THE HEALTH AND ECONOMIC OUTCOMES OF MANAGING COMPLEX PROXIMAL HUMERUS FRACTURES IN THE ELDERLY

Sanjeeve Sabharwal MBBS MRCS MSc

Imperial College London

Department of Surgery and Cancer

2016

Thesis submitted for the degree of Doctor of Medicine (Research)

Declaration of Originality

I hereby declare that this thesis is entirely my own work and that any additional sources of information have been appropriately cited.

Copyright Declaration

The copyright of this thesis rests with the author and is made available under a Creative Commons Attribution Non-Commercial No Derivatives licence. Researchers are free to copy, distribute or transmit the thesis on the condition that they attribute it, that they do not use it for commercial purposes and that they do not alter, transform or build upon it. For any reuse or redistribution, researchers must make clear to others the licence terms of this work.

Abstract

Proximal humerus fractures represent a significant burden to society in terms of disability to patients and healthcare costs. This thesis investigates the costs, health outcomes and cost-effectiveness of treatment strategies for the management of complex proximal humerus fractures in elderly patients.

A meta-analysis of randomised trials comparing treatment strategies was performed. A qualitative clinical study was conducted exploring patient perceptions of their injury and recovery. A cost-analysis based on the principles of time-driven activity base costing was conducted to investigate the institutional burden of treatment costs relative to the national tariff. Finally, two separate health economic evaluations (HEEs) were performed which investigated the cost-effectiveness of existing treatment strategies over a 2-year and a 20-year time horizon.

Sub-group and sensitivity meta-analysis demonstrated that clinical outcomes were improved for patients undergoing hemiarthroplasty for 4-part fractures. Qualitative analysis revealed that patients perceived the following themes as important in their recovery; pain, sleep, shoulder function, emotional state, support networks, relationship with health professionals and experience of healthcare institution. The cost analysis found that there were wide variations in treatment costs and large institutional losses were incurred if hemiarthroplasty was performed. The HEEs found that hemiarthroplasty was the most cost-effective treatment strategy, however the 20-year model was less prone to uncertainty based on sensitivity analysis.

Despite a quantifiable benefit to health outcomes when hemiarthroplasty is performed in an elderly population with complex fractures, the national tariff in the English NHS may not adequately reimburse hospitals that perform this procedure. Furthermore, this inequity in

financial reimbursement extends beyond the penalisation of clinically effective treatment; hemiarthroplasty also represents the most cost-effective treatment strategy for complex proximal humerus fractures in the English NHS. Finally, the measures of health outcomes within this field need further development so that they better represent the perceptions of the target population.

Acknowledgements

The last 2 years have been a thoroughly enjoyable and rewarding experience for me. Many of the people who have supervised and contributed to my research have not only played a role in my academic development, they have become mentors in my clinical practice, and more importantly they have become good friends.

Firstly I would like to thank my supervisors Mr Chinmay Gupte and Mr Peter Reilly. Both have committed a great deal of their time and expertise to shaping, guiding and improving the research presented in this thesis. During the 2 years spent with them, the support and commitment they have offered to improve my clinical and academic skills have been unbelievable. Both are exemplary mentors who have profoundly shaped my outlook on how I wish to develop and practice as an orthopaedic surgeon in the years to come.

I was very lucky to have had the expertise and oversight of Professor Thanos Athanasiou in my meta-analytical work. He is one of the most accomplished and published academics in this field and I am immensely grateful for the time he spent shaping and correcting my methodology and analysis. My qualitative analysis would not have been possible without the efforts and guidance of Dr Stephanie Archer. Stephanie has extensive experience with this kind of work and she helped me design the study, seek ethical approval and conduct the analysis. My cost analysis chapter required a thorough understanding of costing in the NHS. Alex Carter, a health economist at Imperial College invested a great deal of time in working on the project and improving my understanding of the subject matter. Mr Alvin Chen, a previous MD student in the department, had conducted a costing study on total knee replacement which I also contributed to. The paper we published together and our subsequent discussions played an important role in my eventual study design. Professor Anja Kern of DHBW Mosbach in Germany, and a visiting fellow at Imperial College also gave her time to

improve my understanding of global healthcare costing. Other contributors to the study design and analysis were Professor Lord Ara Darzi and Mr Abbas Rashid.

The health economic analysis was perhaps the most taxing part of the thesis. In the early stages of this work I believed that learning and understanding about health economics had accelerated my ageing. However, it was only when I started to learn how to use Treeage, the software for performing decision analytical modelling, that I recognised the complexity of the task I had taken on. Dr Melody Zhifang Ni, a lecturer and postdoctoral fellow in decision analysis at the LSE and Imperial, appeared at the very point I was on the verge of giving up. She has done a remarkable job guiding me through the analysis and educating me on health economic principles. I would also like to thank Mr Dylan Griffiths, who helped with my qualitative study design and contributed to much of the clinical consensus that was required in shaping my decision analytical models.

On a personal note I would like to thank my incredible parents for constantly encouraging me to pursue what was has been a long-standing ambition, to undertake an MD. Their endless commitment and interest in my development never wanes, and it's because of their hard work that I have been able to achieve so many of my life goals. Finally, thank you to my wonderful wife Amita and our amazing children, Ishaan and Anoushka. This break from clinical training has allowed us to spend more time together as a family and has made these 2 years the best of my life. You are the inspiration for all my efforts and I dedicate this work to you.

Table of Contents

List of Tables 10

List of Figures 13

Abbreviations used in Thesis 19

Chapter 1 Introduction 20

1.1 Epidemiology of Proximal Humerus Fractures 20

1.2 Patho-mechanics of injury 22

1.3 Fracture Classification 23

1.4 Limitations of fracture classification systems 28

1.5 Quantitative Outcome Measures 29

1.6 Qualitative Outcomes 34

1.7 An Overview of Treatment Modalities 36

1.8 Health Economics Considerations 41

1.9 Scope of the Thesis 47

1.10 Rationale for the Thesis 47

1.11 Thesis Aims 49

Chapter 2 Meta-analysis evaluating the effect of fracture complexity and choice of surgical intervention on treatment effects in the management of proximal humerus fractures 51

2.1 Introduction 51

2.2 Methods 52

2.3 Results 55

2.4 Discussion 71

Chapter 3 A qualitative study exploring elderly patients' perceptions of their recovery after sustaining a complex proximal fracture 78

3.1 Introduction 78

3.2 Methods 79

3.3 Results 82

3.4 Discussion 96

Chapter 4 Cost analysis of surgical treatment of proximal humerus fractures: an evaluation of cost drivers and comparison of institutional treatment cost with the national tariff 105

4.1 Introduction 105

4.2 Materials and Methods 107
4.3 Results 114
4.4 Discussion 124
Chapter 5 Cost effectiveness analysis of management strategies for complex proximal humerus fractures: a 2 year time horizon based on a decision analytical model 131
5.1 Introduction 131
5.2 Methods 134
5.3 Results 147
5.4 Discussion 165
Chapter 6 Cost effectiveness analysis of different management options for complex proximal humerus fractures: a 20-year time horizon based on Markov decision analysis 170
6.1 Introduction 170
6.2 Methods 172
6.3 Results 182
6.4 Discussion 197
Chapter 7 Discussion 203
7.1 Summary of Findings 203
7.2 Research Limitations 206
7.3 Future Work 209
7.4 Conclusions 211
References 213
Appendix 1: Data Collection Sheets for Meta-Analytical Study 236
Appendix 2: Qualitative Study Documentation 253
Appendix 3: Cost Analysis Documents and Data 271
Appendix 4: Supplementary Data and Methods in Economic Analysis 291
Appendix 5: Supplementary Data and Methods in Markov Economic Analysis 304
Appendix 6: Copyright and Permissions for inclusion of my own published research, as well as figures and tables from other authors. 309

List of Tables

Table 1.1. Adapted Thudichum Classification as described by Dr Stig Broroson[25]. 24

Table 1.2. Components of the Constant-Murley Score and scoring for individual parameters. Adapted from Constant et al[50]. 31

Table 1.3. Summary of types of HEEs. Adapted from Kernick[103] with Permissions from the BMJ (license 3794190641446). 43

Table 2.1. Characteristics of studies included in the meta-analysis 60

Table 2.2. Sensitivity analysis of Constant Scores based on choice of surgical intervention and risk of bias showing no significant effect on treatment effect or heterogeneity between trials 67

Table 2.3. Sensitivity analysis of QALYs based on choice of surgical intervention and risk of bias showing a significant improvement for the study where >80% of cases where treated with hemiarthroplasty compared to conservative management. Moderate heterogeneity was also found within studies with low risk of bias. 68

Table 2.4. Sensitivity analysis of secondary surgery rates based on choice of surgical intervention and risk of bias showing a significantly reduced risk of re-operation for patients managed conservatively compared to surgically in trials where >80% of cases were treated with a locking plate. Similar effect identified on evaluation of trials at low risk of bias. 69

Table 2.5. Sensitivity analysis of adverse events rates based on choice of surgical intervention and risk of bias showing a significantly reduced risk of for patients managed surgically in trials where >80% of cases where hemiarthroplasty. High risk of heterogeneity detected between trials based on predominant type of surgical intervention. 70

Table 2.6. Trials registered in the WHO International Clinical Trials Registry Portal investigating surgical versus conservative treatment of proximal humerus fractures (Search Performed on the 5th January 2016) 74

Table 3.1. Interview prompt schedule that was referred to during patient interviews 82

Table 3.2. Patient demographics and management strategies employed 84

Table 4.1. Case scenario used to define medical condition and patient population. Barthel score fully detailed for staff during interview process. The inpatient length of stay is based on mean length of stay for proximal humerus fractures at our institution. 110

Table 4.2. Table showing examples of how activity cost was estimated within the CDVC. Also included within the analysis were a minimum and maximum capacity cost for staff based on possible variations in earnings, a minimum and maximum activity range based on expected variations in activity times

and a minimum and maximum overall activity cost. Full details on capacity cost assumptions and calculations provided in Appendix 3. 116

Table 4.3. Mean costs for all 3 procedures based on variations in staff capacity-cost rates and proposed activity times. 117

Table 4.4. Implant specific procurement costs for locking plate. 118

Table 4.5. Implant specific procurement costs for soft tissue reconstruction. 118

Table 4.6. Implant specific procurement costs for hemiarthroplasty. Sterilisation costs were included for each tray in the overall theatre consumable cost calculations (£80 per instrument tray). 118

Table 4.7. Calculation of institutional reimbursement based on 2013/2014 Payment by result (PbR) tariffs. Market force factors are valued at 1.2417. 120

Table 5.1. Characteristics of 5 studies used to determine outcome probabilities used in decision tree model. 137

Table 5.2. Summary of model input values for complications. 138

Table 5.3. Summary of model input values for complications requiring secondary surgery. 138

Table 5.4. Input parameters for costing based on national tariffs 140

Table 5.5. Summary of input parameters for QALYs in health economic model 144

Table 5.6. Summary of outputs generated from cost-effectiveness analysis performed on the model. 149

Table 5.7. Summary of variation of input parameters on the decision analytical model. 164

Table 6.1. Characteristics of 5 studies used to determine outcome probabilities used in Markov chain model. 175

Table 6.2. Transitional probabilities for complication rates after primary management for each intervention. Each Markov cycle represents a 2-year time period. 176

Table 6.3. Summary of model input values for complications requiring secondary surgery 177

Table 6.4. Life tables used in MCM. Each cycle is 2 years and ends at the age shown in the table. The probability of death represents the risk of death before the next cycle starts and is based on data from the Office of National Statistics in the UK[287]. 177

Table 6.5. Input parameters for cost based on national tariff. The 'revision state' costs are calculated based on a weighed-mean of the different secondary procedures performed in the 5 RCTs used to inform this HEE. 179

Table 6.6. Summary of input parameters for QALYs in health economic model 181

Table 6.7. Summary of outputs generated from cost-effectiveness analysis performed on the MCM. 183

Table 6.8. Summary outputs generated from MCM analysis performed with increased age-specific mortality. 193

Table 6.9. Summary outputs generated from MCM analysis performed with institutional cost estimates. 196

Table 6.10. Summary of variation of input parameters on MCM. 197

List of Figures

Figure 1.1. Year-on-year increases in admissions to hospitals in the English NHS with a proximal humerus fracture. 21

Figure 1.2. The Neer four fragment classification for proximal humerus fractures[6]. Image used with permissions from Wolters Kluwer (Reference 160119-000702)....26

Figure 1.3. The Binary (Lego) description as proposed by Hertel et al[33]. There are 6 possible fractures dividing the humerus into 2 fragments (1-6). There are 5 possible fractures dividing the humerus into 3 fragments (7-11). There is 1 fracture pattern dividing the humerus into 4 fragments. Image used with permission from Elsevier and Copyright Clearance Centre (License 3792510310271)....28

Figure 1.4. Structured framework of thematic analysis as described by Braun and Clarke[85]. Permissions for use of image obtained from Taylor & Francis Group....36

Figure 1.5. Flowchart by Murray et al[96] depicting factors that influence decision-making in the management of patients with a proximal humerus fracture. Permissions obtained from the Bone and Joint Journal. 39

Figure 1.6. Publication of research on the management of proximal humerus fractures by modality of surgical treatment since 1975. Data obtained from Scopus ® document search.....41

Figure 1.7. Decision analytical model applied to determining large NHS cost-effectiveness study of cemented, cementless and hybrid hip replacement[130]. Data was input to the model from national registry data. Permissions for image use obtained from BMJ (License 3795880171673). 47

Figure 2.1. PRISMA Flow Diagram showing search strategy 59

Figure 2.2. Meta-analysis of health utilities reported at 12 months showing a non-significant trend towards improved outcomes for patients managed surgically as fracture complexity increases....61

Figure 2.3. Meta-analysis of health utilities reported at 24 months showing a non-significant trend towards improved outcomes for patients managed surgically as fracture complexity increases....62

Figure 2.4. Forest plot demonstrating that trials with predominantly 3 part fractures were less likely to undergo secondary surgery if managed conservatively 63

Figure 2.5. Forest plot demonstrating that trials with predominantly 4 part fractures favoured surgery when adverse events were evaluated at a minimum of 1 year follow up....64

Figure 2.6. Cochrane risk of bias summary for 7 included studies (+ represents low risk, ? represents unclear risk, - represents high risk) 65

Figure 2.7. Funnel plot demonstrating risk of publication bias based on A re-operation as an outcome measure and B adverse events as an outcome measure.....66

Figure 3.1. Thematic diagram illustrating 7 overarching themes that informed patients' perceptions of their recovery and outcome after undergoing management for a proximal humerus fracture. 85

Figure 4.1. Outline of steps used in this cost analysis 109

Figure 4.2. Diagram demonstrating how costing was performed for each stage of the different steps that made up the entire Care Delivery Value Chain (CDVC). 115

Figure 4.3. Hemiarthroplasty resulting in a financial loss to the hospital based on mean and maximum cost estimates. 119

Figure 4.4. Sensitivity analysis using 20% fluctuation in cost drivers illustrating that implant cost is the most sensitive cost driver that influences the overall cost of treatment. 121

Figure 4.5. Sensitivity analysis illustrating that within staffing costs, fluctuation in consultant cost has the largest effect on the overall cost of treatment. 122

Figure 4.6. Threshold analysis demonstrating how delays in theatre affected the overall cost of treatment. 123

Figure 5.1. Example of a hypothetical decision tree, demonstrating comparison of different treatments available for Condition X. Pay-offs at terminal nodes include cost and effect (QALYs). The costs and utilities are aggregated and the incremental cost effectiveness ratio of the treatment is compared with a willingness to pay value to determine which treatment is cost-effective. 132

Figure 5.2. The assumed normal distribution of 2-year health utilities reported in existing studies if the mean value was 0.65. 142

Figure 5.3. The estimated health utility for patients with a complication (or the complication state) taken to be 1SD/σ subtracted from the mean. In a normal distribution this accounts for approximately the bottom 15% of the population. Based on a complication rate of between 20-30% this position on the curve is representative of those patients. 143

Figure 5.4. The estimated health utility for patients without a complication (or the well state) taken to be 0.5SD/ σ over the mean. This position on the curve is representative of patient health utilities in upper 67% of a normal population. 143

Figure 5.5. Conceptual model illustrating how a hypothetical patient with a 3 or 4 part proximal humeral fracture would pass through a decision analytical model over a 2 year time horizon. 146

Figure 5.6. Cost-effectiveness graph illustrating how hemiarthroplasty lies within the WTP threshold and has a higher effectiveness and cost than conservative

management, as well as a higher effectiveness and lower cost than internal fixation with a locking plate. 148

Figure 5.7. Three-way sensitivity analysis showing hemiarthroplasty to be the most cost effective strategy provided its complication rate is less than 19%. The complication rate for internal fixation is set at 25%, which is the lowest reported rate. pConservativecomplication is the model's description of the complication rate following conservative management; pHemicomplication is the model's description of the complication rate following hemiarthroplasty. 150

Figure 5.8. Sensitivity analysis showing how hypothetical variation in internal fixation complication rates affects the conclusions of the model. Below a complication rate of 21.9% locking plate fixation becomes more cost effective than hemiarthroplasty. pIFcomplication is the probability of a complication following internal fixation with a locking plate. 151

Figure 5.9. Three-way sensitivity analysis illustrating how the model changes when the probability of a complication falls below 21.9% with locking plate fixation. In this scenario the complication rate for locking plate fixation is set at 21% and locking plate is only more cost effective when the complication rate of hemiarthroplasty is above 18% and the complication rate of conservative management is above 17%. pConservativecomplication is the model's description of the complication rate following conservative management; pHemicomplication is the model's description of the complication rate following hemiarthroplasty. 152

Figure 5.10. Three-way sensitivity analysis illustrating which treatment intervention is the most cost-effective based on a locking plate complication rate of 11 or less% (and a complication rate after hemiarthroplasty less than 10% and after conservative management less than 17%). pConservativecomplication is the model's description of the complication rate following conservative management; pHemicomplication is the model's description of the complication rate following hemiarthroplasty. 153

Figure 5.11. Three-way sensitivity analysis showing that hemiarthroplasty is the most cost effective treatment strategy even if the rate of secondary surgery is modified according to the range of reported values in the literature. Locking plate fixation is set at its lowest value of 25% in relation to the proportion of complicated cases requiring secondary surgery. pHemicomplicationeedsop is the probability of complications after hemiarthroplasty needing surgery and pConservativecomplicationneedsop is the probability of a complication after conservative management needing surgery. 154

Figure 5.12. Two-way sensitivity analysis comparing the variation in success rates after revision surgery for the hemiarthroplasty and non-operative interventions. pImproveafterRevisionHA is the probability of successful secondary surgery after hemiarthroplasty and pImproveafterrevisionCM is

probability of successful secondary surgery after conservative management. 155

Figure 5.13. One-way sensitivity analysis demonstrating a threshold value of 1.684 below which QALYs for patients with a successful outcome after hemiarthroplasty (eHemi), results in conservative management being the most cost effective intervention 156

Figure 5.14. Three-way sensitivity analysis comparing range of values for QALYs obtained for patients that had a successful treatment outcome. Locking plate fixation (eIF) is compared with hemiarthroplasty (eHemi). Conservative management QALY is set at a minimum expected value of 1.545. 157

Figure 5.15. Three-way sensitivity analysis evaluating uncertainty based on QALYs derived for complications after primary management in each treatment arm. Locking plate fixation set a maximum value of 1.492. eConservativecomplication is the range of QALYs for patients with a complication after conservative management. eComplicationHA is the range of QALYs for patients with a complication after hemiarthroplasty..... 158

Figure 5.16. Three-way sensitivity analysis demonstrating the effect of hypothetical values for QALYs after successful secondary surgery for conservative management (eCMrevisionimprove) and hemiarthroplasty (eRevisionHA). Locking plate fixation is set at the highest possible outcome of 2..... 159

Figure 5.17. Three-way sensitivity analysis demonstrating the effect of hypothetical values for QALY after complications following secondary surgery between hemiarthroplasty (eHArevisioncomplicatin) and conservative management (eCMrevisioncomplication). The QALY for locking plate fixation is set at 2 (the maximum possible value). 160

Figure 5.18. Cost-effectiveness graph demonstrating that based on institutional treatment costs conservative management is the most cost effective strategy as locking plate fixation and hemiarthroplasty fall outside the WTP threshold of £20,000/QALY. 161

Figure 5.19. Threshold analysis demonstrating value at which hemiarthroplasty becomes a cost effective treatment strategy when institutional costing is used within the model. cHemiPrimarySurgery is the cost of the primary hemiarthroplasty procedure. 162

Figure 5.20. Threshold analysis demonstrating value at which locking plate fixation becomes a cost-effective treatment strategy within the model. cIFPrimarySurgery is the cost of a primary internal fixation procedure with a locking plate. 163

Figure 6.1. Markov transition state diagram showing possible outcomes for patients undergoing conservative management. The transition states are identical for locking plate fixation and hemiarthroplasty. 174

Figure 6.2. Cost-effectiveness graph illustrating how hemiarthroplasty lies within the WTP threshold and has a higher effectiveness and cost than conservative management, and a higher effectiveness and higher cost than internal fixation with a locking plate. 183

Figure 6.3. Three-way sensitivity analysis graph illustrating that hemiarthroplasty is the most cost-effective treatment strategy based on the cumulative complication rates reported in the included studies for conservative management and hemiarthroplasty. The complication rate in this graph for locking plate fixation is set at the mean reported value (base case) of 0.446. The axes in this graph represent the numerator over the base case value for the complication rate after conservative management (pCMcomplication) and the numerator over the base case value for the complication rate after hemiarthroplasty (pHAcomplication). These values are transitional at each stage in the Markov cycle. 184

Figure 6.4. Three-way sensitivity analysis graph illustrating that hemiarthroplasty is the most cost-effective treatment provided that its complication risk is 1.25 fold its base case value in the MCM with the complication rate of locking plate fixation approximately half (0.561) the base case value for locking plate fixation in the MCM. The axes in this graph represent the numerator over the base case value for the complication rate after conservative management (pCMcomplication) and the numerator over the base case value for the complication rate after hemiarthroplasty (pHAcomplication). These values are transitional at each stage in the Markov cycle. 185

Figure 6.5. Three-way sensitivity analysis demonstrating that hemiarthroplasty remains the most cost effective intervention across full range of secondary surgery rates (locking plate fixation set at minimum value of 0.25). pCMComplicationneeds surgery is secondary surgery probability after conservative management. PHAcomplication needs surgery is secondary surgery probability after hemiarthroplasty. 186

Figure 6.6. Three-way sensitivity analysis that demonstrates that across a wide range of probability outcomes for a complication after secondary surgery hemiarthroplasty remains the most cost effective treatment strategy. Locking plate fixation complication rate after secondary surgery is set at 10%. pCMComplicationneeds surgery is secondary surgery probability after conservative management. PHAcomplication needs surgery is secondary surgery probability after hemiarthroplasty. 187

Figure 6.7. Three-way sensitivity analysis demonstrating effect of uncertainty in relation to 'well state' QALYs. QALY for locking plate fixation set at 1.8. eCMwell is the QALY input parameter for patients in the 'well state' after conservative management. eHAwell is the QALY input parameter for patients in the 'well state' after hemiarthroplasty. 188

Figure 6.8. Three-way sensitivity analysis demonstrating effect of QALY values following a complication on the model. Internal fixation is set at a

maximum QALY value of 1.486. eCMcomplication is QALY value for patients with a complication after conservative management. eHAcomplication is QALY value for patients with a complication after hemiarthroplasty. 189

Figure 6.9. Three-way sensitivity analysis demonstrating the effect of adjusting QALY values for patients that have a successful outcome after secondary surgery. The locking plate fixation QALY is set at 1.5. eCMrevisionwellstate is the 2-year QALY for patients with a successful outcome after secondary surgery in the conservative management group. eHArevisionwellstate is the 2-year QALY for patients with a successful outcome after secondary surgery in the hemiarthroplasty group. 190

Figure 6.10. Three-way sensitivity analysis demonstrating the effect of changing the 2-year QALY values for patients who have suffered a complication after secondary surgery. The QALY input for locking plate fixation patients with a complication after secondary surgery is set at 1.5. eCMrevisioncomplication state is the QALY value for patients with a complication after secondary surgery in the conservative management group. eHAcomplicationrevisionstate is the QALY value for patients with a complication after secondary surgery in the hemiarthroplasty group. 191

Figure 6.11. Cost-effectiveness graph showing that hemiarthroplasty is the most cost effective intervention after adjusting age-specific mortality in MCM. 192

Figure 6.12. One-way sensitivity analysis demonstrating adjustment of cost of hemiarthroplasty as a primary treatment strategy. At a cost of £16,833.91 hemiarthroplasty becomes less cost-effective than conservative management. cHAprimarysurgery is the cost of hemiarthroplasty in £. 194

Figure 6.13. One-way sensitivity analysis demonstrating that adjustment of locking plate fixation cost to £1 results in hemiarthroplasty continuing to be the most cost effective treatment strategy. cIFstatewell is the cost of performing a primary locking plate fixation for a complex proximal humerus fracture. 195

Figure 6.14. Cost-effectiveness graph illustrating that hemiarthroplasty is the most cost-effective treatment when the MCM is run using institutional cost estimates. 196

Abbreviations used in Thesis

AVN	Avascular Necrosis
BPT	Best Practice Tariff
CCA	Cost Consequence Analysis
CEA	Cost Effectiveness Analysis
CMS	Constant Murley Score
CUA	Cost Utility Analysis
HEE	Health Economic Evaluation
ICER	Incremental Cost Effectiveness Ratio
MCM	Markov Chain Modelling
OA	Osteoarthritis
ORIF	Open Reduction and Internal Fixation
OSS	Oxford Shoulder Score
PbR	Payment by Result
PLICS	Patient Level Information Costing Systems
PROM	Patient Reported Outcome Measure
QALY	Quality Adjusted Life Year
RCT	Randomised Controlled Trial
TDABC	Time Driven Activity Based Costing
WTP	Willingness to Pay

Chapter 1

Introduction

1.1 Epidemiology of Proximal Humerus Fractures

In 2008 there were 184,000 fractures of the proximal humerus in the United States[1]. Global estimates of annual injury prevalence are as high as approximately 700,000[2] and epidemiological analysis suggests that over the next three decades, the number of these fractures in an elderly population will triple[3]. This projection is of particular importance because the vast majority of these injuries occur in an elderly population[1,4]. Although almost 77% of these injuries occur in women[5] the age-specific incidence for patients over the age of 60 years is increasing at a faster rate within the male population[3].

The absence of a national registry specific to these injuries makes epidemiological reporting of fracture sub-groups, based on morphology or complexity, limited to observational studies conducted at an institutional level. In the United Kingdom (UK), the largest such study was conducted in Edinburgh and found that over an 8-year time horizon, amongst patients over the age of 65, Neer type 3 and 4 fractures[6] accounted for 17% of all proximal humerus fractures[7]. While conservative management of minimally displaced and 2-part fractures in older patients is considered the norm in patient care[8], the management of more complex fractures remains controversial[9], and therefore an epidemiological description of these injuries at a national level is relevant to the development of clinical research and health policy.

In the UK the burden of these injuries can be extrapolated from Hospital Episode Statistic data which is commonly used to measure surgical activity in the English National Health Service (NHS)[10]. Patient-level data is not publically available, however estimates of the number of inpatient admissions demonstrate an upward trend in the number of cases between

2003 and 2012[11] **(Figure 1.1)**. These figures which range from approximately 7,000 to 15,000 cases per year are likely to grossly underestimate the number of cases because they do not include the large number of patients that suffer a fracture but do not require inpatient management.

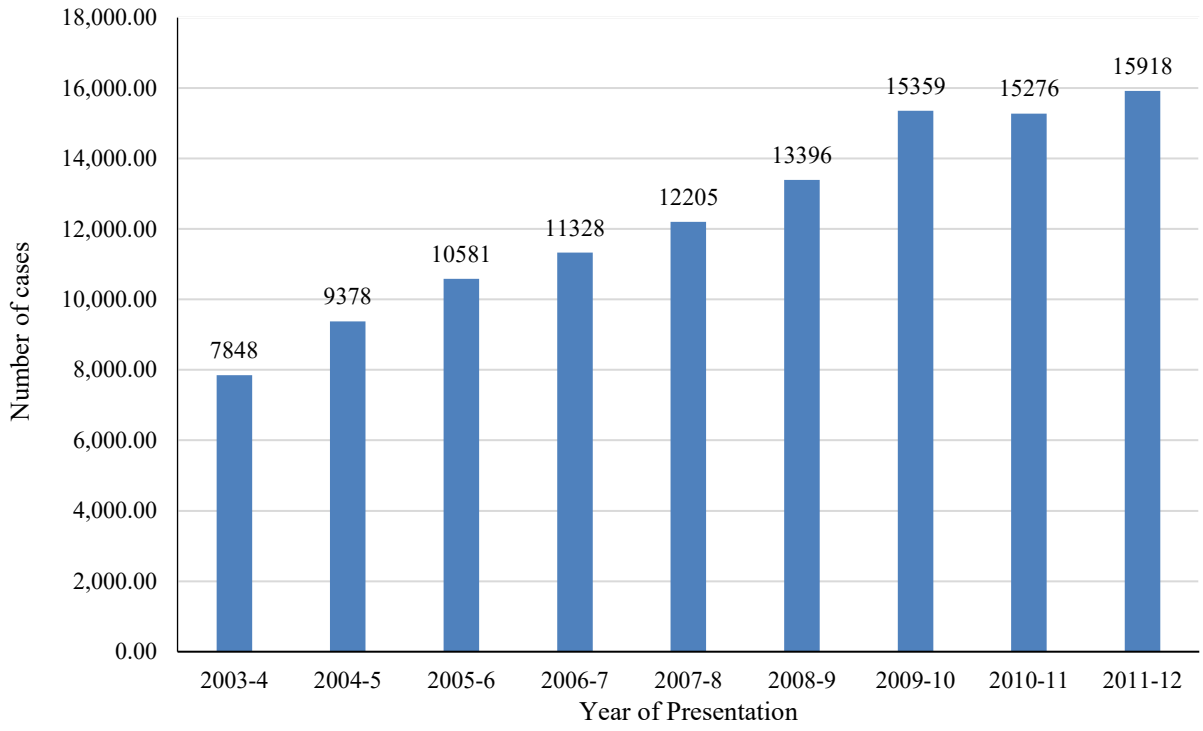


Figure 1.1. Year-on-year increases in admissions to hospitals in the English NHS with a proximal humerus fracture.

Existing research also suggests patients that sustain a proximal humerus fracture have an increased age-specific mortality[12]. The 1-year mortality rate in a British population has been reported to be approximately 10%[7]. Female gender, advanced age and the presence of concurrent medical illness have been found to significantly increase risk of death at 1-year[13], however there is a paucity of epidemiological data that quantifies the effect of fracture morphology or modality of treatment on patient mortality.

Risk factors for proximal humerus fractures include osteoporosis and a history of frequent falls[14]. A history of previous fractures elsewhere in the body and low dietary calcium intake

are also predictors of injury, whilst menopausal hormone replacement therapy and calcium supplementation have been found to have a protective effect[14]. Specifically within a population over the age of 65, a prospective cohort study in the United States (US) that included 9,704 patients found that factors that independently predicted a proximal humerus fracture included a recent decline in health status, type I diabetes mellitus, infrequent walking and indicators of neuromuscular weakness[15]. Ethnicity has also been found to have an effect on global variation in the incidence of these fractures; Japanese populations have less proximal humerus fractures than Caucasian populations[16]. Increased risk in Japanese populations has been rationalised by lower bone mass, however this hypothesis remains controversial primarily because population differences in bone mass have been reported to be small to moderate[17].

The management of proximal humerus fractures is also subject to regional variations. A study of the National Emergency Department Sample in the US for 2010 to 2011 found that admissions to hospital were related to a number of non-medical factors including insurance status and geographic region[18]. Furthermore, examination of Medicare data in the States has also demonstrated that the rates of surgical treatment are also subject to regional variation[19].

1.2 Patho-mechanics of injury

The earliest description of fracture mechanics has been attributed to Dr Ernest Codman, who in 1934 proposed that adult proximal humerus fractures occurred as a result of retained epiphyseal lines that acted as cleavage lines across which the humeral head could divide into 4 main fragments[20]. Codman suggested that fracture displacement occurred as a result of impaction of the articular head on the superior glenoid, however the tuberosity fragments were only partially separated because of the surrounding periosteum and rotator cuff.

In 1970, Charles Neer proposed that fracture position was largely dependent on the forces of muscular attachments on the fracture fragments[6], however the evolution and development of Neer's work in more recent biomechanical research has described the majority of fractures occurring as a result of a "parachute reflex" [21]. The outstretched arm is instinctively held in a flexed, abducted and internally rotated position which results in the head of the humerus to impact on the hard anvil of the glenoid and fracture.

Observational analysis of patients that have sustained a proximal humerus fracture was performed in 2000 by Palvanen et al [22]. In this study. 112 patients who had sustained a proximal humerus fracture were evaluated. The majority of patients reported falling to the side and obliquely forward and experienced a direct impact onto their shoulder. As such, the two main mechanisms reported in the evidence based literature are a "parachute reflex" fall with an outstretched arm and a direct impact injury to the lateral aspect of the proximal humerus. Comparative patho-mechanics of these two injuries and their effect on fracture morphology has yet to be described.

1.3 Fracture Classification

The study and proposals of classification systems for proximal humerus fractures can be traced back to ancient Greece and Rome[23]. The Hippocratic Corpus which is a collection of Greek work on medicine written between 440 and 340 BC, provided very rudimentary descriptions of proximal humerus fractures along with the manoeuvres required for fracture reduction[23]. More descriptive classification systems that reflected existing methods of classification emerged in the 19th century. Johann Ludwig Wilhelm Thudichum was a German physician whose 1851 doctoral dissertation entitled "On the Fractures Appearing at the Upper End of the Humerus", provided a detailed classification system based on the anatomic level of fracture lines[24] **(Table 1.1).**

Table 1.1. Adapted Thudichum Classification as described by Dr Stig Broroson[25].

Classification I -V
I. Anatomic neck fracture
A. Intracapsular without impaction
1. Intracapsular fracture
2. Intracapsular fracture dislocation
B. Intracapsular fracture with impaction
1. Intracapsular with impaction
2. Intracapsular with impaction and tuberosity fracture
II. Fracture of greater tuberosity
III. Fracture of lesser tuberosity
IV. Epiphysiolysis
A. Epiphysiolysis
B. Fracture involving epiphyseal line
V. Surgical neck fracture
A. Extracapsular without impaction
B. Extracapsular fracture with impaction

Towards the late 19th century, Kocher and Böhler developed their own classification system, which was also based on anatomic levels of the fracture[26]. Fractures were either at the level of the anatomic neck, the epiphyseal line or the surgical neck. This classification system, like Thudichum's was limited by a lack of appreciation of fracture or fragment displacement.

In 1934 Codman proposed the 4 segment classification system[20]. Codman's system was based on the recognition that fractures of the proximal humerus typically occurred as a result of cleavage across the epiphyseal scars. The result of this pattern of injury was proposed to be a fracture pattern based on a combination of 4 possible fragments; the articular surface, the shaft and the 2 tuberosities. Codman's work is well recognised in informing the classification system developed by Charles Neer that is commonly applied to modern day clinical practice[27]. Between 1953 and 1967, Neer analysed radiographs and the surgical findings of 300 patients that had sustained a proximal humerus fracture and were treated at New York

Orthopaedic Hospital-Columbia Presbyterian Medical Center[6]. Neer also recognised the 4-segment pattern, but added categories that included articular surface fractures and dislocations, which he considered important prognostic factors **(Figure 1.2).** Neer's classification was considered comprehensive and evolutionary because it linked the patho-mechanics of injury with the characteristics of fracture displacement[27]. Although it has been over 45 years since Neer first introduced this classification system, with the exception of the introduction of the valgus impacted 4 part fracture in 2002[28], it has had few modifications to it, and it remains a commonly applied framework for classifying proximal humerus fractures[29,30]. An interesting aspect of the displacement criteria, > 45° angulation and >1-cm separation, was that this was introduced because of the insistence of the journal editor[27] at the time the classification system was first published[6]. Although universally applied, Neer has acknowledged that these thresholds were arbitrary and not developed in his research[27].

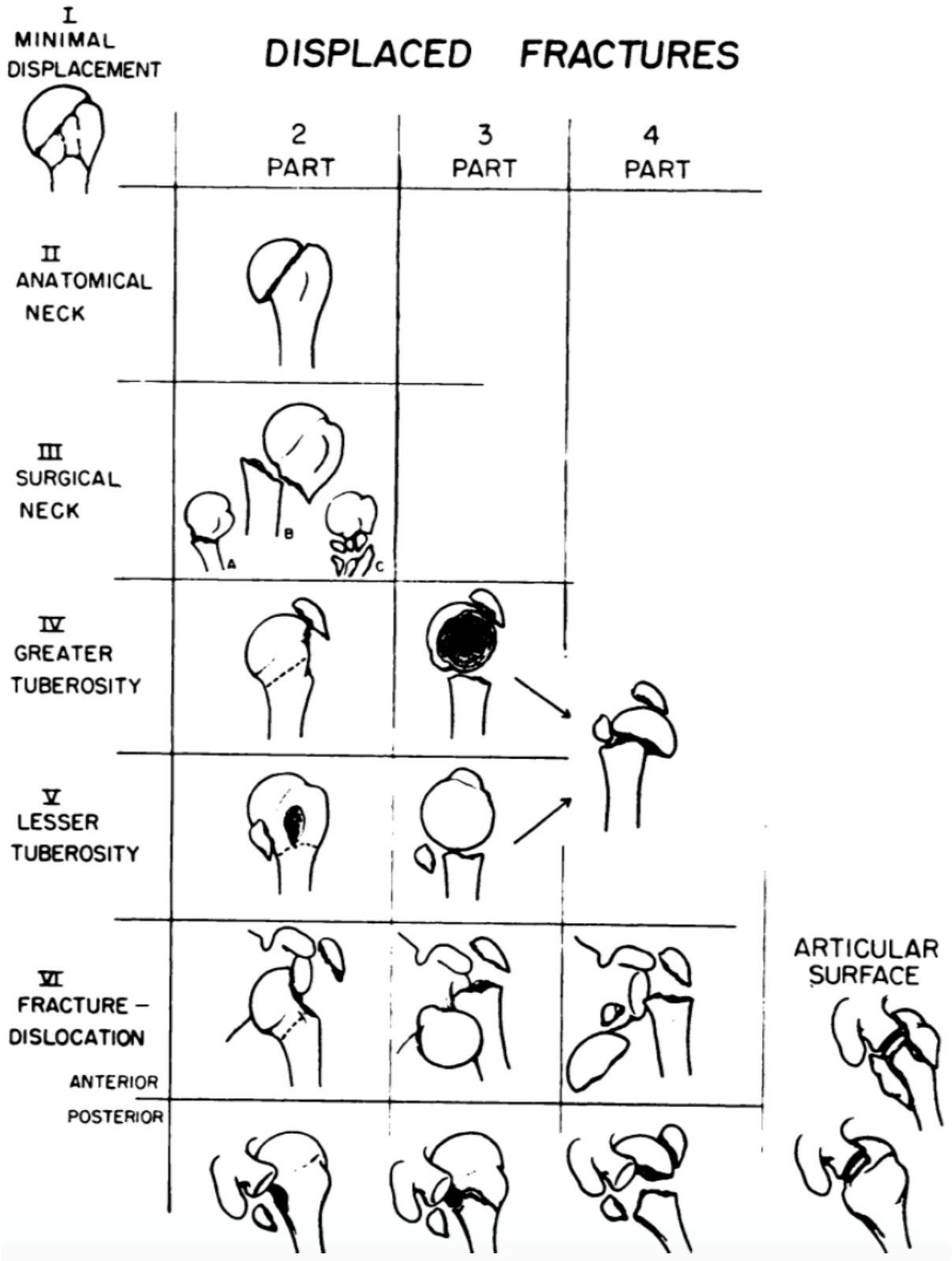


Figure 1.2. The Neer four fragment classification for proximal humerus fractures[6]. Image used with permissions from Wolters Kluwer (Reference 160119-000702).

In the early 1980s, the AO organisation proposed an alternative classification system that was based on their position that the patency of the vascular supply of the articular head, as determined by the number of fragments and degree of displacement, was central to fracture prognosis and classification[31]. Fractures are classified as Type A.B or C. Type A fractures are extra-articular unifocal fractures, with no vascular insult and the smallest risk of avascular necrosis (AVN). Type B fractures are extra-articular bifocal fractures with partial vascular isolation of the articular segment and a slightly higher risk of AVN. Type C fractures are articular fractures that have total isolation of the vascular fragment and a high risk of AVN. Despite the descriptive nature of the AO classification it has not enjoyed the popularity and widespread application of the Neer classification, and this has been suggested to be secondary to its complexity and poor reproducibility[32].

More recently, Hertel et al proposed the Binary (Lego) classification system in 2004[33]. This system was based on the intra-operative examination of 100 intracapsular proximal humerus fractures. Blood flow to the humeral head was measured and poor perfusion was found to correlate with a disrupted medial cortical hinge and metaphyseal head extension of less than 8mm. By combining these positive findings with their Binary fracture configuration **(Figure 1.3)**, the authors concluded that they were able to better inform decision making on management of these fractures. Specifically, their system was predictive of head ischaemia and therefore was indicative of the success of internal fixation. Interestingly in contrast to Neer's classification[6], displacement was less important in prognosis and the Binary classification system has yet to be correlated with AVN. As a result of the limitations of existing classification systems, there is an increasing interest in developing improved methods of classification and a number of newer systems have been put forward over the last 10 years[34-36]. Despite this, an overview of the literature makes it clear that Neer's system remains popular, and this is perhaps underpinned by its simplicity.

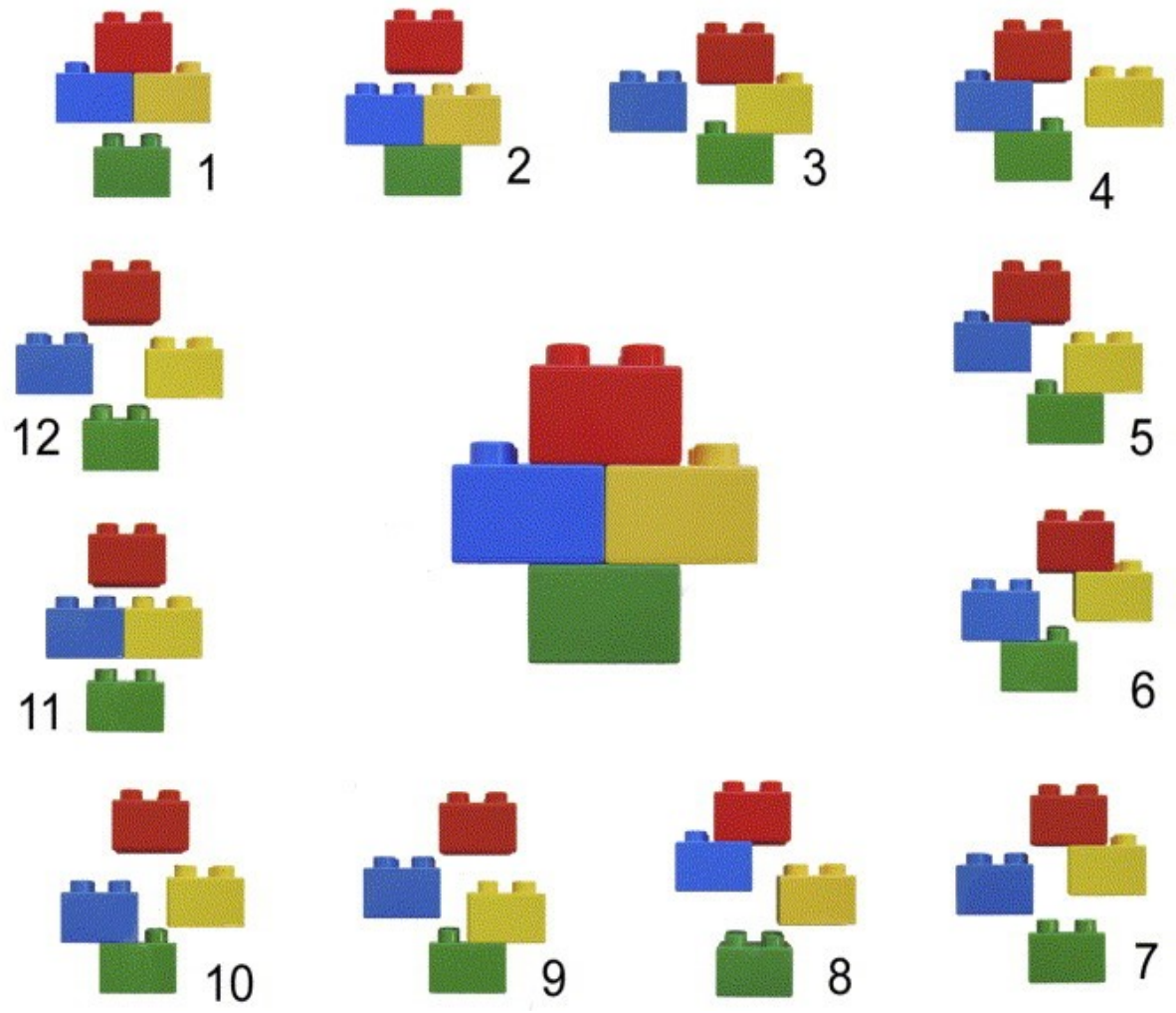


Figure 1.3. The Binary (Lego) description as proposed by Hertel et al[33]. There are 6 possible fractures dividing the humerus into 2 fragments (1-6). There are 5 possible fractures dividing the humerus into 3 fragments (7-11). There is 1 fracture pattern dividing the humerus into 4 fragments. Image used with permission from Elsevier and Copyright Clearance Centre (License 3792510310271).

1.4 Limitations of fracture classification systems

The Neer classification system which is recognised to be the most commonly used for proximal humerus fractures has been reported to suffer from poor inter and intra-observer reliability in research that dates back over 20 years[37,38]. Furthermore, a 2008 systematic review of reliability studies of the Neer classification system for fractures of the proximal humerus reported that existing research suggested that inter and intra-observer agreement levels were unsatisfactory[39]. The review also suggested that agreement was not improved if

tested amongst more senior orthopaedic surgeons, and fracture assessment by Computerised Tomography (CT) scan did not improve classification despite several studies suggesting that the poor quality of radiographs contributed to poor agreement levels.

The AO classification system has also been subjected to research evaluating both 2 and 3-dimensional imaging to determine the reliability of inter-observer agreement[40]. The study authors reported that both plain radiograph and CT evaluation by senior orthopaedic surgeons resulted in poor inter-observer agreement of classification. More recent comparative research that has examined the AO, Neer and the Binary (also called the HGLS) classification systems found that the Binary system had the highest inter and intra-observer reliability scores when classification was performed on the basis of plain radiographs[41]. Evaluation of rapid sequence prototype models of proximal humerus fractures has also found that the Binary system offers better inter-observer reliability than the AO, Neer and a novel classification system developed by Herbert Resch[42]. The importance of these findings is underlined by fact that the majority of published clinical studies have adopted Neer's classification system. The implications of this are that the strength of existing research is degraded by the uncertainty that included patients have not been reliably categorised in relation to their fracture morphology.

1.5 Quantitative Outcome Measures

The interest in outcome measures, or the "End Result" as they were historically termed, has prevailed in orthopaedic practice for over 100 years. In 1904, Codman wrote "The common sense idea that every hospital should follow every patient it treats, long enough to determine whether or not the treatment has been successful, and then to inquire, 'If not, why not?' with a view to prevent similar failures in the future"[43]. While early measures of healthcare outcome were disease centred clinical outcomes, in recent years the pendulum has swung

towards patient centres measures based on the recognition that these two endpoints are not necessarily aligned, and the latter approach more appropriately informs decision making based on patients' needs and perceptions[44]. This paradigm is seen in research evaluating treatment interventions for proximal humerus fractures, with more recent studies favouring the use of patient reported outcome measures (PROMS).

1.5.1 Outcome measures in early research

Ironically one of the earliest published case reports on the management of proximal humerus fractures reported their outcomes using an entirely patient centred approach. Writing in the Annals of Surgery, Dr Charles Brigham from San Francisco stated "The patient writes, January 12, I900, ' For the last ten days I have not experienced any pain whatever; the limits of motion are very much more than before the operation, and the manipulation of the arm does not cause pain as before. I can also sleep on the side without any inconvenience, which I could not do before. I feel satisfied that I shall get at least 75 per cent. of the normal function of the arm'" [45]. Studies published in the 1940s and 1950s provided succinct and subjective observations on range of movement and function[46-48]. The first comprehensive system to evaluate outcomes for patients with a proximal humerus fracture was proposed by Neer in 1970[6]. His rationale for the proposed outcome measure was that the assessment of outcomes extended beyond accurate description of the lesion under discussion, but required a specific objective measurement of functional recovery. Neer included four domains in his assessment system; pain, functional range, strength and anatomy. Neer's system for assessing patient outcomes was still applied 30 years after it was proposed[8], however over the last 10 years proximal humerus fracture studies has adopted more recently developed functional assessment tool, patient reported outcome and health utility measures.

1.5.2 Constant Murley Score

Christopher Constant and Alan Murley developed the Constant Murley Score (CMS) between 1981 and 1986, and their final assessment measure formed part of Constant's Master of Surgery thesis submitted to the University College Cork in 1986[49]. The first publication of the CMS in 1987[50], described the assessment of shoulder function based on 4 components; pain, activities of daily living, range of movement and power **(Table 1.2).**

Table 1.2. Components of the Constant-Murley Score and scoring for individual parameters. Adapted from Constant et al[50].

Scoring for individual domains	
Pain	15
Activities of daily living	20
Range of movement	40
Power	25
Total	100

Overall, content validity analysis of the CMS score has showed that if distinguishes well between different populations and their disability in relation to shoulder function, however there is an absence of published analysis in patients with a proximal humerus fracture[51]. Inter and intra-rater reliability have also been shown to be strong, and the overall strength of the CMS as an outcome measure appears to have been recognised within shoulder research networks, as it has been widely adopted in clinical research[51]. Furthermore, it has been endorsed by the Société Européenne pour la Chiurgie de l'Épaule et du Coude (SECEC), who in 1991 proposed that it should form part of outcome assessments submitted to their society and the Journal of Shoulder and Elbow Surgery[49]. A key limitation of the CMS has been variation in the methods adopted for measuring strength[49]. Updated guidelines for use of the CMS published in 2008[49] are likely to have standardised this aspect of the assessment,

however historical variation in practices does add to the limitations of earlier clinical research that adopted these measures.

1.5.3 The Oxford Shoulder Score

The Oxford Shoulder Score (OSS) was first described in a study published in 1996 by researchers in Oxford who developed a 12-item questionnaire based on patients' perceptions of their shoulder related pathology[52]. The patient population studied included those with a "degenerative or inflammatory condition" of the shoulder, who presented to an elective orthopaedic clinic. Although the development of the OSS was based on a population that excluded patients with proximal humerus fractures, subsequent research was performed to test its correlation with the CMS in the assessment of patients with this injury[53]. The OSS correlated well with the CMS for this group of patients, however an important caveat to these findings was that there is an absence of published research that describes the construct validity of the CMS in relation to patients with a proximal humerus fracture[51].

The uptake of the OSS in recent years has been substantial in upper limb and specifically proximal humerus fracture research, perhaps owing to an increased popularity of PROMs, but also because it addresses the potential reporting bias that non-patient reported measures are inherently vulnerable to[54]. An additional benefit of the use of the OSS is its validity in retrospective application[55]. This is particularly important in the assessment of proximal humerus fractures because it is not possible to capture pre-injury scores if the outcome measure is prone to recall bias. A 2012 review of national shoulder and elbow joint registries found that it was used by 3 out of the 7 national joint replacement registries as an outcome measure[56]. A large number of recently published randomised trials (RCTs) in upper limb orthopaedics have used the OSS as a primary or secondary outcome measure[57-60], and notably the Proximal Fracture of the Humerus: Evaluation by Randomisation (PROFHER) trial, a

pragmatic multicentre RCT comparing surgical and non-operative management of proximal humerus fractures, used the OSS as a primary outcome measure[29]. The OSS has also been validated for use across a vast number of cultures, with published validation studies stretching from China[61], to the Middle East[62], Europe[63] and South America[64]. The prevalence of its application and validation in recent years strongly suggest that it will be adopted in clinical research evaluating proximal humerus fractures in the coming years.

1.5.4 Disabilities of the Arm, Shoulder and Hand (DASH) score

The DASH score is 30 point self administered questionnaire that was developed by the American Academy of Orthopaedic Surgeons (AAOS) in 1996[65]. The rationale for assessment of the entire upper limb rather than the shoulder in isolation is that the upper limb us a single functional unit[66]. Construct validity has been established for a number of elective upper limb musculoskeletal conditions[67], as well as upper limb fractures[68]. The DASH score has also been adopted as a secondary outcome measure in RCTs evaluating interventions for proximal humerus fractures[30,69].

1.5.5 Health Utility Measures

Health utilities are a means of measuring health-related quality of life based on estimates of an individual's health state[70]. The components that define the value of a health state are specific to the rating scale adopted, but generally consist of health attributes such as physical function, social function, psychological well-being and bodily pain. The measure of health utilities is based on a scale from 1 to 0, where 1 is perfect health and 0 is death. The importance of health utilities is that they can be transformed into quality adjusted life years (QALYs) which are a universal endpoint used in health economic analysis[71]. Furthermore they offer clinicians and policy makers an opportunity to compare the treatments benefits across specialties which may help inform decisions on appropriate resource allocation.

Health utilities are generally adopted in combination with shoulder-specific functional measures and this is likely to be because they are unable to evaluate condition-specific dysfunction in isolation[72]. Paradoxically, shoulder-specific outcome measures do not reflect health-related quality of life well enough and therefore their use in isolation is not sufficient to fully draw conclusions on patients' general health state[73,74]. Recent research in the field of proximal humerus fractures has consistently adopted health utility measures[29,30,74] and the published protocols of ongoing RCTs[75,76] also describe the use of these measures in evaluating patient outcomes. The availability of these measures provide health economists with a wider pool of data to conduct cost-effectiveness research, which is often limited when it arises from a single-centre because of a lack of external validity of the data[77]. Furthermore, as the need for health economic research increases because of growing financial pressures on health services, health utilities derived from clinical trials may offer the opportunity to perform less costly and time consuming health economic analyses.

1.6 Qualitative Outcomes

Qualitative analysis in the study of patient outcomes after a proximal humerus is absent from the existing evidence based literature. Commonly overlooked in orthopaedic research[78], qualitative analysis involves research that attempts to uncover or interpret phenomena based on the perceptions of people[79]. The Cochrane Collaboration have described it as involving "an interpretive, naturalistic approach to its subject matter" and giving "priority to what the data contribute to important research questions or existing information"[80]. An example of how qualitative research could be applied might be in an attempt to understand why patients choose to have conservative management rather than surgical treatment after a proximal humerus fracture. The traditional model of quantitative research is too restrictive and rather than testing a priori hypothesis the most suitable means of generating an understanding of the

patient perspective is from the exploratory and interpretive approach offer by a qualitative methodology.

