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Cost Effectiveness Analysis in Orthopaedic Surgery

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Abstract

COST EFFECTIVENESS ANALYSIS IN ORTHOPAEDIC SURGERY.

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The purpose of this thesis was to explore the use of cost effectiveness for interventions in orthopaedics. This was done through three cost effectiveness articles that have been published by the author. In each of these articles, similar methodologies were used. Decision models were constructed for cost-effectiveness analyses of competing orthopaedic interventions. Outcome probabilities and effectiveness values were derived from the literature. Effectiveness was expressed in quality adjusted life years gained. Cost data were compiled and verified from either hospital cost data or from Medicare data. Costs and utilities were discounted in accord with the United States Panel on Cost Effectiveness in Health and Medicine. Principal outcome measures were average incremental costs, incremental effectiveness, incremental quality-adjusted life years, and, in the case of one article, net health benefits. In particular the articles compared the following: 1. Core decompression versus conservative management for osteonecrosis of the hip as a way to delay hip replacement; 2. Total knee arthroplasty versus unicompartmental knee arthroplasty; and 3. Periacetabular osteotomy versus total hip arthroplasty for a young adult with developmental dysplasia of the hip. The more cost effective intervention was identified in each case, along with implications of the results for clinical and operative decision-making. Cost effectiveness was found to be a useful tool in orthopaedic surgery under limited circumstances of either scarce data on new interventions or the need to use more resources to achieve greater effectiveness. It also can provide excellent insight into ways to direct future clinical research.

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Introduction

The goal of clinical research is identify issues of concern to doctors and answer the questions that those issues raise [1]. Randomized trials are the gold standard for providing these answers [2]. Unfortunately, randomized trials pose several inherent difficulties to structure, especially in orthopaedic surgery. Most surgeries in orthopaedics have outcomes that are durable. They last for years without any need for revision. A randomized trial would need to follow patients over an extended span of time, which can be logistically complex. The problem becomes even more challenging when one tracks a cohort large enough to achieve statistical significance. Even if these challenges could be surmounted, they would not provide answers until long into the future. Decisions still need to be made in the short and medium term. The expertise that comes from experience can be used for interim decisions, and that expertise can be supplemented by decision analysis.

The typical use of decision analysis in economic circles has been to assess competing alternatives for achieving a common endpoint. Its use in orthopaedic surgery is to quantify variables for patient outcome and apply these numbers to a model that adequately represents reality [3-5]. To understand how this is the case, one must first have a clear definition of decision analysis.

Decision Analysis

The core idea of decision analysis is that resources are finite and that patient benefit must be maximized given finite resources. This differs from regular clinical judgment in that the information is quantified and the steps of the decision are put into a model. The model usually takes the form of a decision tree, with the choice under consideration at the base of the tree. The tree is built from left to right by adding successive branches. Each branch is made at a node, and each node has an outcome. Outcomes are quantified in a way that represent value for the patient.

In its simplest form a decision tree has only one decision to make, that of the first branch. In orthopaedic surgery this usually means choosing one surgical technique over another. All successive branches are constituted by chance nodes, in which each node is assigned a probability of occurring based on the chance of a certain outcome. The chance may be determined by a complication rate and a consequently mediocre outcome, by no complications and a consequently excellent outcome, by needing a revision, by death, or in fact by any clinically relevant event.

In building such a tree the burden of approximating reality is on the modeler. The outcomes and probabilities must come from the best possible evidence. When randomized trials are not available, other sources may be suitable. Observational trials constitute such a source, as do registries and claims databases. The latter may be especially useful with respect to cost calculations. All these must be accessed through a systematic review of the literature. Systematic review may already have been done in a database such as the Cochrane database, or it may need to be done by the modeler. Inclusion and exclusion criteria should be determined beforehand and should be transparent to anyone looking at the model. The goal of the literature review is to find clinically relevant outcomes and probabilities. Although a decision tree is formed before the onset of reviewing the literature, it should be continuously revised to reflect clinical reality as closely as possible. The literature review itself can help iterate and improve the tree.

Just as the exclusion/inclusion criteria should be transparent, the results of the literature review should be transparent. In fact they should comprise part of the reported methodology. In the ideal case the modeler would present a meta-analysis in which effect size is calculated according to a meta-regression. Study characteristics would be statistically controlled when calculating overall averages. In reality most decision analysis studies will compile simple means. There will also be cases in which the literature does not provide adequate results. This may be especially true for

quantified measurements of health outcomes. In such a case one may need to rely on expert opinion (i.e., the opinion of an experienced doctor involved in the modeling effort).

The quantification of health outcomes is in fact one of the more difficult tasks in developing a decision analysis. One may try to achieve objectivity by measuring an outcome as the absence of a well-known complication. In cardiology, for example, this could be the measurement of whether ventricular remodeling occurs after a myocardial infarction. The administration of an ACE inhibitor reduces the probability of such a complication. The percentage of patients who do not have ventricular remodeling would be the outcome. There are many limitations to such an approach, a discussion of which is outside the scope of this thesis.

The trend among researchers in the field of decision analysis is to include outcomes that represent the value experienced either by the patient directly or by society at large. To be specific, an extra year of life in a vigorous state of health may have a higher value for a patient than an extra year spent undergoing chemotherapy. That year may also be valued differently by society, which loses the benefit of an individual's contributions and, in some form, incurs the cost of treatment. Conventional opinion is that the best way to capture these differences is in the form of quality adjusted life years (QALYs) [6-8]. Numerically, QALYs are defined as the extra years of life achieved by the patient multiplied by a utility that represents the quality of living during those years. The utility is measured on a scale of 0 to 1, with 0 being death and 1 being the highest possible quality of life. In most cases these utilities are obtained from the patients themselves, using measurement techniques such as time tradeoff and standard gamble [6]. In a minority of cases, utilities are determined by a proxy for the patient, such as the doctor [9, 10]. There are questionnaires that assess utility, such as EuroQoL and the Short Forms. Additionally, there are new methods that translate Short Form 36 and Short Form 12 into utilities that range from 0 to 1 [11].

The next step is to cull the literature for probability rates of possible outcomes. The process for doing so is described above, and often the effort of finding appropriate outcomes leads one to discover corresponding probabilities and complications. This activity helps to fill in and further develop the decision tree. Once all of these data are established and appropriately modeled, one can run the tree. It can be run as a Markov model, if the states under consideration are best represented as iterations over an extended period of time. Alternatively, it can be run as a static decision tree, in which final outcomes – that is, outcomes at the far right of the tree – are multiplied by the probability of the branch that leads to them. These are then represented on the node that gives rise to the branch. The process is continued with probabilities and branches that precede each node. It is repeated until the single decision at the left-most side of the tree is reached. That yields a utility of one decision versus another, which in orthopaedics means one procedure versus another.

Such a static model is of course restrictive. Even with the most careful literature review and the most conscientious model development, one still does not capture even a small fraction of clinical reality. Sensitivity analysis offers enough flexibility to address this problem. Input for the model is varied along clinically relevant ranges, which is defined both from the literature and from expert opinion of doctors in the field. When limited evidence supports a particular variable, the range for the sensitivity analysis should be broad. When an abundance of evidence exists, the range can be narrow. In all cases the robustness of variables is assessed. Robustness determines how much a result depends on a specific variable. A result depends greatly on the value of a sensitive variable; it depends very little on the value of a robust variable. Put differently, a small change in a sensitive variable produces a large change in the final result. A large change in a robust variable produces a small change in the final result. Such an understanding of the model comes from one-way, univariate sensitivity analysis – that is, changing one variable at a time and

seeing what the consequent model outcome is. Whenever possible, one should also perform multivariate sensitivity analysis in which 2 or more variables are changed simultaneously and consequent model outcome is assessed. Even for weak models, this activity allows doctors to use results in a way that is much more likely to reflect the reality they face from day to day.

The entire process that has been described is in fact not cost effectiveness analysis. (See Appendix A for the distinction between cost effectiveness and cost utility.) It does not include cost. The inclusion of cost may appear simple at face value; in reality it poses tremendous challenges. First, one must decide whether they use readily available charge data, such as is published in Medicare diagnostic related groups (DRGs). These rarely reflect the actual expenditure to the care provider, and the difference can be either an underestimate or an overestimate. More accurate estimations often require permission to review hospital financial data and are more difficult to access. Fortunately, the accounting software of the hospital's financial department does an adequate job of assessing the resources used by an institution for a given procedure.

The other challenge is the perspective from which cost is calculated. The cost incurred by the individual is different than the cost incurred by the health care system. Premium-based insurance plans in fact create incentives for direct conflict between these two. Furthermore, the cost incurred by society is a third cost altogether. One way to grapple with the issue is to separate direct costs and indirect costs. Direct costs includes goods, services, and other resources that were consumed in the provision of care. Indirect costs include issues such as opportunity costs, which measure what cost an individual incurs when losing one opportunity in order to benefit from another opportunity. For example, a woman who misses several days of work to undergo a procedure benefits from the procedure but loses some amount of wage earnings. Another example of an indirect cost is when a spouse must spend time taking care of a patient in the post-operative

period instead of participating in other activities. In essence indirect costs capture the idea of cost from the perspective of society. For this reason they are favored by practitioners of cost effectiveness.

The assessment of indirect costs can be daunting. There is admittedly no satisfying solution, as of the writing of this thesis, to the challenge. It appears to be a common problem in the world of modeling outside of medicine as well, which suggests that it may be inherent to the methodology of decision analysis. Some physicians suggest that the calculations produced by hospital accounting software serve as adequate proxies for cost from a societal perspective, which includes indirect costs [6, 7].

