simpler and did not include the SN- PSG pathway [45]. Yet, because the same utilities and five-year time-horizon were used, some general comparisons can be made to Chervin's model. Both studies found that FN- PSG studies were more costly and more effective than the UHPSM and that the cost per QALY gained for PSG was reasonable compared to other medical interventions [45].

This study has several limitations. First, the study had to estimate the utility for symptomatic, OSAS-negative patients. However, the results of the physician utility studies suggest these estimates

were valid. Also, it is unlikely that this value affected the model's results since this health state occurred with equal frequency in each diagnostic pathway.

The lack of widely available cost data was another study limitation. In using Medicare reimbursement rates, it was assumed that any variation among these tests would be constant and similarly affect each pathway. There was, however, significant potential for an underestimation of the UHPSM pathway costs because the study did not include costs of lost or damaged equipment [28-32]. Also, the estimated probability for a successful CPAP auto-titration may have been overestimated in that it was based on data from multiple night trials [38,29].

Some potentially useful options for the evaluation and treatment of OSAS were not addressed in this analysis. For example, treatment alternatives to CPAP, such as oral appliances or surgical procedures were not included in the model. The combination of FN- PSG followed by CPAP auto-titration treatment for patients found to have OSAS has been suggested as a more cost-effective alternative [36]. My analysis suggests this could be a promising solution; however, further trials are needed to determine the affect of CPAP auto-titration or long-term CPAP compliance rates [38-42].

In summary, this study sought to compare the cost-effectiveness of three widely used OSAS diagnostic pathways. The modeled scenarios are detailed representations of standard pathways that are used in Unites States. The study finds that SN-PSG is the most cost-effective diagnostic procedure. Further studies assessing other diagnostic approaches can further contribute to policymaker's ability to address this important health issue in the most cost-effective manner possible.

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Appendix I

Appendix I shows a completed example of the questionnaire given to physicians to help determine health state utility values used in this study. The physicians were asked to complete a variety of questionnaires so that the relationship between HRQOL instruments could be measured. The results of the questionnaires show that many of these methods provide valid and responsive measurements of OSAS related QOL.

Appendix II

Appendix II shows a completed example of the HRQOL questionnaires given to patients with OSAS. This questionnaire consisted of the SF-6D and HUI (III) tests. This is the first time these tests have been used to determine the utility of health states associated with OSAS. Overall, the results suggest that these generic, preference-based, HRQOL measures are valid for patients with OSAS.

Appendix III

Appendix III documents Institutional Review Board authorization for eliciting patient utilities.

Appendix IV

Appendix IV documents the licensing agreement for use of the SF-6D Algorithm.

Appendix V

Appendix V shows the SF-36 HRQOL questionnaire. This is a generic, non-preference – weighted, HRQOL instrument. The SF-36 measures health status as an objective index of functioning, not the degree to which patients value this degree of functioning.

Appendix VI

Appendix VI shows the Sleep Apnea Quality of Life Index (SAQLI) questionnaire. This is a disease-specific, non-preference –weighted, HRQOL instrument. Unlike the SF-36, the SAQLI asks more specific questions to determine a patients functioning in health domains affected by OSAS,

Appendix VII

Appendix VI shows the EuroQol 5-D questionnaire. This is a generic, preference –weighted, HRQOL instrument. The pattern of responses to this questionnaire can be converted into a vNM utility value with a regression-based algorithm.