Another key application for qualitative research is in the early stages of developing PROMs[81]. In this area of research, qualitative analysis is used to identify the aspects of patients' health states that are important to them, and subsequently introduced into psychometric evaluation in the final development and validation of PROMs[82]. Such work is limited in orthopaedics and the development of existing PROMs in the upper limb have either been based on aspects of outcome viewed to be important by clinicians[65], or patient perspectives obtained in methods that haven't met the clearly defined and recognised framework of qualitative analysis[52] **(Figure 1.4).** The use of qualitative analysis in elderly patients' perceptions of outcomes after a proximal humerus fracture is particularly relevant, because the suitability of existing quantitative measures may be lacking. This is because the construct validity of commonly used outcome measures such as DASH and the OSS are not based on analysis of a population of elderly patients with proximal humerus fractures. Furthermore, the methods used to generate items that form the basis of these scores might not accurately reflect aspects of well-being that these patients value.

Another important aspect of qualitative research is when it is performed in parallel with RCTs. A systematic review of the literature found that between 2008 and 2010, there were 296 published RCTs that reported qualitative research was performed alongside their trials[83]. The rationale for performing parallel research is that policy makers believe that qualitative work adds value to the findings of clinical trials why providing a context to the findings that make them more easily translatable into health policy[84].

Phase	Description of the process
1. Familiarising yourself with your data:	Transcribing data (if necessary), reading and re-reading the data, noting down initial ideas.
2. Generating initial codes:	Coding interesting features of the data in a systematic fashion across the entire data set, collating data relevant to each code.
3. Searching for themes:	Collating codes into potential themes, gathering all data relevant to each potential theme.
4. Reviewing themes:	Checking in the themes work in relation to the coded extracts (Level 1) and the entire data set (Level 2), generating a thematic 'map' of the analysis.
5. Defining and naming themes:	Ongoing analysis to refine the specifics of each theme, and the overall story the analysis tells; generating clear definitions and names for each theme.
6. Producing the report:	The final opportunity for analysis. Selection of vivid, compelling extract examples, final analysis of selected extracts, relating back of the analysis to the research question and literature, producing a scholarly report of the analysis.

Figure 1.4. Structured framework of thematic analysis as described by Braun and Clarke[85]. Permissions for use of image obtained from Taylor & Francis Group.

1.7 An Overview of Treatment Modalities

The management of proximal humerus fracture has been recorded in surgical texts throughout the last 3 millennia[23]. Modern-day management is either based on non-operative or surgical treatment, with the latter intervention encompassing a wide range of different techniques. Despite a large volume of basic science and clinical research that has investigated the various treatment modalities, they remains substantial controversy and contradiction regarding what is the most appropriate treatment based on different patient populations or fracture types[86-88].

1.7.1 Conservative Management

The vast majority of proximal humerus fractures are undisplaced or minimally displaced and are successfully managed with non operative treatment[89]. This usually consists of a period of shoulder immobilisation in a sling, with concomitant supervised rehabilitation. Some research has indicated that physiotherapy commencing within 2 weeks of injury results in better patient outcomes[90] however adopted practices are largely variable[91] and there is an absence of national or organisational guidance to standardise the non-operative patient pathway.

Decision-making that informs clinician choice of conservative management is based on a myriad of factors. Okike et al performed a retrospective analysis of 229 patients who presented to 2 hospitals in the US with displaced proximal humerus fractures[92]. The authors reported that multivariate analysis found that patients were more likely to be managed conservatively if they were over the age of 70 years and there was an absence of other orthopaedic injuries. Furthermore patients were less likely to undergo surgical treatment if their fracture severity based on the AO classification was lower, there was less displacement of fracture fragments and there had not been an associated dislocation of the glenohumeral joint. The study also found that patients were less likely to undergo surgical treatment if they were under the care of a generalist orthopaedic trauma surgeon, rather than a specialist in shoulder surgery.

Although conservative management does not carry the overt risks such as infection and iatrogenic neurovascular injury that may occur with surgery, complications can occur including malunion, AVN, post-traumatic osteoarthritis, subacromial impingement, rotator cuff deficiency and chronic pain[93]. A number of these patients also go on to require surgical management of the sequelae of their injury; Pascal Boileau reported on the late management of sequelae of proximal humerus fractures[94]. Of the 70 patients that underwent shoulder

arthroplasty at his institution over a 4-year period, 73% had been managed conservatively and 27% had received operative treatment to fix the initial fracture.

1.7.2 Surgical Management

Many of the indications for surgical management are consensus driven or based on expert opinion because the volume of Level I evidence that informs practice remains relatively small with no statistically significant treatment effect seen from surgical intervention[95]. Murray et al provided a framework for treatment and described factors that contributed to how decision-making in the management of patients was informed[96] **(Figure 1.5).** The authors proposed that fractures that may benefit from internal fixation include:

1. Fractures with tuberosity displacement > 1cm
2. Fractures with a displaced fragment of the articular surface of the head attached to a displaced tuberosity fragment
3. Unstable 2-part surgical neck fractures where there is disengagement of the shaft from the humeral head
4. 2,3 or 4-part fractures with varus or valgus deformity of the humeral head to the shaft >30° from the normal head-shaft inclination of 130°
5. 3 or 4-part anterior fracture dislocations caused by propagation of a Hill-Sachs lesion and with retained soft tissue attachments of the humeral head at surgery
6. 3 or 4-part posterior dislocations caused by propagation of a Hill-Sachs lesion and with retained soft tissue attachments of the humeral head at surgery

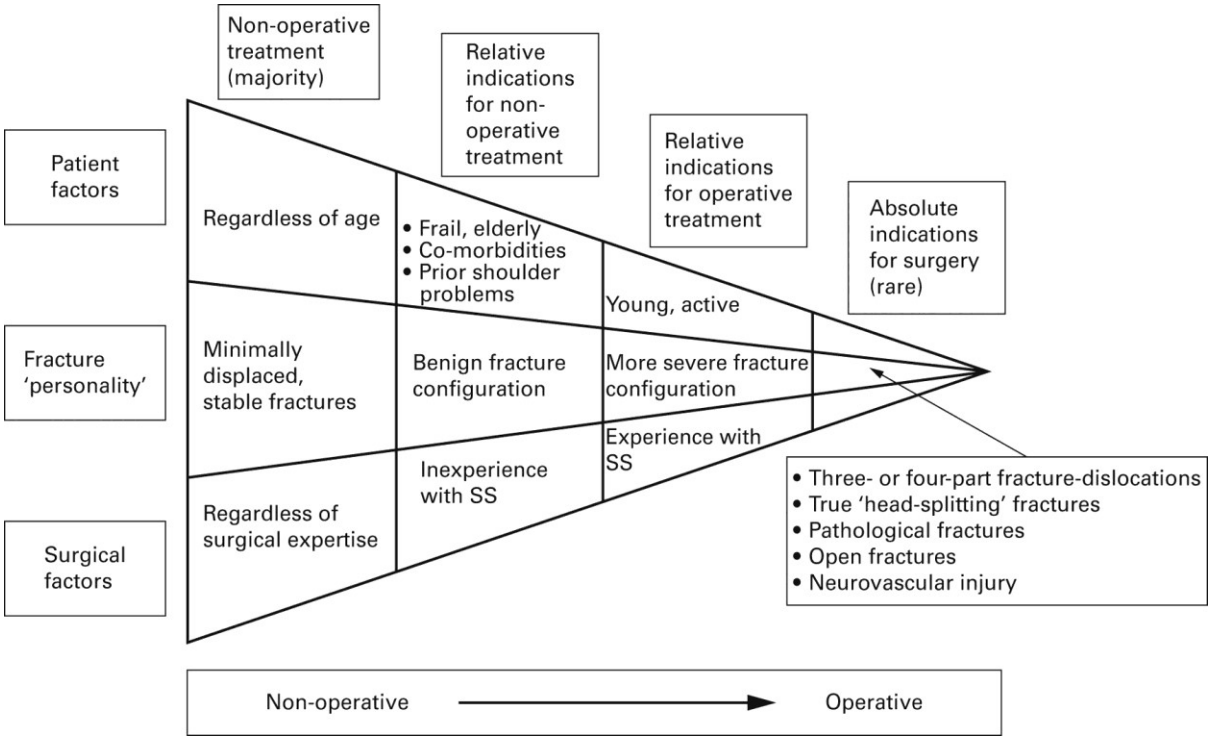


Figure 1.5. Flowchart by Murray et al[96] depicting factors that influence decision-making in the management of patients with a proximal humerus fracture. Permissions obtained from the Bone and Joint Journal.

Although recommendations for treatment such as those described for internal fixation are useful in informing clinical practice, there is a lack of consistency or clinical evidence to support many of the recommendations. For instance in contradiction of some of the recommendations made by Murray et al[96], Voos et al recommended hemiarthroplasty for patients over the age of 70 with displaced 3 or 4 part fractures[97]. Some of contradiction in recommendations of care are likely to occur because of the myriad of fracture classification systems that are adopted in clinical research. It is also possible that performance variability between shoulder surgeons also leads to different surgical techniques being recommended for the same fracture. A further limitation within the literature is that amongst the existing RCTs comparing surgical and conservative management, the sample sizes are not sufficient large enough to produce conclusions on the indications for surgical treatment[95]. One way of overcoming this obstacle is by performing meta-regression or sub-group and sensitivity meta-

analysis to evaluate how fracture morphology or specific treatment interventions affect patient outcomes. To-date no meta-analytical study based on RCTs has adopted these techniques[95]. Another approach in better understanding the outcomes of surgical treatment would be the study of registry data. Large samples of patient data that include clear and descriptive information on patient and fracture characteristics are currently not available for proximal humerus fractures, however their potential importance and application is well recognised by other researchers in this field[29].

A number of surgical techniques are used in the management of proximal humerus fractures including minimally invasive reduction and percutaneous fixation, intramedullary nailing, open reduction and internal fixation (ORIF) and arthroplasty[98]. Generally, 3 or 4-part fractures that undergo surgery are preferentially managed with ORIF or arthroplasty[99]. ORIF is commonly performed using locking plates. These plates have gained popularity over the last 15 years and underpinned an increase in ORIF because of consensus that they represent a more reliable construct than a standard plate, and they offer an opportunity to salvage the humeral head[100]. Hemiarthroplasty is commonly used for elderly patients with fracture comminution or a humeral head split, however their application in the setting of associated rotator cuff injury is challenging and has led to an increased use of reverse shoulder arthroplasty in a trauma setting[98]. The evidence base that informs choice of procedure for more complex fractures has not led to recommendations or treatment criteria that are widely recognised or applied, however the growth of research in this area is indicative that evidence-based guidance may be available in the not too distant future **(Figure 1.6).**

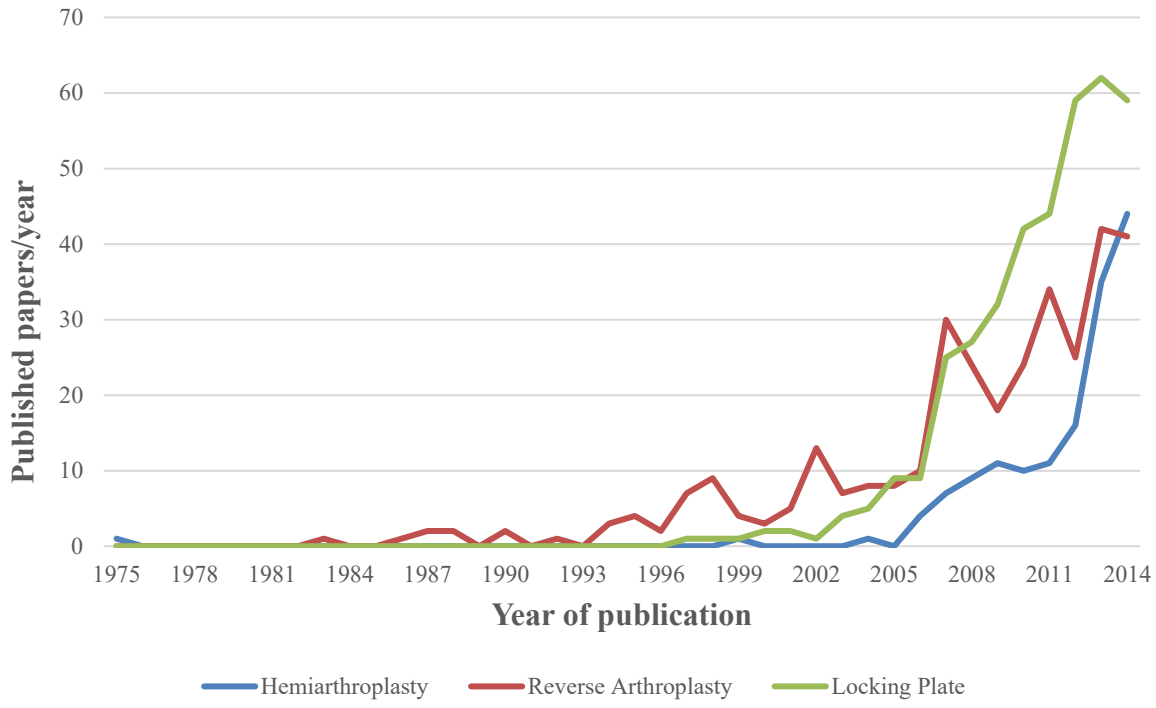


Figure 1.6. Publication of research on the management of proximal humerus fractures by modality of surgical treatment since 1975. Data obtained from Scopus ® document search.

1.8 Health Economics Considerations

Health services around the world face growing pressure to deliver high quality patient care on a finite budget[101]. As the global population expands and the proportion of frail older people with a myriad of treatable medical illnesses grows, the finite financial resources that are available are increasingly stretched[102]. Although it may seem preferable to deliver healthcare that only focuses on patient experiences and outcomes, 'scarcity', the economic principle that that there are insufficient resources to satisfy all human needs[103], underpins why health professionals and policy makers need to be mindful of the cost of treatment.

In the United Kingdom the pressure on health services has been widely recognised in recent years[104]. Although nominal investment in the NHS has been increasing, real term investment which represents investment in relation to inflation, has fallen[105]. A large

number of hospitals report growing deficits and their ability to deliver safe and high quality healthcare is challenged by these financial pressures[106]. There have been various narratives regarding how to overcome these problems, however the concept of value in healthcare is one that is readily recognised by health economists, clinicians and policy makers as being fundamental to delivering high quality health care at the lowest possible cost[107,108]. In health economics value is commonly measured by examination of health outcomes in relation to cost. Health outcomes are quantified by QALYs in the UK and the cost of treatment is either estimated based on the cost of medical treatment, or the overall cost of treatment, social care and loss of opportunity costs which is defined as a societal cost. Acceptable value for medical interventions in the NHS have been set by the National Institute of Health and Care Excellence (NICE) at a willingness to pay (WTP) threshold of £20,000/QALY[109].

1.8.1 Health economic nomenclature

Health economic evaluations (HEEs) consist of a number of different types of analyses, each with its own utility. Cost-analysis studies, where only the cost of two or more interventions are investigated, are not considered HEEs. A HEE is defined as the comparative analysis of alternative courses of action in terms of both their costs and consequences[110]. The types of health economic evaluations are summarised in **Table 1.3.**

Table 1.3. Summary of types of HEEs. Adapted from Kernick[103] with Permissions from the BMJ (license 3794190641446).

Form of evaluation	Measures and valuation of outcomes
1. Cost minimisation analysis (CMA)	Outcomes must be equivalent and the focus is on measurement of costs.
2. Cost effectiveness analysis (CEA)	Natural units (for example life years gained, Oxford Shoulder Score) that are common to competing interventions and costs are combined to determine the incremental net benefit of one intervention over another.
3. Cost utility analysis (CUA)	Health outcomes are based on health utilities represented as QALYs. In combination with the cost of each intervention, an incremental benefit of QALYs and costs between interventions is calculated. This methodology is important because national health policy decisions are based on QALYs. Often used interchangeably with CEA, but if unit of effectiveness is not a utility cannot be called a CUA.

1.8.2 Existing economic research on proximal humerus fractures

Based on the knowledge that proximal humerus fractures are commonly occurring musculoskeletal injuries[4], the economic burden of disease and treatment requires consideration. Cost analysis research within this field has only been conducted in the US, and it is probable that their interest has stemmed from the heated debate on treatment costs that has developed around the implementation of the Affordable Care Act, a law which attempts to enable universal healthcare for all US citizens[111]. A 2013 study performed by Harvard Medical School found that higher surgeon volume was associated with lower hospital costs for proximal humerus fractures[112]. The authors suggested that hospital policy on minimum volume requirements by hospitals could results in substantial financial savings. A 2015 cost analysis performed by the University of Rochester examined cost drivers in the treatment of patients with a proximal humerus fracture and quantified the financial impact of complications of treatment[113]. Such research has an important role in shaping health policy, however these studies like many other cost analyses in medical research rely on hospital or insurance charges rather than actual treatment costs[114]. The distinction is an important one to

make because top-down estimates of treatment cost, which are often adopted when setting charges are viewed to be less accurate than bottom-up estimates[110]. Furthermore, the discrepancy between treatment costs derived by these differing methods is seen across healthcare, and importantly it is seen in orthopaedic surgery[115].

In the United Kingdom cost analysis research on proximal humerus fracture management is limited in the published literature[95]. However, cost-analysis research has generally been of interest to policy makers and clinicians because of the framework through which the NHS reimburses hospitals for healthcare; a system called payment by result (PbR)[116]. This system involves hospital submitting annual estimates of treatment costs to the UK's Department of Health, who then calculate an average tariff for each treatment and reimburse hospitals based on this tariff. A number of studies have found that reimbursement grossly underestimates treatment costs and as a result hospitals are unfairly financially penalised[117,118]. The main problem that hospital managers or clinicians have faced when attempting to estimate true treatment costs has been a lack of robust methodology. In the last few years there has been a rapid increase in the application of a new costing methodology called time driven activity based costing (TDABC)[119]. Developed at Harvard Business School, this bottom-up approach considers the unit cost of all the staff in a treatment pathway, as well as the medical consumables involved in patient care. Although it is time consuming in its design, TDABC is viewed to be the most accurate tool for healthcare costing that is currently available[114]. The importance of such tools in relation to proximal humerus fracture management, is that that they provide an opportunity to accurately understand the financial burden of treatment in relation to national tariffs, they identify cost-drivers that can be subjected to cost-minimisation practices, and they can more accurately inform the costing parameters in HEEs.

To date there have only been 2 health economic evaluations based on interventions for the management of proximal humerus fractures[11,120]. Fjalestad et al[120] published their analysis in 2009 based on a HEE performed in parallel with an RCT they conducted in Norway between 2003 and 2008. This study included 50 elderly patients (>60 years) with complex fractures (3 and 4-part). The authors concluded that there was no significant difference between surgical treatment, with a locking plate, and conservative management. This study does not meet the formal definition of a HEE because it did not aggregate health utilities and costs as an incremental cost effectiveness ratio (ICER), rather the study presented incremental costs and utilities as separate entities. Such research is termed cost-consequence analysis (CCA)[121]. Although CCA has an important role in developing health policy, there are some limitations in the applicability of Fjalestad's study. Firstly, because this analysis was performed in parallel to a single centre RCT it lacks external validity[122]. Surgical practices and costing in different hospitals and countries are likely to vary[123]. As such, informing practices in a clinical setting where this research was not conducted is not appropriate. Furthermore Norwegian and UK health services have recognised differences in health delivery and costing[124,125] which makes application of these findings to the NHS particularly challenging. Another important consideration in the interpretation of this study is that although the mean health utilities in surgically managed patients were higher, costs between the two treatment groups was similar. The high cost of conservative management was driven by a prolonged inpatient stay for patients and the associated inpatient rehabilitation costs. Outpatient care for conservatively managed proximal humerus fractures is generally considered the norm for most patients[126] and therefore the costs that informed Fjalestad et al's conclusions appear inflated for this group of patients. Overall, although this study is an important part of the limited economic literature available in this field, its ability to inform practice based on the economic framework in the NHS is limited.

The 2015 HEE performed alongside the PROFHER trial is the second economic study performed within his field[95]. The strengths of this study are that data was derived from a large multicentre RCT in the UK, and therefore this study has increased external validity and applicability to practice within the NHS. However, the pragmatic design of the PROFHER trial meant that approximately 50% of included patients had a 2-part fracture and the surgical interventions included were broad. The study found that surgical practice was not cost effective in the UK. In the context of evaluating individual interventions in the management of 3 or 4-part fractures in elderly patients a more specific research design is required. To better understand the health economics of commonly adopted management principles for complex proximal humerus fractures in elderly patients, there are 2 potential options that could deliver conclusions to inform clinical practice and health policy. Firstly, the design and implementation of large RCTs like PROFHER, but with more specific inclusion criteria based on fracture complexity, and the segregation of specific surgical interventions would be an ideal basis for a HEE in this field. Secondly the application of decision analytical modelling to data derived from a national registry, or existing RCTs is a method advocated and commonly used by health economists[77]. By comparing the costs and health consequences from multiple data sources, conclusions can be generated with more external validity, and the sensitivity analysis performed in conjunction with the primary analysis offers valuable insight into the uncertainty of conclusions derived from existing research. Decision analytical modelling commonly informs the conclusions of National Institute for Health Research recommendations on cost-effective practices[127-129] **(Figure 1.7),** and its potential application to existing proximal humerus fracture research requires closer examination.

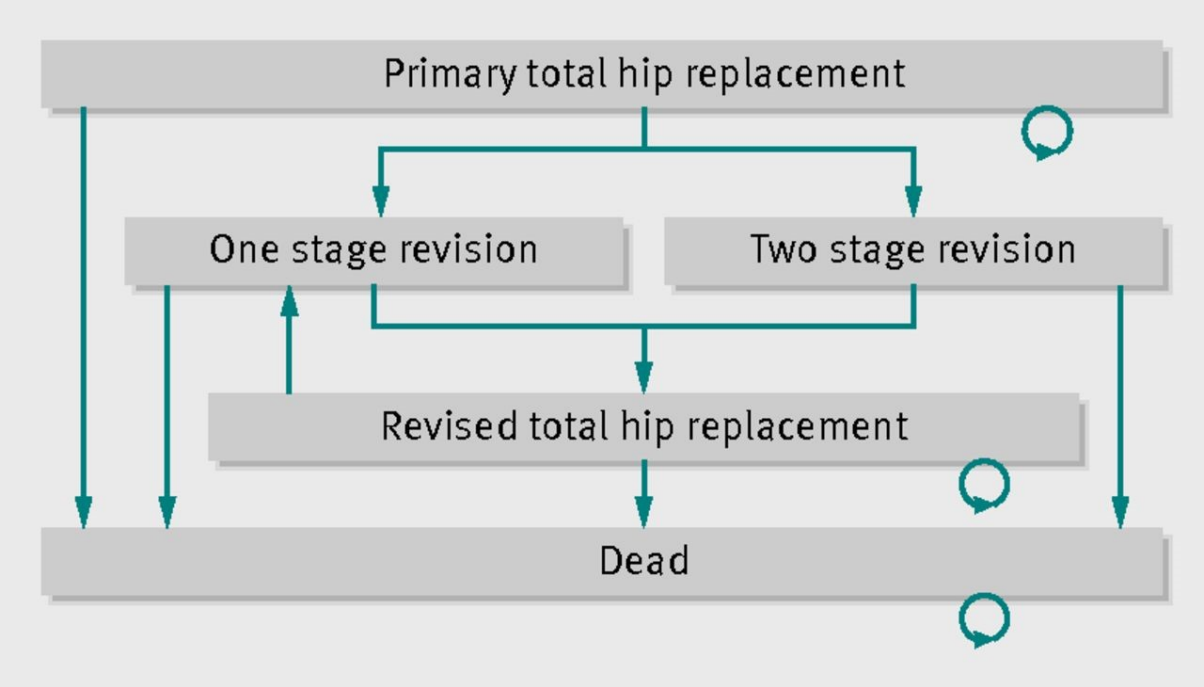


Figure 1.7. Decision analytical model applied to determining large NHS cost-effectiveness study of cemented, cementless and hybrid hip replacement[130]. Data was input to the model from national registry data. Permissions for image use obtained from BMJ (License 3795880171673).

1.9 Scope of the Thesis

This thesis is concerned with evaluating and comparing the health and economic outcomes of different management strategies for elderly patients with 3 and 4-part proximal humerus fractures. An evaluation of health outcomes will be performed using both qualitative and quantitative methodologies. Economic outcomes will be studied using recognised principles for cost analysis and health economic evaluations.

1.10 Rationale for the Thesis

Although the conclusions of existing meta-analyses have indicated that there is no difference in health outcomes between surgical and non-operative of proximal humerus fractures, heterogeneity between the included studies based on fracture complexity and surgical interventions employed makes the conclusions of such research limited in their clinical application. There is a need for the use of meta-analytical methods such as sub-group and

sensitivity analysis which may provide an opportunity to better understand the treatment effects in more complex fractures and for specific treatment interventions in elderly patients.

An absence of published qualitative research that has evaluated elderly patients' perceptions of their health outcomes after sustaining a complex proximal humerus fracture has limited the understanding of whether existing quantitative outcome measures are truly patient-centred. As evidence based medicine moves towards a patient-centred model of care, qualitative analysis in this field may provide better insight into what aspects of recovery elderly patients' value and should be subjected to quantitative measurement.

The true cost of treatment is often inaccurately estimated in health care due to poorly developed tools for accounting for treatment costs. Micro-costing approaches such as TDABC are recognised to be more accurate and are increasingly adopted in healthcare cost analyses in. Using such methodology to estimate the cost of management of proximal humerus fracture treatment is important in the English NHS because it more accurately represents the monetary benefits or losses of individual treatments in relation to national reimbursement.

Health economic evaluations are valuable research tools to inform clinicians and policy makers about how to best inform clinical practice based on scare healthcare resources. Such evaluations for complex fractures in an elderly population are absent within the evidence-based literature. The use of decision analytical modelling can allow the outcomes of existing research to be integrated into an economic analysis with external validity. Such methods inform national recommendations in the NHS yet have not been used for elderly patients with a proximal humerus fracture who represent a sizeable burden amongst musculoskeletal injuries occurring in the UK.

Finally, the rationale for a focus on elderly patients was based on a recognition that these patients represent the largest sub-group of individuals that sustain proximal humerus fractures[3] and the health and economic outcomes of their management may be distinct from a young adult population[131,132]. Elderly age is commonly defined by chronological measures in orthopaedic research as patients ≥ 65 years[133]. As such this was the definition adopted in this thesis. Complex fractures of the proximal humerus can be defined in accordance with specific classification systems. As the Neer system is the most common classification system currently applied to research in this field[134], complex fractures were defined as Neer type 3 or 4 fractures. These fractures are the subject of most the debate that surrounds the management of proximal humerus fractures[87] and therefore a better understanding of their health and economic outcomes is of great value to decision making in clinical practice and guiding health policy.

1.11 Thesis Aims

The overall aim of this thesis is to improve the understanding of health and economic outcomes of treatment strategies for elderly patients (>65 years), with complex proximal humerus fractures (Neer type 3 or 4). More specific objectives are to:

1. Perform a meta-analysis, including sub-group and sensitivity analysis, to evaluate the differences in quantitative health outcomes within existing RCTs that evaluated treatment interventions for elderly patients with a complex proximal humerus fracture.
2. Use a qualitative analytical approach to better understand the experiences of elderly patients who had sustained a complex proximal humerus fracture.
3. Estimate the cost of surgical treatment of fractures of the proximal humerus using a micro-costing methodology, contrast this cost with the national reimbursement tariff and establish the major determinants of cost.

4. Perform a HEE using a decision analytical tree modelled on existing published evidence, and to identify what is the most cost effective treatment option for complex proximal humerus fractures within an English NHS setting over a 2-year time horizon.
5. Perform a HEE using a Markov chain model to determine the most cost-effective treatment intervention for complex proximal humerus fractures in an elderly population within an English NHS setting over a 20-year time horizon.

Chapter 2

Meta-analysis evaluating the effect of fracture complexity and choice of surgical intervention on treatment effects in the management of proximal humerus fractures

2.1 Introduction

Proximal humerus fractures account for almost 10% of all fractures in patients over the age of 65[135]. Epidemiological research has shown an increase in the incidence of this injury, and this is widely regarded to be the result of the growth of an ageing population[136]. A number of classification systems have been proposed over the last 40 years to describe fracture morphology and guide management[42]. Interestingly, there is a recognised upward trend in the incidence of surgical management[19] despite a lack of expert consensus or clinical evidence to support the choice of surgical intervention over non-operative management[91]. Since the 2012 Cochrane Review that concluded that there was insufficient evidence to inform on the management of these fractures [91] there has been emerging Level I evidence[137] within the field. The most recently published of such studies to be published was the PROFHER trial, a multicentre randomised controlled trial (RCT) [29]. Like other RCTs that have previously investigated treatment interventions for proximal humerus fractures[138,139], a variety of fracture types classified according to the Neer's system[6] were included within their study population. Following the publication of the PROFHER trial, updated meta-analysis have been published[95,140], however these have lacked a comprehensive application of sub-group and sensitivity analyses to better understand the effects of fracture complexity or type of surgical intervention.

Heterogeneity amongst RCTs investigating a treatment effect for different interventions in the management of disease and injury is an important and occasionally overlooked research concept[141]. When clinical heterogeneity between RCTs is associated with statistical heterogeneity amongst their treatment effects, decision-making on how to apply research

findings to clinical practice may be affected by the relevant patient or disease related factor[142]. In the case of meta-analysis, pooling data from such trials may also be questionable[142]. Identifying the clinical characteristics that underpin statistical differences in treatment effects provides an opportunity for the design of future RCTs. By conducting RCTs that have inclusion criteria that avoid the clinical heterogeneity identified in previous trials there is a perception that the treatment effects are more clinically applicable and informative[143]. This is particularly relevant to the management of proximal humerus fractures, where the variability in proximal humerus fracture morphology as well as the different surgical treatments available may be a reason for the lack of clinical implementation of findings from pragmatically designed RCTs or meta-analyses.

The aim of this meta-analysis is to provide an updated summary of outcomes of RCTs comparing surgical and non-surgical treatment of elderly patients with displaced proximal humerus fractures, and more specifically to establish whether increasing fracture complexity or type of surgical intervention produce treatment effects that are distinct from the overall meta-analysis.

2.2 Methods

2.2.1 Review protocol

This study was performed in accordance with the guidelines from the preferred reporting items for systematic reviews and meta-analyses (PRISMA)[144].

2.2.2 Search Strategy

A systematic search was performed in PubMed, EMBASE and Cochrane databases (January 1st 1975 – May 1st 2015) using the search term "proximal humerus". Studies were selected for further analysis after reading the individual abstracts. Additional citation review was performed using PubMed's related articles search to identify other studies that may be suitable for analysis.

2.2.3 Inclusion and Exclusion criteria

All randomised controlled trials that compared surgical and non-surgical management of proximal humerus factures were included. Study inclusion was not restricted by the type of surgical repair performed or the fracture-types included. Studies that described conservative treatment that involved a closed reduction under general anaesthesia were excluded. RCTs were only included if the mean age of patients was 65 or above. Only English language studies were included within the analysis and studies that did not include patient follow-up for at least 1 year were excluded. Two reviewers independently selected the relevant articles and reviewed their full texts to assess their eligibility. Discrepancies were resolved following assessment by a third reviewer.

2.2.4 Outcomes of Interest and Data Extraction

The following information was extracted from each study: authorship, year of publication, sample size, single/multicentre status, mean population age, fracture classification system used, fracture types included, surgical procedure performed, non-operative protocol, rehabilitation protocol, duration of follow up and patient outcomes.

Four outcomes of interest were extracted to compare surgical treatment with conservative management:

1. Functional outcome based on the Constant Score (CS).
2. Quality of Life Assessment (QLA) based on the EuroQol or 15-D instrument.
3. Additional surgery (secondary surgery following a complication of primary treatment).
4. Adverse events or complications: avascular necrosis (AVN), post-traumatic osteoarthritis (OA) and non/malunion.

2.2.5 Risk of bias in individual studies

The Cochrane Collaboration's tool for assessing risk of bias in randomized controlled trials[145] was used by two reviewers who independently assessed each domain of every study. A third reviewer was used to resolve potential discrepancies. Sensitivity analysis was performed to investigate whether risk of bias within the studies effected meta-analysis results for the pre-determined outcomes of interest.

2.2.6 Statistical analysis

Meta-analysis was conducted in line with recommendations from the Cochrane Collaboration and PRISMA[144]. Analysis was performed in Review Manager® Version 5.3. The summary statistics for dichotomous data (secondary surgery and adverse events) were odds ratio (OR), whereas the effect measure for continuous data (Constant Score and Quality of life assessment) was mean difference (MD), both reported with 95% confidence intervals (CI). The point estimate of the MD was considered statistically significant at $p < 0.05$ if the 95% CI did not include the value 0. An odds ratio was considered statistically significant at $p < 0.05$ if the 95% CI did not include the value 1. Data was analyzed using a random effects Mantel-Haenszel model.

Publication bias was assessed by graphical exploration with funnel plots. Heterogeneity was assessed using the I^2 statistic. This represents the proportion of total variation between included studies attributable to differences between studies rather than sampling error (chance). The degree of heterogeneity was graded as low (I^2<25%), moderate (I^2 =25-75%) or high (I^2>75%).

Three strategies were used to investigate potential causes of statistical heterogeneity within the included studies: (1) subgroup analysis of RCTs based on the predominant fracture-type within the study (>50% are 2-part, >50 are 3-part and >50% are 4-part; (2) sensitivity

analysis by meta-analysis of studies based on their risk of bias; (3) sensitivity analysis by meta-analysis of studies based on whether arthroplasty or internal fixation was performed for more than 80% of included cases. For sensitivity analysis, both fixed and random effects models were adopted and outcome measures were reported for each. Meta-regression was not performed due to the limited number of RCTs identified.

2.3 Results

Seven studies[29,30,69,138,139,146,147] published between 1975 and 2015 met the inclusion criteria for comparing surgical and non-surgical treatment of displaced proximal humerus fractures **(Figure 2.1).** These included a total of 528 patients; 50% underwent surgical treatment and 50% were managed conservatively. The results from one study group investigating the same group of patients were published as three separate studies that reported on different outcomes as well as outcomes at different follow up periods[120,138,148]. For the purpose of the analysis, these are reported as a single study. Six studies adopted the Neer classification system, with the one study that used the AO/OTA classification system stating that only 3 or 4 part fractures were included. Amongst the 7 studies, there were 3 studies that included only 4 part fractures, 2 studies that included 3 and 4 part fractures, 1 study that included only 3 part fractures and 1 study that included all fracture types **(Table 2.1).**

2.3.1 Outcomes of interest

2.3.1.1 *Constant score*

Four studies[30,69,138,146] reported a CS at 12 month follow up, of which there were 2 subgroups; 1 that included 2 studies with >50% 3-part fractures and another that included 2 studies with > 50% 4-part fractures. Meta-analysis of these studies showed comparable functional outcomes at 12 month follow up based on the CS (MD 2.82, 95% CI -2.17 to 7.82; p = 0.27), with no overall heterogeneity or heterogeneity between the subgroups.

Three studies[30,69,148] reported a CS at 24-month follow up, of which there were 2 subgroups; 1 that included 2 studies with >50% 3-part fractures and another with 1 study with >50% 4 part fractures. Meta-analysis of these studies showed comparable functional outcomes at 24 month follow up based on the CS (MD -0.20, 95% CI -6.68 to 6.39; p = 0.95), with no overall heterogeneity (I^2 = 0%) or heterogeneity between the subgroups (I^2 = 0%). One study with >50% 3-part fractures reported a CS at 50-month follow up and when included in the meta-analysis of 24-month follow up studies there was no statistically significant difference in outcome (MD -1.24, 95% CI -7.07 to 4.59; p = 0.68).

2.3.1.2 *Quality of Life Assessment*

Four studies[29,30,69,148] included quality of life outcomes or health utilities at 12 month follow up. Meta-analysis of these studies revealed that overall there were comparable health utilities at 12 month follow up for surgically and conservatively managed patients (MD 0.02, 95% CI -0.02 to 0.06; p =0.38), with low overall heterogeneity (I^2 = 6%) and low heterogeneity between subgroups (I^2 = 16.4%). These studies also reported health utilities at 24 month follow up and there was also no significant difference between patients treated surgically or conservatively (MD 0.06, 95% CI -0.04 to 0.16; p = 0.22), with moderate overall heterogeneity (I^2 = 55%) and moderate heterogeneity between subgroups (I^2 = 68.2%). There was an observable trend towards favorable outcomes for patients treated surgically as fracture complexity within the studies increased and the single study that included 4-part fractures had a significantly improved health utility score for patients managed surgically at 24 months follow-up **(Figure 2.2 and 2.3).**

2.3.1.3 *Additional surgery*

All seven studies reported on additional surgery following a failure or complication of the primary treatment. Overall, meta-analysis of all the studies **(Figure 2.4)** showed no statistically significant difference between patients who were initially managed surgically

compared to those managed conservatively (OR 1.88, 95% CI 0.92 to 3.85, p = 0.08). Although there was minor heterogeneity (I^2 = 4%) between the 7 studies, sub-group analysis between studies with >50% 2-part fractures, studies with >50% 3-part fractures and studies with > 50% 4-part fractures revealed moderate heterogeneity (I^2 = 60%). Furthermore, sub-group analysis of studies with > 50% 3-part fractures produced a statistically significant OR favoring conservative management (OR 6.47, 95% CI 1.59 to 26.38; p = 0.009).

2.3.1.4 *Adverse events or complications*

All seven studies reported on complications or adverse events occurring as a result of surgical or conservative treatment. Overall, meta-analysis of the studies **(Figure 2.5)** showed no statistically significant difference in the incidence of AVN, post-traumatic OA and mal/nonunion between the two groups (OR 0.51, 95% CI 0.25 to 1.05; p = 0.07). There was moderate overall heterogeneity (I^2= 34%), which was increased when heterogeneity between sub-groups was assessed (I^2= 60.80%). Furthermore, only sub-group analysis of studies with >50% 4-part fractures demonstrated a statistically significant difference in treatment outcomes with less adverse events likely in patients undergoing surgical treatment (OR 0.14, 95% CI 0.25 to 1.05; p=0.003; I^2 = 0%).

2.3.2 Assessment of bias

Using the Cochrane Collaboration's tool for assessment of bias, 5 studies were rated as 'low risk' of bias[29,30,69,146,148], 1 was rated as 'high risk' of bias[147] and 1 was found to have an 'unclear risk' of bias[139] **(Figure 2.6).** Studies that were rated as low risk all had clearly defined randomization methods, however across all 7 studies there a lack of blinding of participants and clinicians noted. These were rated as 'unclear risk' instead of 'high risk' because of a perceived impracticality of blinding patients and clinicians when comparing surgical and non-operative treatment. Selective reporting was difficult to assess across most

the trials, however one study had a published protocol[29] in which the stated outcomes of interest matched those within the final publication and this was judged to be at 'low risk' of bias.

Funnel plots **(Figure 2.6)** based on re-operation and adverse events as outcomes of interest were created to evaluate publication bias. For both evaluations, all the studies were found to lie within a 95% CI as represented by the inverted funnel, suggesting an absence of publication bias.

2.3.3 Sensitivity analysis

Sensitivity analysis was performed on studies based on their risk of bias in order to determine whether methodological heterogeneity influenced statistical heterogeneity of outcome measures, and also to evaluate the effect of type of surgical treatment on outcomes **(Table 2.2 – Table 2.5).** Studies at 'low risk of bias' were subjected to meta-analysis separately from the 2 studies where the risk of bias was 'unclear' or 'high risk'.

When sensitivity analysis was performed on studies based on the predominant surgical procedure carried out, a significant treatment effect in QLA at 24 months was found for the single study that performed hemiarthroplasty (MD, 95% CI 0.04 to 0.28; p = 0.007). Hemiarthroplasty studies were also less likely to result in the pre-defined adverse events (OR 0.14, 95% CI 0.04 to 0.51; p = 0.03). For a fixed effects model, re-operation rates were higher in studies where the predominant surgical treatment was internal fixation (OR 1.98, 95% CI 1 to 3.93). Hemiarthroplasty studies included only 4-part fractures. Internal fixation studies included all fracture types. There was moderate heterogeneity within the internal fixation studies when evaluating re-operation as an outcome of interest ($I^2 = 47\%$). There was no heterogeneity found in any of the meta-analysis performed for hemiarthroplasty studies.

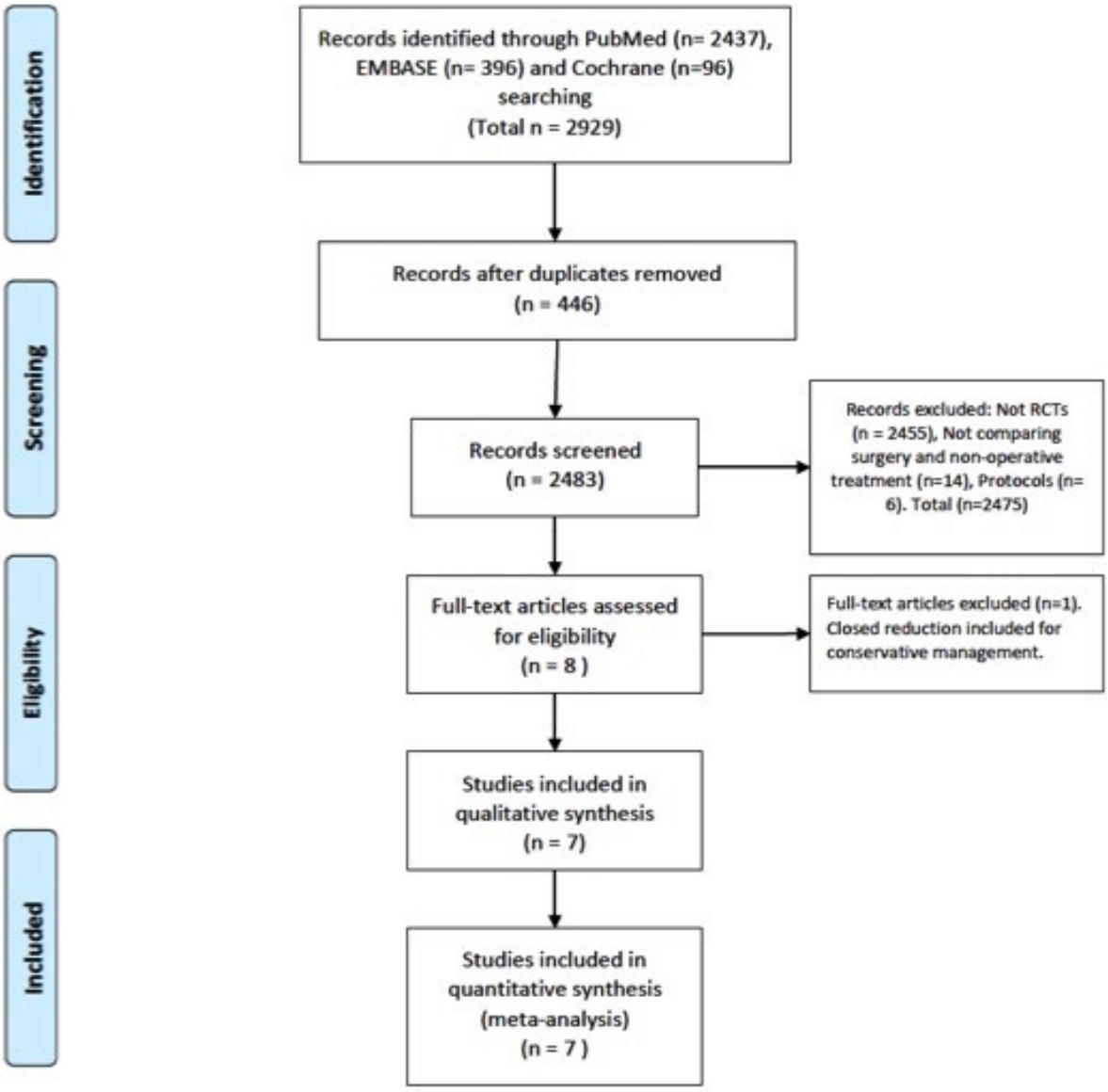


Figure 2.1. PRISMA Flow Diagram showing search strategy

Table 2.1. Characteristics of studies included in the meta-analysis

Author (Year)	Country	Single-centre/ Multicentre	Sample size	Mean age surgical group	Mean age conservative group	Surgical procedure	Fracture type (Neer classification)
Rangan et al. (2015)[29]	United Kingdom	Multicentre	250	66.6	65.4	Plate fixation (82.6%) Hemiarthroplasty (9.2%) Other (8.2%)	2 part (51.2%) 3 part (37.2%) 4 part (4.4%) 1 part (7.2%)
Boons et al. (2012)[146]	Netherlands	Single centre	50	76.4	79.9	Hemiarthroplasty	4 part
Fjalestad et al. (2012) ∗[120,138,148]	Norway	Single centre	50	72.2	73.1	Plate fixation	3 part (52%) 4 part (48%)
Olreud et al. (2011) (H)[30]	Sweden	Single centre	55	75.8	77.5	Hemiarthroplasty	4 part
Olreud et al. (2011) (F)[30]	Sweden	Single centre	60	72.9	74.9	Plate fixation	3 part
Zyto et al. (1997)[139]	Sweden	Single centre	40	73	75	Tension band fixation	3 part (92.5%) 4 part (7.5%)
Stableforth (1984)[147]	United Kingdom	Single centre	32	65.6	70.1	Hemiarthroplasty	4 part

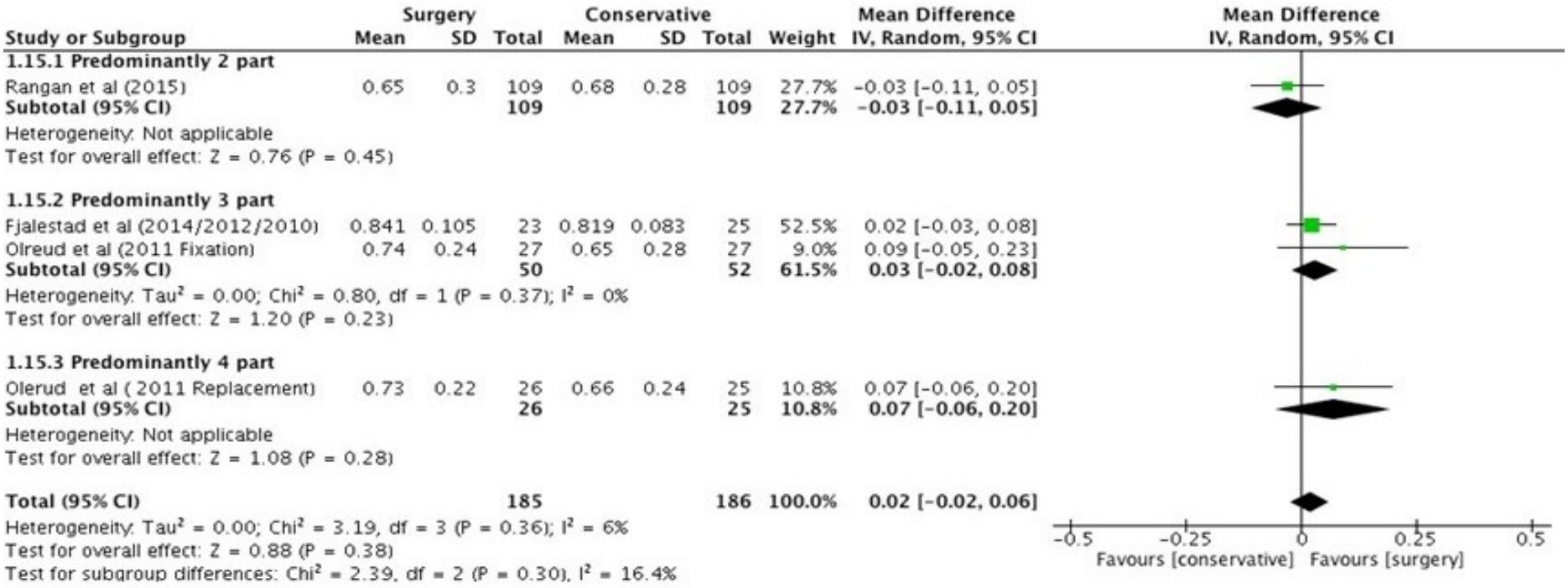


Figure 2.2. Meta-analysis of health utilities reported at 12 months showing a non-significant trend towards improved outcomes for patients managed surgically as fracture complexity increases

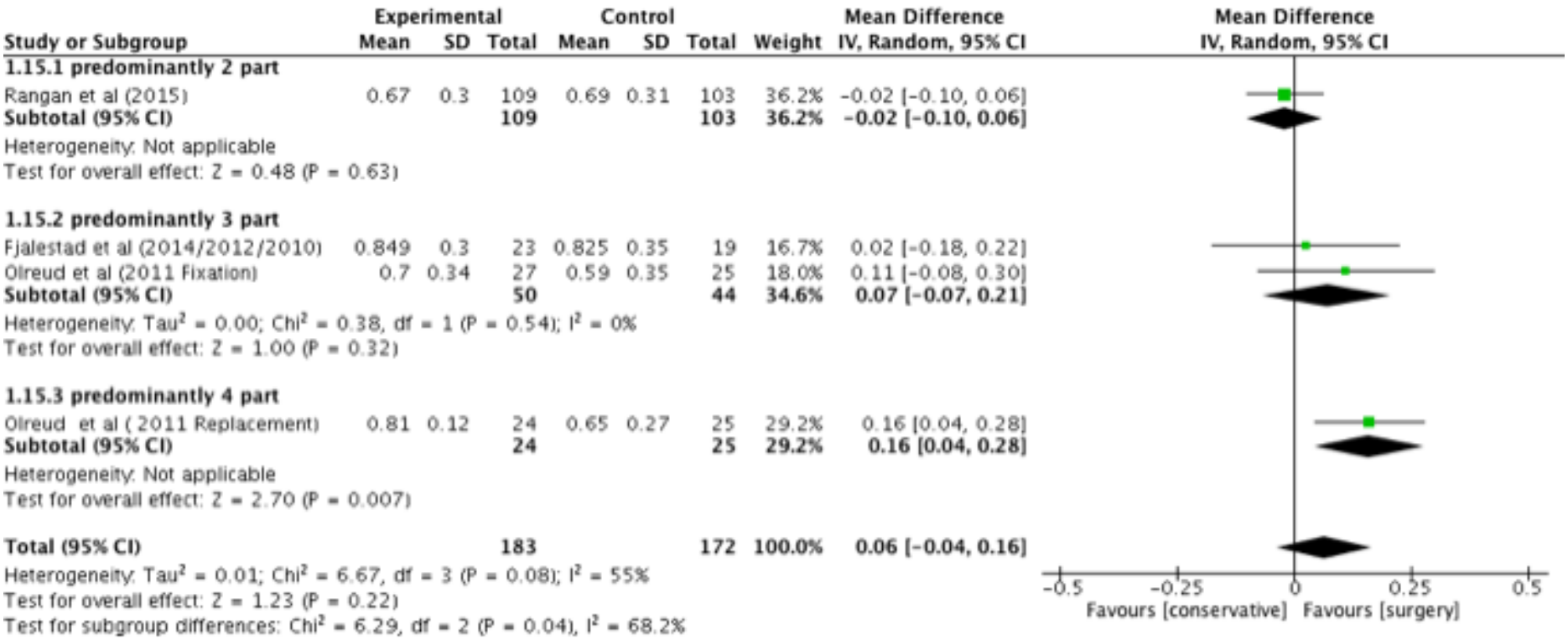


Figure 2.3. Meta-analysis of health utilities reported at 24 months showing a non-significant trend towards improved outcomes for patients managed surgically as fracture complexity increases

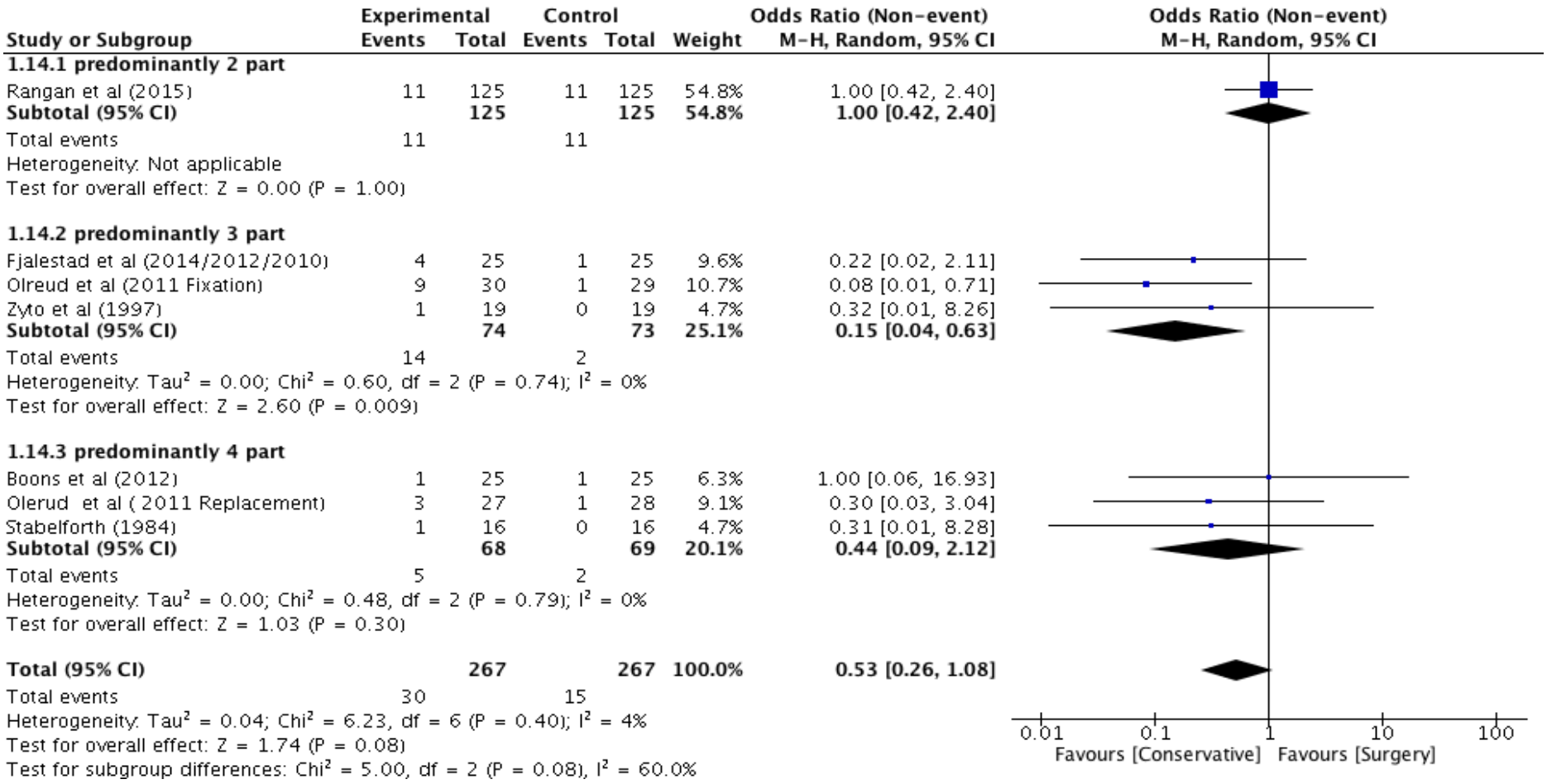


Figure 2.4. Forest plot demonstrating that trials with predominantly 3 part fractures were less likely to undergo secondary surgery if managed conservatively