The final step in the inclusion of cost is to ensure that monetary values accurately reflect the value of money in the present day. In the world of finance, there is enough liquidity and transparency in currency exchange that we can roughly assess the value of a currency with respect to goods and other currencies. This results in historical records of the changing value of money, which in the US has been a rate of inflation of 2-5% for the last 25 years. When data on outcomes are gathered, they must be discounted by a percentage rate that takes into account the real devaluation of our currency. The model can then use cost data expressed in current dollar values. The same requirement applies to projections into the future. Convention dictates that both costs and utilities should be discounted at approximately 5% [6, 7].

Decision analysis in orthopaedic surgery

Orthopaedic surgery as a field can benefit from decision analysis as it is described above. The following 3 articles illustrate the use of cost effectiveness analysis, with the application of the principles that have been laid out. These articles are the product of research conducted and

published by the author of this thesis. The first article analyzes the cost effectiveness of core decompression of a hip with osteonecrosis as a way to delay hip replacement. The second article analyzes the cost effectiveness of total knee arthroplasty versus unicompartmental knee arthroplasty. The third article analyzes the cost effectiveness of periacetabular osteotomy versus total hip arthroplasty in the treatment of the young adult with developmental dysplasia of the hip.

Methods

Cost-effectiveness Analysis of Core Decompression

General Framing and Design

This cost-effectiveness analysis follows the methodological guidelines of the Panel on Cost effectiveness in Health and Medicine convened by the US Public Health Service in 1993[6]. The panel outlined an explicit set of recommendations in a reference case analysis. These reference case guidelines established a common set of standards to improve the comparability of cost-effectiveness analyses. Issues addressed in the reference case analysis include standard practices for framing and perspective of the study, identification of outcomes, estimation of costs, and testing of uncertainty [6]. This study was constructed adhering to these standards.

Consistent with the reference case guidelines, this analysis compares the cost-effectiveness of core decompression to the commonly accepted treatment alternative of observation in the early stages of osteonecrosis. This analysis assumes a target patient population seeking treatment of femoral osteonecrosis at the age of 40 years. The time horizon of this analysis encompasses the remaining life expectancy for this target population.

The cost effectiveness ratios for observation and core decompression were analyzed from the societal perspective. The boundary of the analysis is limited to the costs and health effects directly impacting the target population. Estimates of costs, effectiveness, and the probability of various outcomes were obtained from literature review.

Literature Review

Literature review was used to construct the event pathways following observation and core decompression. A literature search identified 269 articles between 1978 and 2004 using the keywords osteonecrosis, decompression, hip, and outcome. Seventy- eight articles were identified as relevant to the treatment of osteonecrosis with either core decompression or observation. Fifteen publications were review articles and excluded from further analysis. The remaining articles were assessed on their quality. We excluded articles with fewer than 50 subjects. Additional criteria used to select articles included adequate reporting of magnetic resonance imaging staging and standardized surgical technique. A total of 11 studies were identified and selected for abstraction using these criteria. A summary of the abstracted data are included in Appendix B.

Decision Model

Decision tree software (TreeAge Pro; TreeAge Software Inc, Williamston, Mass) was used to create a model for the treatment of femoral head osteonecrosis [8, 12-17]. A simplified schematic of the decision tree is shown in Figure 1. The model begins with the decision for either observation or core decompression. Literature review was used to identify possible outcomes and their probability after each of these treatment alternatives. These event pathways were incorporated as branches in the decision tree. This model assumed a target population of patients seeking treatment of osteonecrosis at the age of 40 years. This age is consistent with the typical age at which core decompression is performed for osteonecrosis of the hip [18]. The time horizon of the model follows events through the remaining life expectancy of 39 years for this age group [19]. The event pathway for observation follows the clinical course of patients with early osteonecrosis and assumes that they become symptomatic and require THA after a 2-year period. This period is consistent with the natural history of osteonecrosis [18, 20, 21].

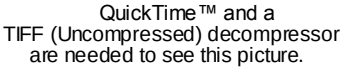

Figure 1: Simplified schematic of decision model for the treatment of femoral head osteonecrosis

The event pathways following core decompression were constructed following literature review. There has been a wide range of results reported on the efficacy of core decompression [22-30]. A reference case was created and assumed a period of 10 years before the need for primary hip arthroplasty after core decompression compared with 2 years with observation. This assumption is consistent with the more favorable reports of the results of core decompression. The efficacy of core decompression in delaying hip arthroplasty for this duration has not been definitively established in the published literature. Given this uncertainty, the effects on the cost-effectiveness of core decompression of both shorter and longer assumptions for its efficacy are examined in the sensitivity analysis. The primary complication included in the model following core decompression is subtrochanteric hip fracture requiring operative intervention. This complication has been infrequently reported, but rates as high as 5% have been published [22-30]. An intermediate value of 2% was selected for the reference case, and sensitivity analysis was used to examine the effect of rates in the range of 0% to 5%.

Subsequent events after observation and core decompression are modeled to include the potential need for hip arthroplasty and revisions over the lifetimes of the target population. Complications after hip arthroplasty include dislocation, infection, and death [31]. The decision model

incorporates the need for subsequent hip revision surgery and the possible complications that can arise. The incidence of complications is assumed to increase with subsequent revision procedures, whereas the durability of revision arthroplasty is assumed to decrease relative to primary arthroplasty [32-34]. The probabilities of infection, dislocation, and mortality used in this model are shown in Table 1. The rates of these complications were selected to fall in the midrange of estimates reported in the literature. Most studies have reported rates of infection leading to implant failure near the value of 1% used in the reference case of this study [32, 33, 35, 36]. Mortality and dislocation rates have not been as definitively established. The reference case of 0.5% for mortality is consistent with the low rates generally reported [37]. The dislocation rate of 2.5% used in the reference case is consistent with reports of large database studies [31, 33]. Sensitivity analysis was used to address the uncertainty of these assumptions for complication rates by examining the effect of higher and lower rates on the results.

Complication	**Probability (%)**
Complication rate primary THA	4
Infection	1
Dislocation	2.5
Mortality	0.5
Complication rate revision THA	10
Complication rate second or third revision THA	15

Table 1: Complication Rates Used in Decision Model After THA

Effectiveness

This study is a special case of cost-effectiveness analysis termed cost-utility analysis. Cost-utility analyses are differentiated by the fact that effectiveness is measured in units that incorporate a

subjective measure of utility such as quality adjusted life years (QALYs). The treatment of osteonecrosis has limited effect on survival but does result in significant changes in the quality of life of patients. The use of QALYs to measure effectiveness allows the survival of patients in different health states to be corrected for health related quality of life using a utility factor.

Utility factors were assigned to all health states in the model to adjust survival for quality of life. The reference case guidelines define utility along a continuum with a factor of 1.0 representing perfect health and a factor of 0.0 representing death [6] . Specific utility values for each health state in this study were assigned following a literature review. Table 2 lists the health states included in the decision model along with their corresponding utility values. Large-scale studies have used questionnaires to establish utility values for a variety of health states. Arthritis has consistently been shown to have a utility value near 0.7 [11, 38-40]. Knee and hip arthroplasties have been shown to increase quality of life weightings close to normal values. Based on these studies, this analysis uses a utility value of 0.9 for successful hip arthroplasty. Revision arthroplasty is given a lower utility value to reflect the diminished clinical results compared with primary arthroplasty. The utility values used for resection arthroplasty and surgical complications were also identified in literature review.

Health state	**Utility value**
Primary THA	0.9
Treatment of dislocation	0.5
Treatment of infection	0.5
Surgery and postoperative recovery	0.5
Death	0.0
Successful core decompression	0.9

Revision THA	0.85
Resection hip arthroplasty	0.6

Table 2: Utility Values for Health States Occurring in Decision Model

The period after successful core decompression was assigned a utility similar to that of successful arthroplasty. This reflects the assumption that successful core decompression results in a well-functioning hip but does not completely restore normal utility. The ability of core decompression to control symptoms and maintain a high level of function has not been definitively documented in the published literature. To address this uncertainty, sensitivity analysis was used to examine the impact of both higher and lower utility values after core decompression on its cost-effectiveness.

Costs

Gross-costing methodology was used to estimate the direct lifetime treatment costs after both observation and core decompression [6]. This methodology relies on global Medicare charge and reimbursement data to approximate the direct costs for various procedures. Indirect costs such as lost productivity were not included in this analysis. The surgical interventions occurring in the decision model were assigned their appropriate International Classification of Diseases, Ninth Revision; diagnosis related groups (DRGs); and Current Procedural Terminology (CPT) codes. Gross cost estimates were then determined for short-term care hospitalizations and physician services based on charge and reimbursement data for these codes. The cost estimates are shown in Table 3.

Procedure	**DRG (cost [$])**
Core decompression	210 (8086)
Primary THA	209 (9183)
Revision THA	209 (9183)
Resection arthroplasty	210 (8086)
Reduction of dislocated hip prosthesis	210 (8086)
Operative treatment of infected hip prosthesis	210 (8086)
Open reduction and internal fixation of hip fracture	210 (8086)

Table 3: Costs for DRG and CPT Codes Occurring in Decision Model Using 1998 Medicare Data

Gross cost estimates for short-term care hospitalizations were determined from mean hospital costs for the DRG associated with each intervention. Mean hospital costs were based on data from the Centers for Medicare and Medicaid Services reported for 1998 [41]. These costs are derived by applying Medicare cost-to-charge ratios to the data from the MedPAR data source [41]. The MedPAR data source is released annually by Medicare and provides cost estimates for each DRG. This study used the MedPAR data for 1998 pertaining to all US hospitals [41, 42].

The gross costs for physician services were determined from mean Medicare reimbursement for the CPT code associated with each surgical intervention. The mean reimbursement reported by the Centers for Medicare and Medicaid Services in 1998 for the Los Angeles, California, carrier was used. This global reimbursement includes preoperative care, surgical fees, and 90 days of postoperative care [43].

Discounting

Cost-effectiveness analysis requires that all future costs and health consequences be discounted and stated in their present-day values. Discounting is performed to correct for the fact that costs that are deferred to the future are preferable to immediate expenditures. Costs and health effects were discounted in the reference case at a constant rate of 3% annually. Sensitivity analyses were conducted with discount rates of 0% and 5% [6, 8].

Sensitivity Analysis

Sensitivity analysis was conducted to test the uncertainty of the reference case results. Cost effectiveness analysis combines information from several data sources to generate estimates of the probability of different outcomes and assign values to their utility and costs. Uncertainty about the true values of these underlying parameters results in uncertainty about the cost-effectiveness ratios generated in the reference case. Sensitivity analysis is used to determine the impact of varying the assumed values for key variables on the conclusions generated by the cost-effectiveness analysis.

Initially, cost effectiveness ratios were calculated using the reference case assumptions for both observation and core decompression. Sensitivity analysis was then performed using different assumptions for the values of the underlying variables [6]. Several key variables were selected for sensitivity analysis. These variables included the delay in hip arthroplasty resulting from core decompression, the functional utility after successful core decompression, the incidence of complications after core decompression, and the incidence of complications after both primary and revision hip arthroplasty.

Cost-Effectiveness Analysis of Unicompartmental Knee Arthroplasty as an Alternative to Total Knee Arthroplasty for Unicompartmental Osteoarthritis

This cost-effectiveness analysis follows the methodological guidelines of the Panel on Cost-Effectiveness in Health and Medicine convened by the United States Public Health Service in 1993[6]. Consistent with these reference case guidelines, the present analysis compares the cost-effectiveness of unicompartmental arthroplasty with the commonly accepted treatment alternative of total knee arthroplasty for unicompartmental arthritis. This analysis assumes a target patient population seeking treatment for unicompartmental arthritis at the age of sixty-five years. The time horizon of this analysis encompasses the remaining eighteen years of life expectancy for this target population [19]. The cost effectiveness ratios for unicompartmental and total knee arthroplasty were analyzed from the societal perspective. The boundary of the analysis is limited to the costs and health effects directly impacting the target population. Estimates of costs, effectiveness, and the probability of various outcomes were obtained from a literature review.

Literature Review

A literature review was used to construct the event pathways following initial treatment with unicompartmental knee arthroplasty and total knee arthroplasty. We identified 345 articles, published from 1975 through 2004, using the following keywords: unicompartmental, unicondylar, knee arthroplasty, results, outcomes, cost, and effectiveness. We included articles published in the years 1994 through 2004 in order to best reflect the results from the current clinical use of unicompartmental knee arthroplasty. We excluded studies involving fewer than fifty subjects. Additional criteria used to select articles included the selection of patients with an intact anterior cruciate ligament and documented unicompartmental disease and the exclusion of patients who had a prior patellectomy or tibial osteotomy. A total of nine studies were identified

and selected for abstraction with use of these criteria [44-52].

Decision Model

Decision-tree software (TreeAge Pro; TreeAge Software, Williamstown, Massachusetts) was used to create a model for the treatment of unicompartmental arthritis [8, 12-17]. A simplified schematic of the decision tree is shown in Figure 2. The model begins with the decision for either unicompartmental or total knee arthroplasty. A literature review was used to identify possible outcomes and their probability following each of these treatment alternatives.

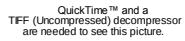

Figure 2: Simplified schematic of the decision model for the treatment of unicompartmental arthritis of the knee. TKA = total knee arthroplasty, and UKA = unicompartmental knee arthroplasty.

The event pathways following unicompartmental knee arthroplasty and total knee arthroplasty were constructed following the literature review. A wide range of results has been reported on the effectiveness of unicompartmental knee arthroplasty [44-53]. The reference case assumes a period of twelve years for the durability of a unicompartmental arthroplasty. This assumption is consistent with results of unicompartmental knee arthroplasty in the nine studies selected for data abstraction [44-52]. Sensitivity analysis was used to examine the effects on the cost-effectiveness of unicompartmental knee arthroplasty of both shorter and longer assumptions for its durability.

Total knee replacement was assumed in the reference case to have a survival of fifteen years. This value is longer than the survival assumed for unicompartmental knee replacement and reflects the fact that long-term outcomes have been more thoroughly documented for total knee replacement [54].

Subsequent events following unicompartmental knee arthroplasty and total knee arthroplasty were modeled to include the potential need for revision total knee arthroplasty as well as complications over the lifetime of the target population. Complications included infection and death[54]. The rates of these complications were selected to fall in the midrange of estimates reported in the literature. Most studies have described rates of infection leading to implant failure near the value of 1% used in the reference case of this study [54-56]. The reference case of 0.5% for mortality is consistent with the low rates generally reported [56].

Effectiveness

Utility factors were assigned to all health states in the model to adjust survival for quality of life. The reference case guidelines define utility along a continuum with a factor of 1.0 representing perfect health and a factor of 0.0 representing death [38]. Specific utility values for each health state in this study were assigned following a literature review (Table 4). Arthritis has been shown to have a utility value near 0.723 [38]. Knee and hip arthroplasty have been shown to increase quality-of-life weightings close to normal values. On the basis of these studies, this analysis uses a utility value of 0.9 for successful unicompartmental and total knee arthroplasty [11, 38-40]. Revision arthroplasty is given a lower utility value to reflect the diminished clinical results compared with primary arthroplasty. Previously published data were used to assign a utility value of 0.6 for resection arthroplasty and 0.5 to periods of surgery and postoperative recovery following complications [40]. Sensitivity analysis was used to examine the effect of uncertainty about the utility values for unicompartmental knee arthroplasty and total knee arthroplasty on the

cost-effectiveness results.

Health State	Utility Value
Primary total knee arthroplasty	0.9
Unicompartmental knee arthroplasty	0.9
Treatment of infection	0.5
Surgery and postoperative recovery	0.5
Death	0.0
Revision total knee arthroplasty	0.85
Resection knee arthroplasty	0.6

Table 4: Utility Values for Health States Occurring in the Reference Case of the Decision Model

Costs

Gross-costing methodology was used to estimate the direct lifetime treatment costs following both unicompartmental and total knee arthroplasty [6]. The surgical interventions occurring in the decision model were assigned their appropriate ICD-9 (International Classification of Diseases–Ninth Revision), DRG (Diagnosis-Related Group), and CPT (Current Procedural Terminology) codes. Gross-cost estimates for acute care hospitalizations were determined from mean hospital costs for the DRG associated with each intervention. The mean hospital costs were based on data from the Centers for Medicare and Medicaid Services reported for 1998 [57]. These costs are derived by applying Medicare cost-to-charge ratios to the data from the Medicare Provider Analysis and Review File (MEDPAR) data source [57]. The MEDPAR data source is released annually by Medicare and provides cost estimates for each DRG [42, 57]. The gross costs for physician services were determined from the mean Medicare reimbursement for the CPT code associated with each surgical intervention (Table 5) [43].

	DRG		**CPT**	
Procedure	*Code*	*Cost*	*Code*	*Cost*
Unicompartmental knee arthroplasty	209	$9183	27446	$1445
Primary total knee arthroplasty	209	$9183	27447	$1951
Revision total knee arthroplasty	209	$9183	27487	$2298
Resection arthroplasty	210	$8086	27488	$1348
Operative treatment of infection around knee prosthesis	210	$8086	27310	$797

Table 5: Costs for DRG and CPT Codes in Decision Model with Use of 1998 Medicare data. Values are based on 1998 United States dollars. DRG = Diagnosis-Related Group, and CPT = Current Procedural Terminology.

Discounting

Cost-effectiveness analysis requires that all future costs and health consequences be discounted and stated in terms of their present-day values. Discounting is performed to correct for the fact that costs that are deferred to the future are preferable to immediate expenditures. Costs and health effects were discounted in the reference case at a constant rate of 3% annually [6, 8].

Sensitivity Analysis

Sensitivity analysis was used to determine the impact of varying the assumed values for key variables on the conclusions generated by this cost-effectiveness analysis. Cost effectiveness analysis combines information from several data sources in order to generate estimates of the probability of different outcomes and to assign values to their utility and costs. Uncertainty about the true values of these underlying parameters results in uncertainty about the cost-effectiveness

ratios generated in the reference case. Sensitivity analysis was performed with use of different assumptions for the values of the underlying variables [6]. Several key variables that were selected for sensitivity analysis included the durability of unicompartmental knee replacements relative to total knee replacements, the functional utility following unicompartmental arthroplasty, and the cost of unicompartmental knee arthroplasty.

Cost-Effectiveness Analysis of Periacetabular Osteotomy

General Model Overview

The model and analysis in this study were constructed according to the guidelines set forth by the Panel on Cost- Effectiveness in Health and Medicine by the United States Public Health Service in 1993 [6, 7, 58].

We compared the cost-effectiveness of periacetabular osteotomy and total hip arthroplasty in young adults with developmental dysplasia of the hip. The upper age limit of our population was forty-five years, and the time horizon of the model was thirty years. The cost-effectiveness for the two procedures is reported from a societal perspective, which accounts for costs and outcomes that are important for society rather than for the payer, the physician, or any other single entity [59]. Effectiveness and outcome probabilities were obtained from the literature or estimated when data were lacking.