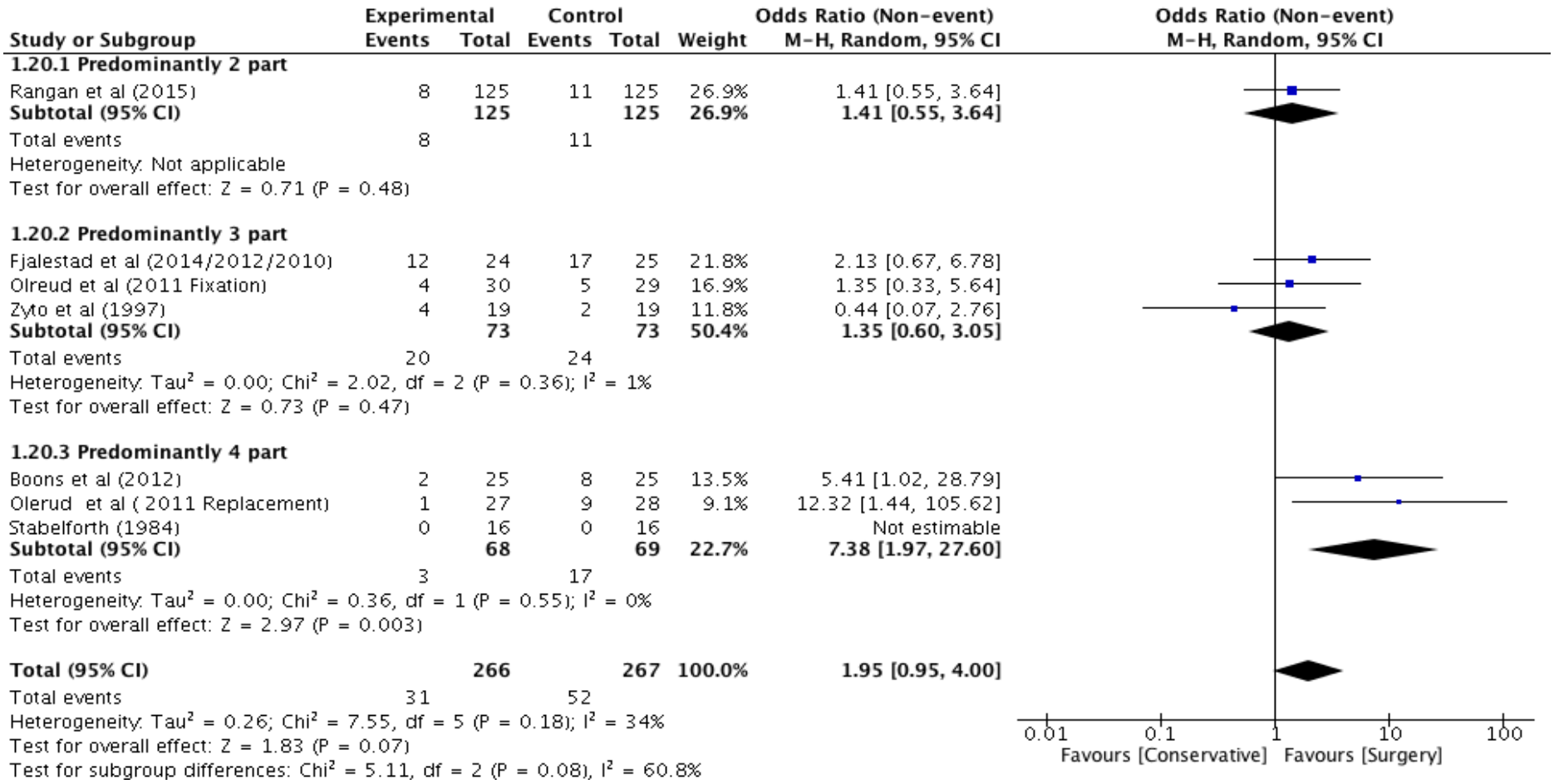


Figure 2.5. Forest plot demonstrating that trials with predominantly 4 part fractures favoured surgery when adverse events were evaluated at a minimum of 1 year follow up

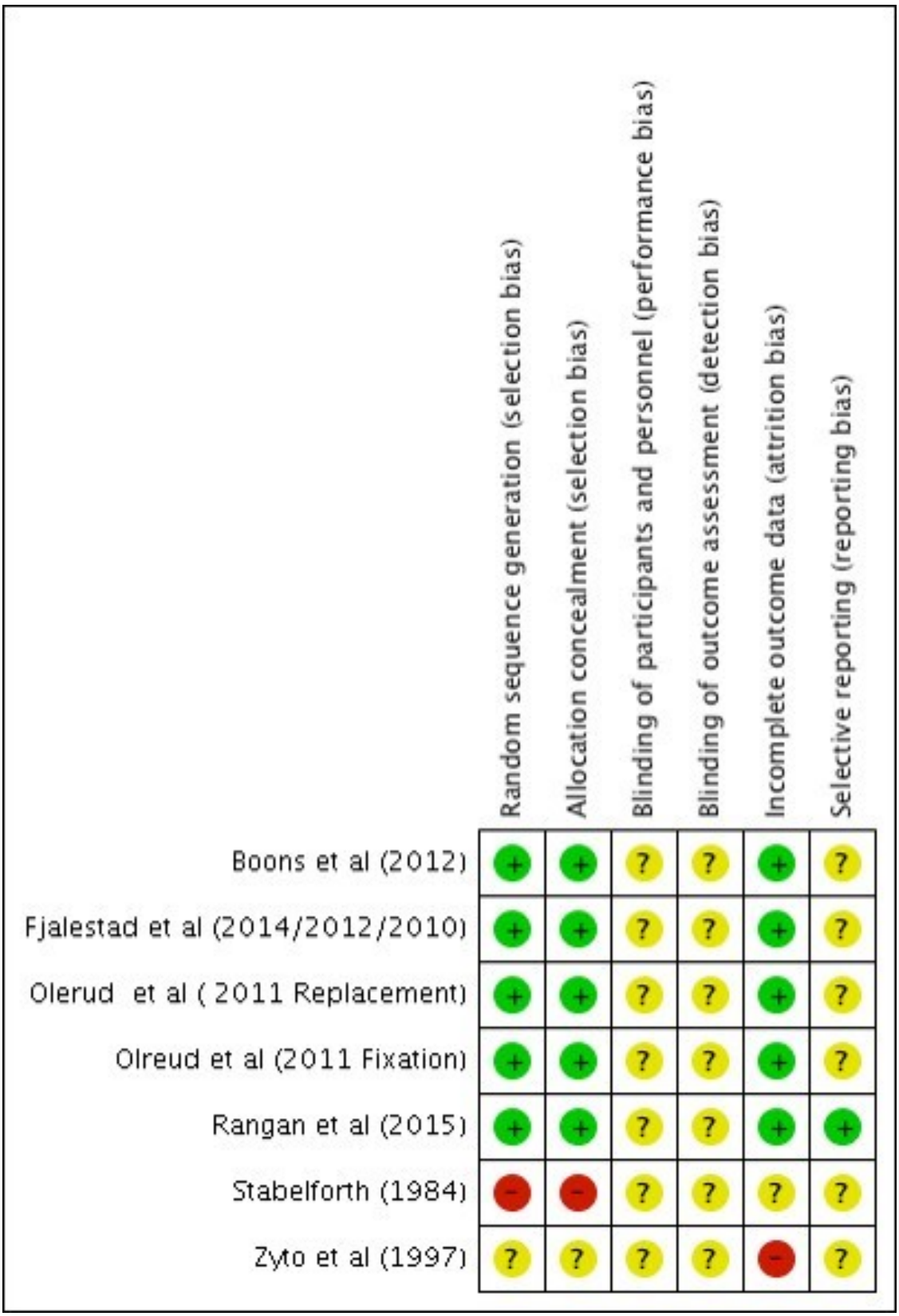


Figure 2.6. Cochrane risk of bias summary for 7 included studies (+ represents low risk, ? represents unclear risk, - represents high risk)

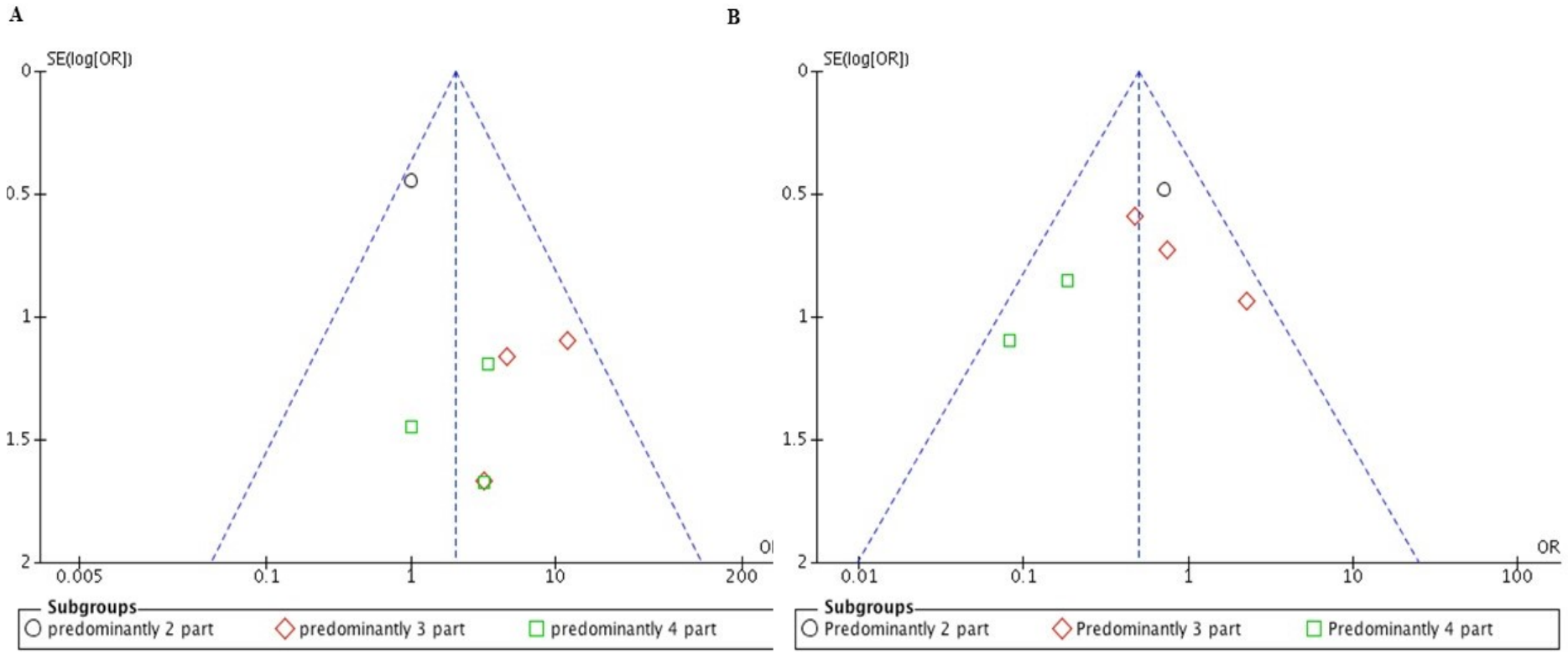


Figure 2.7. Funnel plot demonstrating risk of publication bias based on A re-operation as an outcome measure and B adverse events as an outcome measure

Table 2.2. Sensitivity analysis of Constant Scores based on choice of surgical intervention and risk of bias showing no significant effect on treatment effect or heterogeneity between trials

	Studies where surgery was arthroplasty for >80% cases		**Studies where surgery was fixation for >80% cases**		**Studies with low risk of bias**		**Studies with unclear or high risk of bias**	
Outcome of interest	Fixed effects model	Random effects model	Fixed effects model	Random effects model	Fixed effects model	Random effects model	Fixed effects model	Random effects model
Constant score at 24 months								
Number of studies	1		2		3		0	
Number of patients	49		95		144		-	-
MD	-1.30	-1.30	0.55	0.55	-0.20	-0.20	-	-
95% CI	-11.67, 9.07	-11.67, 9.07	-7.98, 9.07	-7.98, 9.07	-6.78, 6.39	-6.78, 6.39	-	-
P value	0.81	0.81	0.90	0.90	0.95	0.95	-	-
Heterogeneity within group	-	-	$I^2 = 0\%$	$I^2 = 0\%$	$I^2 = 0\%$	$I^2 = 0\%$	-	-
Heterogeneity between groups (fixed effects, random effects)	$I^2 = 0\%$, $I^2 = 0\%$,				-			

Table 2.3. Sensitivity analysis of QALYs based on choice of surgical intervention and risk of bias showing a significant improvement for the study where >80% of cases where treated with hemiarthroplasty compared to conservative management. Moderate heterogeneity was also found within studies with low risk of bias.

	Studies where surgery was arthroplasty for >80% cases		**Studies where surgery was fixation for >80% cases**		**Studies with low risk of bias**		**Studies with unclear or high risk of bias**	
Outcome of interest	Fixed effects model	Random effects model	Fixed effects model	Random effects model	Fixed effects model	Random effects model	Fixed effects model	Random effects model
Quality of life assessment at 24 months								
Number of studies	1		3		4		-	
Number of patients	49		294		357		-	
MD	0.16	0.16	0	0	0.05	0.06	-	-
95% CI	0.04,0.28	0.04,0.28	-0.07, 0.07	-0.07, 0.07	-0.01,0.11	-0.04, 0.17	-	-
P value	**0.007 (favours surgery)**	**0.007 (favours surgery)**	0.92	0.92	0.14	0.22	-	-
Heterogeneity within group	-	-	$I^2 = 0\%$	$I^2 = 0\%$	**$I^2 = 55\%$**	**$I^2 = 55\%$**	-	-
Heterogeneity between groups (fixed effects, random effects)	$I^2 = 12.3\%$, $I^2 = 12.3\%$				-			

Table 2.4. Sensitivity analysis of secondary surgery rates based on choice of surgical intervention and risk of bias showing a significantly reduced risk of re-operation for patients managed conservatively compared to surgically in trials where >80% of cases were treated with a locking plate. Similar effect identified on evaluation of trials at low risk of bias.

	Studies where surgery was arthroplasty for >80% cases		**Studies where surgery was fixation for >80% cases**		**Studies with low risk of bias**		**Studies with unclear or high risk of bias**	
Outcome of interest	Fixed effects model	Random effects model	Fixed effects model	Random effects model	Fixed effects model	Random effects model	Fixed effects model	Random effects model
Reoperation or secondary surgery								
Number of studies	3		4		5		2	
Number of patients	137		397		463		70	
OR	2.34	2.28	1.98	2.78	1.96	2.30	3.18	3.18
95% CI	0.51, 10.82	0.47, 11.05	1, 3.93	0.74, 10.49	1.02, 3.76	0.82, 6.45	0.31, 32.06	0.31,32.06
P value	0.28	0.30	**0.05 (favours conservative)**	0.13	**0.04 (favours conservative)**	0.11	0.33	0.33
Heterogeneity within group	$I^2 = 0\%$	$I^2 = 0\%$	**$I^2 = 47\%$**	**$I^2 = 47\%$**	**$I^2 = 33$**	**$I^2 = 33$**	$I^2 = 0\%$	$I^2 = 0\%$
Heterogeneity between groups (fixed effects, random effects)	$I^2 = 0\%$, $I^2 = 0\%$				$I^2 = 0\%$, $I^2 = 0\%$			

Table 2.5. Sensitivity analysis of adverse events rates based on choice of surgical intervention and risk of bias showing a significantly reduced risk of for patients managed surgically in trials where >80% of cases where hemiarthroplasty. High risk of heterogeneity detected between trials based on predominant type of surgical intervention.

	Studies where surgery was arthroplasty for >80% cases		**Studies where surgery was fixation for >80% cases**		**Studies with low risk of bias**		**Studies with unclear or high risk of bias**	
Outcome of interest	Fixed effects model	Random effects model	Fixed effects model	Random effects model	Fixed effects model	Random effects model	Fixed effects model	Random effects model
Adverse events (AVN, Post-traumatic OA, non/malunion)								
Number of studies	3		4		5		2	
Number of patients	137		397		463		70	
OR	0.13	0.14	0.73	0.73	0.42	0.44	2.27	2.27
95% CI	0.04, 0.48	0.04, 0.51	0.40,1.34	0.39,1.34	0.24,0.74	0.22,0.86	0.36,14.19	0.36,14.19
P value	**0.002 (favour surgery)**	**0.003 (favours surgery)**	0.31	0.31	**0.003 (favours surgery)**	**0.02 (favours surgery)**	0.38	0.38
Heterogeneity	$I^2 = 0\%$	$I^2 = 0\%$	$I^2 = 0\%$	$I^2 = 0\%$	$I^2 = 19\%$	$I^2 = 19\%$	*	*
Heterogeneity between groups (fixed effects, random effects)	**$I^2 = 82.2\%$. $I^2 = 80.4\%$**				**$I^2 = 65.9$, $I^2 = 63\%$**			

2.4 Discussion

The overall meta-analysis suggests there is no significant difference in outcomes between surgical and conservative management. However, the results of the sub-group and sensitivity analysis demonstrated that 4 part fractures treated with hemiarthroplasty had specific health outcomes that were improved compared to when managed conservatively. There was also sub-group analysis which found that patients with 3-part fractures that were treated with locking plates were more likely to require secondary surgery than if managed conservatively. A key implication of the findings of this study is that the heterogeneity between sub-groups based on fracture complexity, and the distinct findings based on type of surgical intervention adopted, underline a need for future RCT design to adopt more specific inclusion criteria based on these clinical variables.

Sub-group analysis of health utilities based on the predominant fracture types within each study demonstrated a trend towards improved outcomes as fracture complexity increased. The single study that included patients with 4-part fractures had significantly improved outcomes for patients managed surgically. Sensitivity analysis of this study demonstrated a statistically significant benefit in surgery over conservative treatment. Studies where the main type of fracture was 3 part had a significantly increased risk of additional surgery for patients who underwent surgical intervention as a primary treatment. Although not statistically significant, there was also an observable difference with an increased OR for additional surgery after surgical management of 4-part fractures compared to 2-part fractures. Within the subgroups separating trials by the fracture complexity there was no statistical heterogeneity, however there was moderate statistical heterogeneity between those subgroups (I^2 = 60%). This heterogeneity was not eradicated, or reduced from moderate to low, when sensitivity analysis was performed based on risk of bias. This suggests that differences in methodology were not underpinning statistical heterogeneity of treatment effects when

considering additional surgery as an outcome of interest. The finding of the sub-group analysis suggest what is intuitive in clinical practice; more complex fractures are more difficult to manage surgically and hence they are likely to require additional surgery to manage failure or complications following the primary surgical procedure.

When evaluating complications after surgical and conservative treatment the selection of type of adverse events was based on inclusion of events that plausible with either intervention. Post traumatic OA, AVN and mal/nonunion are significant indicators of future disability and have been previously been adopted as end-points to compare the incidence of adverse events between the two interventions groups[42,149]. Although the overall analysis suggests there is no statistical difference between surgical and non-operative treatment in relation to these events, sub group analysis of 4 part fractures results in a significant OR that favours surgery (OR 0.14, 95% CI 0.04 to 0.51; p = 0.03) and there was moderate heterogeneity between the subgroups (I^2 = 60.8%). This is likely to be cofounded by the fact that 4 part studies adopted hemiarthroplasty as the surgical intervention and therefore such complications were unlikely to occur when the humeral head was replaced.

The implications of this meta-analysis for future RCT design are clear; homogeny of fracture complexity and the type of surgical procedure are likely to provide clinically applicable findings that aid decision making in this field. While the role of pragmatic trials in this field is greatly important for generating externally valid results that reflect the treatment needs of the wider population[150], there is a potential for misguided interpretation and application; specifically there is potential for a view that outcomes for surgery and conservative management are identical for all displaced proximal humerus fractures[151]. The wide range of fracture patterns that numerous systems have attempted to classify are known to variably

predict clinical outcome[152], and therefore the influence of fracture type on clinical outcome when hypothesizing whether surgical and conservative treatment are comparable is relevant.

At the time the last search was performed within this study, there were 7 ongoing RCTs that included 947 patients, registered in the World Health Organization's International Clinical Trials Registry Platform, that were investigating the difference between surgical and conservative management for proximal humerus fractures **(Table 2.6).** Amongst the 5 RCTs that used the Neer classification system, 2 include 2, 3 and 4 part fractures, 2 include 3 and 4 part fractures and only 1 includes 4 part fractures. The other ongoing trials are investigating complex and displaced fractures based on the AO and Hertel's classification system. While it has often been suggested that the reliability of the current classification systems are poor[42], whichever system is adopted this meta-analysis has underlined that there is need for a more specific fracture type in the inclusion criteria. Within the research community in this field, there is also a need to recognise that appropriate study design has a large role to play in the feasibility of such research. Given that the PROFHER trial was the only study out of the 7 within this meta-analysis that was performed at multiple sites, and it recruited almost 4 times as many patients as the next largest study within the shortest period of time, there is a clear need and benefit to collaboration between research institutions in future RCTs. This will allow appropriate sample size recruitment over

Table 2.6. Trials registered in the WHO International Clinical Trials Registry Portal investigating surgical versus conservative treatment of proximal humerus fractures (Search Performed on the 5th January 2016)

Study name *(ID)*	Country	Single centre or Multicentre	Sample size	Fracture type included	Interventions
Proximal Humerus Fracture Randomized Control Trial *(NCT02362100)*	Canada	Unknown	155	Neer types: 2,3 &4	Locking plate versus conservative
Treatment of Proximal Humeral Fractures (TPHF) *(NCT01246167)*	Finland	Multicentre	290	Neer type: 2,3 &4 (low energy injuries with other specifications described)	Hemiarthroplasty versus plate versus conservative
Treatment of Comminuted Fractures of the Proximal Humerus *(NCT00999193)*	Finland	Unknown	90	Neer type: 3,4 part with > 5mm dislocation of anatomical neck AO C1-2 for non-luxation fractures and C3 for luxation fractures	Hemiarthroplasty versus plate versus conservative
Primary hemiarthroplasty versus conservative treatment for comminuted fractures of the proximal humerus in the elderly (ProCon) *(NTR2040)*	Netherlands	Multicentre	80	Selected Hertel types: 9-12, selected Hertel types 2, or head split fractures based on the judgement of the attending surgeon.	Hemiarthroplasty versus conservative
Comminuted Proximal Humerus Fractures. A Randomised study of Surgical Versus Conservative Treatment *(NCT00863473)*	Norway	Unknown	50	AO B2 or C2 (with further specification on selected types)	Locking plate versus conservative
Effect of Osteosynthesis. Primary Hemiarthroplasty, and Non-surgical Management for Fractures of the Proximal Humerus *(NCT00835562)*	Denmark	Multicentre	162	Neer type 4	Hemiarthroplasty versus plate versus conservative
Operative Versus Non Operative Treatment of Proximal Humerus (Shoulder Joint) Fractures *(NCT0818987)*	Canada	Multicentre	120	Neer type 3 &4	Internal fixation versus conservative

a shorter period of time to be conducted for specific fracture types, which represent smaller cohorts within the general population. Furthermore, conducting multicenter RCTs such as the PROFHER trial will increase the external validity of the research findings[153], which is particularly important in orthopaedics where technical skill is variable and may be a source of performance bias[154].

Functional outcome measures that were adopted in the 7 RCTs included in this meta-analysis were found to vary substantially between trials. Although the majority of these functional assessment measures are valid[52,155], interpretation and comparison of results between studies that have adopted different functional outcome measures is challenging. In hip fracture research, key opinion leaders have proposed core outcome measures for clinical trials in order to improve evidence synthesis within their field[156]**.** The COMET (Core Outcome Measures in Effectiveness Trials) Initiative brings researchers together from multiple fields to standardise outcomes in clinical research[157]. The database includes work to develop standardised core outcomes in upper limb orthopaedics. Consensus and evidence-based guidance on core outcome measures for future proximal humerus fracture trials that have been developed by recognized professional bodies in upper limb orthopaedics could improve the reporting of outcomes as well as the ability to interpret the overall evidence base. Similarly, by going even further and commissioning or sanctioning trials, such organizations can facilitate the multicentre collaboration and clinical trials networking that is required to produce well-designed RCTs[158] that are sufficiently powered to investigate treatment effects for more specific fracture types.

2.4.1 Study Limitations

Our study has 4 main limitations. Firstly, the number of studies included was less than 10. As such, our evaluation of publication bias should be treated with caution as funnel plot

asymmetry is most accurately performed when there are at least 10 studies[159]. Secondly, quantifying heterogeneity using I^2 as a metric that has intervals of severity such as those defined in our methods has been subject to methodological debate[160]. Despite this, the definition of moderate heterogeneity that we used when reporting heterogeneity between fracture-type sub-groups, is based on values described in recognized standards for meta-analysis research[159]. Thirdly, for the 3 studies selected and included in sensitivity analysis of internal fixation as a predominant treatment, 1 involved tension band wiring[139] and the remaining 2 included locking plate fixation[69,148]. Locking plates are a newer technology that are often viewed to be advantageous for internal fixation and therefore some caution is required when considering the results of sensitivity analysis performed on this group, as there are potential differences in efficacy of these 2 variations of internal fixation. Finally, an absence of RCTs that compare reverse arthroplasty with conservative treatment limits the clinical applicability of meta-analysis of the current evidence base, particularly with the growing uptake of this procedure for fracture management[161], and some evidence to suggest that it is superior to hemiarthroplasty for complex proximal humerus fractures in the elderly[162]. Despite this, our results have important implications for the design of future trials, which need to recognize the need for more specific inclusion criteria so that their conclusions can more accurately inform clinical decision-making.

2.4.2 Conclusion

Treatment effects in RCTs evaluating interventions for the management of proximal humerus fractures in elderly patients are likely to be distinct based on fracture complexity and surgical intervention adopted. Existing evidence indicates that patients with 4 part fractures managed with hemiarthroplasty will have health outcomes that are superior to conservatively managed patients. There is quantifiable statistical heterogeneity between current trials and this appears to be based on clinical heterogeneity such as inclusion of patients with different severity of

fracture. Future research within this field may produce more clinically applicable findings if their study design adopts an inclusion criteria based on a more homogenous fracture type or a single philosophy of treatment.

Chapter 3

A qualitative study exploring elderly patients' perceptions of their recovery after sustaining a complex proximal fracture

3.1 Introduction

Proximal humerus fractures are common musculoskeletal injuries and they have a significant effect on patient and healthcare resources[3]. A better understanding of their management is required to improve the health outcomes of patients that sustain these injuries. The volume of quantitative analysis evaluating interventions in the management of proximal humerus fractures has been increasing substantially over the last 30 years[95]. The conventional paradigm for research in orthopaedics has been a quantitative design[78], and this is perhaps why there is an absence of any qualitative research in the evidence based literature that has evaluated patient experiences after sustaining a proximal humerus fracture.

Qualitative research is increasingly viewed to be an important research tool to inform the decision-making of clinicians and health policy makers[84]. The exploratory nature of qualitative research allows researchers to develop an understanding of complex relationships, experiences and decision-making that quantitative work is often too restrictive to address[78]. Furthermore, patients' attitudes towards the treatment of their musculoskeletal conditions have been shown to affect their satisfaction, and therefore understanding the patient perspective is essential in establishing what is the nature of the clinical effectiveness that is being sought[163].

This narrative is seen across clinical medicine, where clinical effectiveness is less commonly quantified using measures important to clinicians; rather the health outcomes that are of value to patients are used to develop patient reported outcome measures (PROMs)[164]. Qualitative analysis has an important role in developing themes that are relevant to the target

population's outlook on their health status, and these themes are then used to develop the various components evaluated within a PROM[165]. This is particularly important in orthopaedics, where a myriad of PROMs have been developed, none of which are specific to an elderly population with proximal humerus fractures. In the absence of a disease-specific measure within the target population, there is a need to better understand what are the aspects of recovery that these patients value.

A qualitative exploration of patients' experiences after surgical and non-surgical treatment of proximal humerus fractures is required to better understand patients' experiences during their recovery. In addition, a comprehensive qualitative analysis of patient experience will allow us to determine what aspects of recovery are important and should be developed as part of a PROM for elderly patients with a complex proximal humerus fracture. The objective of this study was to use a qualitative analytical approach to better understand the experiences and perceptions of recovery of elderly patients who had sustained a complex proximal humerus fracture.

3.2 Methods

A qualitative study design was employed using face-to-face semi-structured interviews to explore elderly patients' perceptions of their recovery after sustaining a complex proximal humerus fracture. Ethical approval for the study was received from the National Research Ethics Service Committee (Research Ethics Committee reference 14/LO/2191).

3.2.1 Participant selection

3.2.1.1 *Inclusion Criteria*

1. Patients aged 65 or above
2. Patients diagnosed with a Neer type[6] 3 or 4-part proximal humerus fracture and treated at Imperial College NHS Trust
3. Patients at least 1 year post injury

3.2.1.2 *Exclusion Criteria*

1. Poly-trauma patients
2. Patients with mental incapacity unable to give informed consent
3. Patients unable to understand verbal and written information in English

3.2.2 Recruitment and sampling

Patients with a diagnosis of a proximal humerus fracture who met the inclusion criteria were identified through hospital records. Purposive sampling of these patients was performed by members of the clinical research team that were familiar with the patients' histories. The sample selected represented both surgically and conservatively managed patients. Patients with differing frailty and clinical outcomes were also chosen so that the sample would be representative of the full range of health outcomes that could be expected. A patient information sheet about the study along with a letter inviting them to participate in the study were sent to patients that met the inclusion criteria **(Appendix 2).** Contact details of the lead author (SS) were provided in the information sheet and patients subsequently contacted him expressing their interest in participation. Based on existing upper limb orthopaedic qualitative research[166] it was expected that a sample size of between 10 and 15 patients would be sufficient for thematic saturation to be achieved.

3.2.3 Data collection

Semi-structured interviews were conducted face-to face at Imperial College NHS Trust. Interviews were conducted by the lead author (SS) and they started by establishing informed consent. The study was discussed at length, the patient information sheet was reviewed with the patient and patients signed a consent form prior to the interview commencing **(Appendix 2).** Interviews were recorded on a digital voice recorder. All the interviews included a range of open-ended questions such as "tell me what happened to you" and "tell me as much as you

can about your experiences during your recovery". Patients were given as much time as they wanted to respond to these questions and report on their experiences. When they had finished talking, an interview prompt form was referred to so data collection covered a consistent and wide range of aspects of recovery that the research team viewed to be important and of interest **(Table 3.1).** Field notes were taken by the interviewer during the interviews to document body language and an obvious change in mood. The interview ended when the patient confirmed they have nothing further to add.

3.2.4 Data analysis

Thematic analysis as outlined by Braun and Clarke was used to analyse the data generated in this study[27]. Thematic analysis is a type of qualitative analysis that is systematic in its application yet allows for nuanced approaches and an interpretative in-depth analysis [167]. It has been applied to recent qualitative research exploring patient perceptions after orthopaedic surgery in other sub-specialties[168,169], and as such its methodology was considered appropriate for this study design. Firstly, interviews were transcribed verbatim and familiarity with the data was gained by extensive reading and re-reading of the transcripts. Notes were also taken during this process to generate ideas for potential codes. In the second stage, coding was performed by systematic assessment through the entire data set, allocating relevant data to each code. Provisional themes were then developed and codes were allocated to each of these themes. Themes were reviewed and refined to develop a set of candidate themes that supported the majority of the data and a thematic map of analysis was constructed. Finally, examples were taken from all the interviews to illustrate the thematic framework.

Table 3.1. Interview prompt schedule that was referred to during patient interviews

Open questions – patients expected to talk at length	
Tell me what happened to you?	
Tell me as much as you can about your experiences during your recovery?	
How did you feel in the days and weeks after your injury?	
How do you feel you responded to the treatment?	
How do you feel your rehabilitation went?	
How are you now?	
Specific questions – to prompt patients if subject matter not already covered	
Tell me about your experience with pain after the injury.	
Tell me about your experience with mobility after this injury.	
Tell me about your experience with sleep after this injury.	
Tell me about your mood after this injury.	
Tell me about your concerns after this injury.	
Tell me about any problems you had with employment or money after this injury.	
Have you needed a lot of help in the last year?	
Is there anything specific you want to mention about your injury, treatment or recovery?	

3.3 Results

A total of 15 patients were recruited to the study that met the inclusion criteria. All 15 were interviewed and included in the qualitative analysis **(Table 3.2).** There were 11 female patients and 4 male patients. The mean age of patients was 71.8 years when they sustained their injury (65 – 84 years). At the time of the interviews the mean time since injury had been 2.4 years (1.1 – 5 years). As the patients had been purposively sampled to represent a broad range of treatment experiences after sustaining a complex proximal humerus fractures, there were 5 patients that had undergone conservative management and 10 patients that had undergone surgical management. Of the 10 patients that had surgical management, 7 had been treated with a locking plate, 1 had a suture fixation and 2 had a hemiarthroplasty.

There were 5 patients included (33.3%) that had a complication. One patient had sustained an axillary nerve neuropraxia at the time at the injury causing some sensory changes and discomfort over the affected shoulder. The symptoms had partially improved 2.4 years after the injury had occurred. One patient was treated with a locking plate and went on to develop painful osteoarthritis in the shoulder. She subsequently had a single stage revision to a hemiarthoplasty 2 years after her primary surgery. Two further patients treated with a locking plate had secondary surgery. One patient had failure of his metal work within the first few weeks and immediately had a re-plating procedure performed. The second had removal of his plate a year after his primary surgery as one of the humeral head screws had migrated and was penetrating into the gleno-humeral joint. Finally, one patient who was managed conservatively had developed painful osteoarthritis 18 months after her injury, however she had decided not to have secondary surgery to manage her symptoms.

Table 3.2. Patient demographics and management strategies employed

ID	Gender	Age at injury (years)	Injury to interview interval (years)	Management method	Complications
1	Male	73	4.5	Conservative management	-
2	Female	65	4.2	Conservative management	-
3	Male	67	1.5	Locking plate	-
4	Female	66	2.4	Locking plate	Axillary nerve injury – on-going sensory disturbance in cutaneous distribution
5	Female	80	5.1	Locking plate	Developed painful OA and AVN and went on to have a hemiarthroplasty
6	Male	75	1.5	Locking plate	Had to have a revision procedure due to screw penetrating into joint
7	Female	75	2.1	Conservative management	Developed painful OA after a year
8	Female	69	2.6	Locking plate	Removal of locking plate after a year – screw penetrating into joint
9	Male	76	2.1	Hemiarthroplasty	-
10	Female	65	1.1	Conservative management	-
11	Female	67	2.2	Locking plate	-
12	Female	84	1.6	Conservative management	-
13	Female	69	1.7	Suture fixation	-
14	Female	72	2.3	Locking plate	-
15	Female	74	1.1	Hemiarthroplasty	-

3.3.1 Thematic analysis

Seven patient reported themes associated with recovery after a proximal humerus fracture were identified and are demonstrated in a thematic map **(Figure 1).** Thematic saturation occurred after the interview of 11 patients.

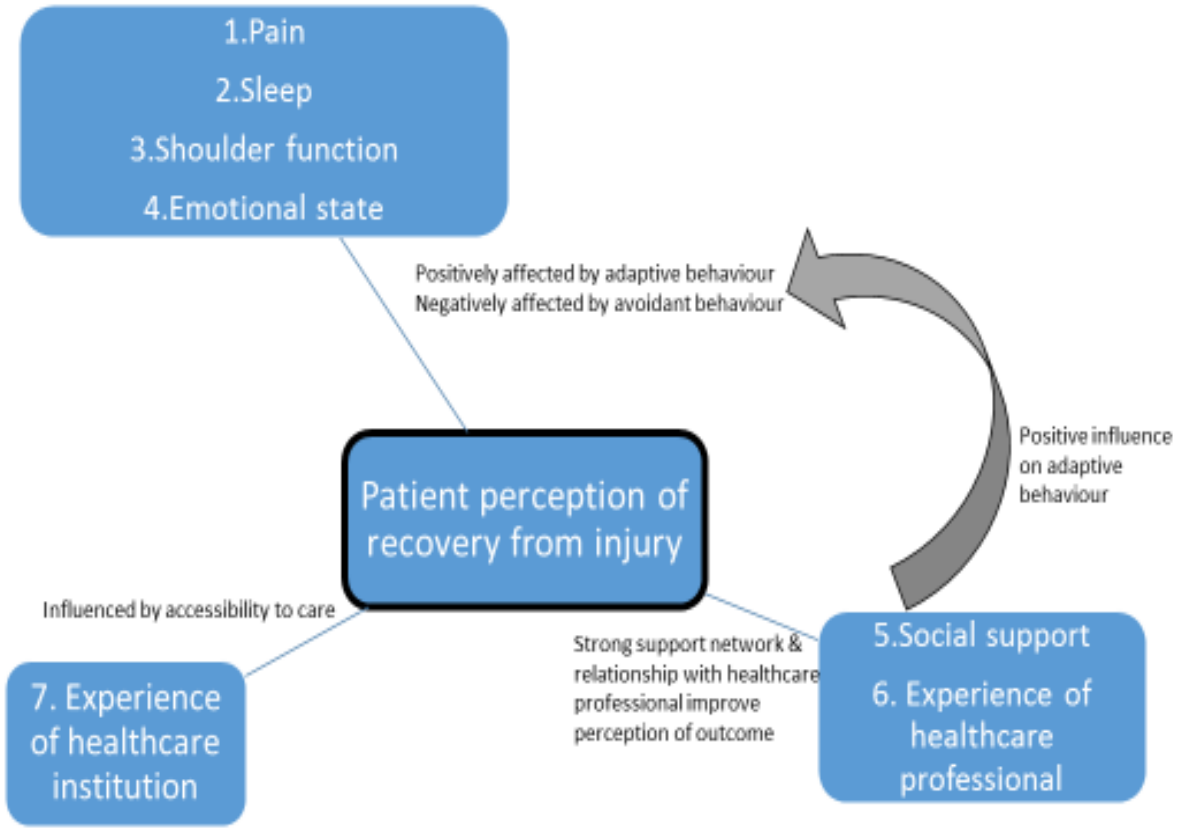


Figure 3.1. Thematic diagram illustrating 7 overarching themes that informed patients' perceptions of their recovery and outcome after undergoing management for a proximal humerus fracture.

3.3.1.1 *Theme 1: Pain*

Pain was a commonly reported problem. Pain in the immediate aftermath of the injury, or surgical management if undertaken, was described as extremely severe and often lasting many months. Patients often compared it to previous experience of pain to highlight its intensity:

As I was saying before, I've had every part of my body broken, but I've never, ever experienced a pain like this. No. It was just extremely painful for quite a few weeks and at least six weeks, or eight weeks (Patient 1).

I mean, I was doing little exercises to begin with also because I was so swollen, you know, and needed to get myself moving, but it was excruciating, I'd never known such pain in any operation I've ever had before, which I've had quite a lot (Patient 13).

Relief from acute pain was of great importance to patients who described both relief and gratitude when there pain was controlled:

It's like when you have a hot shower - it's wonderful [talks about pain and trouble with sleep] the minute I go to the shower and the hot water comes here, I stay there for half an hour in the shower and it's okay. It's good as gold (Patient 3).

I had a lot of pain. I was treated very well so I was given a lot of morphine there and then I started in the hospital to do some movements and then I went back home and the pain continued for months and months and months (Patient 14).

Medication for analgesia often caused side effects that were viewed to be more problematic than pain symptoms and patients often tolerated their acute pain in order to avoid these side effects:

A lot of medicine upset my stomach and I had diarrhoea for a few months because I'm not used to taking medicines or pain killers. All day long. But I'd rather put up with the pain, rather than to put up with pain and running and pain in stomach. And then I stopped the medicine and the painkillers (Patient 3).

So I found that really the constipation was worse than the other thing. So I'm very careful about the amount of codeine that I use. I've still got some of the tablets so when the pain gets really severe I take half the amount. Like instead of 10mg I take 5 or something (Patient 5).

In cases where sequelae of the injury such as osteoarthritis or avascular necrosis occurred, there was severe pain that developed after many months:

But the pain, it developed later on and I had really quite severe pain that developed (Patient 5).

In one case there was reporting of pain accompanied by a sense of disappointment. A patient that had pain after developing avascular necrosis as reported the following:

I am not sure now because I was very disappointed when I heard that I had the necrosis you know. That was a shock because I thought it would have healed. And then thinking back I think well maybe I should have gone for a replacement but now it is too late (Patient 8).

Overall pain was an important aspect of recovery for all the patients. Pain levels in the immediate aftermath of injury or surgery was particularly severe and appropriate management was central to recovery in the first few weeks. In the months that followed pain levels normally settled however patients that developed pain as a result of sequelae of their injury experienced additional symptoms of disillusionment based on an awareness that their discomfort was unlikely to improve without further surgery.

3.3.1.2 *Theme 2: Sleep*

Difficulty with sleep was the most commonly reported theme. In most cases pain was the underlying factor that affected a patient's ability to sleep. Patients would have difficulty lying on their affected side or would wake in the night because they has inadvertently rolled onto the affected side. Patients commonly slept upright in an armchair for the first few weeks after the injury:

It was just extremely painful for quite a few weeks and at least six weeks, eight weeks, I just didn't know what sleep is (Patient 3)

I have a habit of sleeping on my left I couldn't turn, and sleeping was my biggest problem. I tried to sleep on a comfortable chair other than the bed because once I managed to lie down it was difficult to get up without assistance, so I decided it's better to sleep on the sofa because it's a sofa bed and the back goes down and I could bring it up with the lever thing and it was easier for me to sleep on that (Patient 10).

Many patient reported that even a year after their injury they struggled with sleep and had to adopt certain positions or techniques to aid their sleep:

> *I still cannot sleep on, even with the shoulder I could not sleep on my right that was still uncomfortable but about I would say about 18 months, I was able to turn over and sleep on my left which was quite nice (Patient 8).*

> *Of course even now I can't sleep on that side, although if I do I sort of sometimes wake up and I think, "Goodness, here we go again". Whether or not I was sleeping on the muscle or I was sleeping on it badly but now I'm sort of geared to sleeping on my back (Patient 13).*

In one case a patient reported anxiety preceding any physical symptoms and was unable to sleep because of fear of pain coming on:

> *I don't know what happened to me, but I, sort of, went into a panic attack, you know. So when I lay down, I just immediately jumped up again and started walking up and down ... The pain coming on. The pain coming on. I was worried about that (Patient 9).*

Sleep was an aspect of recovery that the majority of patients dwelled on and regarded as important. Difficulty with sleep occurred because of pain arising from lying on the affected side and this often persisted for many months leaving some patients feeling exhausted and anxious.

3.3.1.3 *Theme 3: Shoulder function*

Shoulder function was perceived as extremely important by all patients interviewed in the study. In the first 4 to 6 weeks after the injury activities related to self-care such as showering, use of the toilet, dressing and feeding posed problems to most patients. Family or healthcare support was required as most patients had difficulty performing these activities on their own:

> *There was not much that I could do with my arm I could not lift much so my husband did a lot. He helped washing and dressed me and, one of the worst*

things was not being able to sort of comb your hair and wash but yes those are the first things I remember (Patient 8).

And the only help that I had or needed was help with the showering and I had somebody from Aging UK who came for a few days (Patient 5).

At 9 months to a year, when near-final functional outcome was established, most patients were able to perform most activities related to self or home care. Adaptive or avoidant behaviours played a substantial role in how patients perceived their level of function.

For example I can't do a bra at the back anymore which I don't wear. I wear the stretchy ones (Patient 5).

Having a shirt put on and having it tucked into your trousers. Again, you can't use just one hand. And it's the simple, basic things. Having to read a book: holding a book in there, turning the pages could be hard. And similarly, a newspaper, you had to put it on the table to read because you couldn't hold it in a way with two. It was simple things like that. Having a meal, you find you are using more of the right hand than the left hand because you couldn't get the knife and fork to coordinate. But you adapt. You find the ways around these things and you have to get on with life. (Patient 6)

Many of the longer term functional problems related to activities where there was load applied to the shoulder. Heavy lifting, pulling or pushing activities resulted in pain even a year after the injury and patients generally avoided such activities:

I used to do a lot of shopping and carry heavy things. And also carry things on my back and I just can't. And so I have to have home deliveries and that sort of thing. Or my husband trots out and he's… Although he's... I wouldn't have thought he was stronger than I. But he is much stronger and carries things with me… but I can't carry weights (Patient 5).

If I lift something heavy or I push something heavy, I know that then I will have some pain. Even now I can tell you lifting my arm.... I can lift it well but it's still a bit of pain going here (Patient 14)

In some cases there was a realisation that the final level of function resulted in a degree of disability that prevented participation in activities that the patients enjoyed prior to the

fracture. In such cases this loss of function was of particular importance to the patients who were very active prior to their injury:

> *One sad thing for me is that I absolutely love skiing, … I got osteoporosis but the bad thing was I said I'd stopped skiing and then I didn't throw my boots away for quite a long time because I couldn't quite get mentally over it. I could've skied but my friends said they wouldn't ski with me because they'd be scared stiff if I did (Patient 2).*

> *I used to be climbing mountains, just as a hobby, cycling, swimming. I tried to swim. I was in the Indian Ocean the other week. So I only came back last week. I cannot, you know, dive as such. I used to do scuba diving and a lot of things, which activities that I used to do, I just no longer can do. It's as simple as that, particularly swimming, normal swimming (Patient 3).*

While shoulder function was regarded as an important part of how patients perceived their recovery, many patients adapted their behaviour so that they could partake in the majority of their normal activities of daily living. In such cases the level of function carried less weight in how they viewed their quality of life and final outcome after treatment.

3.3.1.4 *Theme 4: Emotional state*

Although mood and emotional state changed in the early stages after the shoulder fracture, the vast majority of patients reported an affect that was predominantly related to long term disability, pain or loss of function. In some cases patients reported signs and symptoms of depression:

> *And I lost quite a lot of weight, obviously, because you don't move and when you're in pain, you don't feel like eating and so on (Patient 3).*

> *The first time around I suppose it was something new and I thought, 'oh well I have got to get on with it'. It is going to get better. I do not think my mood was too bad… But this time around I have been really bad, I really have, I have been so, it is the frustration, especially when you are so used to doing things in the house and you know cleaning and cooking and doing bits and pieces (Patient 8).*

For six months I couldn't do anything really. I mean, I was doing things but then I was exhausted. And then of course I got quite, you know, despondent about the fact that was it ever going to get better? I mean, I'm a very optimistic person, I don't get depressed, but if I could say if I was ever on the verge of depression that was it because... I was tired all the time (Patient 13).

It was also common for patients to report anxiety or fear of falling. Some patients described avoidant behaviour where activities or environments that could result in a fall were avoided:

I do quite a lot of walking holidays, and it's definitely made me more nervous on a steep decent in particular, and I know that I'm much more careful now and I don't risk – and of course I'm a bit older as well, but I think it's made me (at the back of my mind) there's this fear that if I do have a great tumble (Patient 2).

I suppose one thing ... I'm so frightened of falling now. When I go out walking I feel like I'm walking and watching the pavement which annoys me intensely because the pavements are so uneven anyway that you have to mind it, but I'm a bit more paranoid now that I'm falling, and I do get quite frightened in big crowds because I'm afraid I'll be pushed off balance which I never thought about (Patient 4).

Patients also stated the importance of their independence. Furthermore, the disability sustained in the short and long term was something that many related to in terms of their independence. Some patients had difficulties accepting the loss of their independence, and particularly for those patients living alone, getting help from carer's and family was sometimes quite difficult:

I always looked after myself. I mean, now my boys are grown up and my wife passed away. So I've always been doing things on my own. I live in my own house and there isn't anything I don't do. The first few weeks, no, no. My sons stayed with me for two week. And after that, I said they had to go back to their wives and work, etc. And now I'm just doing the same thing, everything on my own (Patient 3).

So I had a nurse that came in and helped, came in for six weeks to help with my meals. Although I didn't really want help, but that was an awkward part. I was trying to get back on to my feet. I'm an awkward individual in as much as. My wife used to tell me I was too independent for my own good. I don't like help. I like to try and do things[talks about wife passing away briefly then

returns to issue of needing support]. That was awkward and I lost a wee bit of my pride, sort of, always having to ask people to help me to do things and I don't like that (Patient 6).

Patients also described how accepting their disability or loss of function aided their recovery and emotional state. Patients were able to rationalise and accept long term disability by linking their functional decline to old age. Some patients also found the support of their healthcare professionals important in moving forward with their life while still experiencing pain or loss of function:

Well I accepted it at my age as I'm 78, so it's fine for me (Patient 1).

I do see my boys, yes, but probably, yes, it did affect me, but I always keep saying that it happened at that age of mine, rather than when I was young, you know, in my 20s or 30s. Part and parcel of life. Certain things you don't like, but you've got to accept (Patient 3).

I realised that I was treated the proper way and then that helped to accept the pain (Patient 1).

The effect of injury and treatment on a patient's emotional state was a recurring theme identified in the interviews. While some patients felt anxious and frightened of injuring themselves again, the ability to reflect and rationalise on their disability appeared to play a role in how patients perceived their final clinical outcome.

3.3.1.5 *Theme 5: Support network*

In the first 4 to 6 weeks after the injury patients were quite disabled and needed help with activities of daily living. Many patients had family support which was extremely important in managing their symptoms. Family support also allowed long term loss of function to be accommodated; for instance if a patient had difficulty lifting their shopping their husband or children would do the shopping for them. For patients without family support, social care was needed. There were varying levels of frailty within the patients interviewed and as such the

levels of social care needed also varied. Some patients found such social care intrusive or embarrassing. Overall, the level of support patients received from family or social carers was perceived to be necessary or important by the majority of patients and played a key part of their experience of recovery. Some patients had support from their family and close friends during their recovery:

> *It was very difficult, and I needed help the first week really. A friend of mine cared because she was a nurse, and she helped me, and she helped me with my personal care the first week, but after that I managed. I managed to dress myself and look after myself basically (Patient 4).*

> *There was not much that I could do with my arm I could not lift much so my husband did a lot of helped washing and dressed me and, one of the worst things was not being able to sort of comb your hair and wash but yes those are the first things I remember (Patient 8).*

Other patients had support from community health and social workers:

> *So I had a nurse that came in and helped, came in for six weeks to help with my meals. Although I didn't really want help, but that was an awkward part. I was trying to get back on to my feet. I'm an awkward individual in as much as. My wife used to tell me I was too independent for my own good. I don't like help. I like to try and do things … That was awkward and I lost a wee bit of my pride, sort of, always having to ask people to help me to do things and I don't like that (Patient 6).*

Occasionally community health and social care support was felt to be lacking. In one instance a patient who frequently needed the washroom experienced a great deal of difficulty:

> *Well at night the main problem was – well nobody was helping me at night because I was alone (Patient 2).*

Support networks were viewed as important to patients. Whether this took the role of family, friends or health and social workers, there was a physical and psychological need for help throughout recovery.

3.3.1.6 *Theme 6: Experience of health professionals*

The relationship between patients and healthcare professionals, clinicians and non-clinicians, was an important aspect of how patients perceived their recovery and outcome. In the initial consultation and early stages of recovery, the relationship with healthcare professionals often shaped patients outlook:

> *Well it seemed, and there was a young blonde doctor and she was very kind, and she gave me strength to accept it the problem I had … I trust the people – your colleagues and so on, and that helps a lot in my case. Well it helps and in my case and to make it stronger or something, and it helps to recover (Patient 1).*

> *Well to be honest with you once I saw Dr X my mind was at rest because I was comfortable and he explained everything to me and he explained well and he was telling me that – and he was checking me every two weeks I think every 15 days or something … I think the way he handled my situation was absolutely perfect for me (Patient 10).*

Other than affable behaviour and familiarity with the patient's individual case, there was satisfaction of treatment when doctors set goals or established what patient's expectations of their outcome would be:

> *I would say the first thing if you were talking about a patient perception, the first thing that Mr X asked me was, 'What was my lifestyle?' and if I'd say anything to anybody about somebody turning up and had an accident or whatever, and just because you're tired it doesn't mean to say you're not doing anything (Patient 11).*

Even in cases where patients had experienced a complication of treatment and needed secondary surgery, patients accepted their situation and appeared positive based on established trust and a good relationship with their healthcare team. This patient suffered a complication and required secondary surgery. He described his experience after the complication occurred in the following way:

> *So I knew something was wrong and that it was going to be rectified. I was happy that it happened whilst I was in hospital as opposed to being at home. I can't fault the actual treatment I had. I honestly can't. I'm not just saying this for the actual sake of it. I was very well looked after. The doctors were actually first class. When they came to see you, they spoke to you as if they'd known you a long, long time. They showed concern with the questions that they were asking (Patient 6).*

The inter-personal relationship between patients and healthcare professionals played an important role in recovery. A good relationship with a health professional often contributed to a positive outlook on clinical function, even if a complication resulting in discomfort or a disability had occurred.

3.3.1.7 *Theme 7: Experience of healthcare institution*

Experience of healthcare institution was distinct from experience with healthcare professionals. Most patients reported positive experiences in relation to healthcare professionals, however the majority of experiences as a patient in the healthcare institution were negative. The two causes for these negative experiences were difficulties encountered with access to the system as well and busy staff who were unable to dedicate enough time to patients. Problems with access to the system often started in the immediate aftermath of the injury when patients had difficulty getting fracture clinic appointments Delays in time to surgery or discharge were also troublesome to patients and once discharged physiotherapy appointments were often delayed or viewed to occur too infrequently:

We had an absolute nightmare both the GP and me trying to phone through to get somebody to give me an appointment. (Patient 2).