The analysis was performed through a decision tree by using a common decision-analysis package (TreeAge Pro 2005; TreeAge Software, Williamstown, Massachusetts). An essential component of this model was the assumption of a linear annual failure rate for periacetabular osteotomy and total hip arthroplasty. A systematic review of the literature and expert opinion were used to validate the decision tree [9, 60-71]. We searched PubMed through September 2006

for articles using the terms ‘‘periacetabular osteotomy’’ and ‘‘total hip arthroplasty.’’ Inclusion criteria were a sample size of greater than twenty-five hips, follow-up of longer than three years, mean patient age of forty-five years or less, quantitative outcomes reported as Harris hip scores, and outcomes reported by Tonnis grade for periacetabular osteotomy. All data points for total hip arthroplasty, except for cost, were taken from the literature. Where data were not available for periacetabular osteotomy, we took the most conservative estimate based on the expert opinion of two senior orthopaedic surgeons. The model included only objective outcomes. Pain, although not directly assessed, was taken into account by use of the Harris hip score. Because several periacetabular osteotomy studies have shown a correlation between postoperative success and the preoperative radiographic grade of coxarthrosis [65, 70, 72, 73], we ran the model once for each Tonnis grade, measuring costs and outcomes for each run. Total hip arthroplasty outcome was the same regardless of preoperative radiographic coxarthrosis grade [66].

Decision Model

Our decision tree (Fig. 3) consists of two primary treatment arms: periacetabular osteotomy and total hip arthroplasty. Branching points thereafter represent complications and terminate in outcomes. Outcomes were assigned a quantitative health-related quality of-life value derived from the literature. Clinical outcome probabilities, including complications and failure rates, were derived from the literature. The total hip arthroplasty arm of the model is similar to past models of arthroplasty [9, 74, 75]. The weight of each variable was explored by means of multivariate sensitivity analysis.

Figure 3: Main decision tree. PAO = periacetabular osteotomy; THA = total hip arthroplasty; DDH = developmental dysplasia of the hip; OA = osteoarthritis; HO = heterotopic ossification

Table 6 summarizes the sensitive variables used in the model. Sensitive variables yield quantitatively large effects on model outcome and are hence addressed in detail herein. In contrast, robust variables are those that, as determined by sensitivity analysis, do not significantly affect model outcome. Probability inputs for the model were annual probabilities derived by dividing the overall failure rate by the average follow-up time reported in the literature, thereby yielding a linear failure rate. For total hip arthroplasty, the complications modeled were aseptic and septic failure. Our model represents quality of life after a successful revision total hip arthroplasty as being slightly lower than quality of life after a successful primary total hip arthroplasty [76, 77]. Similar to a previously validated total hip arthroplasty model, aseptic failure included prosthetic wear, loosening, and breakage [9]. The literature reports an annual aseptic

failure rate in the range of 1.9% to 3.7% [74, 78-83]. We selected a weighted average of the above studies at an annual aseptic failure rate of 2.6%.

Variable	**Value**
Probability of Primary Aseptic Failure	.026 per annum
Average Lifespan of THA	14 years
Average Lifespan of PAO	10 years
Utility of an Excellent Outcome	1.0

Table 6: Sensitive variables used in the model. Sensitive variables have a significant effect on model outcome.

For periacetabular osteotomy, the complications modeled were periacetabular osteotomy failure resulting in conversion to total hip arthroplasty, periacetabular osteotomy revision secondary to overcorrection or undercorrection, and heterotopic ossification. Failure rates of periacetabular osteotomy were modeled to be different according to Tonnis grade, with rates of 1%, 3%, and 9% for Tonnis grades 1, 2, and 3, respectively [70]. The probability of revision was modeled to be 4% [68], and the probability of heterotopic ossification was 2.4% [70]. Other possible complications, such as neural or vascular injury, were so rare [63] and transient that they exerted no effect on cost and effectiveness and were thus excluded from the model.

The longevity of total hip arthroplasty varies with respect to the population in which the procedure is performed. When it was possible, we used total hip arthroplasty studies that described results in an age group similar to that in which periacetabular osteotomy is a treatment option. By extracting data from articles that directly report a mean or median survival of total hip arthroplasty [80, 82, 84], and by confirming those values by extrapolating median survival

through an assumption of a linear failure rate, we found that survival of total hip arthroplasty ranges from 6.6 to 25.9 years [74, 78-82]. The value we chose to use, fourteen years, is the weighted average of the above trials.

Because of the lack of longer-term follow-up with periacetabular osteotomy, the longevity of the procedure is still unknown. In order to determine a survival range for sensitivity analysis, we extrapolated the median survival of periacetabular osteotomy by assuming a linear failure rate in articles describing follow-up for periacetabular osteotomy beyond four years. The resulting range of values for median survival was 8.6 to 19.6 years, while the weighted mean survival was ten years [60, 68, 70, 72, 73, 85, 86]. For the best and worst-case scenarios, we used empirical data derived from studies describing the survivability of periacetabular osteotomy in hips with more than four years of follow-up [71, 72, 85], ranging from 7.1 years in one study [85] to twelve years (twenty-two of twenty-six hips) in another [73]. The value chosen for our reference case was ten years, and it was based on the weighted mean survival reported above.

Medical Costs

Cost data (not charge data) were compiled and verified with use of our institution's activity-based costing software (IDX, Burlington, Vermont) that tracked our hospital decision support system. Cost data are reported in 2004 U.S. real dollars. The range of values was determined by identifying the lowest and highest costs in our patient cohort. Costs for heterotopic ossification were estimated, and the impact of estimating that cost was assessed in the sensitivity analysis. When we varied the cost of heterotopic ossification from $5000 to $15,000, it changed the breakeven points by less than one month, which is negligible over the multiple year time horizon of our model. Thus, estimating the cost of heterotopic ossification was not deemed important. Costs were discounted at a rate of 5% in order to yield the present monetary value. The time of failure of a hip impacted cost— hips that failed earlier incurred potentially more cost in the time

course of the model.

Utilities

We determined effectiveness in terms of health-related quality of life, which was ascertained by applying the continuous utility assessment method devised by Hazen et al. [10] and applied to total hip arthroplasty by Chang et al. [9]. We mapped health-related quality of- life values to Harris hip scores according to the system of Chang et al., and patient utility analyses done before and after total hip arthroplasty [56, 67, 87]. Consistent with the outcomes reported in the literature, a successful primary periacetabular osteotomy in hips with Tonnis grade-1, 2, and 3 coxarthrosis had health-related quality-of-life values of 1.0, 0.8, and 0.6, respectively [70]. The same health-related quality-of-life value was given to either total hip arthroplasty or periacetabular osteotomy, according to the outcome assessed by Harris hip scores, and a corresponding adjectival rating was given. In our final analysis, utility values were multiplied by the discounted number of years spent in a health state to yield quality adjusted life years (QALYs) gained. QALYs were discounted at a rate of 5% to yield present value [6, 8, 12]. As with cost, the time of failure of a hip impacted the outcome patients with a hip that failed earlier potentially may live longer with a lower health related quality of life. A successful total hip arthroplasty subsequent to failure of a periacetabular osteotomy was assigned a good health-related quality-of-life outcome of 0.8 rather than the excellent outcome of 1.0, associated with a primary total hip arthroplasty.

Incremental cost-effectiveness ratios were used to aid comparison of treatments. The incremental cost-effectiveness ratio presented in the results is averaged over the thirty-year time horizon of the model. The incremental cost-effectiveness ratio is calculated as follows: (CostPAO – CostTHA) / (QALYsPAO – QALYsTHA), with PAO indicating periacetabular osteotomy and THA indicating total hip arthroplasty. The net health benefit was used as a measure of outcome

from a societal perspective because it takes into account the willingness of the health-care system to pay (WTP). The net health benefit may be calculated as QALYs – Cost /WTP [88]. The net health benefit, while not usually reported in the orthopaedic literature, is used in other specialties as it offers the advantage of easy comparison between different treatment strategies. When two cost-saving treatments are compared, the better modality has the higher net health benefit, whereas it would have the lower incremental cost-effectiveness ratios since incremental cost-effectiveness ratios can be expressed in negative terms [88-91].

Sensitivity Analysis

Sensitivity analysis addressed the uncertainty inherent to drawing data from multiple sources [6]. In the case of our model, variables that made a substantial contribution to results were deemed to be sensitive, whereas those that contributed <1% to the total outcome were deemed robust. We varied sensitive variables according to coxarthrosis, measured radiographically as grade 1, 2, or 3 according to the method of Tonnis [92].

An expanded sensitivity analysis was conducted on the average duration of Tonnis-grade 1 and grade-2 hips after periacetabular osteotomy on the basis of a best-case and a worst case scenario for survival. For these two end-point scenarios, we chose the lowest and highest average survival rates reported in the literature for periacetabular osteotomy [73, 85]. We did not do this for Tonnis grade-3 hips because changing the value of hip survival does not change the results substantially.

Results

Cost-effectiveness Analysis of Core Decompression

Reference Case Results

A reference case was created that assumed that core decompression delays the need for THA for 10 years. Given the uncertainty of this assumption, the effects on the cost-effectiveness of core decompression of both shorter and longer assumptions for its efficacy are examined in the sensitivity analysis.

In the reference case, the pathway of core decompression is assumed to delay hip arthroplasty for 10 years and resulted in 20.20 QALYs, whereas observation resulted in 19.75 QALYs. This represents an incremental gain of 0.45 QALYs when core decompression was chosen over observation. Core decompression generated total expected lifetime treatment costs of $27498. This results in an incremental increase in cost of $4298 when compared with the lifetime treatment costs of $23200 for observation followed by arthroplasty. This led to an incremental cost-effectiveness ratio of $9551 for each QALY gained when core decompression was chosen over observation.