> *They thought that was a dislocation, something in that respect. And it took a week, literally, eight days until all of a sudden on a Saturday morning a doctor called, or I think Friday night, to say that I got to come on Saturday morning for an operation at 7 o'clock in the morning. And so it happened and Dr Y was the one who operated on the thing. And that's it. But it took a week and my god, what a week it was (Patient 3).*

> *I felt very frustrated because it's very hard to remember the exercises that you're given to do, and then you don't see them for another week or two weeks, and to me that was very frustrating because I kept worrying all of the time, and they give you diagrams but it's very different if you've never done this kind of thing before to remember how to do them (Patient 4).*

Patients often reported their experience on orthopaedic wards as negative and commented on how busy or understaffed nurses were:

> *In hospital here I found that they are very short of nurses on the ward that I was in. I do not know, but I know the one time that the lady who was washing me, the bells were going and 'I said look, I am alright, go and see to it', she said 'no they will just have to carry on ringing', and I thought 'maybe it is somebody that urgently needs you', they have not got the staff to help (Patient 8).*

> *The nurses were, again, good. The only problem with the nurses is that there wasn't enough and they couldn't always come to you as quickly as you possibly might (Patient 6).*

The relationship patients had with their healthcare institution related to ease of accessibility. Poor accessibility to the care patients wanted had a negative impact on their experience of recovery and was a commonly identified theme amongst a number of patients.

3.4 Discussion

3.4.1 Principle findings

Currently there is an absence of published research reporting on qualitative research exploring patient perceptions of recovery after sustaining a proximal humerus fracture. In this study, thematic analysis was used to explore the experiences of elderly patients who had sustained a complex proximal humerus fracture. The analysis found that patient perception of recovery and outcome was characterised by pain and lack of sleep in the immediate aftermath of the injury. The severity of pain was commonly described as extreme and its effect on sleep left some patients feeling exhausted in the first few weeks. Pain levels settled in the majority of patients approximately 6 months after their injury, however the cohort of patients who

developed sequelae of injury such as osteoarthritis or avascular necrosis began to develop increasing levels of pain after this period of time. Loss of function was an important theme that developed for patients between 6 months and 1 year after their injury. When a near-final level of function became apparent to patients, the inability to perform important activities such as shopping, self-care and home-care resulted in two common methods for managing any residual disability. Firstly, there were adaptive behaviour patterns, where for example patients wore larger jackets that were easier to put on or had trained their non-dominant arm, in cases where it was the unaffected side, to do many daily tasks. Secondly, there were avoidant behaviours such as refraining from walking on busy streets or in supermarkets. The impact of loss of function on the overall patient's perception of their recovery and outcome depended largely on whether they accepted their residual disability and had developed adaptive mechanisms. Family support and a good relationship with healthcare professionals seemed to be crucial for many patients in developing adaptive mechanisms and having a positive outlook, even in cases where a serious complication had occurred after a surgical procedure. For patients that developed avoidant behavioural patterns, there were negative emotional experiences such as anxiety and depressive symptoms. Finally the experience of the healthcare institution was a theme in recovery that many patients dwelled on. This suggested it was a key component of how patients' perceived their management and outcome. Patients described displeasure and occasionally anger at having to manage their injury and at the same time deal with hospital services that were often difficult to access or overly busy and unable to provide the care and experience that they wanted.

3.4.2 Relationship of findings to current knowledge base

To date, there are no patient centred outcome measures which evaluate health outcomes that are specific to elderly patients with a proximal humerus fracture. The Oxford Shoulder Score (OSS)[52] which is increasingly applied to quantitative research in shoulder surgery[29,170,171] was

developed in patients with a mean age of 57.4 years who were undergoing elective orthopaedic treatment[52]. The OSS covers three of the themes identified in this study; pain, sleep and loss of function. Loss of function is given substantial weight within the OSS, with 9 of the 12 questions relating to this theme. Although the level of shoulder function played an important role in how patients perceived their outcomes, in some cases loss of function was not a major contributor to how they viewed their health outcome. A patient's emotional outlook had an important role to play in the experience of loss of function and the impact it had on their lives. Although secondary outcome measures in quantitative research in this field include health utility assessments like the Short-Form 12 (SF-12)[172], and these measures capture a patient's mental state, the absence of an emotional assessment within a PROM evaluating outcomes for elderly patients with a proximal humerus fracture is at odds with the results of this qualitative study.

There has been a growing interest in the effects of shoulder pathology on sleep [173]. Sleep disturbances are recognised to be harmful to an individual's physical and mental health[174], and therefore the contribution of shoulder pathology to sleep disturbances has an association with a patient's clinical outcome. The mechanism of sleep disturbances are hypothesised to be related to peaks in nocturnal pain which possibly occur due to arm position and posture, and their effect on subacromial pressures[173]. The role of shoulder pathology on sleep disturbance is also captured in PROMs like the OSS and the DASH Score, however whether the weight applied to its impact on patient outcomes is appropriate is not known. In relation to proximal humerus fracture, sleep disturbance have had limited evaluation in existing published research. A single study of 1095 patients with proximal humerus fractures, distal radius fractures, tibial plateau fractures and ankle fractures found that patients with proximal humerus fractures had the highest incidence of sleep disturbances 3 months post-injury[175]. The study also found that sleep disturbances were associated with a poor emotional status.

Within our qualitative analysis sleep disturbances were one of the most commonly reported themes. This finding underlines the need for further clinical research on the impact of sleep on recovery and how they should be weighed within patient reported outcome measures.

Adaptive behavioural patterns, family support and a strong inter-personal relationships with healthcare professionals often contributed to a positive outlook and perception of outcome, even when there was loss of function. The role of such factors in moderating the psychological effects of disease or injury have been described in other fields of medicine[176], and this study has demonstrated their relevance in better understanding patient recovery after orthopaedic trauma. The importance of inter-personal relationships, particularly in the case of patients and healthcare professionals is well recognised in clinical practice, as is the positive correlation between clinician-patient relationship and health outcomes[177,178]. Proposed pathways for this relationship include increased patient knowledge, shared understanding, patient empowerment and better management of a patient's emotional state[178]. In orthopaedic practice, the importance of patient-centred consultations has been highlighted by a position statement from the American Association of Orthopaedic Surgeons (AAOS)[179]. The AAOS statement encourages learned communication skills and links better physician-patient communication with improved clinical outcomes and patient satisfaction. Despite the recognition that it is important for orthopaedic surgeons to communicate effectively, establish trust and demonstrate empathy towards their patients, there is a dearth of research that has evaluated the orthopaedic surgeon-patient relationship and its effect on patient outcomes. In this study, the relationship with healthcare professionals played a substantial role in recovery. Patients reported that the support they received from their doctors had an important role in their recovery and accepting long-standing disability. Moreover, patients who suffered a complication had a positive perception of their recovery because of the emotional support and trust they had in their orthopaedic consultant. Complication rates after the surgical

management of complex proximal humerus fractures range from 16% to 64%[180]. Given that the likelihood of a complication is relatively high, the importance of the clinician-patient relationship cannot be overstated and for those patients that have a complication or revision surgery, it could have an important role in maintaining a positive outlook on recovery and their perception of their eventual clinical outcome.

Social support, whether from family or health workers, is a well-established factor that contributes to patient recovery[181,182]. This has been described in relation to elective lower limb arthroplasty[182] yet it is surprising that existing patient outcome tools do not incorporate the quality of support patients receive during their recovery. In the context of elderly patients with a proximal humerus fractures, the level of support patients receive has been emphasised by the findings of this study. A number of the patients included in this study lived alone or had spouses that were frail. The first difficulty such patients encountered was in the immediate aftermath of their injury. Patients were commonly discharged from the casualty department with an outpatient fracture clinic appointment with a view that they were safe for discharge because they were ambulatory. These patients waited up to a week before being seen and during that period they had difficulty with self-care and reported feeling extremely anxious. For those discharged from hospital after surgery there was a similar experience. For up to 6 weeks, many patients were entirely dependent on help from family, friends and carers and in cases where such support was not sufficient there was notable hardship endured by patients during that acute period. Outpatient multidisciplinary care and social support pathways following lower limb orthopaedic surgery are commonplace and have an important impact on patient recovery[183]. It is possible that there is a perception that ambulatory patients with one functioning arm are safe for discharge and can manage the required activities of daily living, however it was clear that for many patients in our study that physical and emotional support was lacking. In the later stages of recovery although physical support was

not as necessary, patients with family support adapted to their loss of function better and had a more positive emotional outlook. The role of a support network in improving patient outcomes after illness has been described in a number of fields in clinical medicine[184,185]. Unfortunately such work is not as well developed in orthopaedic research, and this may be to the detriment of the large proportion of frail older patients we treat.

Patient satisfaction with their treatment has been closely associated with accessibility to their healthcare provider[186,187]. Although patients in this study generally talked positively about their levels of trust and confidence towards healthcare professionals, access to the hospital and its staff was a problem many described. The first period of time in which access to hospital was a problem was in the immediate aftermath of their injury. Patients waited for their clinic appointments or operation days with great uncertainty about what to expect. The time it took for them to meet a consultant and have a management plan established was viewed by most to be excessive. The problems with accessibility in the later stages of injury were mainly related to physical rehabilitation. Patients felt they were not getting enough time with their physiotherapists and this frustrated them because they perceived that it was hindering their progress. Similar experiences have been described in elective joint replacement surgery[188] and underline the need for policy changes to improve access to health care.

3.4.3 Implications of findings to clinicians and policy makers

One of the key implications of this study is that breadth of themes emerging from the qualitative analysis extend beyond the domains reported in quantitative measurement tools[52,189]. Going forward, if health outcomes are to truly reflect the values of the target population with the specified injury, there is a need to develop a validated patient reported outcome measure (PROM). Existing measures are heavily weighted towards function, and

although this is important to elderly patients with complex proximal humerus fractures, improvement in pain and sleep are viewed to be more important in their recovery. Furthermore, the inclusion of emotional recovery, the support patients receive and the relationship of the patient with their clinician and healthcare provider may offer better construct validity to measures of patient outcomes in this field, and further work is needed to evaluate this.

The importance of developing a new PROM for elderly patients with a proximal humerus fracture is also important because currently the myriad of different assessment tools capture a range of different themes. Within the literature it is clear that researchers in this field use a number of different PROMs in their trials to capture as many outcomes of interest as possible. It is likely that this is a burden on patients included in clinical trials as they are required to complete a number assessments during their follow up. A single PROM that captures all the relevant themes that are considered to be important to patients would help overcome this problem and this adds to the rationale of developing a new assessment tool in this field.

3.4.4 Limitations of the study

There are four main limitations to this qualitative study. Firstly, recall of events was quite variable amongst patients. The range of time that had passed since the initial injury ranged from 1 to 5 years. By their own admission, a few patients expressed difficulty recalling some of the events of their recovery. Unfortunately, complications and changes in health states can occur more than 1 years after the initial injury[190] and therefore it was essential to include patients who had suffered their fracture beyond the 1 year threshold. Recall bias could be reduced in future research by conducting a prospective qualitative analysis during patients' recovery. The second limitation of this study is that it does not offer insight into why patients

may perceive benefit from different treatment strategy. Recruitment was only sufficient to develop themes that were common to all the patients, however there is a need for future work to explore the differences in recovery for patients that undergo conservative management, locking plate fixation and hemiarthroplasty. This would provide a better understanding of why quantitative outcomes are better for patients with more complex fractures, as determined in **Chapter 2.** The third limitation of this study is that because it was conducted at a single centre, the external validity and applicability of the findings to other healthcare institutions may be limited. The selection criteria for our patients in this study meant that despite our hospital being a major trauma centre, the patients included had isolated injuries and therefore their treatment and recovery should closely reflect the experiences of elderly patients with a proximal humerus fracture at other hospitals. Service variability between hospitals is well recognised[191] and therefore further work, particularly in the development of a patient reported outcome tool should be performed across multiple centres. Finally, because the patients were purposively selected to represent a wide range of health outcomes following treatment the heterogeneous sample of patients that were included may limited the opportunity of in-depth exploratory analysis within the different cohorts of included patients. Further work should include thematic analysis applied to specific homogenous groups of patients, or a sample large enough to allow for in-depth analysis amongst the different groups of patients.

3.4.5 Conclusions

In total seven themes were found that related to how patients perceived their recovery from their injury and treatment. Pain, sleep and function were three themes that were identified in this qualitative study that overlapped with domains in quantitative measurement tools in the assessment of health outcomes for older patients with a complex proximal humerus fracture. Patients weighed improvement in their pain and sleep more heavily than their level of shoulder function which is contrary to the weights applied to quantitative measures.

Emotional state, the role of support networks, relationships with healthcare professionals and relationships with the healthcare institution emerged as themes that have not been previously described in the existing literature/measures and were identified as key elements of how patients perceived their recovery. Further qualitative research in this field is needed so that patient reported outcome measures can be developed that are supported by qualitative analysis which reflects on the elements of recovery that patients perceive to be important.

Chapter 4

Cost analysis of surgical treatment of proximal humerus fractures: an evaluation of cost drivers and comparison of institutional treatment cost with the national tariff

This chapter is an adapted and unedited pre-publication version of a paper published in the Bone and Joint Journal (Sabharwal S, Carter AW, Rashid A, et al. Cost analysis of the surgical treatment of fractures of the proximal humerus. Bone Joint J 2016; 98-B: 249-259). It has been reproduced with permission from the publisher.

4.1 Introduction

In health economic research, value from the perspective of a service provider is often defined as the health outcome achieved per monetary unit spent[107,192]. The importance of value in health care is underlined by on-going fiscal austerity measures, the burden of an ageing population and the increasing cost of emerging medical technologies, all of which continue to challenge the financial viability of healthcare services[193]. The need to deliver cost effective treatment is now well recognised across all medical specialties and has resulted in a surge in health economic research within trauma and orthopaedic surgery[194,195]. In the United Kingdom (UK), the National Audit Office recommended that the health service achieve efficiency savings of £20 billion between 2011 and 2015[196]. More recent estimates suggest that the funding deficit will grow to £30 billion by 2020, while the demand for health services will continue to rise by 4% annually[197]. As musculoskeletal disease accounts for approximately 10% of all National Health Service (NHS) costs, particular attention has been paid to cost drivers and cost minimisation approaches in orthopaedic surgery[198]. Furthermore, recent orthopaedic research has focused on the financial burden of performing surgical procedures due to insufficient government reimbursement tariffs [117,118].

Costing methodologies can be broadly categorised as top-down costing, where average per diem departmental or disease specific costs are estimated based on overall spending, or bottom-up micro costing, where each resource required for treatment is analysed and used to generate a cost estimate[110]. The latter, although time consuming and often costly, is viewed to be a more systematic and transparent approach to establish treatment costs and to scrutinize cost drivers [110]. Unfortunately, estimates of treatment costs often rely on less accurate top-down costing methods or pre-determined and poorly described hospital charges that lack the granularity required to understand how value can be added to a particular treatment [199]. Patient-level costing approaches are viewed to be superior, and tools for measuring resource use at this level are emerging; Patient Level Information Costing Systems (PLICS) [200] are used in the English NHS, but the system is yet to be validated, which is a limitation to their application to tariff benchmarking or for use in economic evaluation. Time-driven activity based costing (TDABC) was developed by Robert Kaplan and Steven Anderson at Harvard Business School and is a cost-calculation methodology that is commonly employed to perform bottom-up micro costing[119]. It involves a systematic analysis of the patient pathway and estimates the costs of activities based on their unit cost, as well as the time required to perform the service in question. As research continues to highlight how other methodologies fail to provide relevant or accurate information for costing health services, there has been an increase in the uptake and advocacy of TDABC, which is now viewed to be a superior alternative[114].

Although much of the focus on fracture management in older patients is centred on hip fractures, proximal humerus fractures account for approximately 10% of all fractures in patients over the age of 65[135]. The recent publication of the ProFHER trial [11] increases the evidence-base which suggests that surgical treatment may not improve long-term functional outcomes, however future research evaluating specific treatment alternatives, based on a

particular fracture-configuration and a more homogenous patient population may offer more clinical applicability[76]. The volume of existing research that evaluates the cost of surgical treatment of proximal humerus fractures is limited. In the United States (US), a recent study demonstrated how surgeons who performed more of these procedures incurred less overall cost per case for their hospitals[201]. This analysis used Nationwide Inpatient Sample costing values, which are derived from US hospital accounting data. The methodology used to determine these costs is lacking within the medical literature, but it is known to exclude clinician cost [202]. A second study published in this field has used hospital charges and fee schedules to generate overall costs, and the methodology from which many of these charges were derived is not presented [120]. An in-depth micro-costing analysis is required to provide accurate estimates of treatment costs, demonstrate what the major cost drivers are, and allow clinicians and policy makers to review whether further cost minimisation is possible.

The primary objective of this study was to estimate the inpatient cost of surgical treatment of proximal humerus fractures by performing a comprehensive micro costing analysis using TDABC. The secondary objectives were to determine the institutional financial surplus or loss associated with the treatment options reimbursed by the national tariff, and to establish what the major cost drivers in the treatment pathway were.

4.2 Materials and Methods

4.2.1 Cost Analysis Perspective

Although a societal perspective that includes outpatient, community and primary care costs, has the benefit of improving the quality of cost effectiveness research[110], because the purpose of this cost-analysis study was to evaluate inpatient costs and cost drivers, an institutional perspective was considered appropriate. This study was performed at a London teaching hospital and therefore the perspective adopted was that of an English NHS acute hospital.

One of the key differences between the NHS in England and the respective NHS organisations in Scotland, Wales and Northern Ireland, relates to the way healthcare is commissioned[203]. In England there is a purchaser-provider split, where health services are commissioned by organisations called Clinical Commissioning Groups (CCGs). These groups procure NHS Services, including orthopaedic trauma care, which is delivered by English NHS Hospitals whose organisational structure and governance is independent from that of the CCGs. Reimbursement for specific treatments that the CCGs provide these hospitals is based on tariffs that have been calculated from national estimates of treatment costs which are submitted annually by all hospitals in England to the Department of Health. Individual tariffs are known as Healthcare Resource Groups (HRGs). These are often a case mix of similar procedures rather than one specific procedure. Within the NHS in Scotland and Wales, a purchaser-provider split does not exist. Individual health boards in these countries directly employ NHS staff and manage their local healthcare services. Reimbursement is based on locally agreed contracts. In Northern Ireland, although a purchaser-provider split exists, there is close consultation and cooperation between purchasers and providers and reimbursement is also locally negotiated between trusts and commissioning groups[203].

4.2.2 Micro-costing Approach

The steps employed were based on the principles outlined by Kaplan for performing TDABC [119], and incorporate recognised clinical pathway mapping methods[204]. A summary of the steps involved in the methodology is provided in **Figure 4.1**.

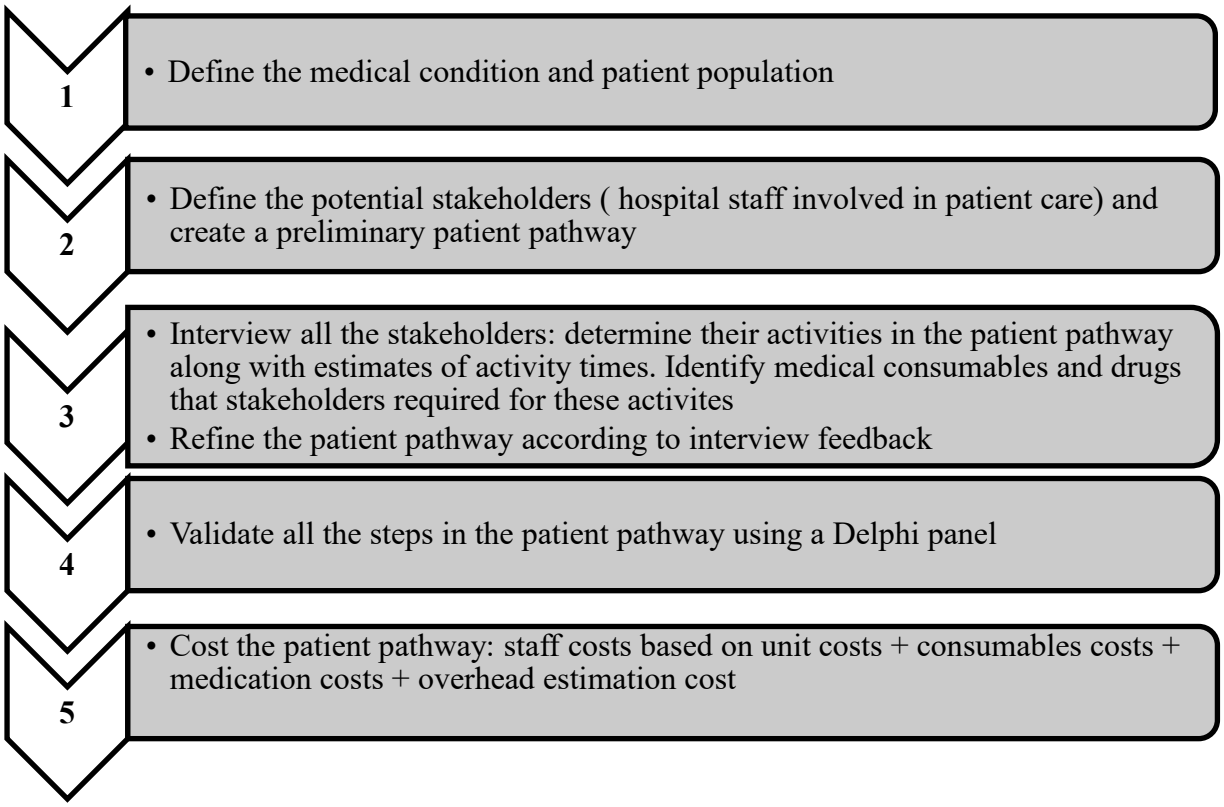


Figure 4.1. Outline of steps used in this cost analysis

4.2.3 Definition of Patient Population and Medical Condition

The patient population and injury definition used in this study are shown in **Table 4.1.** These definitions were based on a consensus between 4 orthopaedic surgeons (myself, Abbas Rashid, Chinmay Gupte and Peter Reilly), of what constituted a common clinical phenotype amongst patients commonly managed at our hospital.

Table 4.1. Case scenario used to define medical condition and patient population. Barthel score fully detailed for staff during interview process. The inpatient length of stay is based on mean length of stay for proximal humerus fractures at our institution.

Patient age	70
Patient injury	Comminuted proximal humerus fracture (Neer type III or IV)
Medical co-morbidities (ASA grade)	Mild systematic disease (ASA grade 2)
Level of mobility	Independently mobile
Barthel score[205] prior to admission	20
Social status	Lives in own house with wife
Expected length of hospital stay	3 nights

4.2.4 Defining the stakeholders and Creating a Preliminary Pathway

A preliminary meeting of three orthopaedic surgeons (myself, Abbas Rashid and Peter Reilly) was used to generate an initial patient pathway, or Care Delivery Value Chain (CDVC) as a means of identifying possible major steps within the patient pathway as well as the stakeholders for each step. For instance, in the case of a patient presenting to the emergency department with a proximal humerus fracture, the stakeholders involved in this single step of the CDVC would be the receptionist, the triage nurse, an emergency department doctor, an emergency department nurse and a radiographer. Furthermore the departmental manager was also defined as a stakeholder because of their role in overseeing the entire process.

4.2.5 Refining the CDVC and Detailing Staff Activities

Semi-structured interviews were then conducted with all the stakeholders. Staff members that were interviewed included doctors, nurses, managers as well as a number of allied health professionals (physiotherapists, occupational therapists, pharmacists) and members of the wider healthcare services (receptionists, porters, domestic staff). Staff members were asked to review the preliminary CDVC and comment whether the overall pathway or individual

components were likely to represent a safe and probable clinical pathway at our institution. Questions were asked about their individual role in the pathway, the time they were likely to spend performing these activities based on a minimum and maximum range, and the consumables or drugs they required for the activities they were involved in. Time ranges were based on an expected range of time required to perform an activity based on differences in patient frailty and staff experience. After reviewing the interview responses, the CDVC was refined to include the opinions of the stakeholders in the pathway.

4.2.6 Validating the CDVC

Following the staff interviews and refinement of the CDVC, content validity of the pathway was established using a Delphi-technique. This is a structured communication technique that is used to gain consensus among a panel of experts[206] and it is a recognised method for establishing the content validity of clinical pathways [207,208].

The CDVC pathway was converted into a 65-step questionnaire linked to a 5-point Likert-scale **(Appendix 3).** Each step included a summarised account of the various activities that formed the overall pathway and the likely time commitments based on a minimum and maximum probable time in minutes. Respondents were asked to rate how much they agreed with each step using the Likert-scale and to provide comments that rationalised their opinions, especially in circumstances where they disagreed with the proposed activity. In total 13 individuals were selected to be part of the Delphi panel and they remained anonymous to each other throughout the Delphi process. They included 5 orthopaedic consultants, 2 senior orthopaedic registrars, 2 anaesthetic consultants, 2 nurses working in management positions and 2 upper limb physiotherapists. Our study protocol defined consensus as being achieved when 9 out of the 13 panellists (69%) agreed with a step. This was based on existing Delphi-based research defining consensus as 60-67% agreement by

respondents[209,210], as well as an awareness that certain members of the panel may be neutral regarding aspects of the patient pathway that they have not previously been exposed to in their clinical practice. When consensus was not met for a particular step it would be modified according to the reviewers' comments, and in the next round of the Delphi-panel assessments the questionnaire would describe how revisions had been made according to feedback from the previous round. A limit on the number of rounds was not set for the Delphi process, and instead the pre-defined protocol was to end the process after consensus had been reached for each of the 65 steps.

4.2.7 Establishing Capacity Costs

Staff capacity cost rates were calculated using wage information acquired from the NHS pay scale[211,212] (2014 costs). For all staff in the pathway, a minimum salary, a mean salary and a maximum salary were estimated based on intensity banding, seniority banding, point level on the pay scale and clinical excellence points achievable in the case of consultants. Further adjustment was made based on national insurance, pensionable income and London Weighting (an allowance that incentivises certain professionals to live in the capital where the cost of living is higher than elsewhere in the UK.) For consultants, the cost per minute was based on assumptions that included a 10 PA weekly job plan and an expectation of 420 PAs worked per year with consideration of annual leave, study leave and professional leave entitlements. For junior medical staff, cost per minute was based on an assumption of 44 weeks worked a year (annual leave and study leave allowances considered) and a probable 48 hours worked in a week. For other healthcare staff, calculations were based on assumptions on hourly wage adapted from the Royal College of Nursing and the NHS Agenda for Change[211,213].

4.2.8 Costing consumables, medications and overheads

All medical consumables, including surgical prosthesis and medications were assigned unit costs at the discounted prices charged to the institution by suppliers (2014 prices). The cost of laboratory investigations were calculated at pre-defined institutional estimates based on the staff cost as well as the equipment and reagent cost of each test. Medical imaging costs formed part of the TDABC analysis, where the cost of radiographers and radiologists for different procedures were estimated based on the time they spent performing or reporting each investigation. The overhead costs (those not directly related to patient care) included infrastructural components, service costs as well as the capital outlay of the hospital and each piece of medical equipment. Estimates of these costs were generated from the accounts of the estates and facilities department that oversees these myriads of non-clinical costs within the hospital. These costs were compared to the hospital's general ledger. At our institution these account for approximately 26 % of the overall financial expenditure, and this proportion represents 35% of direct care costs. Therefore after the TDABC estimates of treatment cost were obtained, these values were increased by an additional 35% to account for overhead expenditure within the inpatient treatment pathway.

4.2.9 Descriptive and Statistical Analysis

The ranges of expected activity times, as well as the different capacity cost rates for individuals within the pathway resulted in a minimum, mean and maximum possible cost estimate for treatment. The individual implant costs for the different procedures performed at our institution were then applied to the costing methodology to produce cost estimate ranges for the different surgical techniques. An overall cost estimate was calculated as the mean value of these procedures and compared to the overall reimbursement tariff. The major cost drivers within the pathway were presented using descriptive analysis. One-way sensitivity analysis using a 20% change for each parameter was used to further scrutinize cost divers.

Threshold analysis was performed using the overall reimbursement tariff to evaluate how delays in the operating theatre would affect surplus. Statistical analysis was performed in SPSS v21.

4.3 Results

4.3.1 CDVC Development Process

The initial CDVC consisted of 10 major steps and 26 stakeholders. During the staff interview process this was refined to 8 major steps that included 32 stakeholders. The updated CDVC was then evaluated by Delphi-panel and there was 100% response rate for both rounds of the process. In the first round there was consensus on 45 out of 65 (69.2%) steps of the summarised pathway. Amendments were made to the pathway in accordance with opinions provided by responders. After a second round, consensus was achieved on all the steps within the pathway.

A total of 130 staff activities were included in the final CDVC (**Figure 4.2**) which was adapted to the 3 main types of surgery performed for comminuted proximal humerus fractures at our institution; open reduction and plate fixation, hemiarthroplasty and soft tissue reconstruction with a third tubular plate. The number of consumables required ranged from 100 – 118, the number of drugs required was estimated at 159 and cost per unit of time was determined for 25 different types of staff members **(Table 4.2).**

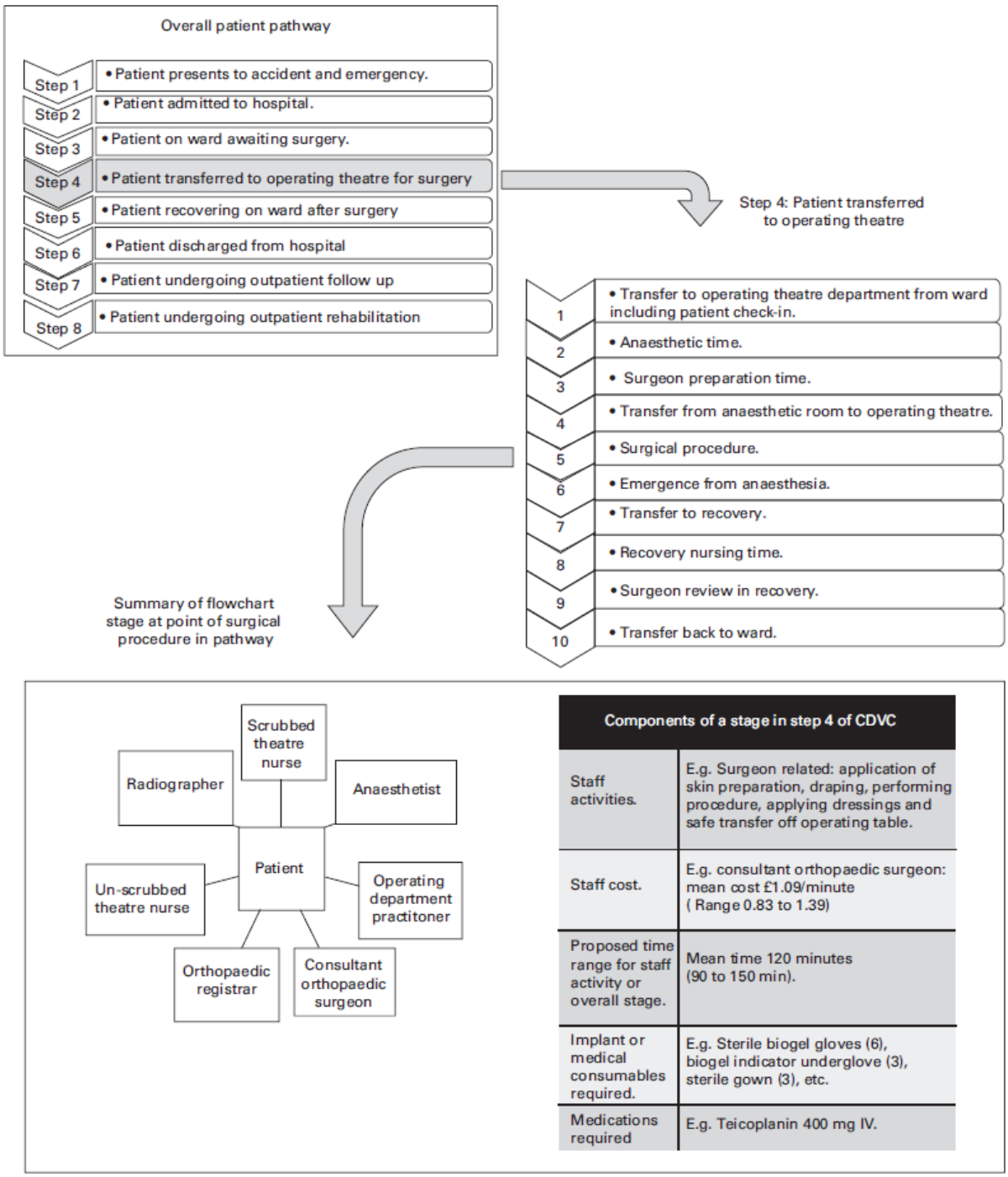


Figure 4.2. Diagram demonstrating how costing was performed for each stage of the different steps that made up the entire Care Delivery Value Chain (CDVC).

Table 4.2. Table showing examples of how activity cost was estimated within the CDVC. Also included within the analysis were a minimum and maximum capacity cost for staff based on possible variations in earnings, a minimum and maximum activity range based on expected variations in activity times and a minimum and maximum overall activity cost. Full details on capacity cost assumptions and calculations provided in Appendix 3.

Staff member	Mean capacity-cost rate (£/minute)	Activity	Mean time required to perform activity (minutes)	Mean cost of activity (£)
Consultant orthopaedic surgeon	1.09	Performing surgical procedure including skin preparation, draping, surgery and safe transfer to bed.	120	130.8
Consultant anaesthetist	1.09	Preparation and performing anaesthetic procedure	30	32.7
Orthopaedic SHO	0.34	Completing electronic discharge summary	12.5	4.25
Ward nurse	0.28	Nursing ward round patient review	7.5	2.1
Casualty department radiographer	0.31	Positioning patient, performing and uploading x-ray	15	5.38
Porter	0.16	Transfer of patient from casualty to ward	15	2.4

4.3.2 Cost of Treatment and Cost Drivers

The overall inpatient cost of surgical treatment based on the mean values of the different treatment options available was estimated to be £3,282.82 **(Table 4.3).** Implant and theatre consumables together formed the largest cost driver at £1,350.74, which was 41.15% of the overall cost.

Table 4.3. Mean costs for all 3 procedures based on variations in staff capacity-cost rates and proposed activity times.

Cost group	Minimum (£)	Maximum (£)	Mean (£)
Accident and emergency staff cost	£39.49	£91.88	£62.35
Accident and emergency consumables	£48.37	£48.37	£48.37
Accident and emergency medications	£0.20	£0.20	£0.20
Wards and Radiology staff cost	£119.21	£338.87	£230.32
Wards and Radiology consumables	£34.63	£34.63	£34.63
Wards and Radiology Drugs	£21.70	£21.70	£21.70
Theatre staff cost	£371.01	£1,026.12	£649.69
Theatre consumables and implant	£1,350.74	£1,350.74	£1,350.74
Theatre Drugs	£33.72	£33.72	£33.72
Overall direct cost	£2,019.07	£2,946.23	£2,431.72
Corporate overheads (35 % of direct costs)	£706.67	£1,031.18	£851.10
Total cost of treatment	£2,725.74	£3,977.41	£3,282.82

Overheads were estimated to be £851.10 based on a pre-determined estimate of overhead costing valued at 35% of overall treatment costs. An average bed day during the inpatient period was valued at £128.40. This estimate was derived from the total healthcare staffing costs for ward-level activities within our CDVC. Staff members included doctors, nurses, physiotherapists, occupational therapists as well as other allied and wider healthcare personnel identified as being necessary within the defined CDVC. Furthermore, all the medication and consumable costs incurred on the ward were included. An overhead estimate was then added to this cost using the pre-defined method for overhead cost calculation, which would account for non-clinical ward costs such as electricity, water and ward-level capital costs. The mean operating theatre cost was valued at £2,746.10 based on theatre staffing, the implants, consumables, medications and overhead estimates. There was a large variation in procedure specific implant costs **(Table 4.4, 4.5 & 4.6)** and this resulted in sub-group costs based on the type of procedure ranging from £2,055.50 for a soft tissue reconstruction, to £4,679.31 for a hemiarthroplasty **(Figure 4.3).**

Table 4.4. Implant specific procurement costs for locking plate.

	Cost	Units	Total cost
Plating procedure			
Plate	£532.08	1	£532.08
3.5mm locking screw	£43.42	6	£260.52
3.5mm cortical screw	£11.91	4	£47.64
Overall cost			**£840.24**

Table 4.5. Implant specific procurement costs for soft tissue reconstruction.

	Cost	Units	Total cost
Soft tissue reconstruction			
Third tubular plate	£25.00	1	£25.00
3.5mm cortical screw	£11.91	2	£23.82
5.0 Ethibond	£3.26	2	£6.52
18G blunt needle	£1.10	1	£1.10
Overall cost			**£56.44**

Table 4.6. Implant specific procurement costs for hemiarthroplasty. Sterilisation costs were included for each tray in the overall theatre consumable cost calculations (£80 per instrument tray).

	Cost	Units	Total cost
Hemiarthroplasty			
Implant Head	£450.00	1	£450.00
Implant Stem	£1,375.00	1	£1,375.00
Cement	£50.00	1	£50.00
Cement Mixer	£45.00	1	£45.00
Overall cost			**£1,920.00**

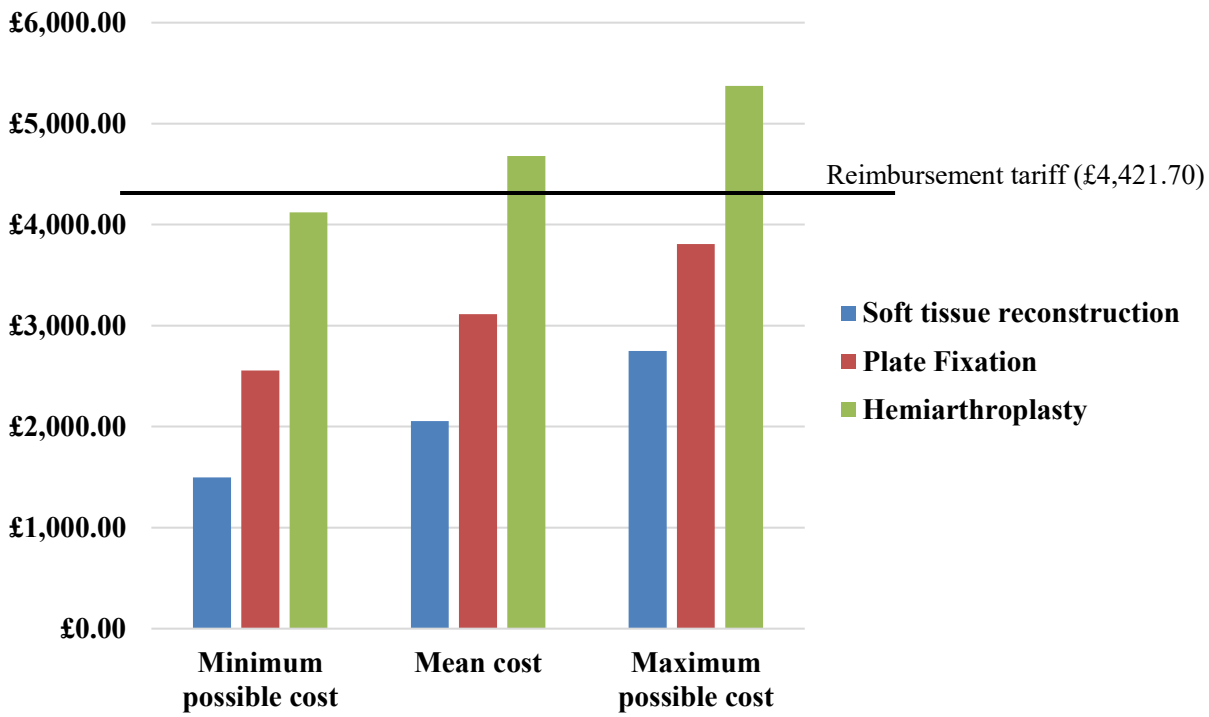


Figure 4.3. Hemiarthroplasty resulting in a financial loss to the hospital based on mean and maximum cost estimates.

4.3.3 Financial profitability relative to national tariff

With reference to the 2013/2014 payment by results (PbR) tariffs [214], the overall reimbursement for inpatient care of patients admitted for surgical treatment of a proximal humerus fracture was calculated to be £4,421.70 **(Table 4.7).** This represented a mean surplus for inpatient care of £1,138.88. The most profitable margin was estimated to be £2,923.27 for a minimum TDABC estimate when performing a soft tissue reconstruction procedure. In the case of a maximum TDABC estimate applied to performing a shoulder hemiarthroplasty there was a net loss of £952.20.

Table 4.7. Calculation of institutional reimbursement based on 2013/2014 Payment by result (PbR) tariffs. Market force factors are valued at 1.2417.

Reimbursement type	Healthcare Resource Group (HRG) Code	HRG name	Tariff adjusted for Institutional market force factors
Accident and emergency episode	VB08Z	Category 2 treatment and category 1 investigation	£136.59
Orthopaedic admission and surgical treatment	HA61C	Major shoulder and upper limb for trauma without complication or comorbidity	£4285.11
Overall reimbursement for admission and treatment			**£4421.70**

Overall sensitivity analysis revealed that surgical implants and theatre consumables represented the cost diver with the biggest effect on overall cost estimates **(Figure 4.4).** Sensitivity analysis applied to staff costing revealed that variations in consultant time were the most sensitive staffing cost driver within the CDVC **(Figure 4.5).** Threshold analysis of the effects of delays to the operating theatre on overall cost revealed that after a 60-minute delay, the hospital would start to incur a net loss on treatment based on mean estimates taken across the 3 types of surgical procedures performed **(Figure 4.6).** This analysis was based on the assumption that a delay had occurred that prevented the anaesthetic procedure from commencing, and all members of the operating department team were redundant during that period. At our institution some of the reasons such delays occur are because of technical problems with operating theatre equipment and lack of availability of appropriate staff to proceed with the operation. Furthermore, after the capacity cost of all the redundant staff members as well as the overhead estimates were calculated, an additional opportunity cost of £15/min was also included based on existing NHS health economic research on theatre efficiency[215].

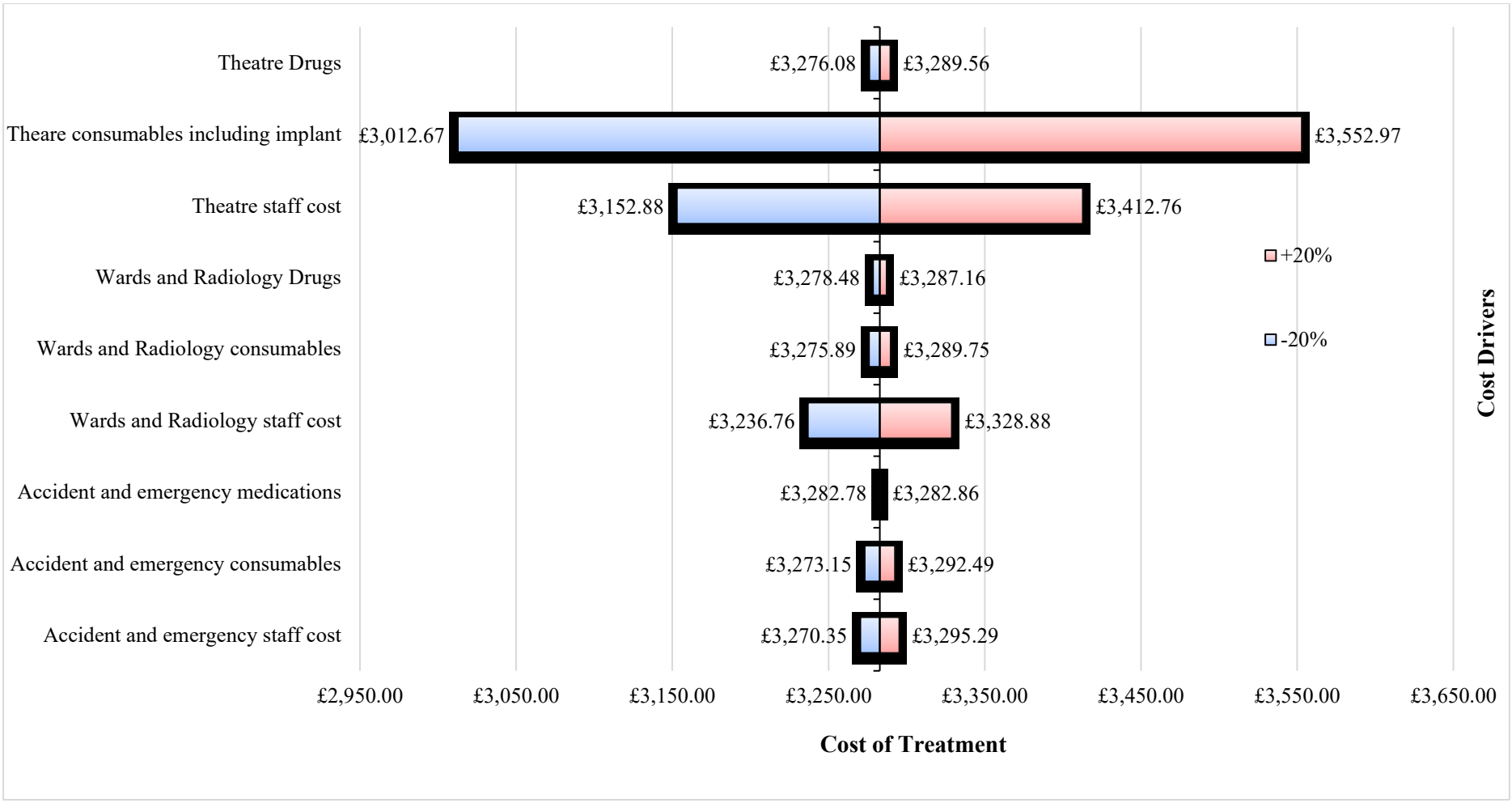


Figure 4.4. Sensitivity analysis using 20% fluctuation in cost drivers illustrating that implant cost is the most sensitive cost driver that influences the overall cost of treatment.

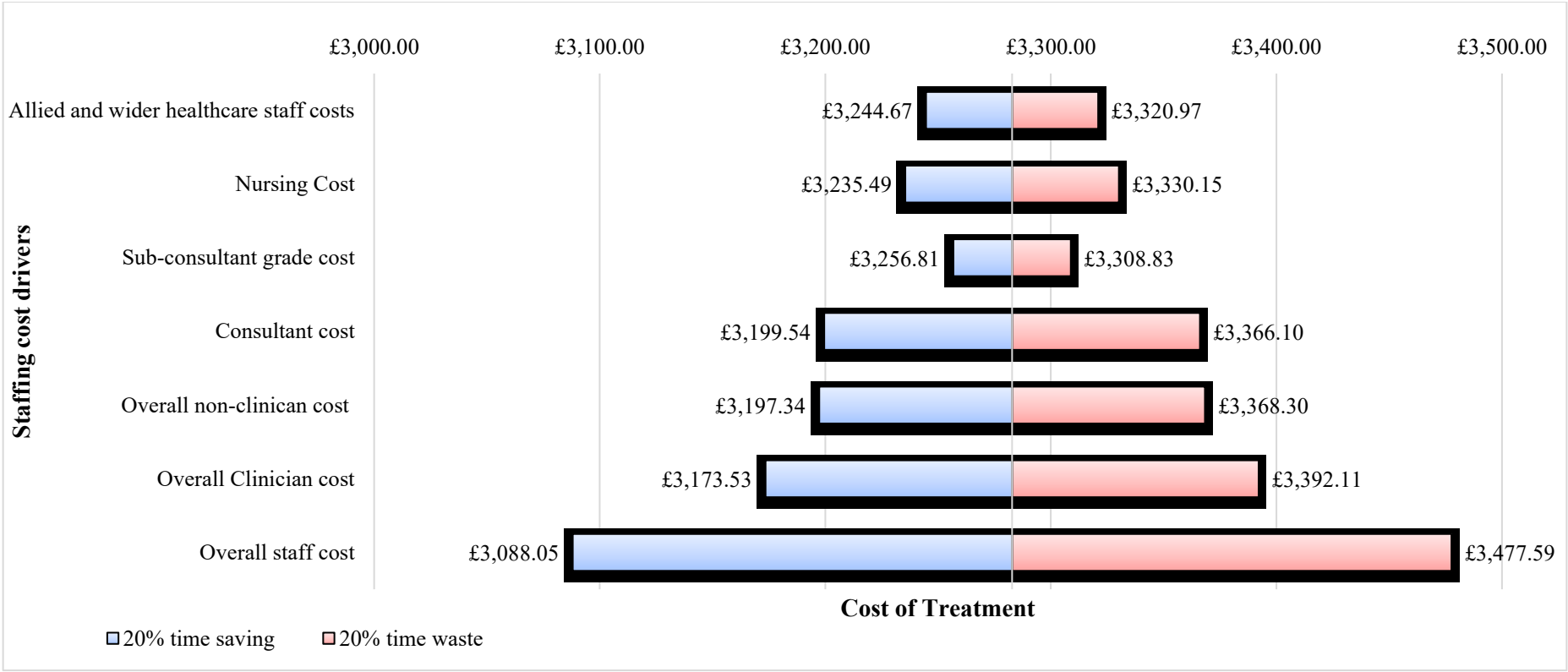


Figure 4.5. Sensitivity analysis illustrating that within staffing costs, fluctuation in consultant cost has the largest effect on the overall cost of treatment.

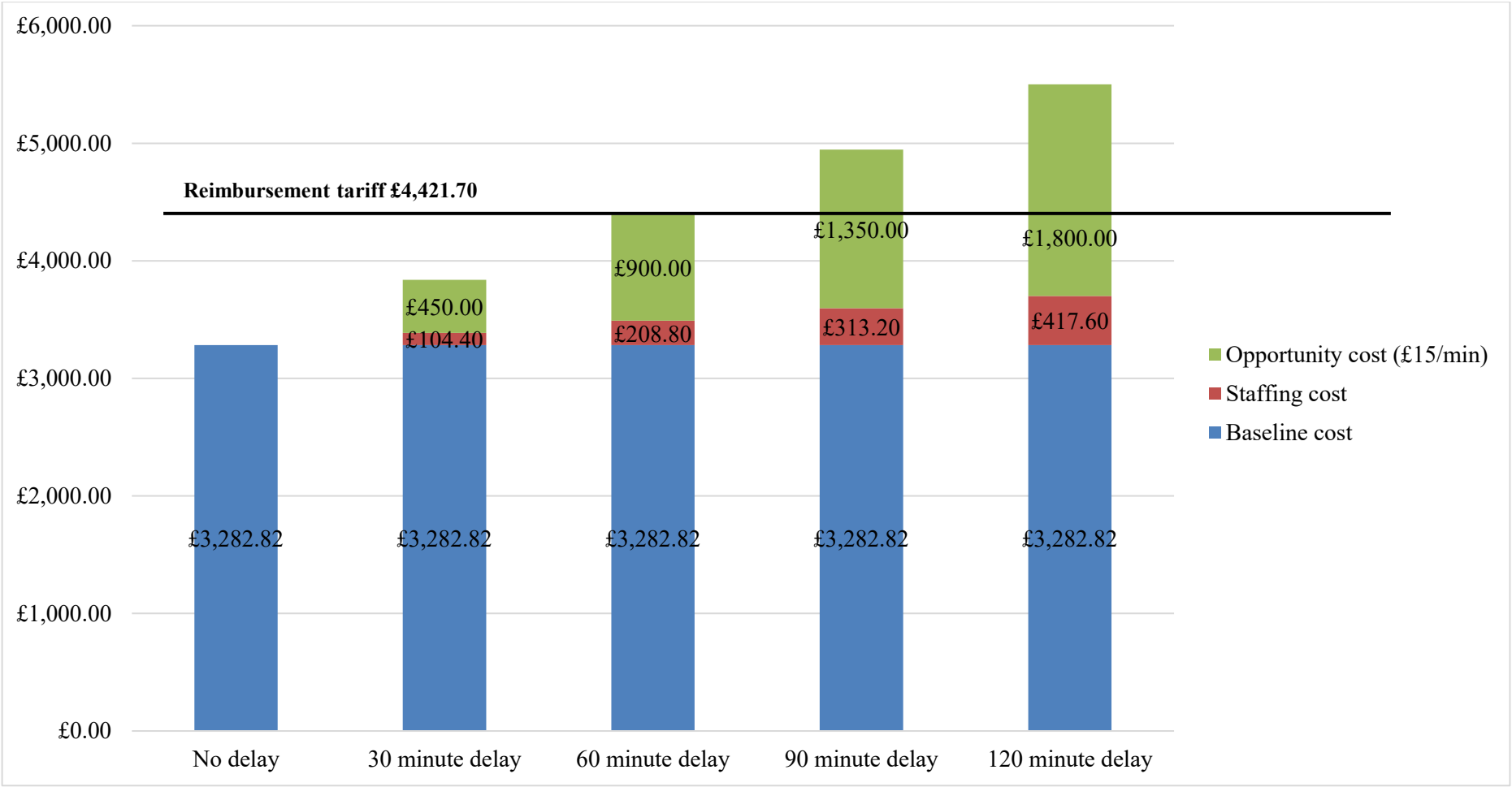


Figure 4.6. Threshold analysis demonstrating how delays in theatre affected the overall cost of treatment.

4.4 Discussion

4.4.1 Summary of findings

This is the first NHS study to utilise TDABC methodology for cost analysis in orthopaedic trauma. The overall inpatient cost for surgical treatment of a proximal humerus factures in an elderly patient was estimated to be £3,282.82. When compared to the reimbursement from the national best practice tariff, this represents a net profit of £1,138.88. However, hemiarthroplasty is likely to result in an institutional loss of up to £952.20 because of substantially higher implant costs. The largest cost driver in the pathway was implant cost and theatre consumables. Theatre staff were the second largest cost driver, and their overall cost was almost 3-times the cumulative costs of staffing the rest of the inpatient pathway. Furthermore, operating theatre inefficiency as defined as redundancy of the operating theatre team for over 1 hour would result in a net loss to the institution. These findings are of particular importance to a large number of NHS trusts that continue to report large financial deficits and need to find ways to achieve efficiency savings [216].

4.4.2 Economic and Policy Implications of Findings

Establishing the cost and clinical outcomes of a treatment are important so that clinicians, healthcare managers and policy makers can scrutinise its value [217]. With much of the focus in clinical research centred on evaluating patient reported outcomes, the standards for measuring these have become well established [218]. In orthopaedic research the development and validation of these outcome measures is also often subjected to peer review[219,220]. Unfortunately, while the cost of a treatment contributes equally to understanding its value, methods for determining these costs, particularly in health economic research within orthopaedics, continue to rely on top-down estimates or the use of national tariffs [221,222]. Top-down costing is often discouraged because it lacks the transparency or detail to produce accurate cost estimates which can be studied and used to deliver cost saving approaches[110]. In

the case of the national tariffs, national guidelines for performing health economic evaluations actually advocate their use [223], despite research consistently showing that these surrogate cost estimates are inaccurate [117,118,224]. Detailed analysis of a treatment using TDABC not only provides more accurate estimates of overall cost, but in-depth analysis of the cost drivers along the patient pathway and as a result the ability to improve efficiency and enhance resource utilisation[217]. In the case of this study, the sensitivity of operating theatre utilisation on the overall cost reveals how efficient and judicious management of just one resource during the inpatient pathway, has the potential to increase profits significantly.