Sensitivity Analysis

Effect of Changing the Assumed Length of the Delay in the Need for THA After Core Decompression.

The reference case assumes that core decompression delays hip arthroplasty for 10 years as compared with 2 years with observation in the early stages of osteonecrosis. Core decompression has not been definitively demonstrated to result in delays of this length. There are conflicting reports in the literature, with some authors showing delays of this length and others reporting

results below this threshold [18, 93]. Sensitivity analysis was used to evaluate the effects of varying the underlying assumption for the success of core decompression on its cost effectiveness ratio. The cost effectiveness of core decompression decreases as its assumed ability to delay hip arthroplasty decreases. The cost effectiveness ratio rises to more than $25000 per life year as the period of delay falls below 7 years. The $50000 cost per life year gained threshold is passed as this period falls below 5 years.

Effect of Function After Core Decompression.

The reference case assumes that successful core decompression prevents painful symptoms during the period it is delaying the need for primary arthroplasty. This control of pain is reflected in the high utility value of 0.9 assigned to patients during this waiting period. Sensitivity analysis was conducted to model clinical situations in which core decompression does not perform well in mitigating the functional limitations caused by advancing osteonecrosis. The cost-effectiveness ratio of core decompression rises to more than $50000 per QALY gained when the utility during the period after the procedure and before conversion to THA is assumed to be lower than 0.86.

Effect of Complication Rate After Core Decompression.

Subtrochanteric hip fractures complicating core decompression have been reported infrequently, although some studies have shown rates as high as 5%. Sensitivity analysis demonstrated that the cost-effectiveness ratio rose or fell only slightly over the range of values from 0% to 5%. Even at an assumed fracture rate of 5%, the cost-effectiveness ratio of core decompression remained lower than $12000 per QALY.

Effect of Complication Rates After Arthroplasty.

The rates of complications after THA have been reported by several authors [31, 33-37]. The assumed durability of hip arthroplasty and incidence of complications including death,

dislocation, and infection were selected to be in the midrange of accepted values. Sensitivity analysis was used to examine the impact of using high- and low-range values for these variables. As the assumed complication rates after hip arthroplasty decrease, core decompression becomes a less cost-effective treatment option. This occurs because some of the cost-effectiveness gains from core decompression result from the delay or avoidance of the costs and negative health impacts that result from these complications. However, these effects were not large and did not alter the conclusions of this study. Even under conditions in which the complication rates of THA are assumed to be negligible, core decompression remained highly cost-effective with an incremental cost effectiveness ratio lower than $13000 per QALY gained.

Effect of Discount Rate.

Analyses assuming discount rates of 0% and 5% in addition to the baseline assumption of 3% were conducted. These variations in the discount rate did not have a large impact on the cost-effectiveness ratios. A discount rate of 0% led to an incremental cost effectiveness ratio for core decompression of $12429 per QALY gained. A discount rate of 5% resulted in a ratio of $9620 per QALY gained. These ratios fall well below the threshold of $50000 per QALY commonly used to judge procedures as moderately cost-effective [6].

Cost-Effectiveness Analysis of Unicompartmental Knee Arthroplasty as an Alternative to Total Knee Arthroplasty for Unicompartmental Osteoarthritis

Reference Case Results

A reference case was created with use of the assumption that unicompartmental arthroplasty results in a high level of function for twelve years. The assumption of twelve years of function is

consistent with that in published clinical series, but there are limited data available that directly compare the durability of unicompartmental knee replacement and total knee replacement [44-53]. Given the uncertainty of this assumption, the impact on the cost-effectiveness of unicompartmental arthroplasty of both shorter and longer assumptions for its effectiveness is examined in the sensitivity analysis.

In the reference case, the pathway of unicompartmental knee arthroplasty resulted in a small gain in effectiveness to 12.21 quality-adjusted life years compared with 12.19 quality adjusted life years when total knee arthroplasty is chosen. There was minimal change in costs, with an increase from $18,995 to $19,000 (in 1998 United States dollars). The incremental cost-effectiveness ratio for unicompartmental knee arthroplasty under the reference case assumption is negligible with a cost of $277 per quality-adjusted life year gained. This ratio indicates that unicompartmental knee arthroplasty was more effective than total knee arthroplasty, and this increased effectiveness required a minimal additional cost.

Sensitivity Analysis

Effect of the Durability of Unicompartmental Knee Replacement Compared with Total Knee Replacement

The durability of unicompartmental knee replacements remains uncertain relative to total knee replacements. Sensitivity analysis was used to evaluate the effects of this uncertainty by varying the underlying assumption for the durability of unicompartmental knee replacements and determining the changes to the cost-effectiveness ratio. The cost effectiveness of unicompartmental knee arthroplasty is lost as the durability of the implant is assumed to decrease. The reference case assumes a survival of fifteen years for primary total knee replacement. The assumption of a longer survival for total knee replacement compared with unicompartmental knee replacement reflects the longer experience and more complete documentation of the durability of

total knee replacement. The cost-effectiveness of unicompartmental knee arthroplasty relies largely on its ability to produce clinical results approaching those of total knee arthroplasty. In sensitivity analyses that assume unicompartmental knee replacement has a survival of eleven years, it becomes both less effective (12.16 compared with 12.19 quality-adjusted life years) and more costly than standard total knee arthroplasty ($19,233 compared with $18,995). This scenario results in total knee arthroplasty becoming a dominant choice. Specifically, total knee arthroplasty becomes both more effective and less costly when unicompartmental knee replacement is assumed to have a survival below the threshold of eleven years (Table 7).

Values Used in Sensitivity Analysis	Incremental Cost of Unicompartmental Compared with Total Knee Arthroplasty	Incremental Effectiveness of Unicompartmental Compared with Total Knee Arthroplasty (QALY)	Incremental Cost-Effectiveness Ratio of Unicompartmental Compared with Total Knee Arthroplasty (Cost/QALY)
Reference case Unicompartmental knee replacement survival assumed to be 12 yr. Total knee replacement survival assumed to be 15 yr.	+$5	+0.02	$277
Scenario 1 Unicompartmental knee replacement survival assumed to be 11 yr. Total knee replacement survival assumed to be 15 yr.	+$238	0.03	TKA is dominant
Scenario 2 Unicompartmental knee replacement survival assumed to be 17 yr. Total knee replacement survival assumed to be 20 yr.	+$6,236	+0.13	$45,958
Scenario 3 Unicompartmental knee replacement survival assumed to be 15 yr. Total knee replacement survival assumed to be 20 yr.	+$6,859	+0.05	$117,103
Cost of unicompartmental knee arthroplasty increased by 25%	+$2,661	+0.02	$165,354
Cost of unicompartmental knee arthroplasty decreased by 25%	-$2,652	+0.02	Unicompartmental knee replacement is dominant

Table 7: Incremental Costs, Effectiveness, and Cost-Effectiveness Ratios with Use of Reference Case and Sensitivity Analyses

Multivariate sensitivity analysis was also performed with use of a broader range of fifteen to twenty years for the expected durability of total knee replacement. These analyses indicated that it is necessary for the assumed survival of the unicompartmental knee replacement to be within three to four years of the assumed survival of the total knee replacement in order to maintain the cost-effectiveness of choosing unicompartmental knee arthroplasty. This is demonstrated by analyses that assume that total knee replacement survival is twenty years. With use of this assumption, the incremental cost-effectiveness ratio of unicompartmental knee arthroplasty is $45,958 per quality-adjusted life-year gained compared with total knee arthroplasty when a unicompartmental knee replacement is assumed to survive for seventeen years. This is below the commonly accepted threshold of $50,000 per quality-adjusted life year often used to determine cost effective procedures [6, 9]. In contrast, when the survival of a unicompartmental knee replacement is assumed to be fifteen years and the survival of a total knee replacement is assumed to be twenty years, the incremental cost-effectiveness ratio increases to more than $100,000 per quality-adjusted life-year gained (Table 7). The incremental cost effectiveness ratio continues to increase, and the cost-effectiveness of unicompartmental knee arthroplasty decreases as the survival of a unicompartmental knee replacement is assumed to be lower relative to the survival of a total knee replacement.

Effect of Function Following Unicompartmental Knee Arthroplasty

The initial published findings indicate that unicompartmental knee arthroplasty results in function that is at least comparable with that seen after total knee arthroplasty [44, 46-52, 94]. The reference case reflects these results by assuming that both unicompartmental knee arthroplasty and total knee arthroplasty result in a high level of function and pain relief. However, there are a limited number of controlled studies that have directly compared the clinical function after unicompartmental knee arthroplasty and total knee arthroplasty. This uncertainty was addressed in a sensitivity analysis that examined the effect of higher and lower values for the utility of unicompartmental knee arthroplasty on its cost effectiveness.

The reference case results show a small gain of 0.02 quality-adjusted life years when unicompartmental knee arthroplasty is chosen over total knee arthroplasty. These gains are lost when the utility of unicompartmental knee arthroplasty is assumed to be less than that of total knee arthroplasty. Conversely, there is a further incremental increase in the cost-effectiveness when the utility of unicompartmental knee arthroplasty is assumed to be >0.9. When unicompartmental knee arthroplasty is assigned the maximal value of 1.0, it results in a total of 13.20 quality-adjusted life years as opposed to 12.19 quality-adjusted life years for a gain of 1.01 quality-adjusted life years. Unicompartmental knee arthroplasty becomes a more cost-effective choice under these assumptions, as the gains in incremental effectiveness increase with no additional cost relative to the reference case.