Although there is a strong emphasis on control of bed-day costs to improve efficiency in the health service[225], within the treatment pathway in this study, operating theatre delays of an hour resulted in an additional £1,108.80 in costs incurred to the hospital. While a comparison with bed-days costs has some limitations, the calculated value of an additional bed-day was £128.40. The difference between these two values underlines the importance of better theatre utilization.

For the purpose of health economic evaluations, TDABC offers more than just an accurate costing approach that improves the level of confidence in the cost-effectivenesss model, it provides an opportunity to consider the effects of cost containment on the overall analysis. In the case of management of proximal humerus fractures in the elderly, previous research has indicated that there is no significant incremental difference of costs and health outcomes between elderly patients who undergo surgery and those treated conservatively[120]. However, by using TDABC as a costing approach instead of charge rates or fee schedules, there is potential to evaluate the treatment pathway in detail, and control cost drivers using operational management techniques. Lean theory and six sigma were initially designed for use in the manufacturing industry, but are increasingly applied to clinical pathways in

surgical practice to deliver efficiency savings[226]. It is possible that such cost minimisation approaches applied to a CDVC, where surgical treatment can significantly improve patient outcomes [69], would improve theatre utilisation or implant procurement discounts to the point that the overall cost of surgery falls and the resulting incremental cost-effectiveness ratio is deemed acceptable to the health service within which the analysis is performed.

In the United States, TDABC has proved to be a valuable tool for achieving efficiency savings in surgical treatment[227] and it has also underlined the limitations of existing healthcare accounting methods[228]. Within the UK, questions remain about whether the structure of the English NHS would allow this tool to apply more accurate treatment costs to tariff benchmarking as well as whether it can improve service efficiency. The basis of this position is that the existing purchaser-provider means that the financial interests of hospitals and commissioning groups do not have to be aligned. Institutional profitability and efficiency will not necessarily benefit commissioning groups. Furthermore, where future TDABC research demonstrates substantial financial losses for specific orthopaedic treatments, English trusts may not be in the same position as hospitals in Scotland, Wales or Northern Ireland. In these countries, financial reimbursement provided by local health boards that are directly responsible for the hospital means that it should be easier to re-negotiate tariffs that TDABC research has demonstrated to be insufficient. The need for improved costing methods and the potential limitations of their application within an English NHS is particularly important at a time when recent health policy research has demonstrated that approximately two thirds of English Trusts are forecasting a deficit within the next year[229].

The overall institutional financial surplus for what is a complex upper limb procedure appears to be add odds with recent research in orthopaedics that has concluded that national reimbursement is often inadequate in orthopaedics[117,118]. However, the range of treatment

costs that were calculated based on acceptable variations in staff activity times and procedural choices, demonstrates that the national tariff is inadequate for benchmarking at a patient level. As such, our findings add credence to the belief that the tariff is often an unsuitable and inaccurate method for costing healthcare in the UK [117,230]. Furthermore, while existing research has determined that the tariff undervalues the cost of surgical treatment, those analyses are based on joint reconstruction surgery [117,118] where arthroplasty implants can be up to four-times the cost of an osteosynthesis prosthesis. Our findings support those results; despite the average cost of treatment being relatively profitable, the cost when performing a hemiarthroplasty has been shown to result in institutional loss of revenue. Although procedure choice may be based on the preferences or experience of the operating surgeon, there are clearly defined indications where hemiarthroplasty is viewed to be a superior alternative[231]. In such cases, data from recognised joint registries [56] should inform decisions on implant choice and institutional procurement based on single-supplier or volume-based discounting may drive prices down considerably.

Consideration must also be given to the use of reverse arthroplasty for proximal humerus fractures. Even though its long term cost-effectiveness has yet to be established, there is growing advocacy for this procedure in a trauma setting[161], with a recent randomised trial demonstrating improved patient outcomes for the reverse prosthesis over hemiarthroplasty[232]. We excluded this implant from our analysis because at the time of our study, on the basis of surgeon preference within our institution, reverse shoulder arthroplasty was not performed for proximal humerus fractures. Should our current practice change we are likely to incur substantial financial losses because the procurement cost for a reverse implant at our hospital is approximately £1,000 more than that of the hemiarthroplasty prosthesis. The financial impact of the use of reverse shoulder replacements for trauma is likely to have nationwide implications. The 2016 National Joint Registry Report indicates a year-on-year increase in

the use of reverse shoulder replacements since 2012 and based on the 2015 data on shoulder fractures, there were 649 reverse shoulder replacements performed, compared to 736 hemiarthroplasty procedures[233]. The potential for such losses raises more questions on the suitability of a national tariff system in adapting to and financially supporting evolving surgical practices.

4.4.3 Limitations

There are 4 main limitations to our study. Firstly, the overall costing model is specific to our organization and therefore the cost estimates derived from our methodology lack external validity. As such, it would be inappropriate to generalise these results for the purpose of cost-effectiveness research performed at other institutions in the UK or abroad. This highlights the complexity of determining costs for health economic research, especially if costs are derived from a single institution. Going forward, national health economic research will continue to be based on tariff costs unless more robust costing systems are developed. Emerging costing tools such as PLICS may be the solution once they have been validated. Second, this study was not conducted as a prospective observational TDABC analysis. Although such a perspective would have been useful in the analysis of resource utilization and staff efficiency, prospectively accounting for every inpatient minute for a large group of trauma patients would require vast financial and staff resources.

Third, our cost calculations may be conservative given the hypothetical patient type used to characterise the care pathway adopted in the study. This is more likely to be the case for physically frail patients. The implications of increasing medical complexity and comorbidities are beyond the scope of our study because of the population description applied to our analysis (Table 1). The financial impact of treating more complex patients warrants further attention because although it might appear intuitive that the cost of

treating them is higher, illness specific HRG codes should provide more reimbursement for patients suffering with concomitant medical illness in hospital. In addition, reimbursement for patients with increased medical comorbidities that undergo surgery would be higher based on a separate HRG code for upper limb trauma that takes into account patients that suffer a complication or have significant medical comorbidities. On the basis these additional reimbursements, it is feasible that patients with substantial medical comorbidities that are treated with a hemiarthroplasty would actually receive reimbursement that are surplus to treatment costs, however further research is required to establish whether this is the case.

Finally, the assumptions for overhead costs were based on overall financial ledger estimates. Although such assumptions are generally excluded from TDABC methodology, these costs comprise a substantial proportion of expenditure within the health service and our research group believed that their exclusion would grossly deflate our cost estimates. Unfortunately, other comprehensive micro-costing approaches that accounts for them at a patient level are lacking, and therefore less rigorous methods were adopted to generate these estimates.

4.4.4 Conclusions

Using TDABC, the inpatient hospital cost of treating a comminuted proximal humerus fracture in an elderly patient was estimated to be £3,282.82. Overall, this represents a net profit of £1,138.88 in relation to national tariff reimbursent, however when hemiarthroplasty is performed there is a potential loss of £952.20. These findings suggest that the national reimbursement tariff does not accurately represent the breadth of surgical treatment options available for this condition. While this has implications for a health service trying to assert more control over its resources and achieve substantial efficiency savings, it should also be

recognised in future health economic research, where the costs of of operative fixation or hemiarthroplasty may be inaccurately represented by the national tariff. Finally, this study has shown that effective operating theatre utlization, specifically appropriate implant selection and staff efficiency are likely to be a more important cost containment approaches than control of bed-day costs.

Chapter 5

Cost effectiveness analysis of management strategies for complex proximal humerus fractures: a 2 year time horizon based on a decision analytical model

5.1 Introduction

As the National Health Service (NHS) and hospital trusts that deliver patient care face a growing deficit [234],there is increasing interest in understanding the health economic benefits of alternative treatment interventions, particularly in orthopaedics[11,235,236]. Although clinical research investigating quantitative outcomes of treatment strategies for proximal humerus fractures is well established[91] [29], there has been little evaluation of what encompasses the safest and most effective method of management, relative to health expenditure within a health service with finite financial resources.

There is a common perception that economic evaluations alongside randomised controlled trials (RCTs) are the most appropriate means for determining the health economic benefits of alternative treatment interventions [237] [110]. This view is derived from a belief that internal validity is improved by prospective data collection within a selected patient and provider population [238]. To date, 2 studies have attempted to investigate the health economic outcomes of alternative treatment strategies for proximal humerus fractures and both have been performed alongside RCTs[11,120]. Handoll et al.'s health economic evaluation[11] was performed alongside the PROFHER trial [29], a large pragmatic multicentre RCT in the United Kingdom that compared surgical and conservative management of proximal humerus fractures. The authors concluded that surgical treatment was not more cost effective than conservative management. The applicability of these findings to decision making for more complex fractures have been challenged, largely because a substantial proportion of 2-part fractures were included in the trial[239]. A smaller single-centre study performed by Fjalestad et al. [120] concluded that there was no significant difference in quality adjusted life

years (QALYs) and treatment costs between locking plate fixation and conservative management for 3 or 4 part proximal humerus fractures. Although this study included patients with more complex fractures, the applicability of its findings to the English NHS is challenging owing to the differences in health service structure between Norway and England [240].

Decision analytical models are a commonly used alternative framework for conducting health economic evaluations(HEEs)[77]. Their application is particularly relevant when the conclusions of HEEs conducted alongside RCTs are weak. This occurs when there is a lack of external validity of the primary study, the number of treatment alternatives included is limited, and there are existing studies that provide relevant, and often contradictory data on costing or health consequences of the treatment strategies[77,122]. Decision analytical models in cost utility analyses adopt parameters on cost and health outcomes from multiple published studies within the existing evidence base, as well as proposed parameters derived from expert opinion[77,241,242]. A decision tree is a basic economic model in which the alternative options and outcomes are represented by pathways in the decision tree model **(See Figure 5.1).**

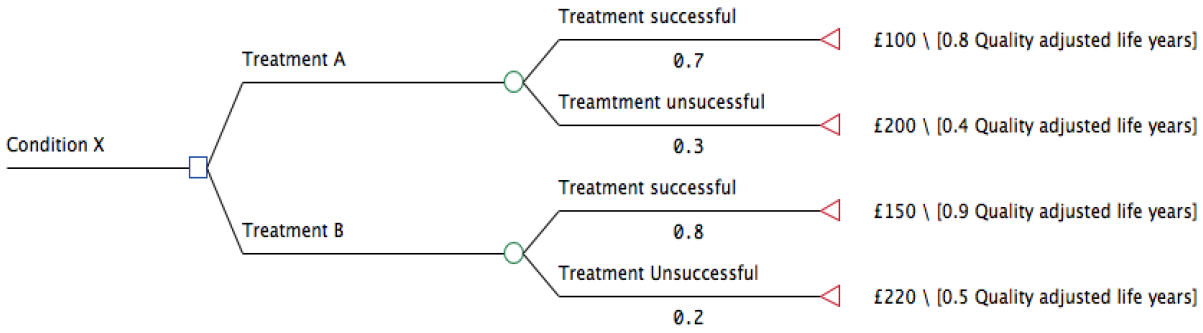


Figure 5.1. Example of a hypothetical decision tree, demonstrating comparison of different treatments available for Condition X. Pay-offs at terminal nodes include cost and effect (QALYs). The costs and utilities are aggregated and the incremental cost effectiveness ratio of the treatment is compared with a willingness to pay value to determine which treatment is cost-effective.

At each stage along the course of the decision tree there is a probability of entering the different pathways and the sum of these probabilities should equate to 1. The pathways

terminate at a terminal node where the pay-offs, which represent the sum costs and clinical outcomes, are assigned [77]. The expected payoffs of each treatment option are calculated and the incremental cost effectiveness ratio (ICER) between treatment options is obtained to determine which is the most cost effective treatment relative to a predetermined willingness to pay (WTP) value. For instance in Figure 5.1 the mean cost per QALY for each treatment is calculated based on the probability of successful and unsuccessful treatment and the incremental difference between each intervention represents the ICER.

Von Neumann and Morgenstern, researchers at the Institute for Advanced Study in Princeton, set the mathematical foundations for decision theory in the book title "Theory of Games and Economic Behaviour" published in 1944[243]. Although this work was credited with the study of strategic decision-making, or game theory, which has been commonly used in economics and political sciences, its potential application in healthcare was first recognised when the journal Science published Ledley and Lusted's study "Reasoning foundations of medical diagnostics: Symbolic logic, probability, and value theory aid our understanding of how physicians reason" [244]. This paper, which was the work of a mathematician (Robert Ledley) and a radiologist (Lee Lusted), considered the probabilities of disease occurring based on different combinations of symptoms and the effectiveness of treatments based on the 'pros and cons of each treatment in relation to the disease complex'. The authors proposed that such mathematical techniques would enable clinicians to 'make a more precise diagnosis' and 'a more scientific determination of the treatment'. Since the publication of this paper in 1959, health economics and decision analytical modelling have matured into a healthcare science which is conducted based on a standardised consensus driven methodology[242]. Furthermore its application now forms the basis of recommendations in national healthcare policy in the UK, Europe and United States[245-247].

The absence of a HEE for management strategies of complex proximal humerus fractures not only weakens the evidence base that should inform decision making, it has created an intellectual vacuum surrounding the understanding of how much treatment or implants can cost within the context of WTP in the English NHS. Application of health economics to this field also has the potential to quantitatively inform orthopaedic surgeons how variability in complication rates or health utilities play a role in determining which treatment is most cost-effective.

This aim of this chapter was to perform a cost-effectiveness analysis using a decision analytical tree modelled on existing published evidence, and to identify what is the most cost effective treatment option for complex proximal humerus fractures within an English NHS setting.

5.2 Methods

This HEE was performed according to Consolidated Health Economic Evaluation Reporting Standards (CHEERS) [242].

5.2.1 Study design

The target population for this HEE was an elderly cohort of patients with a 3 or 4-part proximal humerus fracture. The definition of elderly patients in orthopaedics is most commonly based on chronological age and reported by a heterogeneous group of values[133]. The most commonly reported chronological age in orthopaedic research is a patient at or above 65 years[133] and this was adopted as the definition of an elderly patient in this study. Therefore data were only selected from existing research in which the mean age of patients included was 65 years or more. As discussed in earlier chapters, elderly patients represent the largest proportion of patients that sustain complex proximal humerus fractures and this made the population definition relevant to the economic evaluation

The setting of this study was the English NHS and the perspectives adopted were based on the recommendations provided by the National Institute for Health and Clinical Excellence (NICE), for the evaluation of health technologies[248]. The primary perspective of the study was that of an NHS payer based on treatment reimbursement costs acquired from nationally reported tariffs for Healthcare Resource Groups (HRGs). The strength of such a perspective is that the cost estimates apply to the NHS across England and therefore the results of a cost utility analysis would have greater external validity. However, as pointed out in the NICE guidance[248], micro-costing data may also be appropriate because different treatments reimbursed by the same HRG can have different institutional costs. Therefore cost estimates acquired from the micro-costing study reported in Chapter 4 formed part of the sensitivity analysis in which a cost utility analysis based on institutional treatment costs would be performed. More comprehensive societal costs such as those incurred from primary healthcare services, social care or productivity losses were not included because there is no available research or data to support their estimates.

The intervention strategies in this analysis included all reported treatment methods for managing 3 or 4 part proximal humerus fractures, for which there was exiting Level I evidence[249] reporting on probability outcomes of treatment and the measures of effectiveness (health utilities) used in this cost utility analysis. The time horizon of a HEE evaluation refers to length of time over which the costs and consequences are evaluated[242]. A 2-year time horizon was used for this study based on the findings of a systematic review of the literature reported in Chapter 2, which found that most RCTs had a maximum 2-year follow up. Furthermore long-term retrospective studies have shown that complication rates after 2 years are low [190,250] and therefore it was felt that this further justified the design of an economic model based on a 2-year time horizon. Other agreed assumptions for the economic model included that only 1 secondary surgical or revision procedure would be performed within the

stated time horizon and outpatient follow up appointments were equivalent between the selected interventions. These assumptions were based on the expert consensus of four orthopaedic surgeons, a health economist and a decision analyst, after it was determined that pre-existing data for these factors was not present in the scientific literature.

Discounting in a health economic evaluation relates to different weights given to costs and health outcomes relative to the time at which they occur. It is a principle based on the belief that current costs and benefits are higher, as there is an opportunity cost from loss of investment return for money spent, and society has a preference to gain health outcomes today rather than in the future[251]. Discounting costs along a time horizon is used to reflect the return of investment on money spent in the future. It was not performed within this health economic evaluation because a 2 year time horizon was built into a decision tree, not a Markov chain, and therefore transitional costs at 1 year could not be accounted for.

A decision tree model was constructed and the health economic analysis was performed using the decision analysis software (TreeAge Pro; TreeAge Software, Williamstown, Massachusetts). This model included the cumulative outcome probabilities of each treatment strategy reported in published RCTs for 3 or 4-part proximal humerus fractures. Costs for each outcome of treatment were incorporated into the model as were 2 year quality adjusted life years (QALYs) which were derived from published RCTs. In cases where there was paucity of outcome data from Level I studies, retrospective research and expert consensus was used to create surrogate values. These values were subsequently subjected to sensitivity analysis to establish their effect on the constructed decision model.

5.2.2 Model Inputs

5.2.2.1 *Outcome probabilities*

Outcome probabilities were based on the reporting of 2-year follow up by 5 RCTs [30,69,148,232,252] **(Table 5.1).** The only treatment interventions with published outcome data in the form of health utilities were conservative management, locking plate fixation and hemiarthroplasty. As such, these 3 management strategies and their cumulative outcome probabilities from the 5 identified RCTs were used to build an economic model.

The probability values for of a complication for each intervention is summarised in **Table 5.2** and the probability values for complications requiring secondary surgery is summarised in **Table 5.3**. A full description of these complications and revisions as reported by each study is available in **Appendix 4**.

Table 5.1. Characteristics of 5 studies used to determine outcome probabilities used in decision tree model.

Author (Year)	Country	Sample size	Mean age	Treatment strategies	Fracture type (Neer classification)	Health utilities reported (Type)
Cai et al. (2012)	China	32	71.9	Hemiarthroplasty Locking plate	4 part	Yes (15D)
Fjalestad et al. (2012)	Norway	50	72.56	Locking plate Non-operative	3 part (52%) 4 part (48%)	Yes (EQ5D)
Olreud et al. (2011)	Sweden	55	76.65	Hemiarthroplasty Locking plate	4 part	Yes (EQ5D)
Olreud et al. (2011)	Sweden	60	73.9	Locking plate Non-operative	3 part	Yes (EQ5D)
Sebastiá-Forcada et al (2014)	Spain	62	-	Hemiarthroplasty Reverse arthroplasty	4 part (83.9%) 3 part (16.1%)	No

Table 5.2. Summary of model input values for complications.

	Total cases	Total complications	Mean probability of a complication	Probability range for a complication
Locking Plate	65	29	0.446	0.25 – 0.696
Hemiarthroplasty	72	14	0.194	0.083 – 0.3
Conservative	78	32	0.410	0.357 – 0.64

Table 5.3. Summary of model input values for complications requiring secondary surgery.

	Total complications	Total number of secondary operations	Probability of complication requiring secondary surgery	Probability range for complications requiring secondary surgery
Locking Plate	29	16	0.551	0.25 – 1
Hemiarthroplasty	14	13	0.928	0.889 – 1
Conservative	32	3	0.094	0.0625 – 0.167

Reported outcomes probabilities following revision surgery are not described in published RCTs. Only a handful of case series have reported on secondary surgery following complications of management of proximal humerus fractures[190,253,254], and these Level IV studies have shown that complication rates and outcomes are worse than those reported following primary management. Expert consensus was adopted for modelling outcome probabilities after secondary surgery with an assumption that half of patients would experience a complication. This probability was then modified according to a broad range of values within the sensitivity analysis, for each of the 3 treatment interventions. This sensitivity analysis was important as it scrutinized how input parameters that were not derived from published clinical evidence affected the overall cost-effectiveness results.

5.2.2.2 *Costs*

The costs used in this health economic evaluation were based on national reimbursement tariffs in the NHS in England. These costs are referred to as Payment by Result (PbR) tariffs

and are set every year by the Department of Health (DoH) in England. These values are based on estimates of treatment costs for case-mixes of conditions, called Healthcare Resource Groups (HRGs) that are submitted to the DoH by hospital trusts in the NHS in England. The values used within this study are based on the PbR national prices set for 2014 to 2015[214]. Reimbursement for different treatments, such as hemiarthroplasty and plate fixation, is often the same because HRGs can encompass a wide range of treatments. Although this does not reflect actual differences in treatment costs, these values have national applicability and micro-costing surrogate values may lack external validity because of variations in treatment costs between hospitals[255]. After primary analysis using PbR costs was performed, sensitivity analysis using institutional costs of treatment derived from a micro-costing study reported in Chapter 4, were used to evaluate the effect on the overall results.

Reimbursement tariffs included those related to inpatient treatment as well as outpatient follow up. An assumption used within this model was that following each treatment a patient would have 6 outpatient clinic reviews. Outpatient physiotherapy costs were excluded because these are not based on national tariffs, but rather are negotiated locally as block contracts by each hospital. Another assumption related to costing was that patients managed non-surgically were not admitted into the hospital and therefore the only costs incurred were those related to outpatient clinic attendance.

The PbR costs used in this study are listed in **Table 5.4** and they exclude market force factors (MFFs). These indices, which are used to reflect differences in overhead costs between institutions based on their geographic location, were not felt to add value to a HEE based on an overall English NHS perspective. Each unit of treatment in **Table 5.4** relates to a chargeable unit of healthcare based on the potential outcomes identified from the RCTs used to build this economic model. The institutional cost estimates are listed in **Appendix 4.**

Table 5.4. Input parameters for costing based on national tariffs

Unit	HRG Reference code	Description	Cost (£)
Primary locking plate procedure	HA61C	Major Shoulder and Upper Arm Procedures for Trauma without CC	3413
Primary hemiarthroplasty procedure	HA61C	Major Shoulder and Upper Arm Procedures for Trauma without CC	3413
Post procedure first clinic follow up appointments	WF01B	First Attendance – Single Professional	119
Subsequent clinic follow up appointments	WF01A	Follow Up Attendance – Single Professional	70
Re-plating for locking plate procedure	HB61B	Major Shoulder and Upper Arm Procedures for Non-Trauma with CC	5490
Removal of locking plate	HB62B	Intermediate Shoulder and Upper Arm Procedures for Non-Trauma with CC	3136
Revision of infected locking plate	HB61B	Major Shoulder and Upper Arm Procedures for Non-Trauma with CC	5490
Revision of locking plate to hemiarthroplasty	HB61B	Major Shoulder and Upper Arm Procedures for Non-Trauma with CC	5490
Revision of hemiarthroplasty to other hemiarthroplasty	HB61B	Major Shoulder and Upper Arm Procedures for Non-Trauma with CC	5490
Wound revision of infected hemiarthroplasty or locking plate	HB62B	Intermediate Shoulder and Upper Arm Procedures for Non-Trauma with CC	3136
Intra-operative hemiarthroplasty fracture treated with cerclage wire	HA61B	Major Shoulder and Upper Arm Procedures for Trauma without CC	4330
Manipulation under anaesthesia of stiff hemiarthroplasty		Minor Shoulder and Upper Arm Procedures for Non-Trauma	1028
Revision of hemiarthroplasty to reverse arthroplasty	HB61B	Major Shoulder and Upper Arm Procedures for Non-Trauma with CC	5490
Acromioplasty and release of adhesions after hemiarthoplasty	HB62B	Intermediate Shoulder and Upper Arm Procedures for Non-Trauma with CC	3136
Fixation of tuberosity after hemiarthroplasty	HB62B	Intermediate Shoulder and Upper Arm Procedures for Non-Trauma with CC	3136
Locking plate fixation for acute displacement of conservatively managed fracture	HA61C	Major Shoulder and Upper Arm Procedures for Trauma without CC	3413

Unit	HRG Reference code	Description	Cost (£)
Hemiarthoplasty for acute displacement of conservatively managed fracture	HA61C	Major Shoulder and Upper Arm Procedures for Trauma without CC	3413
Sub-acromial decompression for impingement after conservatively managed fracture	HB63Z	Minor Shoulder and Upper Arm Procedures for Non-Trauma	1028

5.2.2.3 *Health Utilities and Quality Adjusted Life Years*

Quality adjusted life years (QALYs) are summary measures used for health outcomes in economic analysis that incorporate both the quantity and quality of an individual's life[256]. They were the measure of clinical effectiveness employed within this study. These values were derived from health utilities reported in 4 RCTs[30,69,148,252]. The health utilities were transformed into QALYs using an area under the curve (AUC) methodology[256] in Microsoft® Excel®, Mac Version 2011. A description of this methodology is detailed in **Appendix 4.**

When HEEs are performed in parallel to RCTs it is possible to use population specific health utility values to reflect different clinical outcomes. However, when sub-group means are not available, which is often the case when performing secondary analysis, estimates of health utilities are often based on expert opinion[77]. More than a third of cost utility analyses use utilities based on the authors' judgements[257] and such assumptions are commonly adopted in orthopaedic research[258-260]. Provided these assumptions are subjected to sensitivity analysis which demonstrates their effect on the study's results, such methodology is viewed to be acceptable[77].

The health utilities presented in the 4 RCTs[30,69,148,252] included the mean 2-year health utilities along with standard deviation (SD) values. For instance at 2-year follow up the health utility for patients managed conservatively in an RCT may have been reported as 0.65 and the SD as 0.15. Although this result is indicative of the clinical outcome for the overall population it is

not directly informative of how patients who fared well reported their health utilities relative to those that had a complication. A consensus-derived methodology by the authors of this study was based on an assumption that subjective reporting of health utilities would be normally distributed. This assumption was established by expert opinion, however existing research also suggests that functional shoulder outcomes in a normal population of elderly patients[261] as well those who have undergone shoulder surgery[262], is normally distributed. Based on this assumption the health utilities of the cohort of patients who had fared better for each intervention was calculated by adding 0.5 SD to each health utility. For those who sustained a complication, the health utility was calculated by subtracting 1 SD from the mean health utility of each intervention.

The rationales for these calculations are demonstrated in **Figure 5.2, 5.3, and 5.4.**

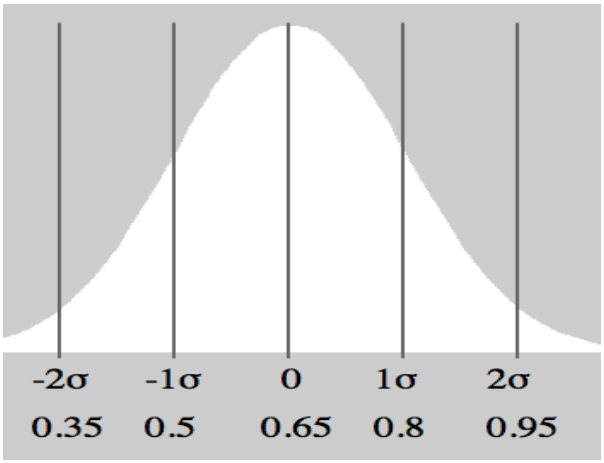


Figure 5.2. The assumed normal distribution of 2-year health utilities reported in existing studies if the mean value was 0.65.

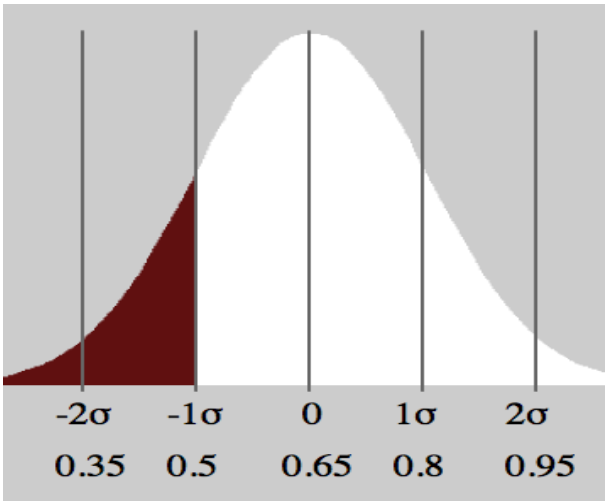


Figure 5.3. The estimated health utility for patients with a complication (or the complication state) taken to be 1SD/σ subtracted from the mean. In a normal distribution this accounts for approximately the bottom 15% of the population. Based on a complication rate of between 20-30% this position on the curve is representative of those patients.

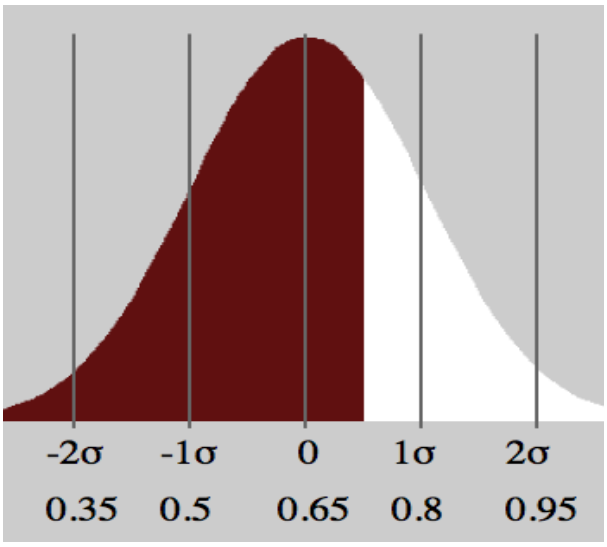


Figure 5.4. The estimated health utility for patients without a complication (or the well state) taken to be 0.5SD/ σ over the mean. This position on the curve is representative of patient health utilities in upper 67% of a normal population.

There is also an absence of published data that reports on health utilities after revision surgery or management of proximal humerus fracture sequelae. The study authors agreed that because of the disutility encountered from further surgery and the likelihood that function and health state after successful secondary surgery were unlikely to be at the same level as after

successful primary management, the utility estimate for successful secondary surgery would be half way between the primary 'well state' and the primary 'complication state'.

The estimates for health utilities after complications of secondary surgery were based on a methodology adopted from a cost utility study comparing hemiarthroplasty and reverse total shoulder arthroplasty for rotator cuff tear arthropathy[259]. The authors of this study used the ratio of the primary well and complication states to determine the complication utility value after secondary surgery. For instance if the primary management well state was 0.65 and the complication state was 0.5, then a ratio of 0.77 would be adopted and applied to a post-secondary surgery well state utility of 0.575 to derive a post-secondary surgery complication state of 0.443. The impact of uncertainty surrounding these assumptions would form part of the sensitivity analysis.

The input parameters for QALYs are summarised in **Table 5.5.**

Table 5.5. Summary of input parameters for QALYs in health economic model

	Value			
QALY Description	**Base Case**	**Low**	**High**	**Origin of QALY values**
Well state after conservative management	1.605	1.545	1.719	Fjalestad et al[148], Olreud et al[69], Olreud et al[30]
Well state after locking plate fixation	1.704	1.647	1.756	Cai et al[252], Olreud et al[69], Fjalestad et al[148]
Well state after hemiarthroplasty	1.713	1.682	1.744	Cai et al[252], Olreud et al[30]
Complication state after conservative management	1.029	0.76	1.486	Fjalestad et al[148], Olreud et al[69], Olreud et al[30]
Complication state after locking plate fixation	1.165	0.958	1.492	Cai et al[252], Olreud et al[69], Fjalestad et al[148]
Complication state after hemiarthroplasty	1.165	1.154	1.175	Cai et al[252], Olreud et al[30]
Improvement after secondary surgery for conservative management	1.317	1.196	1.603	Expert opinion

QALY Description	Value			Origin of QALY values
	Base Case	Low	High	
Improvement after secondary surgery for locking plate fixation	1.434	1.333	1.624	Expert opinion
Improvement after secondary surgery for hemiarthroplasty	1.439	1.418	1.460	Expert opinion
Complication after secondary surgery for conservative management	0.658	0.486	0.951	Expert opinion
Complication after secondary surgery for locking plate fixation	0.792	0.651	1.014	Expert opinion
Complication after secondary surgery for hemiarthroplasty	0.792	0.785	0.799	Expert opinion

The health utilities that were used to determine these QALY's are provided in **Appendix 4**. QALYs are reported as an expected gain in quality adjusted life years at 2 year follow up. Therefore, unlike 1 year health utility reporting where 1 represents perfect health and 0 represents death, in this analysis a value of 2 represents perfect health and 0 represents death.

5.2.3 Cost Utility Statistical Analysis

The input parameters derived from a systematic review of the literature, expert opinion, national costing data and institutional treatment costs resulted in the design of a decision tree illustrated in **Figure 5.5**. The complete decision tree which describes all the surgical strategies included after a complication is included in **Appendix 4**.

Cost-effectiveness analysis was performed on the basis of a willingness-to-pay (WTP) of £20,000/QALY. This value is cited by NICE as the upper limit of how much treatments within the NHS should cost in order to be deemed cost-effective[248]. The differences in cost effectiveness between interventions is determined using a measure called the incremental cost-effectiveness ratio (ICER). The ICER is calculated by dividing the net costs between

treatments from the net QALYs. For instance the ICER of hemiarthroplasty (HA) relative to conservative management (CM) would be based on the equation;

[(Cost $_{HA}$ – Cost $_{CM}$) / (QALY$_{HA}$ -QALY$_{CM}$)].

If a treatment strategy is more expensive and provides less effectiveness it is said to be dominated and is immediately viewed to be less cost effective. If a treatment requires increased cost but is more effective, cost-effectiveness is established if the ICER falls within the WTP of the model (£20,000/QALY). Cost effectiveness-analysis was performed and presented as graphical illustrations of the cost-effectiveness plane, as well as text summarising the rankings.

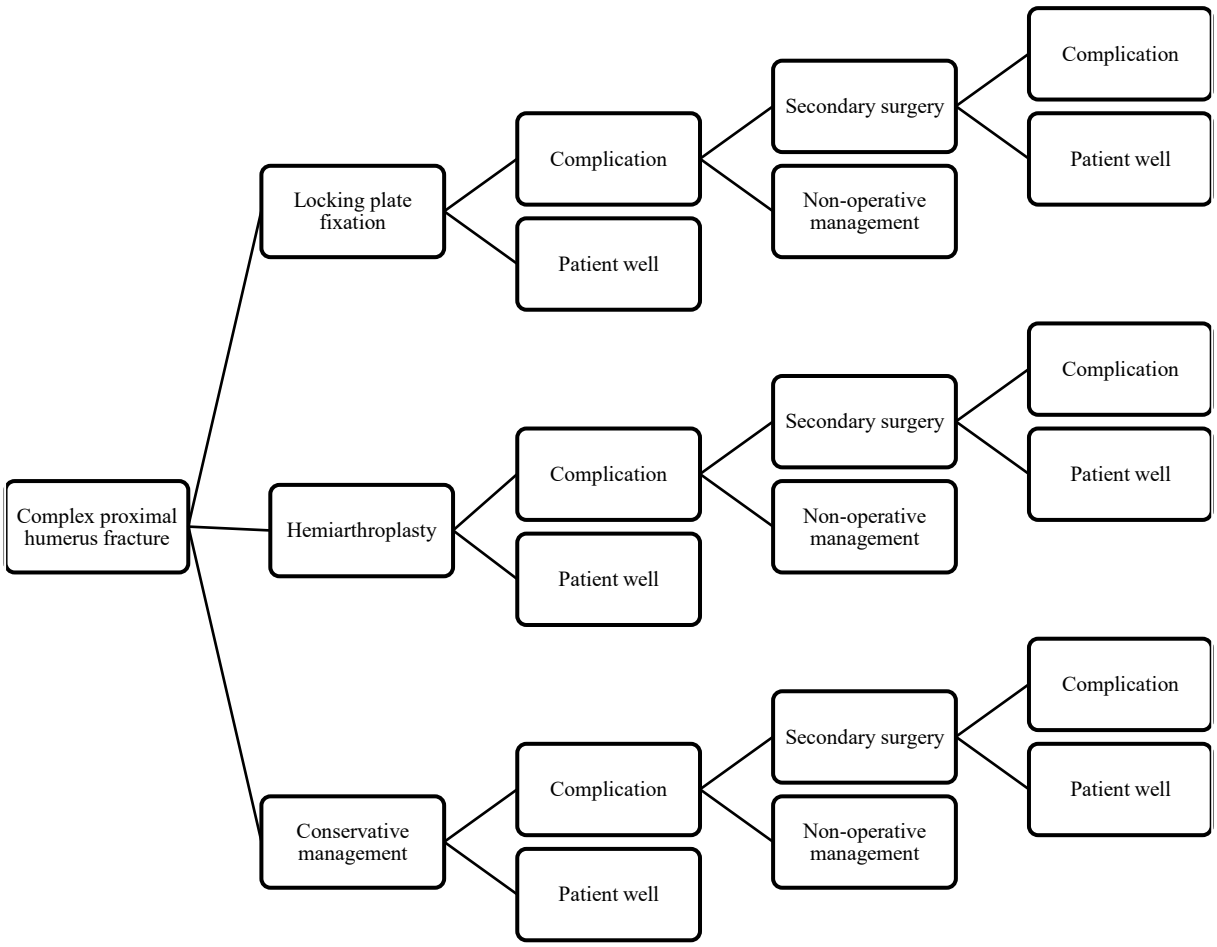


Figure 5.5. Conceptual model illustrating how a hypothetical patient with a 3 or 4 part proximal humeral fracture would pass through a decision analytical model over a 2 year time horizon.

5.2.4 Sensitivity Analysis

Multi-way sensitivity analysis was performed to evaluate uncertainty within the economic model. Uncertainty based on input parameters was evaluated through sensitivity analysis with 2 approaches. Firstly the range of values for each input parameter established from the literature search, or expert opinion, were adopted to test uncertainty in the model. Additionally, hypothetical values were input to determine the thresholds at which the model would become unstable if the range of values from the literature review did not affect the overall results.

Sensitivity analysis in Treeage Pro determines cost-effectiveness based on net monetary benefit (NMB). NMB is calculated using the following equation:

NMB = (Effectiveness Intervention A × WTP) - Cost Intervention A

NMB is commonly employed in health economic studies, particularly for sensitivity analysis because it is viewed to be more transparent in the comparison of multiple strategies than cost-effectiveness ratios[263]. Furthermore, as they incorporate WTP within their formula they are easier to interpret as the higher the NMB of an intervention, the more cost-effective it is.

Finally, cost parameters were subjected to sensitivity analysis by replacing national tariff costs with estimates of institutional treatment cost, which were obtained from a micro-costing study performed in **Chapter 4** (summary of these values presented in **Appendix 4**).

5.3 Results

Within this health economic model, hemiarthroplasty was found to be the most cost-effective treatment strategy for the management of 3 and 4-part proximal humerus fractures **(Figure 5.6).** Internal fixation was dominated by hemiarthroplasty because it had a lower estimated effectiveness and a higher cost. Although hemiarthroplasty was more expensive than

conservative management, it had a higher estimated effectiveness and its ICER was calculated to be £18,000.31/QALY. Within a framework of a WTP of £20,000 this made it the most cost-effective treatment.

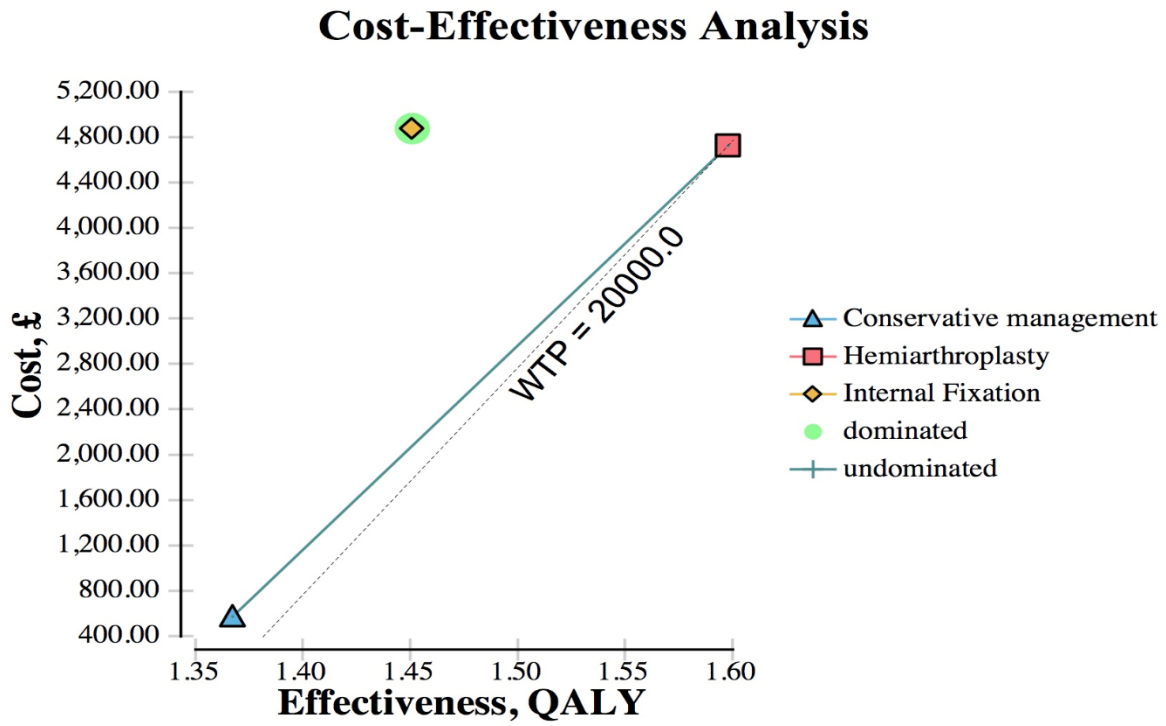


Figure 5.6. Cost-effectiveness graph illustrating how hemiarthroplasty lies within the WTP threshold and has a higher effectiveness and cost than conservative management, as well as a higher effectiveness and lower cost than internal fixation with a locking plate.

The summary of outputs generated from the cost-effectiveness analysis is provided below in **Table 5.6**.

Table 5.6. Summary of outputs generated from cost-effectiveness analysis performed on the model.

Strategy	Cost, £	Incremental Cost, £	Effect, QALYs	Incremental Effect, QALYs	ICER, £/QALY gained	NMB
Conservative management	575.87	-	1.37	-	-	26,768.94
Hemiarthroplasty	4,725.59	4,149.72	1.60	0.23	18,000.31	27.229.94
Internal Fixation	4,876.38	4,300.51	1.45	0.08	51,449.71	24,140.16

5.3.1 Sensitivity analysis

5.3.1.1 *Outcome probabilities reported in the literature*

In 3-way sensitivity analysis, in which primary complication rates were varied according to the complication rates in **Table 5.2**, hemiarthroplasty remained the most cost effective strategy provided the complication rate was less than 19% **(Figure 5.7).**

Within the context of testing uncertainty using hypothetical values, below a locking plate complication rate of 21.9%, the decision model becomes unstable **(Figure 5.8).** However, complication rates above 36% for conservative management and above 19% for hemiarthroplasty would be required to make locking plate fixation the most cost effective intervention at this threshold **(Figure 5.9).** As the value drops further to 11%, the complication rate of conservative management needs to be above 25% for locking plate to be the most cost effective option **(Figure 5.10).**

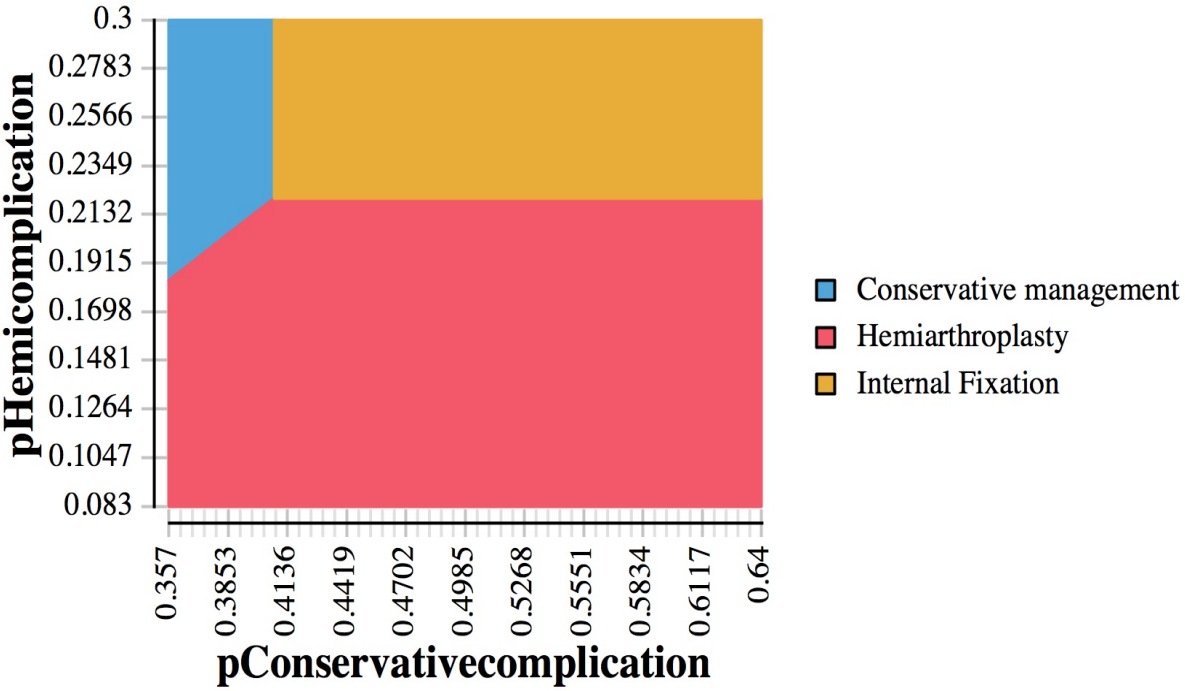


Figure 5.7. Three-way sensitivity analysis showing hemiarthroplasty to be the most cost effective strategy provided its complication rate is less than 19%. The complication rate for internal fixation is set at 25%, which is the lowest reported rate. pConservativecomplication is the model's description of the complication rate following conservative management; pHemicomplication is the model's description of the complication rate following hemiarthroplasty.

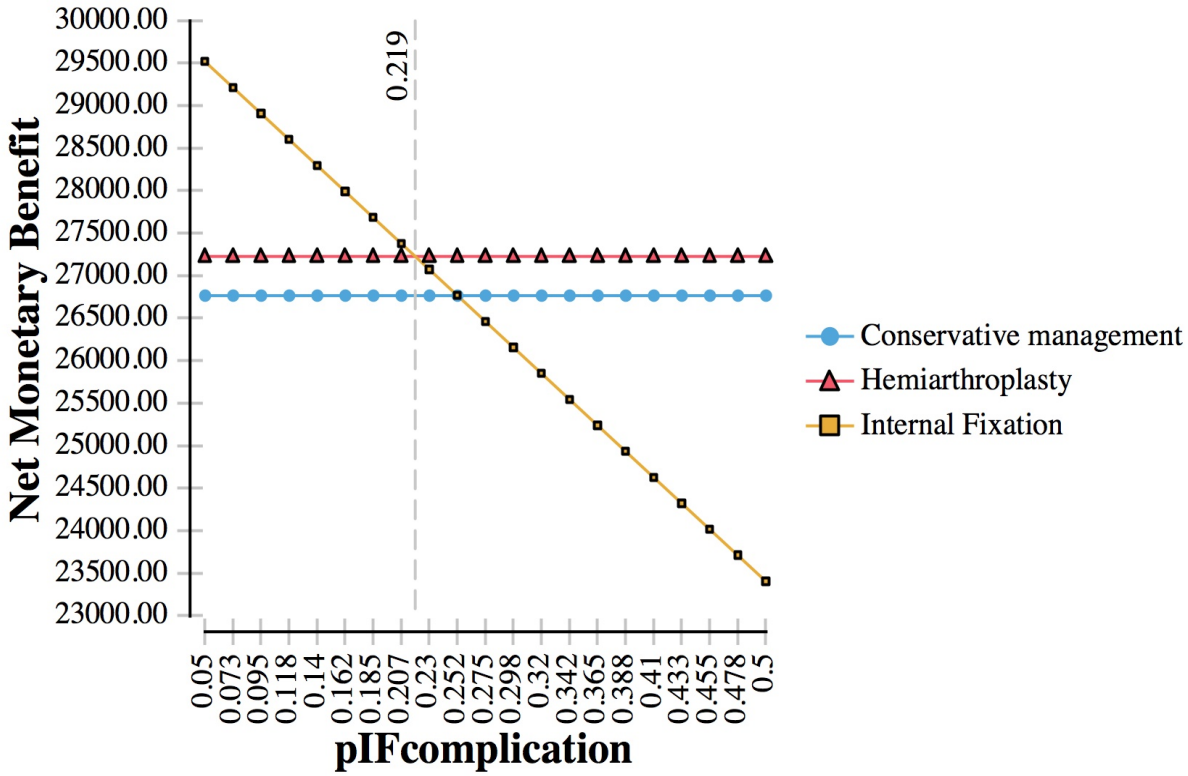


Figure 5.8. Sensitivity analysis showing how hypothetical variation in internal fixation complication rates affects the conclusions of the model. Below a complication rate of 21.9% locking plate fixation becomes more cost effective than hemiarthroplasty. pIFcomplication is the probability of a complication following internal fixation with a locking plate.

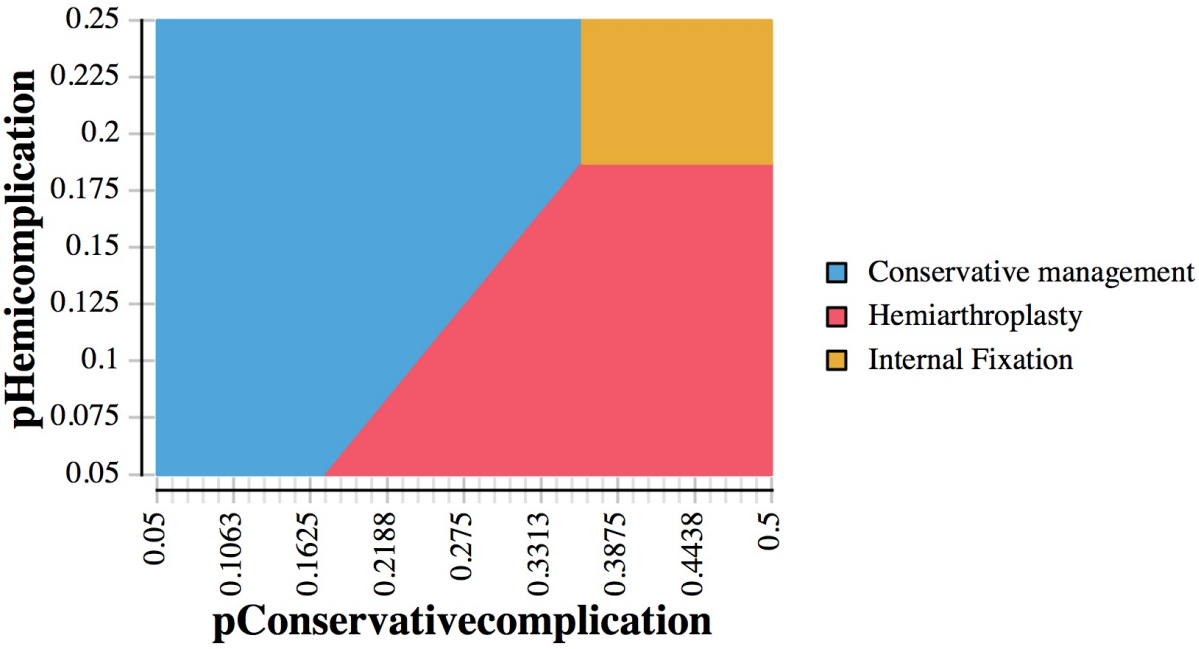


Figure 5.9. Three-way sensitivity analysis illustrating how the model changes when the probability of a complication falls below 21.9% with locking plate fixation. In this scenario the complication rate for locking plate fixation is set at 21% and locking plate is only more cost effective when the complication rate of hemiarthroplasty is above 18% and the complication rate of conservative management is above 17%. pConservativecomplication is the model's description of the complication rate following conservative management; pHemicomplication is the model's description of the complication rate following hemiarthroplasty.

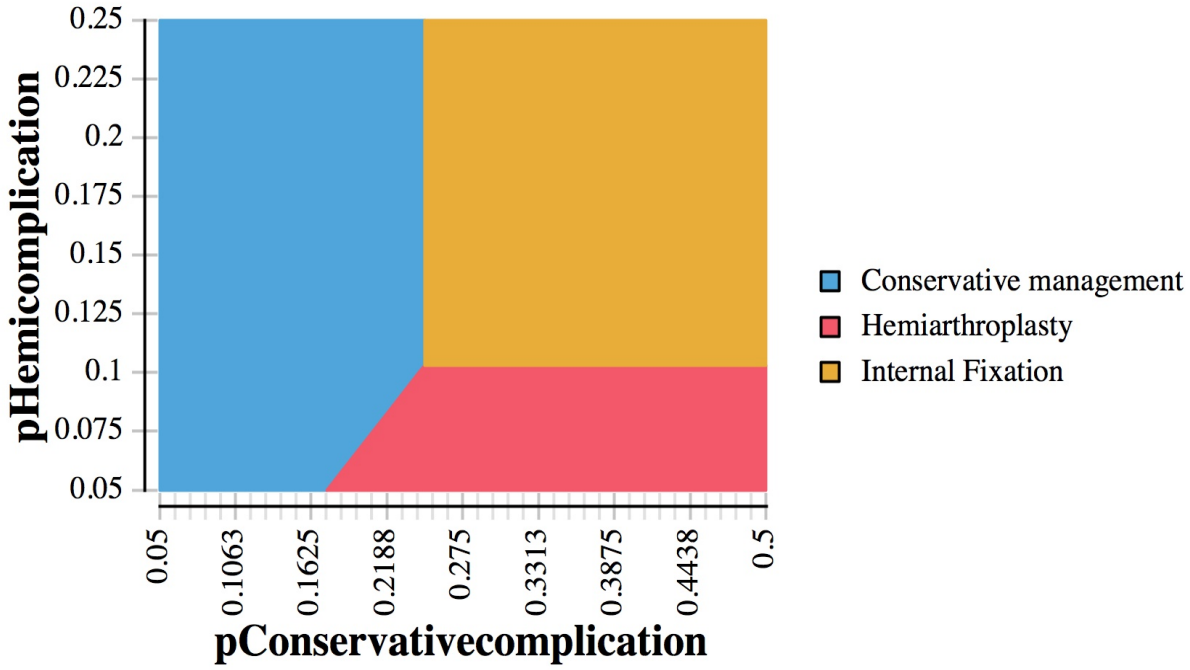


Figure 5.10. Three-way sensitivity analysis illustrating which treatment intervention is the most cost-effective based on a locking plate complication rate of 11 or less% (and a complication rate after hemiarthroplasty less than 10% and after conservative management less than 17%). pConservativecomplication is the model's description of the complication rate following conservative management; pHemicomplication is the model's description of the complication rate following hemiarthroplasty.