Effect of Cost of Unicompartmental Knee Arthroplasty

There is a small incremental additional cost from unicompartmental knee arthroplasty with use of the reference case assumptions for the relative costs of unicompartmental and total knee arthroplasty. The minimal cost increase in the reference case results from the assumption that there is a decrease in the physician's fee for unicompartmental knee arthroplasty relative to the fee reimbursement for total knee arthroplasty. Unicompartmental knee arthroplasty becomes a

less cost-effective alternative in a sensitivity analysis in which the cost of unicompartmental knee arthroplasty is assumed to be higher than the cost of total knee arthroplasty. An increase of 25% resulted in an incremental cost-effectiveness ratio of $165,354 per quality adjusted life year gained when unicompartmental knee arthroplasty was chosen over total knee arthroplasty. This indicates that the cost-effectiveness of unicompartmental knee arthroplasty may be lost if it requires a large relative increase in cost compared with total knee arthroplasty (Table 7 above).

The use of gross costing based on Medicare reimbursement does not account for the potential savings of unicompartmental knee arthroplasty from implant costs or decreased hospital length of stay. This is due to the fact that both unicompartmental knee arthroplasty and primary total knee arthroplasty are assigned the same DRG, resulting in a similar cost assumption for the hospital stay. A sensitivity analysis was performed to examine the effect of a 25% cost-savings in a comparison of unicompartmental knee arthroplasty with total knee arthroplasty. A decrease of 25% in the assumed costs of unicompartmental knee arthroplasty resulted in an overall savings of $2652 in the lifetime treatment costs compared with those of primary total knee arthroplasty (Table 7 above).

Cost-Effectiveness Analysis of Periacetabular Osteotomy

Cost

Costs were averaged over the thirty-year time horizon of the model. The average cost of total hip arthroplasty in all three Tonnis grades of coxarthrosis was $32,790. In Tonnis grade-1 and grade-2 hips, periacetabular osteotomy yielded a cost of $26,592 and $30,673, respectively. The cost of periacetabular osteotomy in Tonnis grades 1 and 2 was cost-saving compared with total hip arthroplasty, i.e., it was below the abscissa in Figure 4. Periacetabular osteotomy in Tonnis grade 3 was associated with a cost of $33,465, which resulted in an incremental cost (above the abscissa

in Figure 4) of $675.

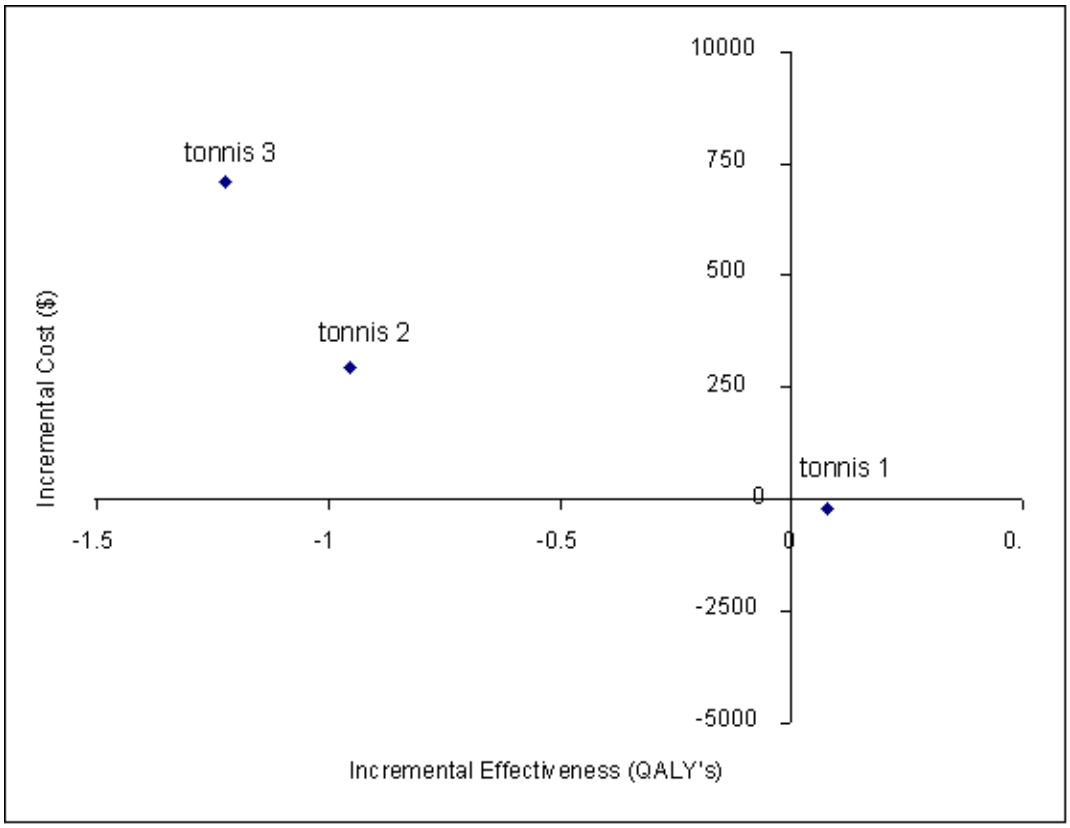

Figure 4. Average incremental costs and incremental quality-adjusted life years for peri-acetabular osteotomy (PAO) compared with total hip arthroplasty (THA).

Effectiveness

QALYs gained were averaged over the thirty-year time horizon of the model. In each of the three Tonnis grades of coxarthrosis, total hip arthroplasty resulted in an average of 4.7QALYs gained. Periacetabular osteotomy in Tonnis grade-1, 2, and 3 hips yielded an average of 4.85, 3.3, and 3.2 QALYs gained, respectively. Compared with the QALYs gained with total hip arthroplasty, the increment in QALYs gained with periacetabular osteotomy in Tonnis grade-1 coxarthrosis was 0.15 (represented in Figure 4 by the data point for Tonnis grade-1 hips lying to the right of the ordinate). In addition, for Tonnis grade-2 and grade-3 hips, total hip arthroplasty yielded, on the

average, more QALYs (both data points lie to the left of the ordinate) than did periacetabular osteotomy (Fig. 4).While over thirty years, total hip arthroplasty is more effective (i.e., it yields more QALYs) on the average than periacetabular osteotomy in Tonnis grade-2 coxarthrosis, periacetabular osteotomy becomes the more effective treatment by year 19.4 of the model. For Tonnis grade-3 coxarthrosis, total hip arthroplasty is and remains more effective throughout the time period of the model.

Cost-Effectiveness and Incremental Cost-Effectiveness

Cost-effectiveness ratios were averaged over the thirty-year time horizon of our model. The cost-effectiveness ratio of total hip arthroplasty was $11,631/QALY for all three Tonnis grades. In Tonnis grade-1, 2, and 3 coxarthrosis, periacetabular osteotomy had a cost-effectiveness ratio of $7856/QALY, $10,807/ QALY, and $15,005/QALY, respectively. Since periacetabular osteotomy in Tonnis grade-1 coxarthrosis is, on the average, both more effective than total hip arthroplasty and more cost-saving (lower right quadrant in Figure 4), it is the dominant procedure in this setting. For Tonnis grade-1 coxarthrosis, periacetabular osteotomy is more cost-effective over thirty years and surpasses total hip arthroplasty in cost-effectiveness at 5.5 years. In Tonnis grade-2 coxarthrosis, periacetabular osteotomy is less costly than total hip arthroplasty on the average but also less effective (lower left quadrant in Figure 4). While both incremental cost and effectiveness are negative for periacetabular osteotomy in Tonnis grade-2 coxarthrosis, the former effect is greater than the latter effect, making periacetabular osteotomy ultimately more cost-effective than total hip arthroplasty in this grade, with an associated incremental cost-effectiveness ratio of –$824/QALY. For Tonnis grade-2 coxarthrosis, periacetabular osteotomy is more cost-effective over thirty years and surpasses total hip arthroplasty in cost-effectiveness at 18.25 years. Periacetabular osteotomy was both more costly and less effective on the average than total hip arthroplasty in Tonnis grade-3 coxarthrosis (upper left quadrant in Figure 4); as a result, total hip arthroplasty is the dominant procedure in this setting.

Net Health Benefits

Figures 5 and 6 depict the results for the two treatments in terms of net health benefits. In Tonnis grade-1 coxarthrosis (Fig. 5), periacetabular osteotomy yields a greater net health benefit after 10.1 years in comparison with total hip arthroplasty. In Tonnis grade-2 coxarthrosis (Fig. 6), periacetabular osteotomy reaches equivalence by 19.1 years, after which it becomes dominant. If periacetabular osteotomy can be expected to have a greater longevity than the crossover points of 10.1 years and 19.1 years for Tonnis grade 1 and 2, respectively, then periacetabular osteotomy as a treatment would be preferable to total hip arthroplasty in terms of net health benefits. Finally, at no point does periacetabular osteotomy yield a negative net health benefit in both Tonnis grades 1 and 2, whereas total hip arthroplasty does so at 23.5 years and 25.1 years, respectively. These results are summarized in Table 8, which shows how long (in years) a periacetabular osteotomy must survive to become the preferred treatment modality.