When secondary surgery rates were analysed using the range of values reported in the literature **(Table 5.3)** there was no effect on the model and hemiarthroplasty remained the most cost effective model **(Figure 5.11).** This was found to be the case in testing hypothetical uncertainty, with an extreme scenario demonstrating how insensitive the model is to these outcome probabilities; if the secondary surgery rate for complications of hemiarthroplasty is 100% and for internal fixation or conservative management it is 5%, hemiarthroplasty still remains the most cost effective strategy. This is likely to reflect existing research, which reports a lower complication rate for hemiarthroplasty, however a substantially higher re-operation rate when a complication has occurred.

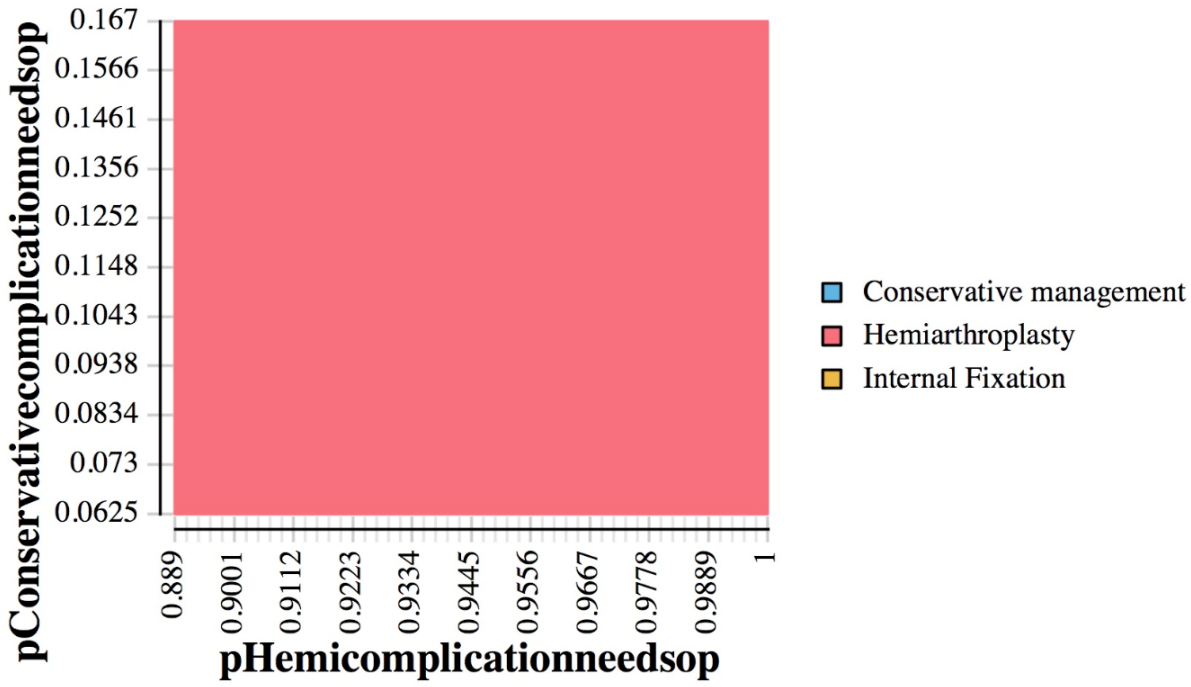


Figure 5.11. Three-way sensitivity analysis showing that hemiarthroplasty is the most cost effective treatment strategy even if the rate of secondary surgery is modified according to the range of reported values in the literature. Locking plate fixation is set at its lowest value of 25% in relation to the proportion of complicated cases requiring secondary surgery. pHemicomplicationeedsop is the probability of complications after hemiarthroplasty needing surgery and pConservativecomplicationneedsop is the probability of a complication after conservative management needing surgery.

5.3.1.2 *Outcome probabilities based on expert consensus*

Uncertainty was tested on the basis that for each intervention the likelihood of improvement after secondary surgery ranged from 10% to 100%. Testing different ranges for locking plate fixation had no effect on the model. Hemiarthroplasty was the more cost effective intervention when different values of improvement after revision surgery were tested between the conservative management and hemiarthroplasty arms in the model **(Figure 5.12).** Such was the insensitivity to variation on these input parameters that if all patients who underwent secondary surgery in the conservative management group had a favourable outcome, hemiarthroplasty would still be more cost-effective intervention if only 40% of revision procedures had a favourable outcome.

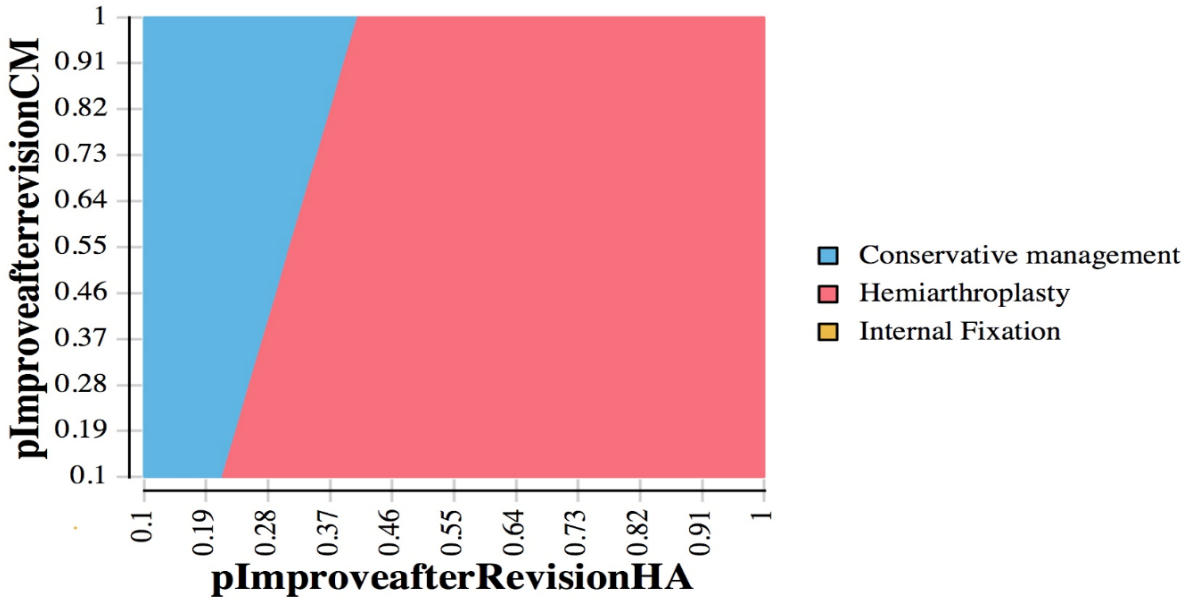


Figure 5.12. Two-way sensitivity analysis comparing the variation in success rates after revision surgery for the hemiarthroplasty and non-operative interventions. pImproveafterRevisionHA is the probability of successful secondary surgery after hemiarthroplasty and pImproveafterrevisionCM is probability of successful secondary surgery after conservative management.

5.3.1.3 *Uncertainty in QALYs*

The model was highly sensitive to variation in QALYs for patients with an uncomplicated primary management. While hemiarthroplasty was found to be the most cost-effective intervention, below a 2-year QALY of 1.684, it was surpassed by conservative management (**Figure 5.13).** From the range of QALYSs derived within the existing literature, a minimum reported QALY of 1.682 from Olreud et al's study[30] underlines the uncertainty within the model based on QALYs for patients that were managed successfully.

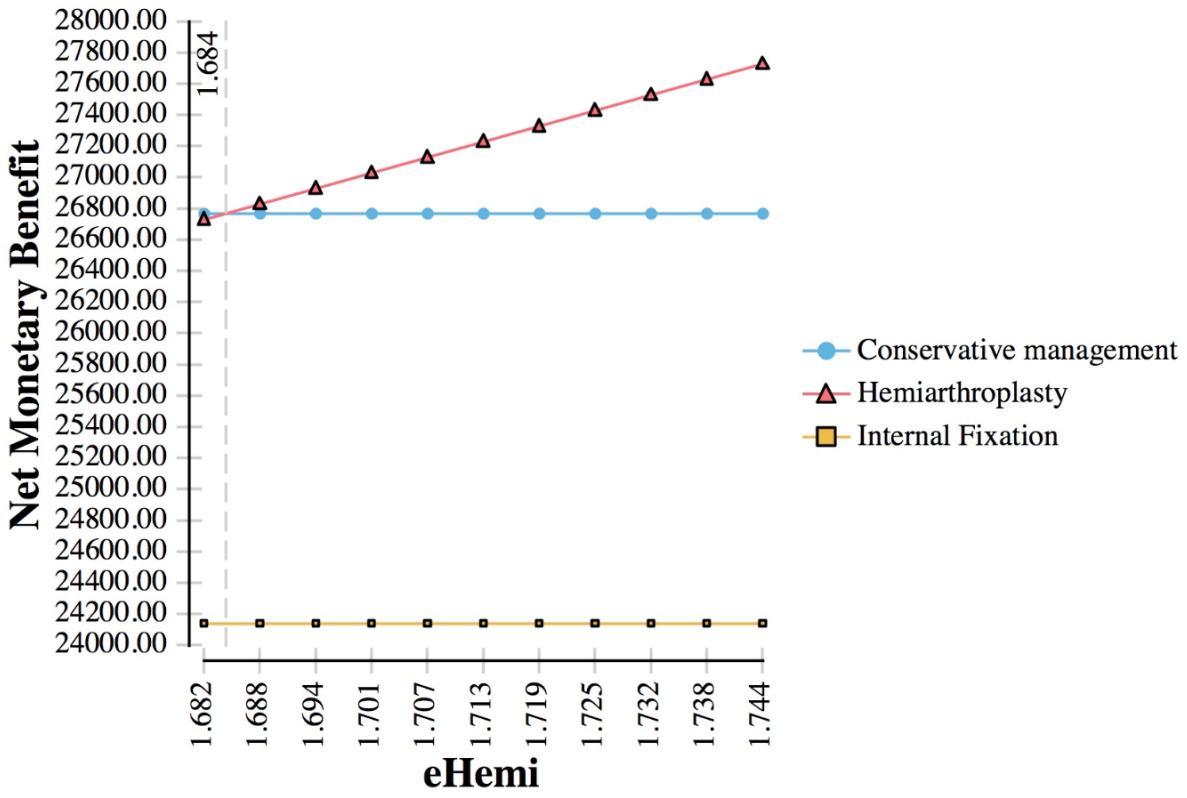


Figure 5.13. One-way sensitivity analysis demonstrating a threshold value of 1.684 below which QALYs for patients with a successful outcome after hemiarthroplasty (eHemi), results in conservative management being the most cost effective intervention

Despite the sensitivity of the model to QALY variation for hemiarthroplasty and conservative management values, evaluating the range of values for locking plate fixation had no effect on the outcome of the model. Hemiarthroplasty remained the most cost effective intervention when it was compared with locking plate fixation QALY values for patients with a successful outcome **(Figure 5.14).**

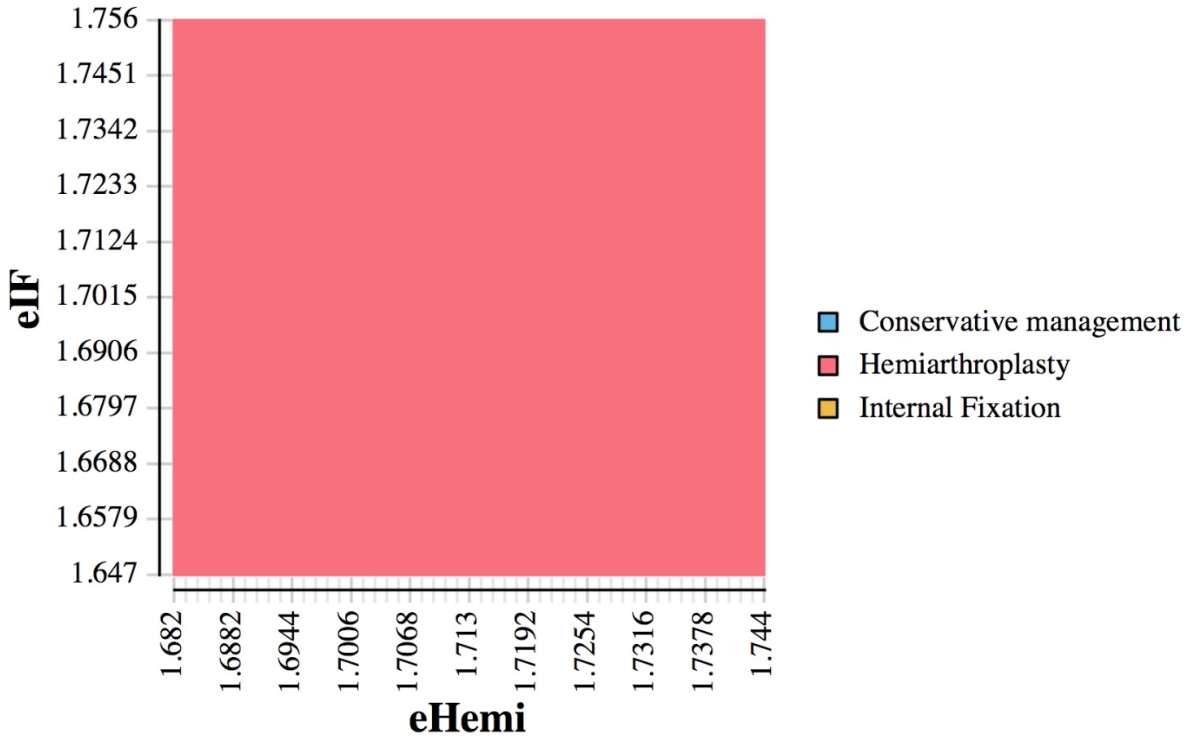


Figure 5.14. Three-way sensitivity analysis comparing range of values for QALYs obtained for patients that had a successful treatment outcome. Locking plate fixation (eIF) is compared with hemiarthroplasty (eHemi). Conservative management QALY is set at a minimum expected value of 1.545.

With regards to uncertainty based on QALYs derived for patients that had a complication after primary management, the model was sensitive to variation within the range of values for conservative management. Above a threshold of 1.09 QALYs for conservative management, the model would always favour conservative management as the most cost-effective intervention **(Figure 5.15).** Variation in locking plate fixation values had no effect on the model.

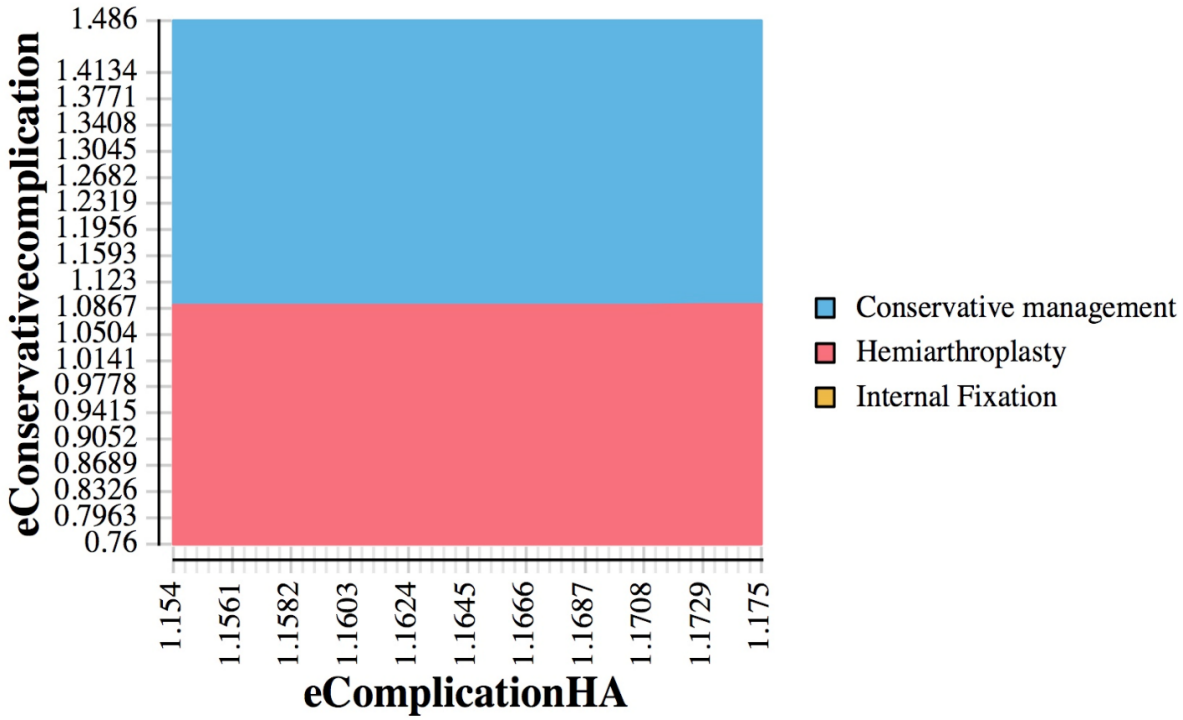


Figure 5.15. Three-way sensitivity analysis evaluating uncertainty based on QALYs derived for complications after primary management in each treatment arm. Locking plate fixation set a maximum value of 1.492. eConservativecomplication is the range of QALYs for patients with a complication after conservative management. eComplicationHA is the range of QALYs for patients with a complication after hemiarthroplasty.

All QALYs derived using expert opinion were tested within the model and the range of expected values had no effect on the outcome of the overall model. When hypothetical values beyond the range of expected values were tested, the model also favoured hemiarthroplasty. In relation to successful treatment outcomes after revision surgery, provided the QALY for patients undergoing secondary surgery after complicated hemiarthroplasty was greater than 1.32, hemiarthroplasty would always be the most cost effective treatment strategy **(5.16.)**

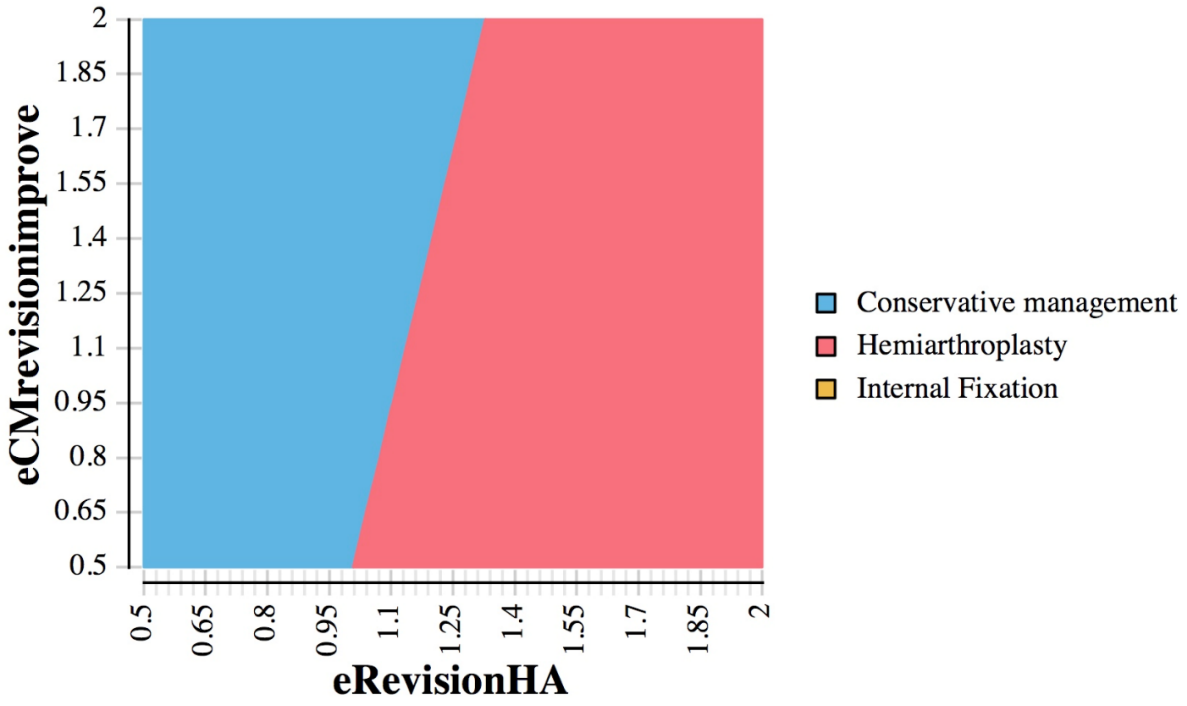


Figure 5.16. Three-way sensitivity analysis demonstrating the effect of hypothetical values for QALYs after successful secondary surgery for conservative management (eCMrevisionimprove) and hemiarthroplasty (eRevisionHA). Locking plate fixation is set at the highest possible outcome of 2.

Similarly when evaluating hypothetical uncertainty in relation to QALYs for patients who had a complication after secondary surgery, hemiarthroplasty remained the most cost-effective strategy provided that the 2-year QALY was above 0.8, even in the context of perfect health utilities for patients that were managed conservatively or by locking plate fixation **(Figure 5.17).**

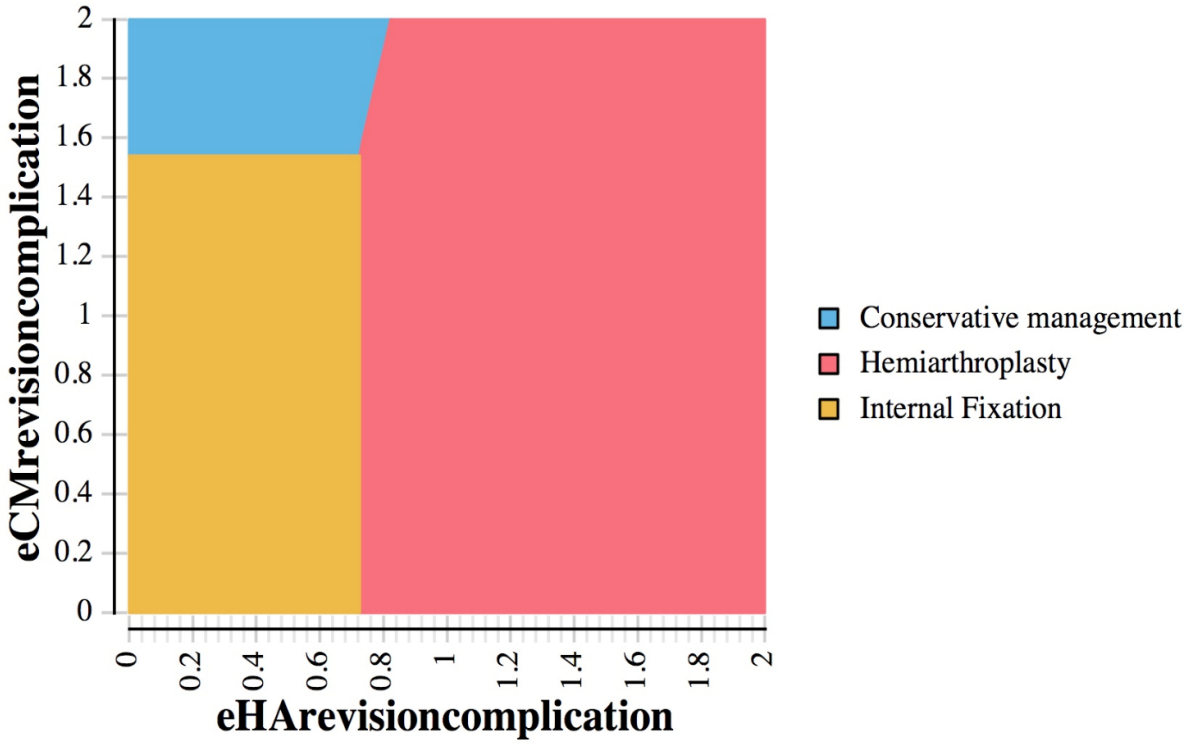


Figure 5.17. Three-way sensitivity analysis demonstrating the effect of hypothetical values for QALY after complications following secondary surgery between hemiarthroplasty (eHArevisioncomplicatin) and conservative management (eCMrevisioncomplication). The QALY for locking plate fixation is set at 2 (the maximum possible value).

5.3.1.4 *Uncertainty in costing: consideration of institutional costs*

When institutional costs were applied to the model instead of costs based on the national tariff, conservative management was the most cost-effective treatment strategy **(Figure 5.18).** This was because the ICER for hemiarthroplasty was £23,274.19/QALY and the ICER for locking plate fixation was £42,345.04/QALY relative to conservative management.

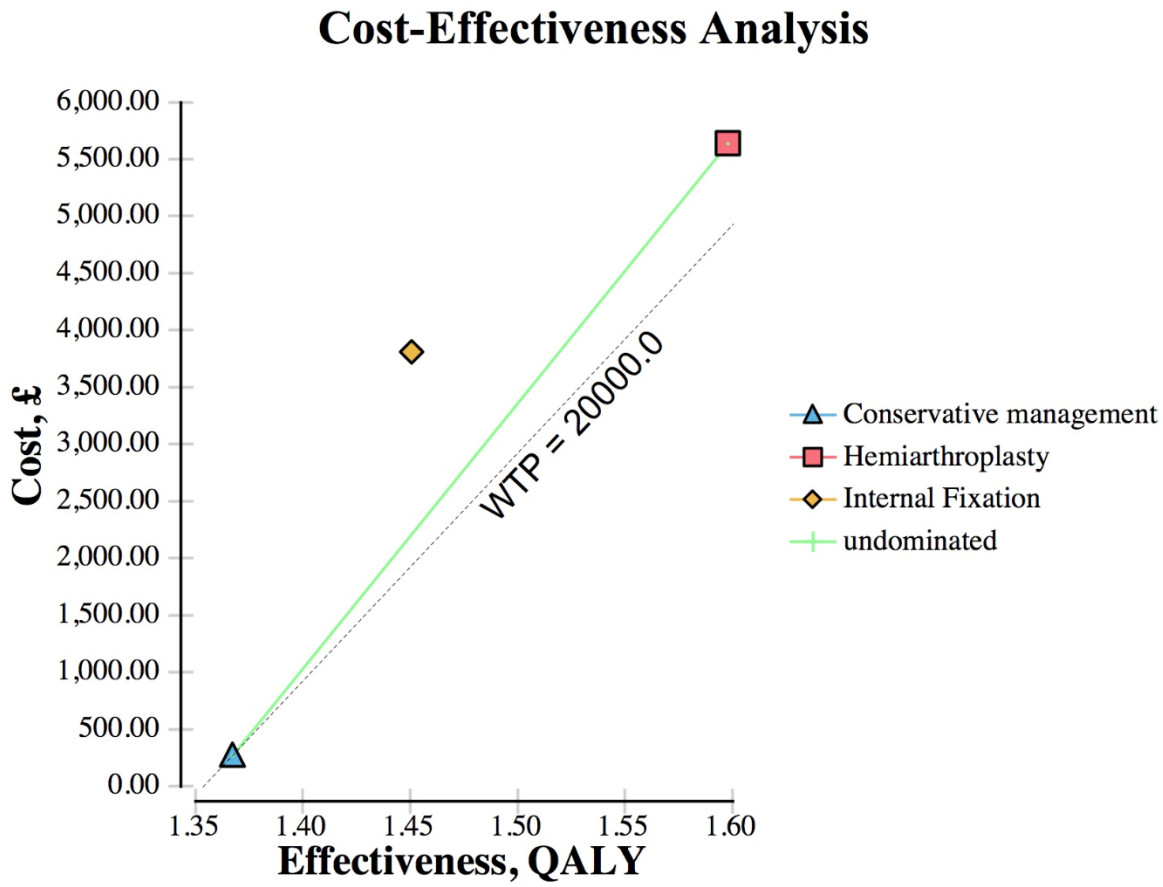


Figure 5.18. Cost-effectiveness graph demonstrating that based on institutional treatment costs conservative management is the most cost effective strategy as locking plate fixation and hemiarthroplasty fall outside the WTP threshold of £20,000/QALY.

Threshold analysis revealed that for hemiarthroplasty to be cost-effective for the hospital primary management would need to cost less than £3,924.49 **(Figure 5.19)** and for internal fixation to be cost-effective it would need to be less than £1,245.25 **(Figure 5.20).**

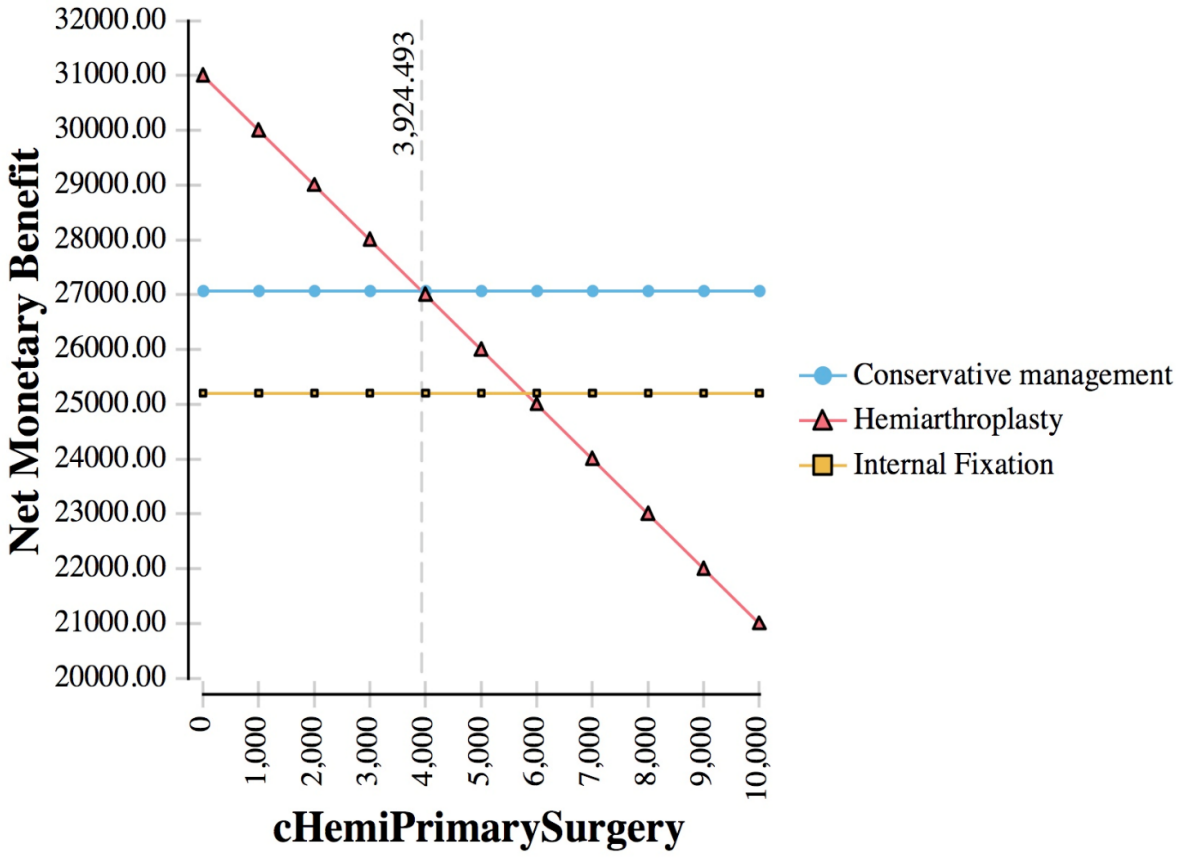


Figure 5.19. Threshold analysis demonstrating value at which hemiarthroplasty becomes a cost effective treatment strategy when institutional costing is used within the model. cHemiPrimarySurgery is the cost of the primary hemiarthroplasty procedure.

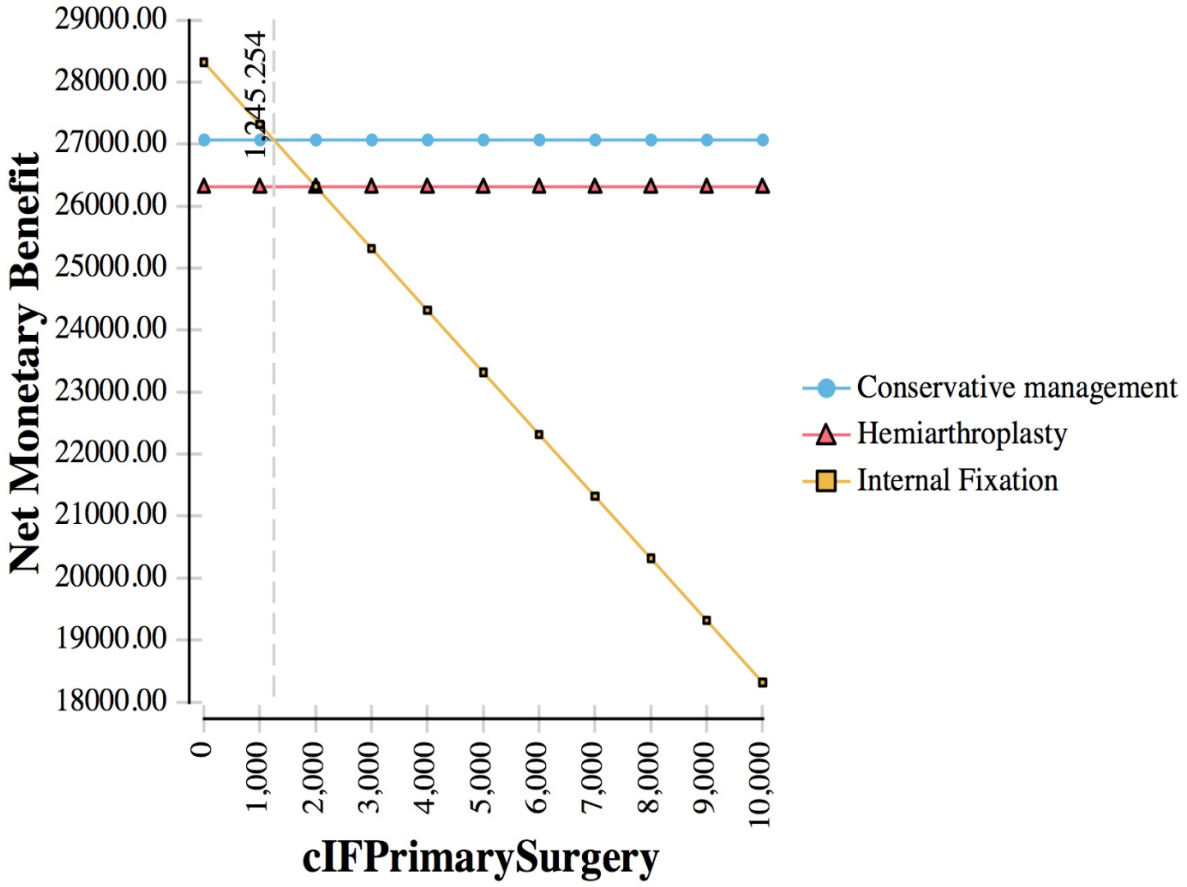


Figure 5.20. Threshold analysis demonstrating value at which locking plate fixation becomes a cost-effective treatment strategy within the model. cIFPrimarySurgery is the cost of a primary internal fixation procedure with a locking plate.

5.3.1.5 *Sensitivity analysis: summation of findings*

Based on the range of input parameters generated from a literature review and expert consensus, the model was sensitive to changes in primary management complication rate, QALYs following primary management and adjustment of the costing methodology to an institutional perspective. Hemiarthroplasty was displaced by conservative management as the most cost-effective intervention, if conditions within the models changed according to those parameters **(Table 5.7).**

Table 5.7. Summary of variation of input parameters on the decision analytical model.

Parameter	Intervention found to be most cost effective	Parameter assumption
Complication rate after primary management	Hemiarthroplasty	Complication rate for hemiarthroplasty ≤ 19%
	Conservative management	Complication rate for hemiarthroplasty >19%
	Locking plate	Hemiarthroplasty complication rate >22%, locking plate complication rate ≤ 25%
Secondary surgery rate	Hemiarthroplasty	All
Probability of improving after secondary surgery	Hemiarthroplasty	>30% of hemiarthroplasty patients undergoing secondary surgery have a successful outcome.
	Conservative Management	≤30% of hemiarthroplasty patients undergoing secondary surgery have a successful outcome.
QALY values for patients with a successful outcome after primary management	Hemiarthroplasty	QALY for hemiarthroplasty patients with a successful outcome ≥ 1.684
	Conservative Management	QALY for hemiarthroplasty patients with a successful outcome < 1.684
QALY values for patients with an unsuccessful outcome after primary management	Hemiarthroplasty	QALY for hemiarthroplasty patients with an unsuccessful outcome ≥ 1.09
	Conservative management	QALY for hemiarthroplasty patients with an unsuccessful outcome < 1.09
QALY values for successful outcome after secondary surgery	Hemiarthroplasty	QALY for successful secondary surgery in hemiarthroplasty ≥ 1.32
	Conservative management	QALY for successful secondary surgery in hemiarthroplasty < 1.32
QALY values for complication after secondary surgery	Hemiarthroplasty	QALY value for complication after secondary surgery in hemiarthroplasty ≥ 0.8
	Conservative management	QALY value for complication after secondary surgery in hemiarthroplasty <0.8
Institutional costing perspective	Conservative management	Cost of hemiarthroplasty >£3,924.49 and cost of internal fixation >£1,245.25.

5.4 Discussion

This health economic evaluation compared conservative management, locking plate fixation and hemiarthroplasty in the management of complex proximal humerus fractures within an elderly population. A decision-analytical model was built based primarily on the outcomes from RCTs, with some parameters derived from expert opinion. Within the existing literature there is limited economic research evaluating the management of complex proximal humerus fractures[120] and an absence of any evidence that relates to cost-effectiveness for these injuries in the English NHS. Within a health service struggling to manage a £22 billion shortfall in funding[264], health economic research amongst common musculoskeletal injuries like proximal humerus fractures provides an opportunity to understand the value of different treatment interventions and pursue effective clinical practice that is mindful of the scarcity of financial resources.

In this decision analytical model, hemiarthroplasty was found to be the most cost effective treatment intervention for the management of 3 or 4 part proximal humerus fractures in elderly patients. The model was sensitive to variation amongst reported health utilities and complication rates. However, conservative management rather than locking plate fixation was the more cost-effective intervention when sensitivity analysis was performed using the full range of reported input parameters. Furthermore, when the evaluation was performed using institutional costing estimates, conservative management was the most cost effective treatment intervention. The existing treatment costs within the institution from which the estimates were obtained, would need to fall by approximately 17% for hemiarthroplasty and 60% for locking plate fixation for the clinical benefits of each intervention to be deemed as cost-effective, relative to the WTP framework in the English NHS.

Clinical trials have shown hemiarthroplasty to be an effective treatment in the management of complex proximal humerus fractures[30,252]. Expert narrative supported by clinical evidence have highlighted that complication rates for head preserving procedures are very high and this is reflected within the literature review that informed this study[265]. Avascular necrosis and metal work failure amongst the population included in within this economic analysis **(See Appendix 4)** were major contributors to a reported complication rate that was twice as high for locking plate fixation compared to hemiarthroplasty. Although the secondary surgery rates for patients with a complication after hemiarthroplasty were almost double the secondary surgery rates after a complication following locking plate fixation, the mean secondary surgery rate for the entire cohort of patients was 6% less in the hemiarthroplasty group. In addition, the health utilities reported amongst the studies that informed this decision analytical model favoured surgical management over conservative management. Health utility scores were higher amongst patients that underwent hemiarthroplasty compared to locking plate fixation and the aggregated disutilities brought about by an increased complication rate are likely to have contributed to an ICER for locking plate fixation that exceeded the threshold WTP value (£20,000/QALY.)

The sensitivity of the model to conservative management when input variables were modified was driven by its cost. The cost of conservative management is substantially smaller than that of surgical treatment. Staffing costs of the operating theatre, implant procurement costs and bed costs are absent within this group of patients. When patients undergoing non-operative management are admitted to hospital, it is normally due to concomitant medical illness or social care needs[18]. Such admissions would attract a separate reimbursement and as such these costs were excluded from our analysis. As a result of conservative management being substantially less costly, sensitivity analysis that adopted improved outcome probabilities or health utilities resulted in the model showing it to be the most cost-effective intervention.

This finding underlines the need for surgical intervention to offer a clear benefit over conservative treatment. However, the broad range of reported complication rates and health utilities for each intervention does confound the benefits of each intervention. Fjalestad et al[148] reported that approximately 70% of patients that underwent a locking plate fixation had a complication, whilst this figure was only 33% in Olreud et al's RCT[69]. It is possible that inter-study variability regarding what constitutes a complication results in such disparate outcomes. A possible route to overcoming this limitation within existing research could be a consensus definition for core outcomes and complications. This approach has already been adopted for hip fracture research[156]. A further observation of the included studies was that originated from a single centre. The external validity of such research can be restricted by local performance bias[153] and national registry data may provide outcome data that has more validity.

The findings of this study have generalizability across the English NHS. While institutional treatment costs and national reimbursement vary substantially within the service[117,118] a determination of what constitutes an appropriate costing perspective is needed. The use of both perspectives in this study informs decision making at a national and local level. It also draws attention to how the results of cost-effectiveness research in the English NHS can vary based on these different perspectives. The national costing perspective found hemiarthroplasty to be the most cost effective intervention, whilst feeding institutional treatment costs estimates into the model resulted in conservative management being the most cost effective approach. The purchaser-provider divide within the health service possibly makes the national tariff more relevant in relation to resource allocation based around a central NHS budget, however it masks the true costs of treatment. These costs feed into the growing institutional deficit that inevitably has an effect on the financial stability of the NHS as a whole[266]. The limitation of incorporating institutional treatment costs into health

economic analysis, is that treatment costs can vary significantly between hospitals, and therefore the generalizability of such research is limited. However, the results of our analysis performed using institutional costs are of interest because they underline the importance of capturing treatment costs and measuring patient outcomes. Although hemiarthroplasty would need to be 17% cheaper to be the most cost-effective intervention at the hospital where institutional treatment costs were obtained, these costs could be brought down dramatically by improving operating department efficiency and volume based discounting of implant procurement. Furthermore if local audit or registry data demonstrates patient outcomes that are more favourable than those reported in the literature, this could increase the cost threshold at which the clinical benefits of each surgical procedure are deemed to be cost-effective.

5.4.1 Limitations

There are inherent limitations to most health economic analysis because variability in costs and outcomes often make individual clinical cases distinct from the assumptions on which the model is based[267]. There are four main limitations to this analysis. Firstly, the outcomes were determined from a small group of clinical trials. In addition, as all these trials were single-centre studies, their external validity can be challenged. However, these RCTs represent the highest level of evidence within this field and the full range of reported outcomes were subjected to sensitivity analysis. Furthermore, the reported threshold values that affect the stability of the model provide a subtext that informs choice of treatment where individual surgical or departmental performance is known to differ from that reported in the literature. Secondly, a societal perspective was not adopted in this study. Such a perspective that considers primary and social care costs, is viewed to carry more weight for national health policy[268], however there was an absence of any such costing data in the evidence-based literature and therefore this analysis was based on a more restrictive perspective. This perspective was clearly defined in the methodology and despite its limitations it accounts for

approximately 75% of health economic research on hip fractures[269] and 25% of health economic research on shoulder injuries[195]. Thirdly, because this was not a health economic evaluation run in parallel with an RCT, primary data was not available to evaluate the effect of clinical heterogeneity on cost effectiveness by means of sub-group analysis. The availability of registry data that characterises patient groups and fracture morphology offers the potential to evaluate cost and effectiveness based on parameters that have more applicability in a clinical setting. Finally, the limitation in available trials that reported health utilities meant that health utilities derived from different health utility instruments were combined to generate outcomes. Three trials used the EQ-5D instrument[270] and 1 trial used the 15-D instrument[271]. Mapping between different health utilities in upper limb orthopaedics has not yet been performed and therefore there is likely to have been some variation between the two instruments. The sensitivity analysis that was performed covered a wide range of values and any uncertainty that resulted from very small changes in health utilities may be secondary to the small differences in discriminative capacity and responsiveness of both instruments[272].

5.4.2 Conclusion

This health economic evaluation performed using decision analytical methodology compared conservative management, locking plate fixation and hemiarthroplasty in the management of complex proximal humerus fractures in elderly patients. Within the setting of the English NHS and based on national tariff pricing, hemiarthroplasty is the most cost effective treatment intervention. The findings of this study are limited by the small number of trials that informed the analysis, and the uncertainty within the economic model demonstrated by the sensitivity analysis performed. A national registry of patient outcomes for proximal humerus fractures and future RCTs on more complex proximal humerus fractures would help develop clinical and economic research in this field further.

Chapter 6

Cost effectiveness analysis of different management options for complex proximal humerus fractures: a 20-year time horizon based on Markov decision analysis

6.1 Introduction

In chapter 5, the cost-effectiveness for treatment interventions in the management of complex proximal humerus fractures in elderly patients was explored. The decision-tree analysis that was performed was limited to a 2-year time horizon. Within the specified population, an evaluation that includes the health effects of advancing age and life expectancy, adds value to the conclusions of cost-effectiveness research[273,274]. Markov chain modelling (MCM) is a form of decision analytical modelling that enables such evaluations to be performed in health economic research[77].

Andrey Markov was a Russian mathematician who developed and gave his name to this domain of probability theory in the early 20th century [275]. Interestingly, Markov's first application of this process, in 1913, was an attempt to use mathematics to better understand the poetry of Alexander Pushkin[275]. Although the findings of this study yielded little in relation to understanding Pushkin's poems, the methodology that was employed has evolved into modern-day MCM[275]. In decision analytical modelling in health economics, Markov chain analysis adopts the assumption that at any point in time, all patients occupy a set of finite health states. Patients make transitions between health states at the end of a predefined time interval and the probability of entering different health states is based on transitional probabilities. These transitional probabilities reflect the effect of time on changing health states, but are also important because they can accommodate for expected age related mortality[110,276]. The costs and health outcomes of different interventions are aggregated at each cycle, as pay-offs are at the end of a decision-tree, and when the last cycle terminates,

the incremental cost effectiveness ratio (ICER) is calculated between treatment interventions to determine which treatment is most cost-effective in relation to the established willingness to pay (WTP) threshold.

Markov chains in decision analytical models are commonly adopted in health economic evaluations across a range of clinical specialties[277]. In orthopaedic policy within the United Kingdom (UK), Markov models have been used to inform national health technology assessments for hip replacement surgery[278,279]. Its applications have also been found to be useful in health economic research in upper limb orthopaedics[259,280], however to-date there is no published cost-effectiveness research on proximal humerus fractures where MCM has been adopted. Both of the published health economic evaluations that have investigated treatment interventions for proximal humerus fractures were performed in parallel to randomised controlled trials (RCTs) [11,120]. The applicability of the Proximal Fractures of the Humerus: Evaluation by Randomisation (ProFHER) trial[11] to complex fractures is limited because almost half of the included patient population had a 2-part fracture. Similarly Fjalestad et al's study[120] was based on a Norwegian health-service model of care, and therefore has limited external validity in relation to the UK and the National Health Service (NHS). Although the decision-tree model constructed in Chapter 5 integrated evidence and expert opinion to provide recommendations based on the English NHS, a 2-year time horizon does not inform the understanding of long-term cost-effectiveness between treatment options. MCM enables extrapolation of costs and health effects beyond the 1 or 2 years outcomes reported in most RCTs, and therefore is an important analytical tool to inform wider health economic policy[273,281]. This is particularly relevant for patients with a proximal humerus fractures because epidemiological research underlines that this injury occurs predominantly in patients over the age of 65 years, and age-related mortality can be accelerated [7,282].

The aim of this chapter is to perform a health economic evaluation (HEE) using a MCM to determine the most cost-effective treatment intervention for complex proximal humerus fractures in an elderly population over a 20-year time horizon.

6.2 Methods

This HEE was performed according to Consolidated Health Economic Evaluation Reporting Standards (CHEERS)[283].

6.2.1 Study design

The target population included in this study was elderly patients with a complex proximal humerus fracture. Elderly patients were defined as patients at or above the age of 65 years. Although frailty measures are increasingly viewed to be a more clinically applicable method for defining elderly age, their use is limited in existing orthopaedic literature, and most studies adopt chronological measures and define elderly patients as those who are at or above 65 years old[133]. Complex proximal fractures fractures were defined as type 3 or 4 based on the Neer Classification System[6].

The setting and perspectives adopted in this HEE were identical to those used in the decision-tree analysis performed in Chapter 5. An NHS-payer perspective was adopted within the English NHS. The English NHS is distinct from health services in Scotland, Wales and Northern Ireland[284]. Hospitals are reimbursed for surgical treatment by Clinical Commissioning Groups (CCGs) that are independent from the hospitals in the context of leadership and governance. Reimbursements for individual treatments are based on national tariffs allocated to treatment specific Healthcare Resource Groups (HRGs)[214]. Individual HRGs commonly include a case mix of procedures. In the case of proximal humerus fractures, the same HRG is used to reimburse surgical management with either a locking plate or a hemiarthroplasty implant. National Institute for Health and Clinical Excellence

(NICE) guidance recommends use of the tariff in health technology assessments, as this costing perspective has more external validity[248], especially because treatment costs can vary greatly between healthcare institutions[255]. There are limitations to this methodology especially if true treatment costs vary and they are represented by the same HRG. As a result a secondary perspective using estimates of institutional cost acquired from the micro-costing study performed in Chapter 3, formed part of the sensitivity analysis.

The evidence-based literature was systematically reviewed to identify RCTs that reported on clinical outcomes and health utilities for management strategies in patients with a proximal humerus fracture. On the basis of existing Level I evidence; conservative management, internal fixation with a locking plate and hemiarthroplasty were the interventions included within this HEE. The time horizon in this study was selected to base the analysis on an expected life expectancy of an elderly patient with a proximal humerus fracture. The current World Bank estimate for life expectancy in the United Kingdom is 81 years of age[285]. As such, a 20-year time horizon was viewed to be representative for cost-effectiveness research conducted along the expected life-horizon of the patient population in this HEE. Discounting principles that are recommended in health economic research[283] were employed for both costs and health outcomes within the analysis. Future costs and health outcomes were discounted at 3.5% a year based on NICE guidance for discounting principles in cost-effectiveness research[248].

The model structure was based on patients in each intervention group existing in one of 6 health states. The ‘well state’ represented patients that had undergone primary management with an uncomplicated outcome. The ‘complication state’ included patients who had undergone primary management and suffered a complication. The ‘revision state’ included patients that had suffered a complication and then gone on to have secondary surgery, the

'revision well state' included patients that had a successful outcome after secondary surgery and the 'revision-complication state' included patients that had a complication after secondary surgery. A 'dead state' related to death occurring based on age specific mortality. Patients could transition between the different health states at the end of each Markov cycle, which represented a 2-year time period **(Figure 6.1).** Along with the allocation of finite health states, another key assumption within this model was that only one secondary surgery would be performed after a complication.

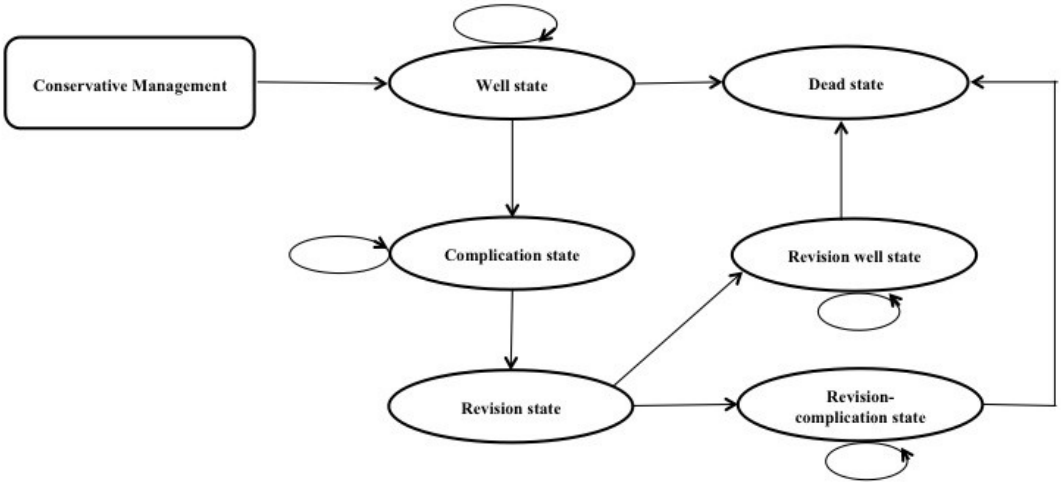


Figure 6.1. Markov transition state diagram showing possible outcomes for patients undergoing conservative management. The transition states are identical for locking plate fixation and hemiarthroplasty.

6.2.2 Model Inputs

6.2.2.1 *Outcome probabilities*

Outcome probabilities were based on the same 5 RCTs that informed the decision-tree model performed in Chapter 4 [30,69,148,232,252] **(Table 6.1).**

Table 6.1. Characteristics of 5 studies used to determine outcome probabilities used in Markov chain model.

Author (Year)	Country	Sample size	Mean age	Treatment strategies	Fracture type (Neer classification)	Health utilities reported
Cai et al. (2012)	China	32	71.9	Hemiarthroplasty Locking plate	4 part	Yes
Fjalestad et al. (2012)	Norway	50	72.56	Locking plate Non-operative	3 part (52%) 4 part (48%)	Yes
Olreud et al. (2011)	Sweden	55	76.65	Hemiarthroplasty Locking plate	4 part	Yes
Olreud et al. (2011)	Sweden	60	73.9	Locking plate Non-operative	3 part	Yes
Sebastiá-Forcada et al (2014)	Spain	62	-	Hemiarthroplasty Reverse arthroplasty	4 part (83.9%) 3 part (16.1%)	No

The probability values for outcomes were reported at 2-year follow up for the included RCTs. The MCM that was constructed in this analysis was based on a 20 year time horizon and therefore further input parameters were required to inform the transitional probabilities after each cycle. Within the existing literature there is an absence of research that reports on outcome over such an extensive period of time. A small number of case series have been published that report that there is an attrition in complications or functional decline after 1 or 2 years[190,213,286]. This was also the experience of the orthopaedic upper limb specialists who contributed to this analysis (Peter Reilly and Dylan Griffiths), and therefore a further assumption that was integrated into the MCM was that transitional probabilities for complications would fall over the course of the 20-year life horizon. Based on the fact that all 5 RCTs that informed this analysis reported 2-year outcomes, a 2-year cycle was used within the MCM to reduce the number of assumptions and extrapolation from existing data within the field. To reflect substantial decline in complication rates over time, after each 2-year cycle, formulae was introduced into the MCM to decrementally reduce the complication rates by 25% **(Table 6.2).**

Table 6.2. Transitional probabilities for complication rates after primary management for each intervention. Each Markov cycle represents a 2-year time period.

	Conservative Management	Hemiarthroplasty	Internal Fixation
Cycle Number	**Probability of a complication after primary management**		
1	0.410	0.194	0.446
2	0.103	0.049	0.112
3	0.026	0.012	0.028
4	0.006	0.003	0.007
5	0.002	0.001	0.002
6	0.000	0.000	0.000
7	0.000	0.000	0.000
8	0.000	0.000	0.000
9	0.000	0.000	0.000
10	0.000	0.000	0.000

With regards to the probability of needing secondary surgery, transitional probabilities were not assigned to the MCM. There is no existing literature that reports on timing of complications influencing a decision to offer secondary management. Expert opinion from the authorship also viewed static probabilities to be more appropriate. These probabilities were calculated from the cumulative number of secondary surgeries performed that were reported within the 5 RCTs **(Table 6.3).**

Table 6.3. Summary of model input values for complications requiring secondary surgery

	Total complications	Total number of secondary operations	Probability of complication requiring secondary surgery	Probability range for complications requiring secondary surgery
Locking Plate	29	16	0.551	0.25 - 1
Hemiarthroplasty	14	13	0.928	0.889 – 1
Conservative	32	3	0.094	0.0625-0.167

Static probabilities were also assigned to outcomes after secondary surgery. Using the assumptions adopted in Chapter 4, the outcomes were based on a small number of Level IV studies[190,253,254] and the expert opinion of this study's authorship; it was assumed that half of patients would experience a complication after a secondary surgical procedure was performed within the MCM.

Life tables from the UK's Office of National Statistics were used to inform the age-related mortality within the MCM[287] **(Table 6.4).**

Table 6.4. Life tables used in MCM. Each cycle is 2 years and ends at the age shown in the table. The probability of death represents the risk of death before the next cycle starts and is based on data from the Office of National Statistics in the UK[287].

Age	Probability of death
66	0.0137
68	0.0164
70	0.0209
72	0.0259
74	0.0309
76	0.0372
78	0.047
80	0.0587
82	0.0757
84	0.0946

Although a number of studies demonstrate increased long-term mortality rates for patients with a proximal humerus fractures[7,288,289], no research to date has found variation in mortality

rate according to the management the patient received. Therefore uniform mortality rates were adopted between the treatment interventions in the MCM. However, a secondary evaluation formed part of the sensitivity analysis, where risk of death was increased 5-fold per Markov cycle. The authorship viewed this increase in mortality rate to reflect 1-year mortality rates of approximately 10%[15,36] reported within the literature. The purpose of this secondary analysis was to determine whether the ICER of the more costly interventions (internal fixation and hemiarthroplasty) would exceed the WTP as Quality Adjusted Life Years (QALYs) fall with life expectancy.

6.2.2.2 *Costs*

The costing values employed within this analysis were based on the 2014-2015 national tariffs set by the Department of Health (DoH) in the English NHS[214]. As discussed in Chapter 5, these costing parameters make the analysis generalizable across the English NHS. However, they lack the accuracy of micro-costing estimates which paradoxically have poor external validity because of variation in treatment costs between hospitals[255]. The micro-costing estimates which were derived from the costing study performed in Chapter 4, formed part of the sensitivity analysis conducted within this HEE.

The 'revision states' within the Markov model included a number of different secondary surgical procedures which attracted a wide range of tariffs. In order to accommodate the different treatment costs to a single 'revision state' cost, a mean cost was calculated which was weighed on the proportions of the different secondary procedures reported amongst the 5 RCTs.

Costing for conservative management was based on outpatient ambulatory care. All patients were given 6 outpatient clinic appointments following primary or secondary management. Physiotherapy costs were excluded as these are based on locally negotiated block contracts

and therefore have poor applicability across the English NHS. The cost parameters used in this analysis are shown in **Table 6.5**. These values exclude Market Force Factors (MFF). The micro-costing estimates used to perform sensitivity analysis based on an institutional costing perspective, are included in **Appendix 5.**

Table 6.5. Input parameters for cost based on national tariff. The 'revision state' costs are calculated based on a weighed-mean of the different secondary procedures performed in the 5 RCTs used to inform this HEE.

Unit	HRG Reference Code	Description	Cost (£)
Primary management options			
Primary locking plate procedure	HA61C	Major Shoulder and Upper Arm Procedures for Trauma without CC	3413
Primary hemiarthroplasty procedure	HA61C	Major Shoulder and Upper Arm Procedures for Trauma without CC	3413
Post procedure first clinic follow up appointments	WF01B	First Attendance - Single Professional	119
Subsequent clinic follow up appointments	WF01A	Follow Up Attendance - Single Professional	70
Secondary surgery after conservative management (3 cases)			
Locking plate fixation for acute displacement of conservatively managed fracture (1 case)	HA61C	Major Shoulder and Upper Arm Procedures for Trauma without CC	3413
Hemiarthoplasty for acute displacement of conservatively managed fracture (1 case)	HA61C		3413
Sub-acromial decompression for impingement after conservatively managed fracture (1 case)	HB63Z	Minor Shoulder and Upper Arm Procedures for Non-Trauma	1028
Weighed mean cost for conservative management 'revision state'			**3047**
Secondary surgery after Hemiarthroplasty (13 cases)			
Revision of hemiarthroplasty to other hemiarthroplasty (2 cases)	HB61B	Major Shoulder and Upper Arm Procedures for Non-Trauma with CC	5490
Wound revision of infected hemiarthroplasty or locking plate (1 case)	HB62B	Intermediate Shoulder and Upper Arm Procedures for Non-Trauma with CC	3136
Intra-operative hemiarthroplasty fracture	HA61B	Major Shoulder and Upper Arm Procedures for Trauma without CC	4330

Unit	HRG Reference Code	Description	Cost (£)
treated with cerclage wire (1 case)			
Manipulation under anaesthesia of stiff hemiarthroplasty (1 case)		Minor Shoulder and Upper Arm Procedures for Non-Trauma	1028
Revision of hemiarthroplasty to reverse arthroplasty (6 cases)	HB61B	Major Shoulder and Upper Arm Procedures for Non-Trauma with CC	5490
Acromioplasty and release of adhesions after hemiarthroplasty (1 case)	HB62B	Intermediate Shoulder and Upper Arm Procedures for Non-Trauma with CC	3136
Fixation of tuberosity after hemiarthroplasty (1 case)	HB62B	Intermediate Shoulder and Upper Arm Procedures for Non-Trauma with CC	3136
Weighed mean cost for hemiarthroplasty 'revision state'			**4743**
Secondary surgery after locking plate fixation (16 cases)			
Re-plating for locking plate procedure	HB61B	Major Shoulder and Upper Arm Procedures for Non-Trauma with CC	5490
Removal of locking plate	HB62B	Intermediate Shoulder and Upper Arm Procedures for Non-Trauma with CC	3136
Revision of infected locking plate	HB61B	Major Shoulder and Upper Arm Procedures for Non-Trauma with CC	5490
Revision of locking plate to hemiarthroplasty	HB61B	Major Shoulder and Upper Arm Procedures for Non-Trauma with CC	5490
Wound revision of infected hemiarthroplasty or locking plate	HB62B	Intermediate Shoulder and Upper Arm Procedures for Non-Trauma with CC	3136
Weighed mean cost for locking plate fixation ' revision state'			**4187**

6.2.2.3 *Health Utilities and QALYs*

QALYs were the measure of clinical effectiveness used in this HEE. The QALYs used in this analysis were identical to those used in Chapter 5; 2 year health utilities derived from 4 RCTs[30,69,148,252] were converted into QALYs using and Area Under the Curve (AUC) methodology[256]. The existing literature on proximal humerus fractures does not distinguish health utilities of patients with a successful outcome from those who suffered a complication.

Furthermore there is no research reporting on the health utilities of patients undergoing secondary surgery. The methodology used to obtain surrogate values for this HEE and the assumptions they were based on are detailed in the methodology of the decision-tree analysis performed in Chapter 5. A summary of these values that were used in this analysis is presented in **Table 6.6.**

Table 6.6. Summary of input parameters for QALYs in health economic model

	QALY Value		
QALY Description	**Base Case**	**Low**	**High**
Well state after conservative management	1.605	1.545	1.719
Well state after locking plate fixation	1.704	1.647	1.756
Well state after hemiarthroplasty	1.713	1.682	1.744
Complication state after conservative management	1.029	0.76	1.486
Complication state after locking plate fixation	1.165	0.958	1.492
Complication state after hemiarthroplasty	1.165	1.154	1.175
Conservative management revision-well state	1.317	1.196	1.603
Locking plate fixation revision-well state	1.434	1.333	1.624
Hemiarthroplasty revision well state	1.439	1.418	1.460
Conservative management revision-complication state	0.658	0.486	0.951
Locking plate fixation revision-complication state	0.792	0.651	1.014
Hemiarthroplasty revision-complication state	0.792	0.785	0.799

6.2.3 Cost Utility Statistical Analysis

The cost and QALY input parameters derived from a systematic review of the literature and expert consensus, were used to inform the MCM constructed in this model. The complete Markov tree is included in **Appendix 5** each of the three main branches is based on the transition state diagram shown in **Figure 1.** Discounting principles were adapted to accommodate for a 2-year time horizon. 1 year of discounting outcomes at 3.5% translates to 2-year practices of 6.9% and this was the value used for discounting within the model. The

analysis was based on a WTP threshold of £20,000/QALY, which is the recommendation for healthcare technologies in the UK by NICE[248]. A treatment is viewed to be cost effective if it is less costly and more clinically effective. For treatments that are more costly but result in improved clinical effectiveness, they are viewed to be cost effective if they fall under the WTP threshold. The cost-effectiveness output that is used to measure cost and clinical effectiveness between interventions is the ICER. Sensitivity analysis was performed using Net Monetary Benefit (NMB). The formulae for ICER and NMB are detailed in Chapter 5. The analysis was performed within Treeage Pro; graphical and text ranking tables were produced to support the results of the cost-effectiveness analysis.

6.2.4 Sensitivity Analysis

Multi-way sensitivity analysis was performed to evaluate uncertainty within this MCM. Uncertainty in relation to cost was calculated by performing a secondary analysis using institutional estimates of treatment cost (summary values presented in **Appendix 5**). Uncertainty in the context of clinical outcomes was tested by performing sensitivity analysis based on the full range of clinical outcome probabilities reported in the literature. This was also performed for health utility values across all treatment strategies and for all health states in the MCM. Finally, the cost-effectiveness analysis was repeated with life table mortality rates inflated 5-fold, to determine whether an increased mortality rate amongst elderly patients with a proximal humerus fracture would affect the overall study findings.

6.3 Results

Within this HEE which was performed using a MCM, hemiarthroplasty was found to be the most cost-effective treatment strategy in the English NHS for the management of 3 or 4-part proximal humerus fractures in elderly patients over a 20 year time-horizon **(Figure 6.2).** This finding was based on an incremental cost of £4,379.88 per QALY for hemiarthroplasty

relative to conservative management, compared with an incremental cost of locking plate fixation relative to conservative management of £63,734.58 per QALY **(Table 6.7).**

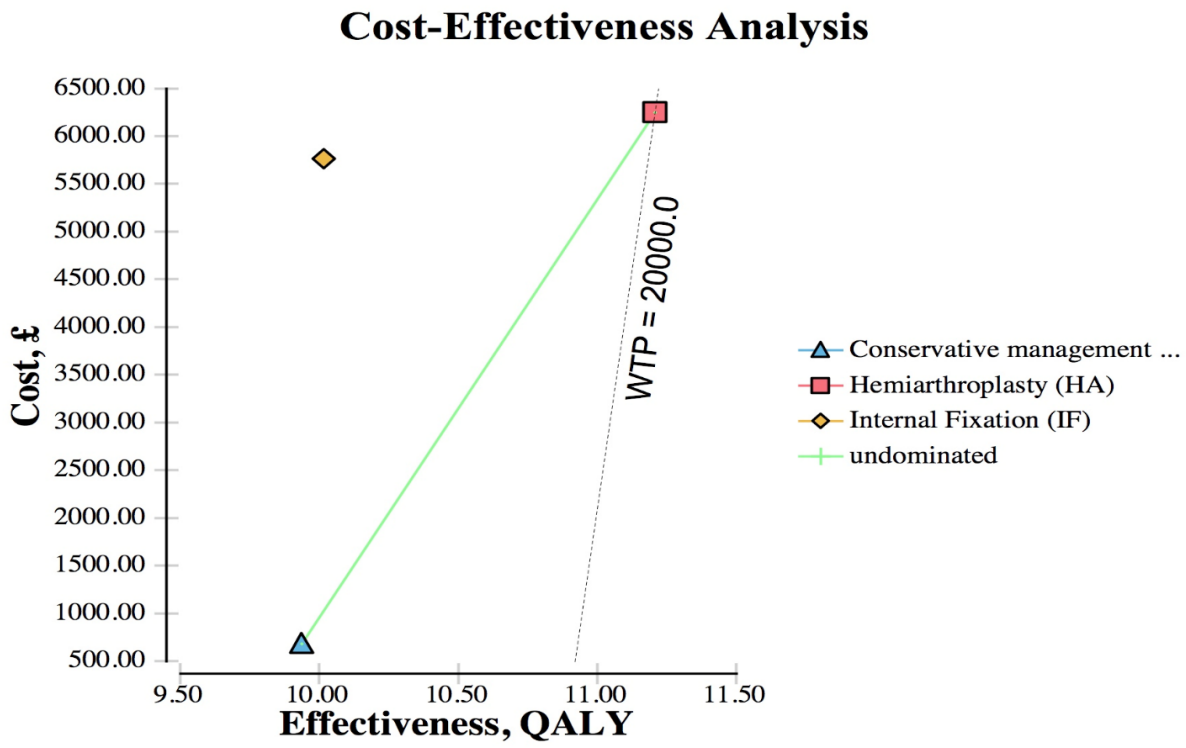


Figure 6.2. Cost-effectiveness graph illustrating how hemiarthroplasty lies within the WTP threshold and has a higher effectiveness and cost than conservative management, and a higher effectiveness and higher cost than internal fixation with a locking plate.

Table 6.7. Summary of outputs generated from cost-effectiveness analysis performed on the MCM.

Strategy	Cost, £	Incremental Cost, £	Effect, QALYs	Incremental Effect, QALYs	ICER, £/QALY gained	NMB
Conservative management	682.80	-	9.94	-	-	198,037.97
Hemiarthroplasty	6250.15	5567.34	11.21	1.27	4,379.88	217,892.98
Internal Fixation	5763.95	5081.14	10.02	0.08	63,734.58	194,551.29

6.3.1 Sensitivity analysis

6.3.1.1 *Outcome probabilities*

3-way sensitivity analysis that examined the reported range of complication rates after primary management demonstrated that the MCM calculated hemiarthroplasty to be the most cost-effective intervention across the majority of probable model scenarios. At the base-rate probability for complication after conservative management (0.41), hemiarthroplasty was the most cost-effective strategy across the range of complication rates reported for conservative management and hemiarthroplasty **(Figure 6.3).** At the lowest reported complication rate for locking plate fixation (0.25), hemiarthroplasty was more cost effective than locking plate fixation provided that its own complication rate for hemiarthroplasty was below 24% **(Figure 6.4).**

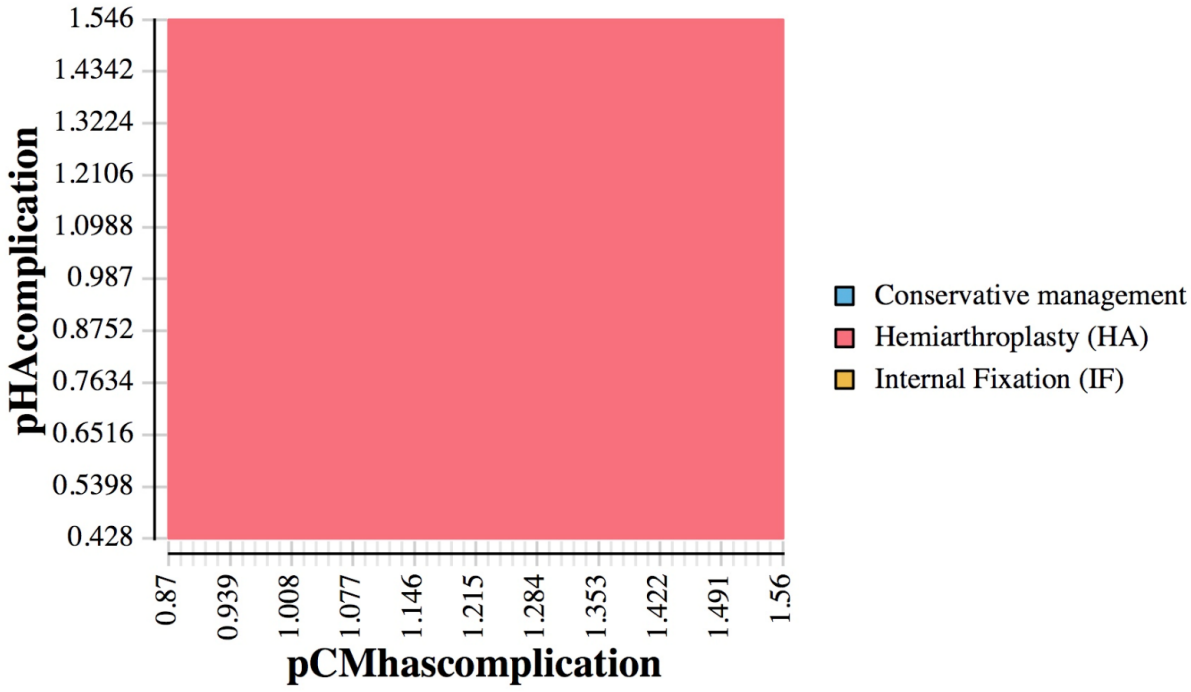


Figure 6.3. Three-way sensitivity analysis graph illustrating that hemiarthroplasty is the most cost-effective treatment strategy based on the cumulative complication rates reported in the included studies for conservative management and hemiarthroplasty. The complication rate in this graph for locking plate fixation is set at the mean reported value (base case) of 0.446. The axes in this graph represent the numerator over the base case value for the complication rate after conservative management (pCMcomplication) and the numerator over the base case value for the complication rate after hemiarthroplasty (pHAcomplication). These values are transitional at each stage in the Markov cycle.

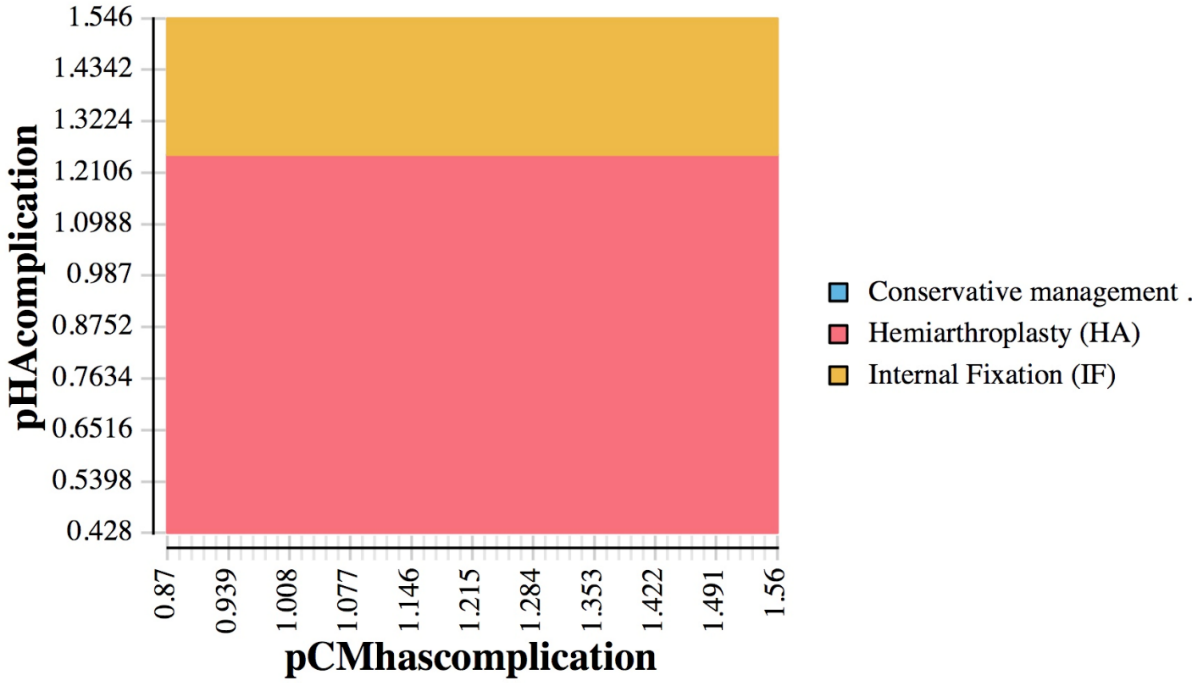


Figure 6.4. Three-way sensitivity analysis graph illustrating that hemiarthroplasty is the most cost-effective treatment provided that its complication risk is 1.25 fold its base case value in the MCM with the complication rate of locking plate fixation approximately half (0.561) the base case value for locking plate fixation in the MCM. The axes in this graph represent the numerator over the base case value for the complication rate after conservative management (pCMcomplication) and the numerator over the base case value for the complication rate after hemiarthroplasty (pHAcomplication). These values are transitional at each stage in the Markov cycle.

The model was not sensitive to uncertainty introduced in relation to the probability ranges reported for patients needing secondary surgery, after a complication had occurred **(Figure 6.5).** Hemiarthroplasty remained the most cost-effective intervention, even if all patients that had a complication after hemiarthroplasty had occurred required secondary surgery and the secondary surgery probabilities for conservative management and locking plate fixation were at the minimum reported values (0.0625 and 0.25 respectively). Extrapolation beyond the reported values also found that secondary surgery probabilities had no effect on the model. Even if all patients that had a complication after hemiarthroplasty required secondary surgery and only 10% of patients with a complication after locking plate fixation required secondary surgery, hemiarthroplasty remained the most cost-effective treatment strategy.

The probability of a complication after secondary surgery that was adopted for this analysis was 0.5 and was based on the expert opinion of the study's authorship as well as the reporting of a small number of retrospective studies. Multi-way sensitivity analysis demonstrated that across all permutations input into the MCM for this outcome, hemiarthroplasty remained the most cost-effective treatment strategy **(Figure 6.6).**

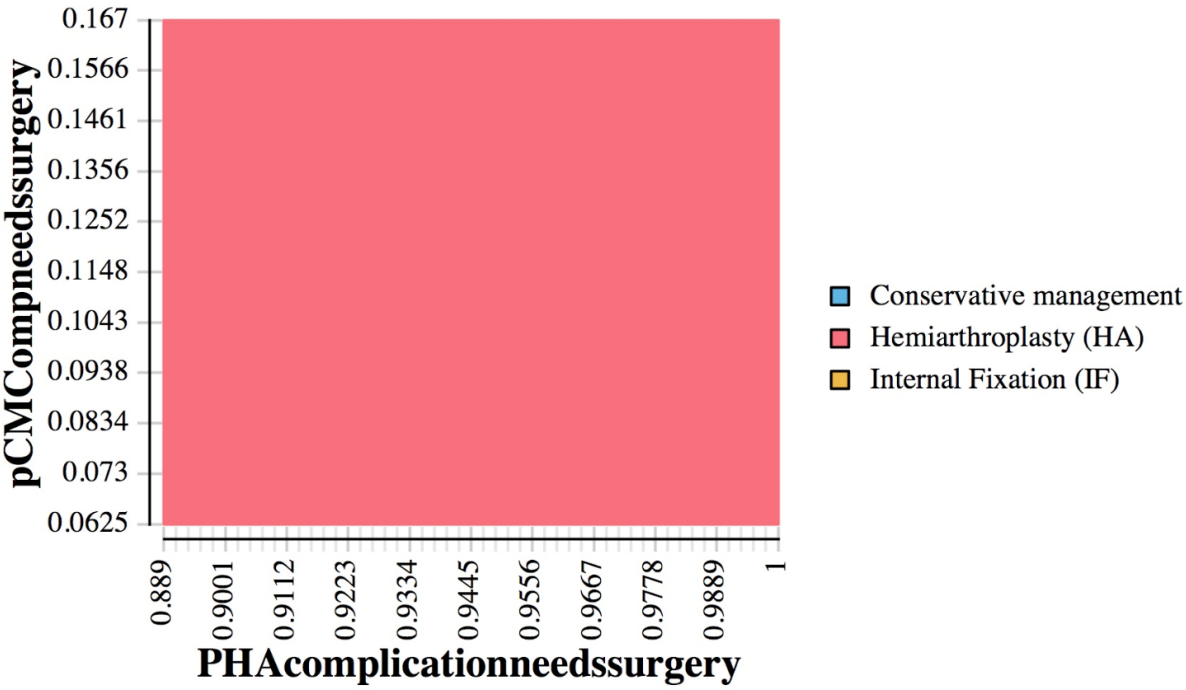


Figure 6.5. Three-way sensitivity analysis demonstrating that hemiarthroplasty remains the most cost effective intervention across full range of secondary surgery rates (locking plate fixation set at minimum value of 0.25). pCMComplicationneeds surgery is secondary surgery probability after conservative management. PHAcomplication needs surgery is secondary surgery probability after hemiarthroplasty.

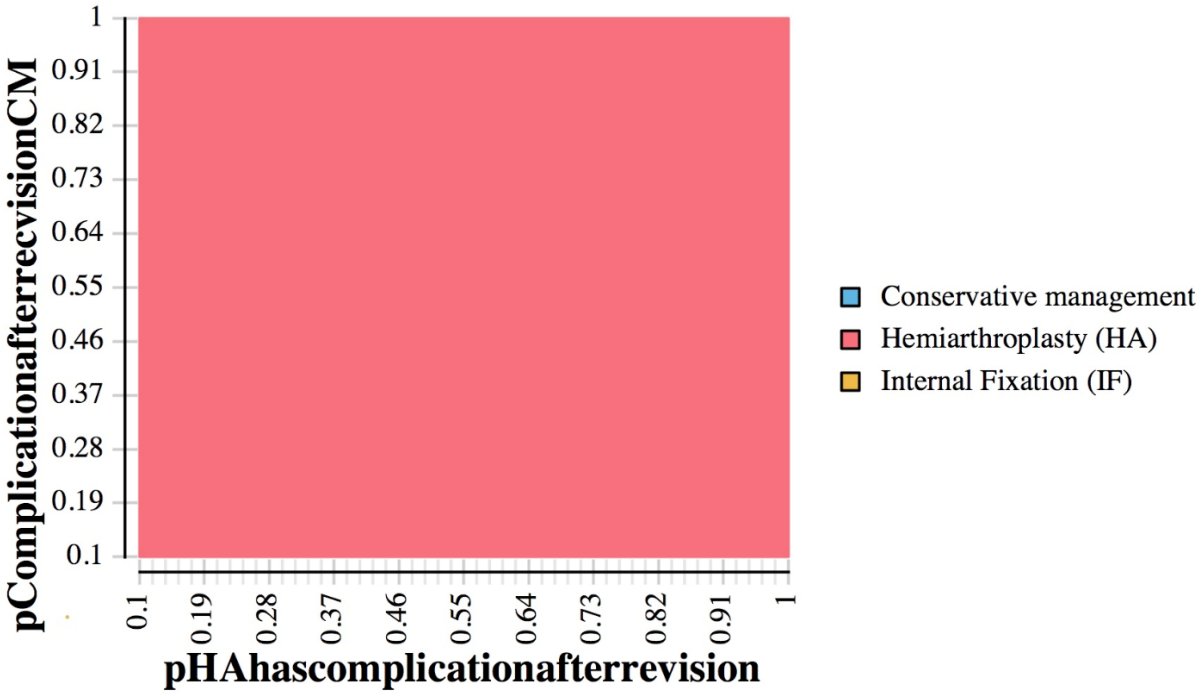


Figure 6.6. Three-way sensitivity analysis that demonstrates that across a wide range of probability outcomes for a complication after secondary surgery hemiarthroplasty remains the most cost effective treatment strategy. Locking plate fixation complication rate after secondary surgery is set at 10%. pCMComplicationneeds surgery is secondary surgery probability after conservative management. PHAcomplication needs surgery is secondary surgery probability after hemiarthroplasty.

6.3.1.2 *Uncertainty in QALYs*

The MCM was not sensitive to the full range of reported health utilities within the existing literature, for patients with a successful outcome after primary management. Hemiarthroplasty remained the most cost effective treatment strategy when 3-way sensitivity analysis was performed using the QALYs derived from these health utilities. When QALYs for patients with a successful outcome were extrapolated beyond the pre-determined range, provided the 2-year QALYs for the hemiarthroplasty 'well-state' were above 1.53, it was the most cost-effective treatment unless the QALY for the conservative management 'well state' was above 1.63. Beyond this threshold there was a linear relationship between the two values **(Figure 6.7).**

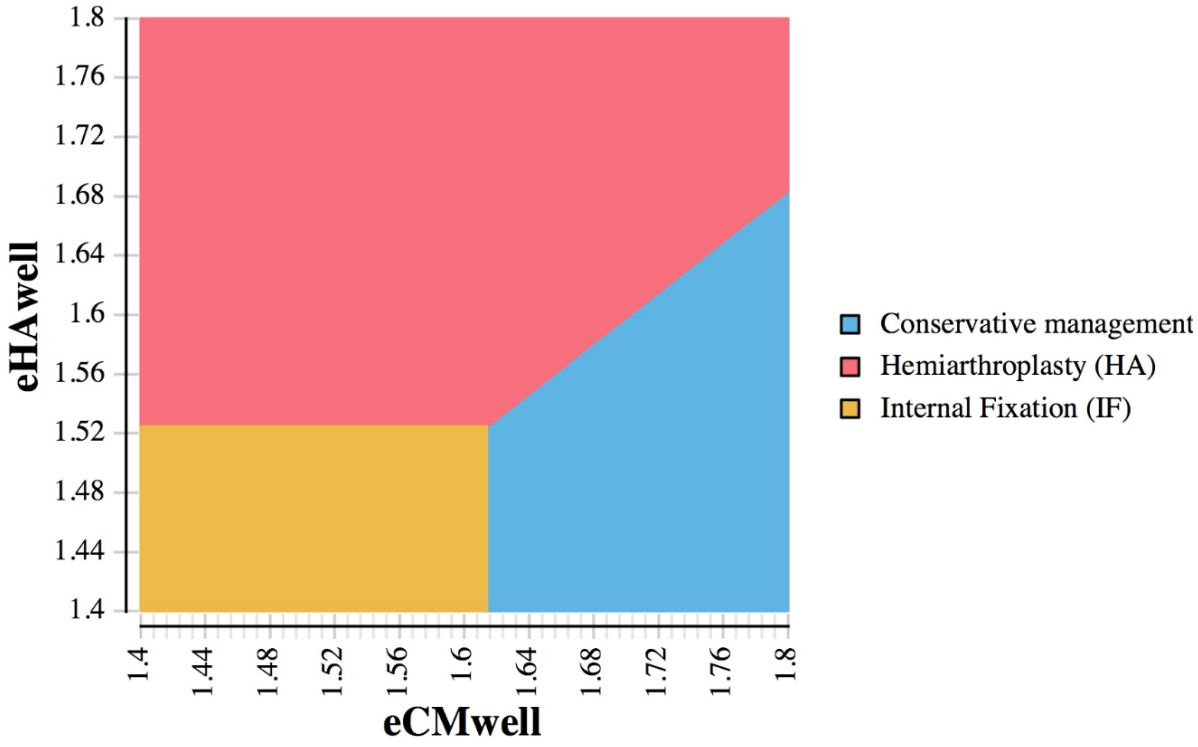


Figure 6.7. Three-way sensitivity analysis demonstrating effect of uncertainty in relation to 'well state' QALYs. QALY for locking plate fixation set at 1.8. eCMwell is the QALY input parameter for patients in the 'well state' after conservative management. eHAwell is the QALY input parameter for patients in the 'well state' after hemiarthroplasty.

Multi-way sensitivity analysis performed on QALY values applied for patients who had suffered a complication also revealed that the model favoured hemiarthroplasty with the exception of the scenario that the QALY for patients with a complication had QALY of greater than 1.39 after conservative management **(Figure 6.8).** Further analysis on health states after revision surgery found that hemiarthroplasty would always be the most cost-effective intervention provided that the 2-year QALY after a successful secondary surgery was greater than 0.3 **(Figure 6.9).** The model also favoured hemiarthroplasty if the complication state after secondary surgery had a 2-year QALY value of greater than 0.3 **(Figure 6.10).**

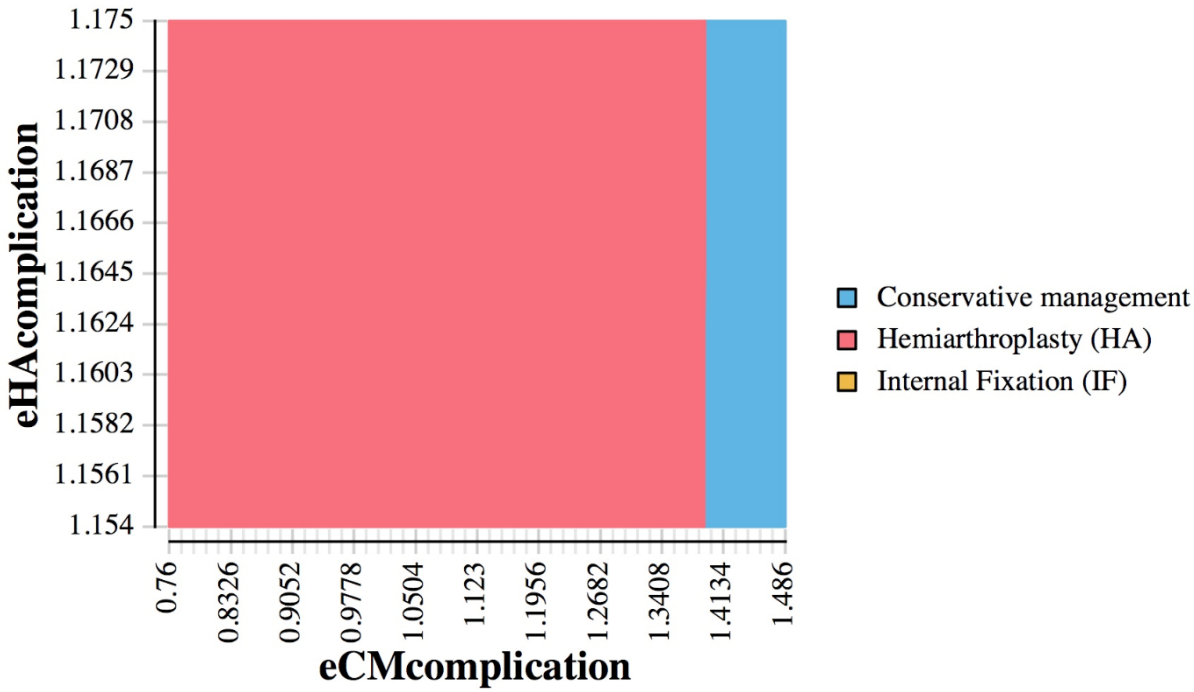


Figure 6.8. Three-way sensitivity analysis demonstrating effect of QALY values following a complication on the model. Internal fixation is set at a maximum QALY value of 1.486. eCMcomplication is QALY value for patients with a complication after conservative management. eHAcomplication is QALY value for patients with a complication after hemiarthroplasty.

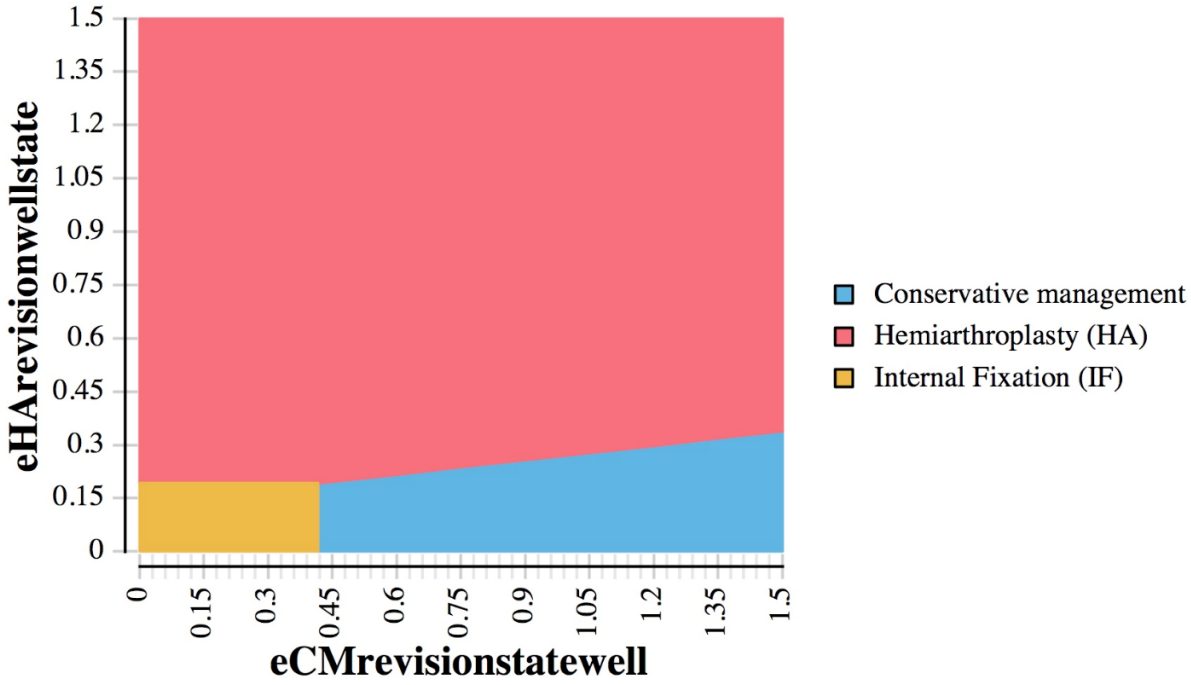


Figure 6.9. Three-way sensitivity analysis demonstrating the effect of adjusting QALY values for patients that have a successful outcome after secondary surgery. The locking plate fixation QALY is set at 1.5. eCMrevisionwellstate is the 2-year QALY for patients with a successful outcome after secondary surgery in the conservative management group. eHArevisionwellstate is the 2-year QALY for patients with a successful outcome after secondary surgery in the hemiarthroplasty group.

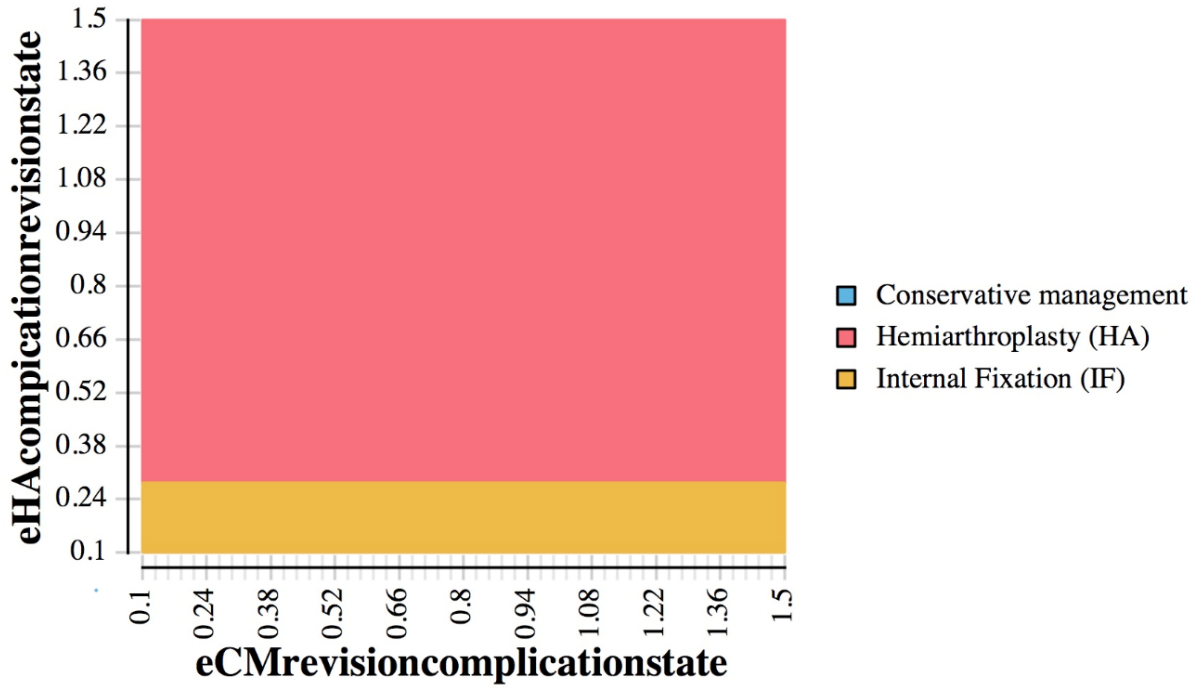


Figure 6.10. Three-way sensitivity analysis demonstrating the effect of changing the 2-year QALY values for patients who have suffered a complication after secondary surgery. The QALY input for locking plate fixation patients with a complication after secondary surgery is set at 1.5. eCMrevisioncomplication state is the QALY value for patients with a complication after secondary surgery in the conservative management group. eHAcomplicationrevisionstate is the QALY value for patients with a complication after secondary surgery in the hemiarthroplasty group.

6.3.1.3 *Adjustment of age-specific mortality*

Repeating the analysis with increased age-specific mortality yielded the same overall result; hemiarthroplasty was the most cost-effective treatment strategy **(Figure 6.11).** The main difference in the quantitative analysis was that the incremental cost of internal fixation fell more for the locking plate fixation group and their incremental effectiveness increased marginally compared to the base line analysis. While the incremental cost of hemiarthroplasty also fell, the incremental effectiveness was lower than that calculated in the baseline analysis. Despite this finding the ICER for hemiarthroplasty fell within the WTP threshold and this was not the case for locking plate fixation **(Table 6.8).**

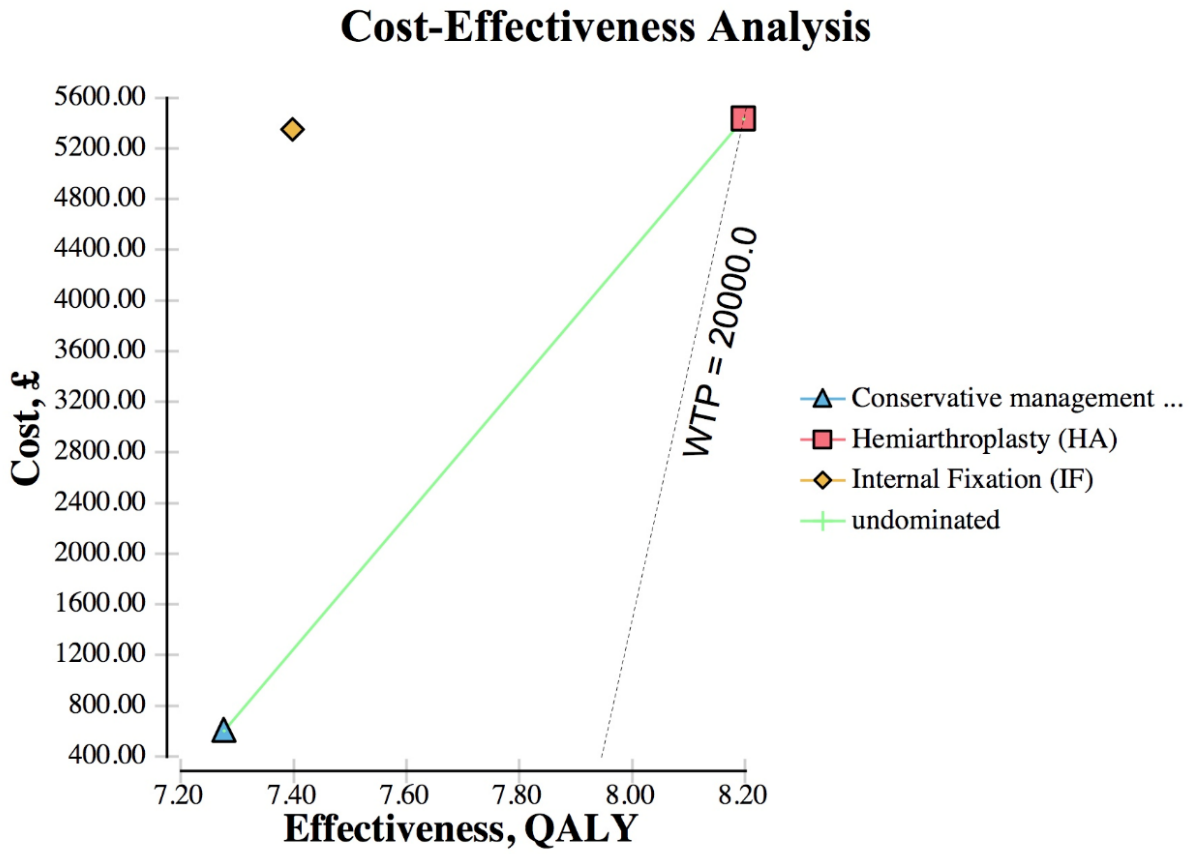


Figure 6.11. Cost-effectiveness graph showing that hemiarthroplasty is the most cost effective intervention after adjusting age-specific mortality in MCM.

Table 6.8. Summary outputs generated from MCM analysis performed with increased age-specific mortality.

Strategy	Cost, £	Incremental Cost, £	Effect, QALYs	Incremental Effect, QALYs	ICER, £/QALY gained	NMB
Conservative management	604.96	-	7.28	-	-	144919.78
Internal Fixation	5349.92	4744.96	7.4	0.12	39024.12	142606.63
Hemiarthroplasty	5435.48	4830.52	8.2	0.92	5246.33	158504.13

6.3.1.4 *Uncertainty in relation to cost*

One-way sensitivity analysis performed to determine the effects of cost adjustment for hemiarthroplasty and locking plate fixation revealed that the MCM favoured hemiarthroplasty. The cost of a primary hemiarthroplasty for a complex proximal humerus fracture could rise to £16,833.91 before its ICER climbed above the WTP threshold and conservative management became the most cost-effective treatment **(Figure 6.12).** Furthermore, extrapolation of the cost of primary locking plate fixation to £1 still resulted in hemiarthroplasty being the most cost effective treatment strategy in the MCM (**Figure 6.13).**

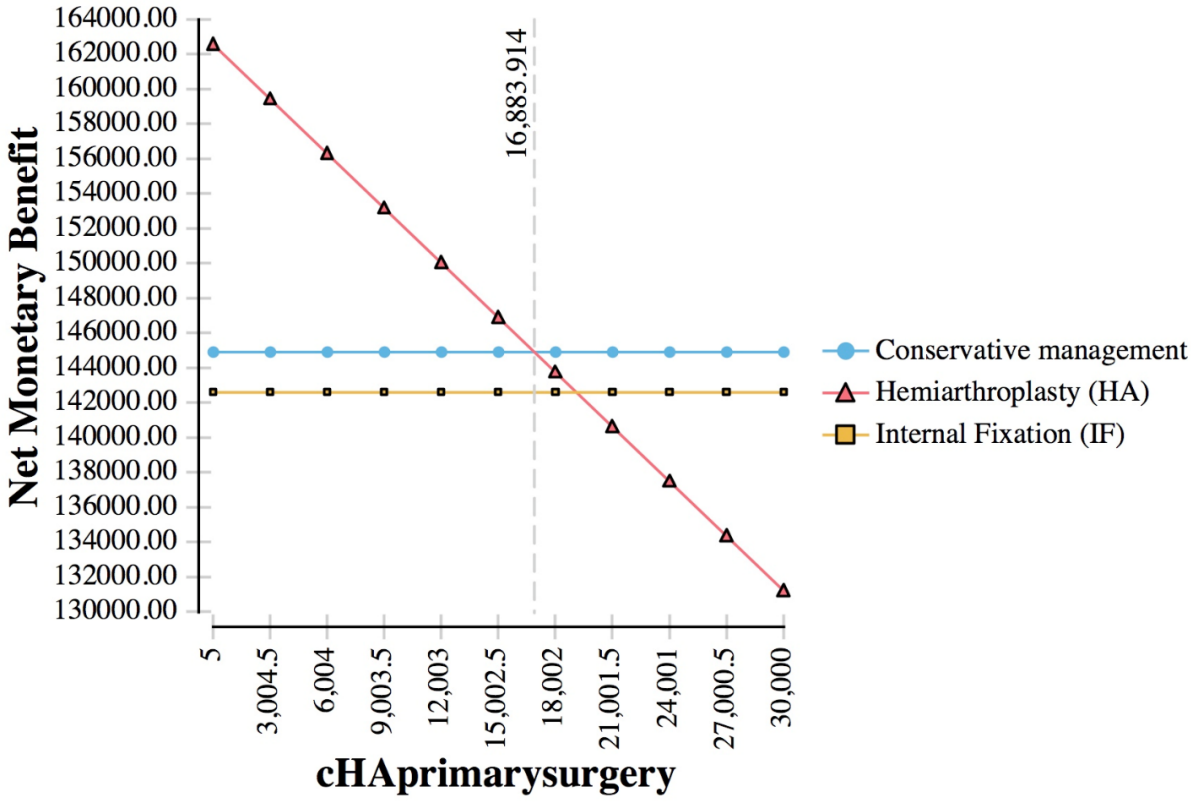


Figure 6.12. One-way sensitivity analysis demonstrating adjustment of cost of hemiarthroplasty as a primary treatment strategy. At a cost of £16,833.91 hemiarthroplasty becomes less cost-effective than conservative management. cHAprimarysurgery is the cost of hemiarthroplasty in £.

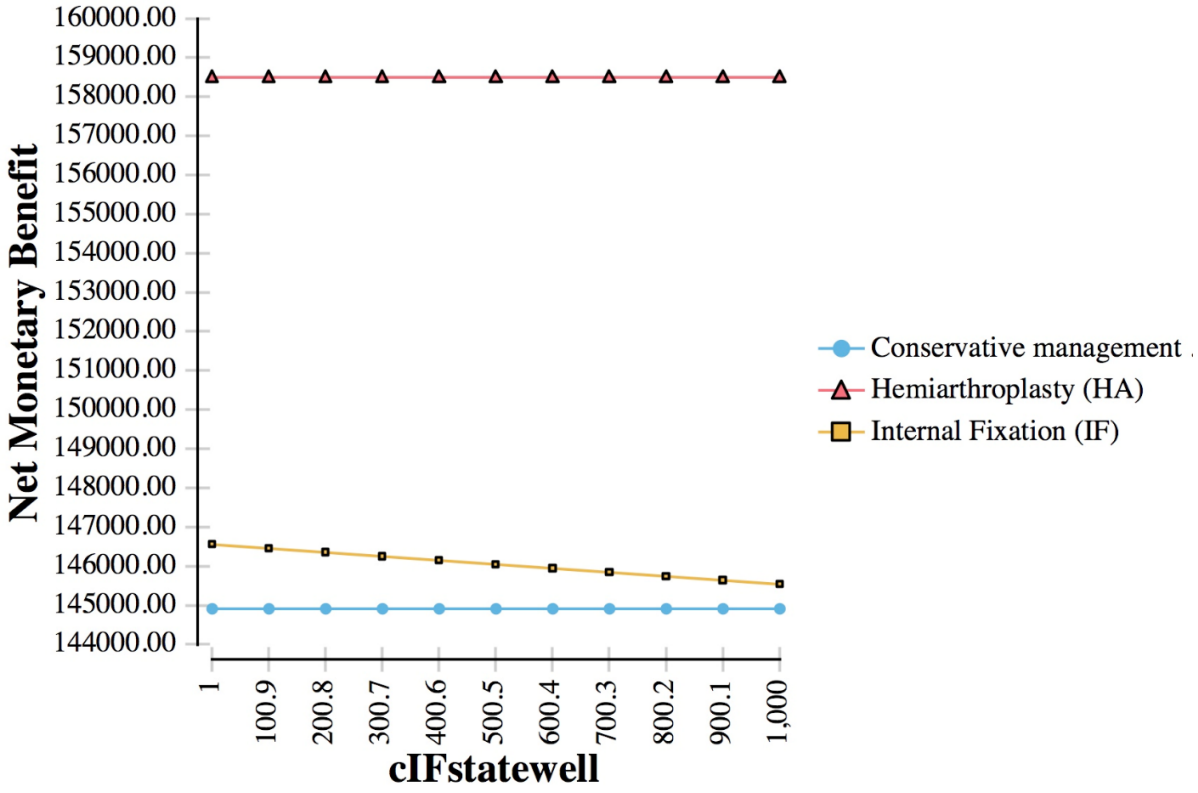


Figure 6.13. One-way sensitivity analysis demonstrating that adjustment of locking plate fixation cost to £1 results in hemiarthroplasty continuing to be the most cost effective treatment strategy. cIFstatewell is the cost of performing a primary locking plate fixation for a complex proximal humerus fracture.

Using institutional estimates of treatment cost adopted from the cost-analysis study performed in Chapter 4, the cost-effectiveness analysis was repeated in the MCM. The results were the same as the baseline analysis; hemiarthroplasty was the most cost effective treatment strategy (**Figure 6.14).** Although the overall cost for treatment from an institutional perspective is higher for hemiarthroplasty (£7,068 in institutional analysis versus £5,567 based on the national tariff), the incremental effectiveness is high enough to result in an ICER that falls within the WTP threshold **(Table 6.9).**

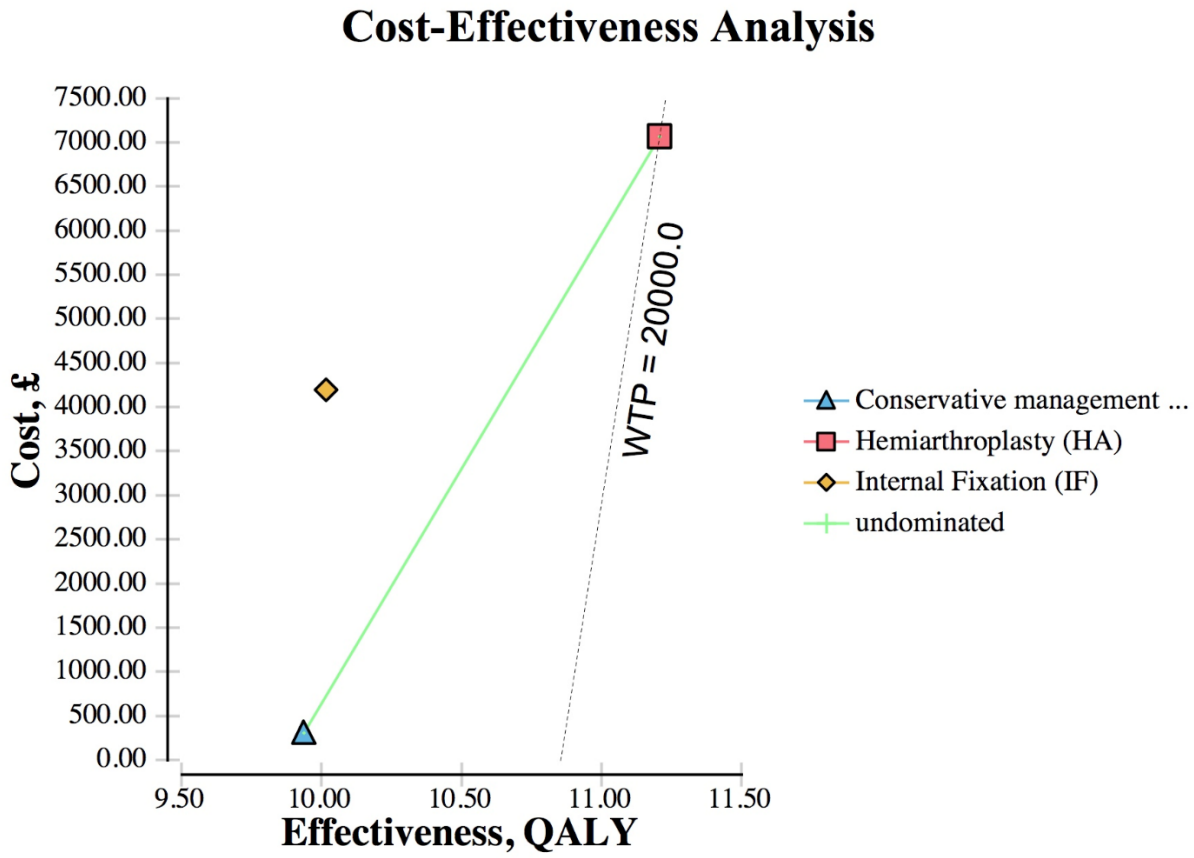


Figure 6.14. Cost-effectiveness graph illustrating that hemiarthroplasty is the most cost-effective treatment when the MCM is run using institutional cost estimates.