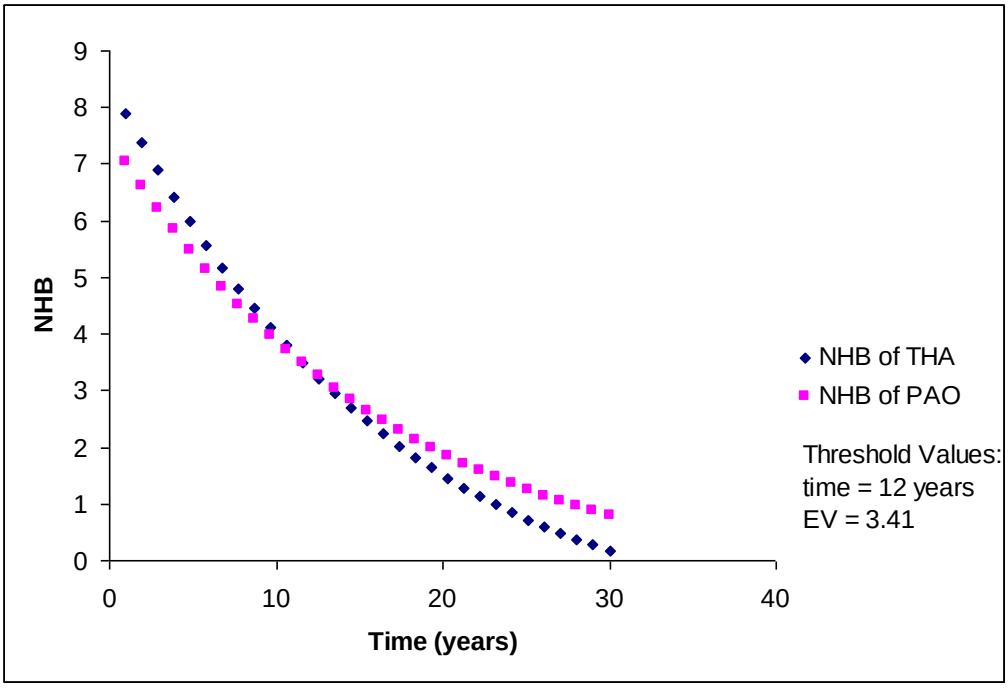

Figure 5. Tönnis 1 Incremental Net Health Benefits $/QALY's (WTP = $50,000).

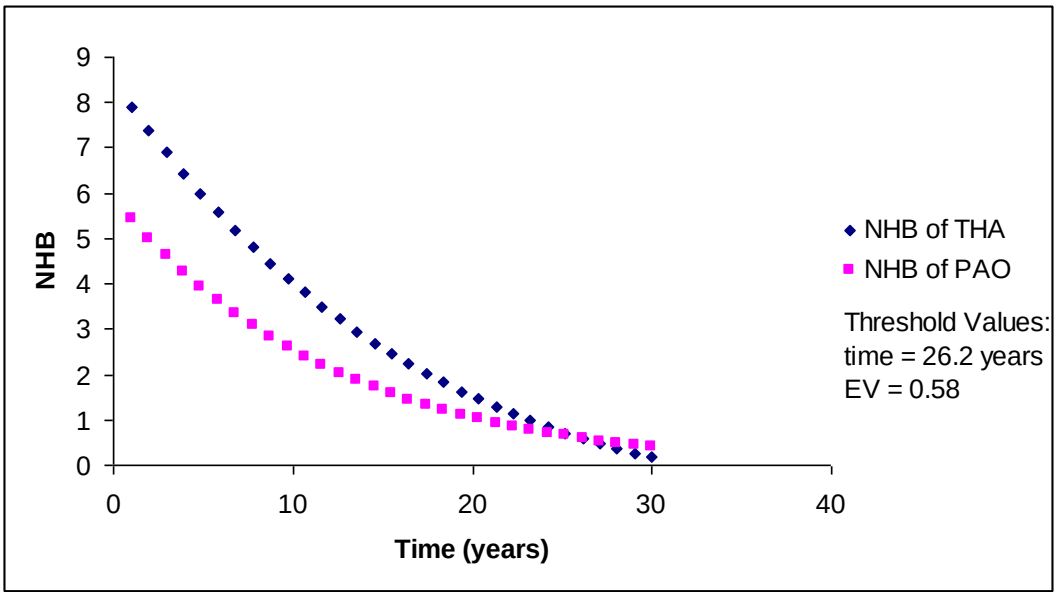

Figure 6. Tonnis 2 Incremental Net Health Benefits $/QALY's (WTP = $50,000).

		Effectiveness	**Cost**	**Cost Effectiveness**	**NHB**
Survival of PAO needed to be preferred treatment (years)	**Tönnis grade 1**	10.8	PAO always preferred	5.5	10.1
	Tönnis grade 2	19.4	PAO always preferred	18.25	19.1
	Tönnis grade 3	THA always preferred	THA always preferred	THA always preferred	THA always preferred

Table 8. The number of years PAO needs to survive for it to be a preferred treatment over THA, given assessment by either Effectiveness, Cost, Cost-Effectiveness or NHB (Net Health Benefits).

Sensitivity Analysis

We performed a multivariate sensitivity analysis for each Tonnis grade. Multivariate analysis identified five consistently sensitive variables for Tonnis grades 1 and 2 that contributed >99% of the total variability in outcome: (1) average lifespan of the periacetabular osteotomy, (2) probability of a failed periacetabular osteotomy, (3) average lifespan of a total hip arthroplasty, (4) probability of an aseptic revision, and (5) utility of excellent outcome.

We summarize the results of our worst and best-case analyses in Table 9. The cost-effectiveness and effectiveness of periacetabular osteotomy improved considerably as the functional life of the Tonnis grade-1 hip after periacetabular osteotomy increased. In the worst-case scenario, periacetabular osteotomy is, on the average, more cost-effective than total hip arthroplasty and reaches equivalence at 11.45 years for Tonnis grade-1 coxarthrosis. In the worst-case scenario for Tonnis grade-2 coxarthrosis, periacetabular osteotomy, while it is not more cost-effective, on the average, than total hip arthroplasty, reaches equivalence at 18.6 years. The range of reaching equivalence is broader from best-case to worst-case scenarios for Tonnis grade-1 compared with Tonnis grade-2 coxarthrosis because periacetabular osteotomy survival is not as sensitive a variable for the latter. For both Tonnis grade-1 and grade-2 hips, periacetabular osteotomy always remained below $50,000 per QALY gained for all of the values we tested in our sensitivity analysis.

	Tönnis grade 1		**Tönnis grade 2**	
	Avg CE ($/QALY) : EV time (years)	**Avg E (QALYs) : EV time (years)**	**Avg CE ($/QALY) : EV time (years)**	**Avg E (QALYs) : EV time (years)**
Worst case scenario	- 5689 : 11.45	-1.1 : 16.35	200 : 18.6	-1.9 : 19.8
Reference	-7856 : 5.5	.15 : 10.8	- 824: 18.25	- 1.4 : 19.4

case				
Best case scenario	- 8800 : 2.45	1.0 : 5.9	- 1152 : 17.8	-1.1 : 19.2

Table 9. Sensitivity analysis based on worst case and best case durability of a PAO hip showing average incremental cost-effectiveness (Avg CE), average incremental effectiveness (Avg E), the time point where equivalence between PAO and THA is attained (EV time) in terms of cost-effectiveness and effectiveness, and the peak effectiveness of PAO in terms of maximum potential gain in QALYs over the time span of our model.

Discussion

With each passing year, healthcare costs consume an ever increasing percentage of our Gross Domestic Product (GDP) [95]. Disease burden in the US is no greater than in peer countries of the Organization for Economic Co-operation and Development (OECD), but our input costs are intrinsically more expensive [96]. Unfortunately, we are getting a bad deal for this high price, at least by the metrics we claim to be important. Within the group of OECD countries, the US has among the highest infant mortality rates, the lowest life expectancies, and the greatest level of obesity [97]. We pay a premium cost for an inferior result.

One possible reason for this combination is our reimbursement structure. Before 1982, the government reimbursed physicians according to the cost of a procedure. Resource intensive procedures predictably acquired favor. Diagnostic related groups (DRGs) were instituted to address the perverse incentive of trying to use more resources in order to increase reimbursements. The new incentive created by DRGs, however, was to spend less time per procedure in order to perform as many procedures as possible. We still do not know with precise statistics how this dynamic has affected outcomes in medical practice.

Most recently, there have been attempts to link reimbursement to outcome metrics, such as quality or efficiency [98]. There are several potential requirements to make a value-based reimbursement structure that focuses first and foremost on patient welfare while still accounting for resource constraints. Two of the most prominent requirements are unambiguous measures of quality and accurate measurements of cost. Within the realm of orthopaedic surgery, this thesis presented 3 articles that compared quality and cost for alternative treatments.

Defining costs

Costs can be direct or indirect, as was discussed in the introduction. In terms of cost effectiveness analysis, this is usually where researchers end their measurements. That is a mistake. Considerations of other types of cost are crucial, in particular fixed cost, variable cost, average total cost, and marginal cost.

Fixed cost is defined as a cost that does not vary with usage. The cost of an operating room table is an example. The hospital buys the table and installs it. The cost of doing so remains the same no matter how many times it is used. Fixed costs can change over the long term, however, especially if the product depreciates. The operating table may require, for example, more maintenance as it gets older. A subset of fixed costs that cannot change over the long term is sunk costs. These costs occur when an item with a fixed cost cannot be used for any other purpose in the short term or long term. An old operating table might be used for instructional purposes in another setting, but the operating suite itself has only one purpose. The former is a regular fixed cost; the latter is a sunk cost.

Variable costs change according to the amount of output being produced. The salaries of scrub nurses paid on a per time basis are examples of variable costs, as they increase with both longer surgeries and with the number of surgeries performed. The amount of gloves and towels used for a surgery constitute another example. Total costs equal fixed costs plus variable costs.

Average total cost is simply the total cost divided by the quantity produced. Marginal costs are the cost of producing one extra unit. Marginal cost differs from average total cost when the production of an extra unit raises or lowers the variable cost. In the corporate world the difference between the two is obvious. When workers in a car factory make their first car, they become more proficient at their job. Production of their second car is therefore done more rapidly and with fewer mistakes (i.e., variable cost goes down). Production of their third car improves as well,

although data show that the rate of improvement decreases – that is, there is a negative second derivative that represents diminishing returns. This means that marginal cost is less with each subsequent car, up to a certain plateau.

Perhaps the same applies to the learning curve of a surgeon for a new procedure. The state of surgery research, however, is that none of this has been studied. From an economics perspective, we do not have good data on marginal costs in the healthcare environment. This is acceptable when deciding whether to apply a new intervention to a population that is receiving no intervention at all. In that case average total costs can be used. It is a problem in cases such as the articles in this thesis, in which one compares a newer procedure to a more established procedure. Marginal cost is a more sensible approach for comparing competing procedures [99, 100].

Interpreting results

The driving reason for doing a cost effectiveness analysis is ambiguity. If a newer intervention were both more effective and less costly, it would be adopted without hesitation – indeed, without analysis. Analysis is necessary for two reasons: 1. Cases in which the effectiveness and cost of the newer intervention are not known with accuracy; and 2. Cases in which the newer intervention is superior in just one category, typically in being more effective, but inferior in the other category, typically in being more costly.

For the first reason, cost effectiveness analysis is done to give a range of values that a doctor can use in his practice. This was the case for the knee arthroplasty article in this thesis. The costs of the procedures were not easily available to the researchers, especially the indirect costs as usually represented in hospital accounting software. We were compelled to use DRG charge data and validate these data with costs from the literature. Additionally, the outcome of the newer procedure, the unicompartmental knee arthroplasty, was not known with any statistical power.

We therefore conducted a sensitivity analysis with several scenarios to explore how long the unicompartmental knee arthroplasty would need to last before revision in order to be as cost effective as a total knee arthroplasty. The take-home message for an orthopaedic surgeon is that a UKA does not need to last as long as a TKA to be as cost effective. It could last 3 - 4 years less, and this difference held whether the duration of the TKA were 20 years, 15 years, or some value in between. The experienced orthopaedic surgeon could assess how long his total knees last and prognosticate accordingly.

The PAO article illustrates both cases. There is an ambiguity about the effectiveness of PAO, and PAO may be superior in only one category, cost or effectiveness. Data on the outcomes of PAO are scarce. This was one of the motivations for conducting research on it. We wanted to understand, at a minimum, how long a PAO must last in order for it to be a worthwhile procedure compared to THA. The answer to this question happened to differ according to Tonnis grade. For it to be worthwhile just in terms of effectiveness in Tonnis grade 1, it needed to last 10.8 years. For it to be worthwhile just in terms of effectiveness in Tonnis grade 2, it needed to last 19.4 years. In Tonnis grade 3 it was never more effective, and when cost was factored in, these numbers changed. PAO was found to be less costly in Tonnis grades 1 and 2 and more costly in Tonnis grade 3. For example, when factoring in cost and effectiveness for Tonnis grade 1, a PAO needed to last only 5.5 years to be the preferred choice. In Tonnis grade 2 it needed to last 18.25 years to be preferred.

By reporting the results in this manner, we gave the orthopaedic surgeon the option to use them as he wishes. If money were no object, it would mean that the surgeon would use only the duration thresholds for effectiveness. In resource-limited environments, by contrast, the duration threshold for cost-effectiveness could be considered.

This approach also demonstrates the situation in which PAO may be better in only certain settings. Specifically, PAO was found to be much less costly on average in Tonnis grade 1. It was also found to be slightly more effective. If one believes that these assertions are well founded, the decision to use PAO is automatic. In this setting PAO is the dominant choice. Similarly, in Tonnis grade 3 PAO is both more costly and less effective. If one believes that these particular assertions are well founded, one must conclude that THA in this setting is dominant. Beyond the usefulness of quantifying these issues and analyzing them in a transparent structure, cost effectiveness analysis is a worthy exercise in the middle scenario. For PAO, this was Tonnis grade 2, where PAO is less costly than THA but on average is also less effective. This grey zone is where the orthopaedic surgeon will seek out data to make a judgment. In the absence of data, a model such as ours can be used, which is precisely what was represented in Figure 4 in the results section for PAO.

Limitations of cost effectiveness

Perhaps one of the greatest limitations of this kind of research comes from the state of research in orthopaedic surgery. There is such a shortage of well-conducted, large randomized trials in orthopaedics that the data sources for the models are limited. Even the most well constructed model has little value when its inputs are of low quality. The gold standard for assessing clinical benefits is the randomized controlled trial. In the case of many orthopaedic procedures, and certainly in the case of the ones assessed in this thesis, this is not easily feasible. Such trials would take years to complete and would have prohibitive costs. By the time they were completed, the technology of the field would have evolved to a new stage.

Large registries are an acceptable alternative, such as the nationwide hip registry in Sweden. Indeed, much of my THA data comes from that registry. Whether or not such a registry is

possible in a country without a national healthcare system, such as the US, is still an open question.

Another problem with assessing cost and effectiveness in medicine in general is that the best way to do so would be to integrate these factors into the very methodology of every prospective clinical trial. Tracking resource use and assessing outcomes should in fact be done simultaneously in order to understand specific links between which resources lead to which outcomes. Unfortunately, the data points required to achieve statistical significance for economics variables are much greater than those needed for clinical variables. The addition of economic analysis to a clinical trial is therefore highly likely to make the trial underpowered [100, 101].

Given this situation, we face a problem of "garbage in, garbage out." The only time the issue can be avoided is when the older technology has an established abundance of data, such as with THA. In that case we can use sensitivity analysis on the newer technology to assess when and how it can be useful. As pointed out, this approach was used in the analysis of PAO and THA.

There is also a concern with the methodology of cost effectiveness analysis. QALYs are by definition subjective measurements of value. They depend on individual preferences, translated into utilities, and these individual preferences are then applied to the general public. There may be huge variations for any given patient on how they value an extra year of life with, for example, the ability to walk free of pain [102, 103]. Furthermore, differences in these preferences may vary dramatically across cultures as well as within professions that have greater physical demands [104]. There is also the considerable ethical problem that QALYs by definition will be less for older patients with fewer remaining years of life and for patients with co-morbidities that guarantee a lower baseline utility. All of these issues highlight that cost effectiveness is a relative

measure. It should be used to enhance clinical judgment with the comparative thresholds and benchmarks it can produce. Absolute statements of cost effectiveness are not useful.

Cost effectiveness analysis can also be used to advance the state of research. Models allow us to estimate, for example, an adequate population size needed to conduct a randomized trial. They would also inform us how much time would be required for completion. These models can help identify which variables (i.e., duration of the implant, complication rates, patient characteristics) are most influential in determining the total cost effectiveness of the procedure. A doctor can then pay particular attention to these in the decision process. A researcher can use these to target fruitful areas of inquiry [105], and in fact the model itself may prove simply that no conclusions can be drawn until more powerful data are gathered on sensitive variables. Finally, cost effectiveness helps us determine whether the information in the literature is specific enough. If in fact it is too general, then it serves as a warning to the researcher or surgeon that patients should be subdivided depending on characteristics. For PAO versus THA, for example, this could mean subdivision of THA into several categories of implants, such as ceramic on ceramic, metal on metal, and ultra-high molecular weight polyethylene.

Appendix A – Definition of Cost Utility Analysis

Each article contained the term cost effectiveness in it, but this term is a misnomer. A cost effectiveness analysis, in the strict sense, measures health outcomes in units that are specific to the two procedures under comparison. For example, a fractured femur could potentially be fixed by external fixation or by internal fixation. One common outcome shared by these two methods is the rate of nonunion. The cost of each procedure would be compared with nonunion rates in a cost effectiveness analysis. In essence a cost effectiveness analysis uses an outcome that is deemed important by the doctor.

By contrast, a cost utility analysis uses units that are standardized to all potential procedures, and the unit of outcome takes into account the preferences of the patient. The current consensus for a standardized unit is the quality adjusted life year (QALY), which equals the number of extra years of life, or in the typical case for orthopaedics, extra years of function, multiplied by the utility of those years for the patient. While utility assessment can be difficult, there are methods for its calculation. One example is the Rosser Index Matrix, which determines patient utility on a scale of 0 to 1 by comparing disability ratings of orthopaedics patients to the self-reported distress of the patient [106]. Once these standardized utilities are obtained, a cost utility analysis can be performed, as was done in the articles here.

Nonetheless, convention favors the use of cost effectiveness to mean cost utility. For the sake of ease, I follow this convention.

Appendix B – Literature Review for Core Decompression

A.1. Summary of Literature Search

A.1.1 Search Strategy

Keywords (in permutation)	**Osteonecrosis, decompression, hip, outcome**
Dates	1978-2004
Total articles	269
Articles not relevant	191
Relevant articles analyzed	78
Excluded reviews	15
Excluded articles <50 subjects	30
Excluded articles that failed criteria	22
Articles remaining from 78	11

A.1.2. Randomized Control Trial Used for Core Decompression and Conservative Treatment

A.1.2.1. Randomized control trial, more than 50 subjects

• Ref [30]

A.1.3. Articles Used for Core Decompression

A.1.3.1. Prospective, more than 50 subjects

• Refs [22, 24-26, 28, 29].

A.1.3.2. Retrospective, more than 50 subjects

• Refs [23, 27].

A.1.4. Articles Used for Conservative Treatment

• Refs [20, 21].

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