Table 6.9. Summary outputs generated from MCM analysis performed with institutional cost estimates.

Strategy	Cost, £	Incremental Cost, £	Effect, QALYs	Incremental Effect, QALYs	ICER, £/QALY gained	NMB
Conservative management	309.16	-	9.94	-	-	198,411.61
Internal Fixation	4,194.92	3,885.77	10.02	0.08	48,740.58	196,120.31
Hemiarthroplasty	7,068.68	6,759.52	11.21	1.27	5,317.78	217,074.45

6.3.1.5 *Sensitivity analysis: summation of findings*

Based on the full range on input parameters that informed this MCM, sensitivity analysis demonstrated that in the vast majority of parameter adjustments hemiarthroplasty remained the most cost effective treatment strategy **(Table 6.10).**

Table 6.10. Summary of variation of input parameters on MCM.

Parameter	Intervention found to be most cost effective	Parameter assumption
Complication rate after primary management	Hemiarthroplasty	Complication rate for hemiarthroplasty ≤ 24%, locking plate fixation ≥25%
	Locking plate	Hemiarthroplasty complication rate ≥25%, locking plate complication rate ≥25%
Secondary surgery rate	Hemiarthroplasty	All
Probability of improving after secondary surgery	Hemiarthroplasty	All
QALY values for patients with a successful outcome after primary management	Hemiarthroplasty	All reported parameters
	Conservative Management	Extrapolation beyond reported values: hemiarthroplasty well state QALY ≤ 1.53 and conservative management well state QALY ≥ 1.63
	Locking plate fixation	Extrapolation beyond reported values: hemiarthroplasty well state QALY ≤ 1.53, conservative management well state QALY ≤ 1.63, locking plate well state ≥ 1.8
QALY values for patients with an unsuccessful outcome after primary management	Hemiarthroplasty	QALY of conservative management complication state <1.39
	Conservative management	QALY for conservative management well state ≥ 1.39
QALY values for successful outcome after secondary surgery	Hemiarthroplasty	QALY for successful secondary surgery in hemiarthroplasty ≥ 0.3
	Conservative management	QALY for successful secondary surgery in hemiarthroplasty <0.3
QALY values for complication after secondary surgery	Hemiarthroplasty	QALY value for complication after secondary surgery in hemiarthroplasty ≥ 0.3
	Conservative management	QALY value for complication after secondary surgery in hemiarthroplasty < 0.3
Age specific mortality increased	Hemiarthroplasty	Based on repeated analysis using increased age-specific mortality in life tables
Institutional costing perspective	Hemiarthroplasty	Cost of hemiarthroplasty <£19,972 (£16,883 for national tariff perspective)

6.4 Discussion

This health economic evaluation investigated the cost-effectiveness of conservative management, locking plate fixation and hemiarthroplasty for proximal humerus fractures in the English NHS. It was conducted using a MCM over a 20-year time horizon for an elderly

cohort of patients with a 3 or 4-part proximal humerus fracture. The analysis found that hemiarthroplasty was the most cost-effective treatment strategy. This finding was based on improved clinical outcomes over the alternative treatment strategies, with an increased cost that was justified by an ICER of £4,380/QALY, which is within the national WTP margin. The input parameters that informed the MCM included clinical outcomes and probabilities derived from RCTs and expert opinion. Compared to the 2-year analysis performed in Chapter 5, sensitivity analysis demonstrated that the model found hemiarthroplasty to be the most cost-effective treatment across the vast majority of clinical scenarios. In relation to the parameters generated from expert consensus, the introduction of extreme and extrapolated values did not introduce uncertainty into the MCM. The overall lack of uncertainty demonstrated by the sensitivity analysis underlines the strength of this HEE and its findings.

Over the last 30 years, life expectancy in England has grown at a rate of 1.2% per year for men and 0.7% per year for women[290]. The health costs for older patients are significantly greater than those of the general population[291] and therefore there is an acute need for cost-effectiveness health policy that aligns the long-term needs of elderly patients with the financial resources of the health service[292]. MCMs provide an opportunity to forecast cost and health outcomes over a lifetime horizon in elderly patients. This generates a more expansive analysis to inform health policy and decision making which is usually restricted to the 1 or 2 year outcomes reported in clinical trials[273]. The findings of this cost-effectiveness study performed using a MCM over a 20-year time horizon were consistent with the results of the decision-tree analysis conducted in Chapter 5, which was based on a 2-year time horizon. Uncertainty within the MCM was smaller and therefore the strength of recommendations for management of elderly patients is greater based on a time frame that reflects their life expectancy.

The superiority of hemiarthroplasty over locking plate fixation and conservative management is driven by improved health utilities reported for hemiarthroplasty within the existing literature[30,252]. The improved health states of patients who underwent this procedure are possibly the result of less disutilities being incurred due to the reduced rate of secondary surgery compared to locking plate fixation (6% less). Avascular necrosis and metal work failure were sizeable contributors to locking plate fixation complications within the evidence base that informed this study. Advocates of hemiarthroplasty for more complex fractures rationalise their opinion based on such complications occurring after internal fixation[265]. The existing literature and its applications to health economic research provides weight to such opinions. However, the lack of registry data limits the understanding of performance bias when trying to generate consensus on recommendations for management. For instance, clinical research has shown that surgeon volume is inversely proportional to risk of complications after total hip replacement[293]. Therefore, it is possible that the complication rates for proximal humerus fractures reported from single-centre RCTs do not necessarily reflect individual or overall complication rates within the United Kingdom. High-volume orthopaedic units that have experience and a preference for locking plate fixation may have significantly lower complication rates and better functional outcomes for their patients. It is important that such variability in practice and patient outcomes is transparent, as well as available so that long-term clinical practice can be informed by more comprehensive data. The benefits of a national registry for patients with a proximal humerus fracture also offer health economic researchers time dependent clinical outcomes and more accurate age-specific mortality data. Cost-effectiveness work on total hip replacement surgery has benefited from the National Joint Registry[130], and Handoll et al's HEE conducted in parallel to the ProFHER Trial also concluded that the creation of a national database should be the basis for future work in this field[11].

This study is generalizable across the English NHS because it uses the national tariff for treatment costs. As discussed in Chapter 5, the inaccuracy of the tariff in reflecting true treatment costs[118] underlines the limitations of cost-effectiveness research done within the English NHS that endeavours to be applicable across the service. Institutional cost estimates vary greatly between hospitals due to differences in procurement methods and capital overhead expenditure[255], and therefore there is poor external validity to using such costs to inform national health economic policy. Despite this, the MCM that was constructed in this study revealed important findings in relation to treatment cost. Based on the reported clinical outcomes for hemiarthroplasty, the treatment cost could rise to £16,833 from £4,679 (institutional cost of treatment), and it would still be the most cost-effective treatment within the English NHS. In Chapter 4, it was found that true treatment costs for hemiarthroplasty outweigh the national tariff, and as a result it was a financial burden for the hospital to provide this treatment. It appears counterintuitive that hospitals should be financially penalised when providing treatments that are cost-effective. This inequity in health policy possibly occurs because the reimbursement structure in the English NHS does not commonly account for, or reward cost-effective practices. In relation to hip fractures or joint replacement surgery, the Best Practice Tariffs that rewards evidence based standards of care, appears to add value to patient care[294]. These costing methods form such a small proportion of secondary care reimbursement that they are almost an aberration within an antiquated and inaccurate costing system. The possibility that inadequate reimbursement for cost-effective treatments are increasing hospital deficits or deterring services from better practices needs further examination. However, on the basis of the findings in this study there are definite policy implications; hospitals with comparable clinical outcomes to those that informed this study have a stronger case in asking for more reimbursement so that they can deliver cost-effective treatment for elderly patients with complex proximal humerus fractures.

Reverse shoulder arthroplasty for complex proximal humerus fractures in elderly patients is increasing in popularity[295]. A number of studies have reported functional and clinical benefits to using this implant[296], and there appears to be an attrition of the high complication rates that were reported in earlier research[297]. To-date, there is no clinical research that uses health utilities as measures of patient outcomes, and as a result this intervention could not be incorporated into this economic analysis. One of the financial concerns with using a reverse shoulder replacement has been the high cost of the implant[259]. Within the English NHS, the use of such a costly implant may stretch hospital services that are inevitability feeling the effects of economic austerity in the public sector[298]. Considering that the one-way sensitivity analysis found hemiarthroplasty to be cost-effective with a treatment cost as high as £16,833, it is feasible that the use of a reverse implant would be cost-effective if its outcomes were comparable or better than hemiarthroplasty. Existing research suggests this is the case [232,297], however outcomes that include health utilities are needed to perform further health economic research to establish this.

6.4.1 Limitations

Like the decision-tree analysis performed in Chapter 5, one of the limitations of this study was the small number of trials that informed the analysis. These trials represent the highest level of published evidence reporting on patient outcomes for proximal humerus fractures, and the MCM was largely unaffected by uncertainty introduced by sensitivity analysis. Even though this underlines the strength of the findings of this study, future work would be better informed by larger patient samples from a national database. Patent-level data with long-term follow up from such a national database would also overcome a further limitation within this analysis, which was a reliance on assumptions for transitional probabilities and patient utilities. Moreover, because of the absence of registry data, clinical heterogeneity could not be assessed through sub-group analysis. Nevertheless, the inclusion criteria for the studies

that informed the analysis were similar and therefore the findings of this cost-effectiveness study adds to the current knowledge base for treatment of the target population defined within the methodology. Finally, although societal costs are commonly viewed to improve the quality and applicability of HEEs[110], a restrictive costing perspective was adopted using NHS-payer costs. Such methods are commonly employed in health economic research when societal costs are not available[269], as was the case for this study. Measuring social and primary care costs requires substantial resources[268]. In the future, a HEE performed in parallel to an RCT for 3 or 4-part fractures would offer the opportunity to measure such costs. In the absence of societal costing data, the analysis performed in this study provides important recommendations on maximising health outcomes based on the constraints of the healthcare budget, and this is important finding for orthopaedic health policy [268].

6.4.2 Conclusions

This HEE using a MCM examined the cost-effectiveness of treatment interventions for complex proximal humerus fractures in elderly patients. In the setting of the English NHS and over a 20-year time horizon, hemiarthroplasty was found to be the most cost-effective strategy when compared with locking plate fixation and conservative management. Sensitivity analysis revealed that when input parameters were adjusted according to the wide range of expected clinical outcomes, health utilities and treatment costs that were reported in the literature or generated from expert opinion, in the vast majority of scenarios hemiarthroplasty remained the most cost-effective treatment strategy. Furthermore, the current cost of treatment could be increased by approximately 3-fold, and hemiarthroplasty would still offer health benefits that would fall within the WTP threshold that exists the NHS. The data that informed this analysis was based on a small number of trials and a large number of assumptions. Future work will have stronger external validity and rely on fewer assumptions if a national database is generated that records patient outcomes after this injury.

Chapter 7

Discussion

7.1 Summary of Findings

This thesis aimed to improve the understanding of health and economic outcomes for complex proximal humerus fractures in elderly patients. Both quantitative and qualitative analytical methods were used to evaluate health outcomes. Economic outcomes were investigated using recognised principles of cost analysis and health economic evaluation. The results of each experimental chapter and the overall aims of the thesis will be summarised in this final section.

7.1.1 Quantitative Evaluation of Health Outcomes: Meta-Analysis of RCTs

A meta-analysis of 7 RCTs comparing surgical and non-operative management was performed. Sub-group analysis based on increasing fracture complexity and sensitivity analysis that examined trials by the type of surgical procedure was also performed. While the overall meta-analysis reinforced the findings of existing research[95] that there is no significant difference in treatment effects between surgery and non-operative management, the extended meta-analytical methods employed in this chapter offer food for thought. Sensitivity analysis of 4-part fractures managed by hemiarthroplasty showed statistically significant improved health outcomes for patients at 24 months. Subgroup analysis of 4-part fractures also revealed they were less likely to result in osteoarthritis, osteonecrosis and non/malunion if treated surgically. Patients who underwent locking plate fixation for 3-part fractures were more likely to require secondary surgery than patients with the same injury managed conservatively. Evaluation of heterogeneity between the published studies found that statistical heterogeneity of treatment effects was not driven by methodological bias, but rather clinical heterogeneity between the trials.

The findings of this study have 2 key implications. Firstly, this meta-analysis demonstrates that within the existing evidence base, 4-part fractures managed with hemiarthroplasty in elderly patients have specific health outcomes that are better than when managed conservatively. Secondly, the heterogeneity between trials and the results of sub-group and sensitivity analysis which were distinct from the overall analysis indicate that future RCT design may provide more clinically applicable conclusions if the inclusion criteria are more specific in relation to fracture complexity and the type of surgical procedure performed.

7.1.2 Qualitative Analysis of Elderly Patients' Perceptions of Recovery

To-date, there is no published qualitative analysis of patient perceptions after sustaining a proximal humerus fracture. A structured framework of thematic analysis was adopted in the evaluation of the experiences of 15 patients aged 65 or above, who had sustained a 3 or 4-part proximal humerus fracture. Seven themes were identified that related to how patients perceived their recovery and treatment; pain, sleep, shoulder function, emotional state, support network, experience of healthcare professional and experience of healthcare institution. Pain and trouble with sleep were the most important aspects of recovery for patients. Existing PROMs have an emphasis on limb function[52,65] and do not consider or measure concepts such as emotional state, support network, experience of healthcare professional and experience of healthcare professional. Based on the findings of this qualitative study, there is a need to develop PROMs that better reflect the views of this specific population in relation to recovery after sustaining a complex proximal humerus fracture.

7.1.3 Cost Analysis of Surgical Management

This study employed TDABC as a micro-costing methodology to estimate the cost of surgical management of 3 and 4-part proximal humerus fractures in patients aged 65 years or above.

The study found that the mean institutional cost for the three surgical procedures performed at a single hospital varied substantially; the cost of a soft tissue reconstruction was £2,055, the cost of a locking plate fixation was £3,113 and the cost of a hemiarthroplasty procedure was £4,679. Reduced staff experience and increased patient frailty increased the estimates of treatment costs. National reimbursement for surgically managing this injury was £4,421. The findings of this study indicate that widespread use of hemiarthroplasty for these injuries can be a financial burden for hospitals as treatment costs are not appropriately reimbursed. Furthermore, the 2 main direct cost drivers that were identified within the patient pathway were implant cost and operating theatre staffing. Threshold analysis of theatre utilization demonstrated that delays in the operating theatre were likely to result in large increases in treatment cost and therefore better management of theatre utilization is likely to control treatment costs when managing these injuries.

7.1.4 Health Economic Evaluation Over a 2-year Time Horizon

This HEE performed using a decision analytical tree compared conservative management, locking plate fixation and hemiarthroplasty in the management of complex proximal humerus fractures in elderly patients over a 2 year time horizon. Within the setting of the English NHS and based on national tariffs, hemiarthroplasty is the most cost-effective treatment strategy with an incremental cost effectiveness ratio (ICER) of £18,000/quality adjusted life year (QALY). Sensitivity analysis indicated that the findings of this economic model had a great deal of uncertainty as adjustment of model parameters based on expected differences in clinical outcomes and costing based on an institutional perspective, resulted in conservative management being more cost effective within the defined willingness to pay threshold of £20000/QALY in the English NHS.

7.1.5 Health Economic Evaluation Over a 20-year Time Horizon

This HEE used a Markov chain model (MCM) to examine the cost-effectiveness of treatment interventions for complex proximal humerus fractures in elderly patients. In the setting of the English NHS and over a 20-year time horizon, hemiarthroplasty was found to be the most cost-effective strategy when compared with locking plate fixation and conservative management. It offered an ICER of approximately £4,380/QALY which represented a benefit in QALYs over alternative treatments, which was well within the recognised WTP threshold. Furthermore, extensive sensitivity analysis based on adjustment of input parameters and cost found that hemiarthroplasty remained the most cost-effective treatment intervention across the majority of probable scenarios. One-way sensitivity analysis also demonstrated that the cost of treatment could increase by almost 3-fold and hemiarthroplasty would remain the most cost effective intervention. This has important implications in the development of newer technologies and the application of more costly treatments such as reverse arthroplasty for the management of these injuries. It is strongly suggestive that such technologies would be cost-effective within the English NHS if they can meet or exceed the health outcomes specific to those currently reported after hemiarthroplasty for the management of complex proximal humerus fractures in elderly patients.

7.2 Research Limitations

The individual limitations of the methodology for each study are detailed in the corresponding chapters. The principle limitation of the meta-analysis study was that the number of included RCTs was less than 10. As such, the evaluation of publication bias amongst the studies needs to be treated with caution[299]. Furthermore, because less than 10 RCTs were available, meta-regression was not possible[300]. Meta-regression is a meta-analytical tool that allows the impact of moderator variables to be statistically evaluated in relation to study effect size. The presence of 10 or more RCTs would have allowed for more

robust statistical testing to establish the causes of heterogeneity between studies, and specifically it would determine whether studies with increased fracture complexity respond better to surgical treatment. As reported in Chapter 2, a large number of trials investigating proximal humerus fracture management are ongoing. The publication of these studies will make possible more comprehensive meta-analysis of studies based on a specific inclusion criteria of complex fracture-types, as well as meta-regression of moderator variables to better understand drivers of clinical heterogeneity between trials.

The main limitation of the qualitative analysis was that patients included in the study were recruited from one hospital. While there may be acceptable internal validity to these findings, they are not representative of hospitals across the NHS. This restricts the generalisation of the conclusions, particularly in the development of a validated PROM. The study findings do suggest that patient perceptions may be not be adequately measured using current PROMs, and there is a need to extend and develop this research across a larger number of hospitals. The cost-analysis study was also limited because it was conducted at one hospital. However, there are inherent inaccuracies in deriving estimates across a number of hospitals because treatment costs greatly vary[255,301]. This study has demonstrated the feasibility of using more accurate costing methodologies in this field and it has highlighted how the reimbursement structure in the English NHS can actively penalise hospitals for performing appropriate and uncomplicated treatments.

The health economic evaluations that were performed were limited in their strength because they was driven by a small select group of RCTs. The health utilities reported amongst these studies were presented as a mean value of all included patients. Such reporting methods make it difficult for to apply the findings of primary analyses to decision analytical economic models. Assumptions were made to delineate between successful outcomes of treatment and

complications and these assumptions were subjected to sensitivity analysis to quantify the extent of uncertainty they introduced into the models. Overall, the evaluation performed using a MCM over a 20-year time horizon had stronger conclusions because comprehensive sensitivity analysis supported the overall recommendations that hemiarthroplasty was the most cost-effective treatment strategy in the English NHS.

There are two fundamental limitations to this work, both of which arise from the use of existing research. Firstly, there is a widely recognised deficiency in the classification of proximal humerus fractures[134]. Although reliability of commonly used systems such as those described by Neer and the AO have been challenged, there is a more concerning debate about whether these classification systems appropriately describe fractures, guide management and provide an accurate prognosis[134]. Until a more valid classification system is developed, this problem will limit the quality of research in this field. Secondly, there is a dearth of evidence that examines the effect of surgical skill on performance bias in orthopaedic surgery. Within our evidence synthesis there was a wide range of reported complication rates for surgical management of identical procedures. Although there can be a number of explanations for this including selection, detection and reporting bias, the effect of surgical skill requires consideration. A 2013 US study found that there was a significant correlation between the technical skills of bariatric surgeons and patient outcomes[302]. The effect of technical skill on outcomes in the management of proximal humerus fractures may also have a similar effect. As such, the findings of clinical and economic research such as that conducted in this thesis should come with the caveat; this research may reflect the outcomes of a large proportion of surgeons, however it is unable to fully encapsulate the full spectrum of surgical skill and performance.

7.3 Future Work

The qualitative analysis provided new and important patient-centred views on recovery after sustaining a complex proximal humerus fracture. Concepts such as patients' emotional state, their support networks, and their experience of healthcare professionals and the healthcare institution overseeing their care, do not form part of conventional measures of their health outcomes. As the shape of healthcare evolves, and the perceptions of patients' own health state supersedes the clinician perspective[303], there is a need to build upon the findings of this study and construct a PROM that is valid for elderly patients with complex proximal humerus fractures. Existing scores that are heavily weighted in favour of function may not be truly reflective of the needs of this group of patients and further study in this field is required.

Another aspect of the qualitative analysis that requires development is the comparative assessment of patients that have undergone different management strategies for their proximal humerus fractures. The effects of complications, secondary surgery, functional improvement and symptomatic relief between treatment groups requires an exploratory analysis that quantitative assessment is likely to be too restrictive in design to provide. For instance, the meta-analysis in Chapter 2 demonstrated how patients who underwent a locking plate had a significantly increased risk of secondary surgery. Head preserving surgery for complex fractures is often adopted because of the perception by clinicians that it improves function[304,305]. An in-depth patient centred qualitative analysis offers the opportunity to better understand how an elderly cohort of patients value the benefits and risks of locking plates and hemiarthroplasty, and such an analysis is likely to improve and better inform shared decision making between clinician and patient.

The cost analysis chapter posed some important questions for health policy in the English NHS that extend beyond the core subject matter in this thesis. However, having examined

existing costing methods while performing this study, I personally believe that there are substantial limitations in the accounting of treatment costs in the English NHS that require urgent further analysis. At a time when there is great financial strain on hospitals across England[305], the study of improvement of costing methodology is crucial for health services. Patient level information costing systems (PLICS), is an information system driven tool that is being unrolled across the NHS as a means to estimating the costs of individual episodes of patient care[306]. This system draws data from a myriad of variables that range from prescribed drugs to implants used during surgery. These are then aggregated to calculate the cost of patient care. In the preliminary study design, this data was examined to determine whether it would be appropriate for use in the micro-costing analysis. Only a cursory observation of the data was required to recognise that it was greatly flawed; for example, implant costs for patients with a proximal humerus fracture included estimates of £2 to £20 for a large number of patients who had been managed with locking plates or hemiarthroplasty. Considering that implant cost was identified as the largest cost driver in Chapter 4, with costs of approximately £800 and £1,900 for a locking plate and hemiarthroplasty respectively, such gross inaccuracies requires further investigation. I believe one solution to identifying inaccuracies within PLICS would be to perform TDABC analysis, such as that conducted in Chapter 4 to identify inaccurate cost variables. Those variables could then be subjected to root cause analyses to identify why they have been inaccurately accounted for.

There is also substantial scope for the development of health economic research in this field. A large number of trials that are currently ongoing will shape and improve the validity of future decision analytical models used to conduct a HEE comparing treatment interventions. The interest in the use of reverse shoulder implants, particularly for an elderly population with complex proximal humerus fractures, has resulted in their inclusion in ongoing RCTs[307]. The high cost of this implant is well recognised, and as such the cost-effectiveness of its

application will be particularly important to clinicians and policy makers alike. Another area that requires development and has also been highlighted by other researchers in this field, has been the implementation of a proximal humerus fracture registry[11]. A national record of patient outcomes would allow for more valid and robust clinical and economic analyses. One of the problems encountered while performing the HEE in this thesis was that the health utilities reported in the results of RCTs were quite restrictive and as a result assumptions need to be made to satisfy the full range of clinical outcomes. Registry data would allow this limitation to be overcome and this has been demonstrated in the use of such data to inform UK based health economic research in other orthopaedic sub-specialties[308,309].

The clinical applicability of research as a whole in this field is likely to benefit from more valid classification of these injuries. Furthermore, there is a need for appropriately powered multi-centred RCTs with specific inclusion criteria based on patient and fracture characteristics. Single-centre studies have limited external validity and given that the PROFHER trial is the only multi-centred RCT in this field, there is a need for the development of research networks to facilitate multicentre trials. Finally, future research should evaluate the impact of a surgeon's technical skill and case-load volume on patients' outcomes following surgery for a proximal humerus fracture. Such work is likely to characterise the role of performance bias which is relevant to more informed decision making on appropriate management.

7.4 Conclusions

This thesis has addressed the health and economic outcomes following management of complex proximal humerus fractures in elderly patients. It has found that quantitative health outcomes for 4 part fractures are more favourable following hemiarthroplasty. It has also demonstrated that this treatment represents the most cost-effective intervention for complex

fractures in elderly patients within the English NHS. Despite the health and economic benefits of this procedure, cost analysis showed that performing a hemiarthroplasty resulted in a financial loss for a hospital in the English NHS based on the national reimbursement tariff. The inequity of a financial framework that allows cost and clinically effective practice to be penalised requires further attention. Qualitative analysis has also demonstrated that the measures of health outcomes within this field need further development so that they better represent the perceptions the target population. This body of work has also outlined that there is a great deal of uncertainty that exists around the health and economic outcomes of complex proximal humerus fracture management. To address this uncertainty, there is a need for further clinical and health economic research and the development of a national registry.

References

1. Kim SH, Szabo RM, Marder RA. Epidemiology of humerus fractures in the United States: nationwide emergency department sample, 2008. *Arthritis Care Res (Hoboken) 2012;64-3:407-14.*

2. Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. *Osteoporos Int 2006;17-12:1726-33.*

3. Palvanen M, Kannus P, Niemi S, Parkkari J. Update in the epidemiology of proximal humeral fractures. *Clin Orthop Relat Res 2006;442:87-92.*

4. Court-Brown CM, Caesar B. Epidemiology of adult fractures: A review. *Injury 2006;37-8:691-7.*

5. Kristiansen B, Barfod G, Bredesen J, Erin-Madsen J, Grum B, Horsnaes MW, Aalberg JR. Epidemiology of proximal humeral fractures. *Acta Orthop Scand 1987;58-1:75-7.*

6. Neer CS, 2nd. Displaced proximal humeral fractures. I. Classification and evaluation. *J Bone Joint Surg Am 1970;52-6:1077-89.*

7. Clement ND, Duckworth AD, McQueen MM, Court-Brown CM. The outcome of proximal humeral fractures in the elderly: predictors of mortality and function. *Bone Joint J 2014;96-B-7:970-7.*

8. Court-Brown CM, Garg A, McQueen MM. The translated two-part fracture of the proximal humerus. Epidemiology and outcome in the older patient. *J Bone Joint Surg Br 2001;83-6:799-804.*

9. Gallinet D, Clappaz P, Garbuio P, Tropet Y, Obert L. Three or four parts complex proximal humerus fractures: hemiarthroplasty versus reverse prosthesis: a comparative study of 40 cases. *Orthop Traumatol Surg Res 2009;95-1:48-55.*

10. Slavin JP, Deakin M, Wilson R. Surgical research and activity analysis using Hospital Episode Statistics. *Ann R Coll Surg Engl 2012;94-8:537-8.*

11. Handoll H, Brealey S, Rangan A, Keding A, Corbacho B, Jefferson L, Chuang LH, Goodchild L, Hewitt C, Torgerson D. The ProFHER (PROximal Fracture of the Humerus: Evaluation by Randomisation) trial - a pragmatic multicentre randomised controlled trial evaluating the clinical effectiveness and cost-effectiveness of surgical compared with non-surgical treatment for proximal fracture of the humerus in adults. *Health Technol Assess 2015;19-24:1-280.*

12. Johnell O, Kanis JA, Oden A, Sernbo I, Redlund-Johnell I, Petterson C, De Laet C, Jonsson B. Mortality after osteoporotic fractures. *Osteoporos Int 2004;15-1:38-42.*

13. Wilson LA, Gooding BW, Manning PA, Wallace WA, Geoghegan JM. Risk factors and predictors of mortality for proximal humeral fractures. *Shoulder & Elbow 2014;6-2:95-9.*

14. Chu SP, Kelsey JL, Keegan TH, Sternfeld B, Prill M, Quesenberry CP, Sidney S. Risk factors for proximal humerus fracture. *Am J Epidemiol 2004;160-4:360-7.*

15. Kelsey JL, Browner WS, Seeley DG, Nevitt MC, Cummings SR. Risk factors for fractures of the distal forearm and proximal humerus. The Study of Osteoporotic Fractures Research Group. *Am J Epidemiol 1992;135-5:477-89.*

16. Hagino H, Yamamoto K, Ohshiro H, Nakamura T, Kishimoto H, Nose T. Changing incidence of hip, distal radius, and proximal humerus fractures in Tottori Prefecture, Japan. *Bone 1999;24-3:265-70.*

17. Davis JW, Ross PD, Wasnich RD. Relation of height and weight to the regional variations in bone mass among Japanese-American men and women. *Osteoporos Int 1995;5-4:234-8.*

18. Menendez ME, Ring D. Factors associated with hospital admission for proximal humerus fracture. *Am J Emerg Med 2015;33-2:155-8.*

19. Bell JE, Leung BC, Spratt KF, Koval KJ, Weinstein JD, Goodman DC, Tosteson AN. Trends and variation in incidence, surgical treatment, and repeat surgery of proximal humeral fractures in the elderly. *J Bone Joint Surg Am 2011;93-2:121-31.*

20. Codman EA. *The shoulder : rupture of the supraspinatus tendon and other lesions in or about the subacromial bursa.* Malabar, Fla.: R.E. Kreiger, 1984, 1934.

21. Edelson G, Kelly I, Vigder F, Reis ND. A three-dimensional classification for fractures of the proximal humerus. *J Bone Joint Surg Br 2004;86-3:413-25.*

22. Palvanen M, Kannus P, Parkkari J, Pitkajarvi T, Pasanen M, Vuori I, Jarvinen M. The injury mechanisms of osteoporotic upper extremity fractures among older adults: a controlled study of 287 consecutive patients and their 108 controls. *Osteoporos Int 2000;11-10:822-31.*

23. Brorson S. Management of fractures of the humerus in Ancient Egypt, Greece, and Rome: an historical review. *Clin Orthop Relat Res 2009;467-7:1907-14.*

24.Thudichum L. U¨ber die am oberen Ende des Humerus vorkommende Knochenbruche. Giessen, Germany: Ricker'sche Buchhandlung, 1851.

25. Brorson S. Management of proximal humeral fractures in the nineteenth century: an historical review of preradiographic sources. *Clin Orthop Relat Res 2011;469-4:1197-206.*

26. Kocher T. *Beitrage zur Kenntnis Einiger Praktisch Wichtiger Fracturenformen.* Basel: Carl Sallman Verlag, 1896.

27. Carofino BC, Leopold SS. Classifications in brief: the Neer classification for proximal humerus fractures. *Clin Orthop Relat Res 2013;471-1:39-43.*

28. Neer CS, 2nd. Four-segment classification of proximal humeral fractures: purpose and reliable use. *J Shoulder Elbow Surg 2002;11-4:389-400.*

29. Rangan A, Handoll H, Brealey S, Jefferson L, Keding A, Martin BC, Goodchild L, Chuang LH, Hewitt C, Torgerson D, Collaborators PT. Surgical vs nonsurgical treatment of adults with displaced fractures of the proximal humerus: the PROFHER randomized clinical trial. *JAMA 2015;313-10:1037-47.*

30. Olerud P, Ahrengart L, Ponzer S, Saving J, Tidermark J. Hemiarthroplasty versus nonoperative treatment of displaced 4-part proximal humeral fractures in elderly patients: a randomized controlled trial. *J Shoulder Elbow Surg 2011;20-7:1025-33.*

31. Bateman JE, Welsh RP. *Surgery of the shoulder.* Philadelphia: Decker ; Saint Louis ; London : Mosby, 1984.

32. Williams GR. *Shoulder elbow arthroplasty.* Philadelphia, Pa. ; London: Lippincott Williams & Wilkins, 2005.

33. Hertel R, Hempfing A, Stiehler M, Leunig M. Predictors of humeral head ischemia after intracapsular fracture of the proximal humerus. *J Shoulder Elbow Surg 2004;13-4:427-33.*

34. Resch H, Tauber M, Neviaser RJ, Neviaser AS, Majed A, Halsey T, Hirzinger C, Al-Yassari G, Zyto K, Moroder P. Classification of proximal humeral fractures based on a pathomorphologic analysis. *J Shoulder Elbow Surg 2015.*

35. Mutch J, Laflamme GY, Hagemeister N, Cikes A, Rouleau DM. A new morphological classification for greater tuberosity fractures of the proximal humerus: validation and clinical implications. *Bone Joint J 2014;96-B-5:646-51.*

36. Boileau P, Chuinard C, Le Huec JC, Walch G, Trojani C. Proximal humerus fracture sequelae: impact of a new radiographic classification on arthroplasty. *Clin Orthop Relat Res 2006;442:121-30.*

37. Kristiansen B, Andersen UL, Olsen CA, Varmarken JE. The Neer classification of fractures of the proximal humerus. An assessment of interobserver variation. *Skeletal Radiol 1988;17-6:420-2.*

38. Sidor ML, Zuckerman JD, Lyon T, Koval K, Cuomo F, Schoenberg N. The Neer classification system for proximal humeral fractures. An assessment of interobserver reliability and intraobserver reproducibility. *J Bone Joint Surg Am 1993;75-12:1745-50.*

39. Mahadeva D, Mackay DC, Turner SM, Drew S, Costa ML. Reliability of the Neer classification system in proximal humeral fractures: a systematic review of the literature. *European Journal of Orthopaedic Surgery and Traumatology 2008;18-6:415-24.*

40. Bruinsma WE, Guitton TG, Warner JJ, Ring D, Science of Variation G. Interobserver reliability of classification and characterization of proximal humeral fractures: a comparison of two and three-dimensional CT. *J Bone Joint Surg Am 2013;95-17:1600-4.*

41. Sukthankar AV, Leonello DT, Hertel RW, Ding GS, Sandow MJ. A comprehensive classification of proximal humeral fractures: HGLS system. *J Shoulder Elbow Surg 2013;22-7:e1-6.*

42. Majed A, Macleod I, Bull AM, Zyto K, Resch H, Hertel R, Reilly P, Emery RJ. Proximal humeral fracture classification systems revisited. *J Shoulder Elbow Surg 2011;20-7:1125-32.*

43. Brand RA. Ernest Amory Codman, MD, 1869-1940. *Clin Orthop Relat Res 2009;467-11:2763-5.*

44. Gartlehner G, Flamm M. Is the Cochrane collaboration prepared for the era of patient-centred outcomes research? *Cochrane Database Syst Rev 2013;3:ED000054.*

45. Brigham CB. VIII. Dislocation at the Shoulder complicated by Fracture through the Anatomical Neck of the Humerus. *Ann Surg 1900;31-5:614-6 1.*

46. Milch H. The treatment of recent dislocations and fracture-dislocations of the shoulder. *J Bone Joint Surg Am 1949;31A-1:173-80.*

47. Michaelis LS. Comminuted fracture-dislocation of the shoulder; result 7 years after excision of fragments and treatment on abduction splint. *Proc R Soc Med 1949;42-8:597.*

48. Thompson FR, Winant EM. Unusual fracture-subluxations of the shoulder joint. *J Bone Joint Surg Am 1950;32-A-3:575-82.*

49. Constant CR, Gerber C, Emery RJ, Sojbjerg JO, Gohlke F, Boileau P. A review of the Constant score: modifications and guidelines for its use. *J Shoulder Elbow Surg 2008;17-2:355-61.*

50. Constant CR, Murley AH. A clinical method of functional assessment of the shoulder. *Clin Orthop Relat Res 1987-214:160-4.*

51. Roy JS, MacDermid JC, Woodhouse LJ. A systematic review of the psychometric properties of the Constant-Murley score. *J Shoulder Elbow Surg 2010;19-1:157-64.*

52. Dawson J, Fitzpatrick R, Carr A. Questionnaire on the perceptions of patients about shoulder surgery. *J Bone Joint Surg Br 1996;78-4:593-600.*

53. Baker P, Nanda R, Goodchild L, Finn P, Rangan A. A comparison of the Constant and Oxford shoulder scores in patients with conservatively treated proximal humeral fractures. *J Shoulder Elbow Surg 2008;17-1:37-41.*

54. Dawson J, Rogers K, Fitzpatrick R, Carr A. The Oxford shoulder score revisited. *Arch Orthop Trauma Surg 2009;129-1:119-23.*

55. Wilson J, Baker P, Rangan A. Is retrospective application of the Oxford Shoulder Score valid? *J Shoulder Elbow Surg 2009;18-4:577-80.*

56. Rasmussen JV, Olsen BS, Fevang BT, Furnes O, Skytta ET, Rahme H, Salomonsson B, Mohammed KD, Page RS, Carr AJ. A review of national shoulder and elbow joint replacement registries. *J Shoulder Elbow Surg 2012;21-10:1328-35.*

57. Chen CY, Hu CC, Weng PW, Huang YM, Chiang CJ, Chen CH, Tsuang YH, Yang RS, Sun JS, Cheng CK. Extracorporeal shockwave therapy improves short-term functional outcomes of shoulder adhesive capsulitis. *J Shoulder Elbow Surg 2014;23-12:1843-51.*

58. Wang A, McCann P, Colliver J, Koh E, Ackland T, Joss B, Zheng M, Breidahl B. Do postoperative platelet-rich plasma injections accelerate early tendon healing and functional recovery after arthroscopic supraspinatus repair? A randomized controlled trial. *Am J Sports Med 2015;43-6:1430-7.*

59. Poon PC, Chou J, Young SW, Astley T. A comparison of concentric and eccentric glenospheres in reverse shoulder arthroplasty: a randomized controlled trial. *J Bone Joint Surg Am 2014;96-16:e138.*

60. Svendsen SW, Christiansen DH, Haahr JP, Andrea LC, Frost P. Shoulder function and work disability after decompression surgery for subacromial impingement syndrome: a randomised controlled trial of physiotherapy exercises and occupational medical assistance. *BMC Musculoskelet Disord 2014;15:215.*

61. Xu X, Wang F, Wang X, Wei X, Wang Z. Chinese cross-cultural adaptation and validation of the Oxford shoulder score. *Health Qual Life Outcomes 2015;13-1:193.*

62. Naghdi S, Nakhostin Ansari N, Rustaie N, Akbari M, Ebadi S, Senobari M, Hasson S. Simple shoulder test and Oxford Shoulder Score: Persian translation and cross-cultural validation. *Arch Orthop Trauma Surg 2015;135-12:1707-18.*

63. Frich LH, Noergaard PM, Brorson S. Validation of the Danish version of Oxford Shoulder Score. *Dan Med Bull 2011;58-11:A4335.*

64. Lima ED, Natour J, Moreira E, Jones A. Translation, cultural adaptation and reproducibility of the Oxford Shoulder Score questionnaire for Brazil, among patients with rheumatoid arthritis. *Sao Paulo Med J 2015.*

65. Hudak PL, Amadio PC, Bombardier C. Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand) [corrected]. The Upper Extremity Collaborative Group (UECG). *Am J Ind Med 1996;29-6:602-8.*

66. Davis AM, Beaton DE, Hudak P, Amadio P, Bombardier C, Cole D, Hawker G, Katz JN, Makela M, Marx RG, Punnett L, Wright JG. Measuring disability of the upper extremity: a rationale supporting the use of a regional outcome measure. *J Hand Ther 1999;12-4:269-74.*

67. Gummesson C, Atroshi I, Ekdahl C. The disabilities of the arm, shoulder and hand (DASH) outcome questionnaire: longitudinal construct validity and measuring self-rated health change after surgery. *BMC Musculoskelet Disord 2003;4:11.*

68. Wang Y, He Z, Lei L, Lin D, Li Y, Wang G, Zhai H, Xu J, Zhang G, Lin M. Reliability and validity of the Chinese version of the Short Musculoskeletal Function Assessment questionnaire in patients with skeletal muscle injury of the upper or lower extremities. *BMC Musculoskelet Disord 2015;16:161.*

69. Olerud P, Ahrengart L, Ponzer S, Saving J, Tidermark J. Internal fixation versus nonoperative treatment of displaced 3-part proximal humeral fractures in elderly patients: a randomized controlled trial. *J Shoulder Elbow Surg 2011;20-5:747-55.*

70. Garza AG, Wyrwich KW. Health utility measures and the standard gamble. *Acad Emerg Med 2003;10-4:360-3.*

71. Brinker MR, O'Connor DP. Stakeholders in outcome measures: review from a clinical perspective. *Clin Orthop Relat Res 2013;471-11:3426-36.*

72. Patel AA, Donegan D, Albert T. The 36-item short form. *J Am Acad Orthop Surg 2007;15-2:126-34.*

73. Beaton DE, Richards RR. Measuring function of the shoulder. A cross-sectional comparison of five questionnaires. *J Bone Joint Surg Am 1996;78-6:882-90.*

74. Oh JH, Jo KH, Kim WS, Gong HS, Han SG, Kim YH. Comparative evaluation of the measurement properties of various shoulder outcome instruments. *Am J Sports Med 2009;37-6:1161-8.*

75. Verbeek PA, van den Akker-Scheek I, Wendt KW, Diercks RL. Hemiarthroplasty versus angle-stable locking compression plate osteosynthesis in the treatment of three- and four-part fractures of the proximal humerus in the elderly: design of a randomized controlled trial. *BMC Musculoskelet Disord 2012;13:16.*

76. Den Hartog D, Van Lieshout EM, Tuinebreijer WE, Polinder S, Van Beeck EF, Breederveld RS, Bronkhorst MW, Eerenberg JP, Rhemrev S, Roerdink WH, Schraa G, Van der Vis HM, Van Thiel TP, Patka P, Nijs S, Schep NW. Primary hemiarthroplasty versus conservative treatment for comminuted fractures of the proximal humerus in the elderly (ProCon): a multicenter randomized controlled trial. *BMC Musculoskelet Disord 2010;11:97.*

77. Petrou S, Gray A. Economic evaluation using decision analytical modelling: design, conduct, analysis, and reporting. *BMJ 2011;342:d1766.*

78. Beaton DE, Clark JP. Qualitative research: a review of methods with use of examples from the total knee replacement literature. *J Bone Joint Surg Am 2009;91 Suppl 3:107-12.*

79. Denzin NKe, Lincoln YSe. *The SAGE Handbook of Qualitative Research.* Fourth Edition ed.

80. Higgins J, Green S. *Cochrane handbook for systematic reviews of interventions.* Oxford: Wiley-Blackwell, 2008.

81. Patchick EL, Horne M, Woodward-Nutt K, Vail A, Bowen A. Development of a patient-centred, patient-reported outcome measure (PROM) for post-stroke cognitive rehabilitation: qualitative interviews with stroke survivors to inform design and content. *Health Expect 2015;18-6:3213-24.*

82. Willert CB, Holmich LR, Thorborg K. [Developing and validating of patient-reported questionnaires - part 2]. *Ugeskr Laeger 2015;177-42:V04150290.*

83. O'Cathain A, Thomas KJ, Drabble SJ, Rudolph A, Hewison J. What can qualitative research do for randomised controlled trials? A systematic mapping review. *BMJ Open 2013;3-6.*

84. Whitty CJ. What makes an academic paper useful for health policy? *BMC Med 2015;13:301.*

85. Braun V, Clarke V. Using thematic analysis in psychology. *Qualitative research in psychology 2006;3-2:77-101.*

86. Pretell-Mazzini J, Murphy RF, Kushare I, Dormans JP. Unicameral bone cysts: general characteristics and management controversies. *J Am Acad Orthop Surg 2014;22-5:295-303.*

87. Resch H. Proximal humeral fractures: current controversies. *J Shoulder Elbow Surg 2011;20-5:827-32.*

88. Hageman MG, Jayakumar P, King JD, Guitton TG, Doornberg JN, Ring D, Science of Variation G. The factors influencing the decision making of operative treatment for proximal humeral fractures. *J Shoulder Elbow Surg 2015;24-1:e21-6.*

89. Jo MJ, Gardner MJ. Proximal humerus fractures. *Curr Rev Musculoskelet Med 2012;5-3:192-8.*

90. Lefevre-Colau MM, Babinet A, Fayad F, Fermanian J, Anract P, Roren A, Kansao J, Revel M, Poiraudeau S. Immediate mobilization compared with conventional immobilization for the impacted nonoperatively treated proximal humeral fracture. A randomized controlled trial. *J Bone Joint Surg Am 2007;89-12:2582-90.*

91. Handoll HH, Ollivere BJ, Rollins KE. Interventions for treating proximal humeral fractures in adults. *Cochrane Database Syst Rev 2012;12:CD000434.*

92. Okike K, Lee OC, Makanji H, Harris MB, Vrahas MS. Factors associated with the decision for operative versus non-operative treatment of displaced proximal humerus fractures in the elderly. *Injury 2013;44-4:448-55.*

93. Vachtsevanos L, Hayden L, Desai AS, Dramis A. Management of proximal humerus fractures in adults. *World J Orthop 2014;5-5:685-93.*

94. Boileau P, Trojani C, Walch G, Krishnan SG, Romeo A, Sinnerton R. Shoulder arthroplasty for the treatment of the sequelae of fractures of the proximal humerus. *J Shoulder Elbow Surg 2001;10-4:299-308.*

95. Handoll HH, Brorson S. Interventions for treating proximal humeral fractures in adults. *Cochrane Database Syst Rev 2015;11:CD000434.*

96. Murray IR, Amin AK, White TO, Robinson CM. Proximal humeral fractures: current concepts in classification, treatment and outcomes. *J Bone Joint Surg Br 2011;93-1:1-11.*

97. Voos JE, Dines JS, Dines DM. Arthroplasty for fractures of the proximal part of the humerus. *J Bone Joint Surg Am 2010;92-6:1560-7.*

98. Mauro CS. Proximal humeral fractures. *Curr Rev Musculoskelet Med 2011;4-4:214-20.*

99. Gupta AK, Harris JD, Erickson BJ, Abrams GD, Bruce B, McCormick F, Nicholson GP, Romeo AA. Surgical management of complex proximal humerus fractures-a systematic review of 92 studies including 4500 patients. *J Orthop Trauma 2015;29-1:54-9.*

100. Badman BL, Mighell M. Fixed-angle locked plating of two-, three-, and four-part proximal humerus fractures. *J Am Acad Orthop Surg 2008;16-5:294-302.*

101. Appleby J, Helderman JK, Gregory S. The global financial crisis, health and health care. *Health Econ Policy Law 2015;10-1:1-6.*

102. Bloom DE, Chatterji S, Kowal P, Lloyd-Sherlock P, McKee M, Rechel B, Rosenberg L, Smith JP. Macroeconomic implications of population ageing and selected policy responses. *Lancet 2015;385-9968:649-57.*

103. Kernick DP. Introduction to health economics for the medical practitioner. *Postgrad Med J 2003;79-929:147-50.*

104. Roberts A. NHS funding projections. *2015.* http://www.health.org.uk/sites/default/files/FundingOverview_NHSFundingProjections.pdf [Accessed: 1st July 2016]

105. Gainsbury S. What the Spending Review really means for the NHS. Nuffield Trust, 2015. http://www.nuffieldtrust.org.uk/blog/what-spending-review-really-means-nhs[Accessed: 1st July 2016]

106. Walshe K, Smith J. Comprehensive spending review and the NHS. *BMJ 2015;351:h6477.*

107. Kim JY, Farmer P, Porter ME. Redefining global health-care delivery. *Lancet 2013;382-9897:1060-9.*

108. Bozic KJ. Value-based healthcare and orthopaedic surgery. *Clin Orthop Relat Res 2012;470-4:1004-5.*

109. Appleby J, Devlin N, Parkin D. NICE's cost effectiveness threshold. *BMJ 2007;335-7616:358-9.*

110. Drummond MF. *Methods for the economic evaluation of health care programmes.* 3rd ed. ed. Oxford: Oxford University Press, 2005.

111. Jick H. Lifting the fog of health delivery and costs. *Pharmacotherapy 2014;34-12:1227-9.*

112. Jain NB, Kuye I, Higgins LD, Warner JJP. Surgeon Volume is Associated With Cost and Variation in Surgical Treatment of Proximal Humeral Fractures. *Clinical Orthopaedics and Related Research 2013;471-2:655-64.*

113. Thorsness R, Shields E, Iannuzzi JC, Zhang L, Noyes K, Voloshin I. Cost Drivers after Surgical Management of Proximal Humerus Fractures in Medicare Patients. *J Orthop Trauma 2015.*

114. Mercier G, Naro G. Costing hospital surgery services: the method matters. *PLoS One 2014;9-5:e97290.*

115. Akhavan S, Ward L, Bozic KJ. Time-driven Activity-based Costing More Accurately Reflects Costs in Arthroplasty Surgery. *Clin Orthop Relat Res 2016;474-1:8-15.*

116. Dixon J. Payment by results--new financial flows in the NHS. *BMJ 2004;328-7446:969-70.*

117. Kallala RF, Vanhegan IS, Ibrahim MS, Sarmah S, Haddad FS. Financial analysis of revision knee surgery based on NHS tariffs and hospital costs: does it pay to provide a revision service? *Bone Joint J 2015;97-B-2:197-201.*

118. Vanhegan IS, Malik AK, Jayakumar P, Ul Islam S, Haddad FS. A financial analysis of revision hip arthroplasty: the economic burden in relation to the national tariff. *J Bone Joint Surg Br 2012;94-5:619-23.*

119. Kaplan RS, Anderson SR. Time-driven activity-based costing. *Harv Bus Rev 2004;82-11:131-8, 50.*

120. Fjalestad T, Hole MO, Jorgensen JJ, Stromsoe K, Kristiansen IS. Health and cost consequences of surgical versus conservative treatment for a comminuted proximal humeral fracture in elderly patients. *Injury 2010;41-6:599-605.*

121. Mauskopf JA, Paul JE, Grant DM, Stergachis A. The role of cost-consequence analysis in healthcare decision-making. *Pharmacoeconomics 1998;13-3:277-88.*

122. Baltussen R, Leidl R, Ament A. Real world designs in economic evaluation. Bridging the gap between clinical research and policy-making. *Pharmacoeconomics 1999;16-5 Pt 1:449-58.*

123. Rothwell PM. Factors that can affect the external validity of randomised controlled trials. *PLoS Clin Trials 2006;1-1:e9.*

124. Bohm K, Schmid A, Gotze R, Landwehr C, Rothgang H. Five types of OECD healthcare systems: empirical results of a deductive classification. *Health Policy 2013;113-3:258-69.*

125. Ingleby D, McKee M, Mladovsky P, Rechel B. How the NHS measures up to other health systems. *BMJ 2012;344:e1079.*

126. Twiss T. Nonoperative Treatment of Proximal Humerus Fractures. In: *Proximal Humerus Fractures*: Springer, 2015:23-41.

127. Sharma P, Boyers D, Scott N, Hernandez R, Fraser C, Cruickshank M, Ahmed I, Ramsay C, Brazzelli M. The clinical effectiveness and cost-effectiveness of open mesh repairs in adults presenting with a clinically diagnosed primary unilateral inguinal hernia who are operated in an elective setting: systematic review and economic evaluation. *Health Technol Assess 2015;19-92:1-142.*

128. Freeman K, Connock M, Cummins E, Gurung T, Taylor-Phillips S, Court R, Saunders M, Clarke A, Sutcliffe P. Fluorouracil plasma monitoring: systematic review and economic evaluation of the My5-FU assay for guiding dose adjustment in patients receiving fluorouracil chemotherapy by continuous infusion. *Health Technol Assess 2015;19-91:1-322.*

129. Westwood M, Joore M, Whiting P, van Asselt T, Ramaekers B, Armstrong N, Misso K, Severens J, Kleijnen J. Epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation testing in adults with locally advanced or metastatic non-small cell lung cancer: a systematic review and cost-effectiveness analysis. *Health Technol Assess 2014;18-32:1-166.*

130. Pennington M, Grieve R, Sekhon JS, Gregg P, Black N, van der Meulen JH. Cemented, cementless, and hybrid prostheses for total hip replacement: cost effectiveness analysis. *BMJ 2013;346:f1026.*

131. Gopinath B, Harris IA, Nicholas M, Casey P, Blyth F, Maher CG, Cameron ID. A comparison of health outcomes in older versus younger adults following a road traffic crash injury: a cohort study. *PLoS One 2015;10-4:e0122732.*

132. Ossendorf C, Scheyerer MJ, Wanner GA, Simmen HP, Werner CM. Treatment of femoral neck fractures in elderly patients over 60 years of age - which is the ideal modality of primary joint replacement? *Patient Saf Surg 2010;4-1:16.*

133. Sabharwal S, Wilson H, Reilly P, Gupte CM. Heterogeneity of the definition of elderly age in current orthopaedic research. *Springerplus 2015;4:516.*

134. Mora Guix JM, Pedros JS, Serrano AC. Updated classification system for proximal humeral fractures. *Clin Med Res 2009;7-1-2:32-44.*

135. Baron JA, Karagas M, Barrett J, Kniffin W, Malenka D, Mayor M, Keller RB. Basic epidemiology of fractures of the upper and lower limb among Americans over 65 years of age. *Epidemiology 1996;7-6:612-8.*

136. Kannus P, Palvanen M, Niemi S, Parkkari J, Jarvinen M, Vuori I. Osteoporotic fractures of the proximal humerus in elderly Finnish persons: sharp increase in 1970-1998 and alarming projections for the new millennium. *Acta Orthop Scand 2000;71-5:465-70.*

137. Oxford Centre for Evidence Based Medicine. OCEMB Levels of Evidence Working Group. http://www.cebm.net/ocebm-levels-of-evidence/[Accessed: 1st July 2016]

138. Fjalestad T, Hole MO, Hovden IA, Blucher J, Stromsoe K. Surgical treatment with an angular stable plate for complex displaced proximal humeral fractures in elderly patients: a randomized controlled trial. *J Orthop Trauma 2012;26-2:98-106.*

139. Zyto K, Ahrengart L, Sperber A, Tornkvist H. Treatment of displaced proximal humeral fractures in elderly patients. *J Bone Joint Surg Br 1997;79-3:412-7.*

140. Xie L, Ding F, Zhao Z, Chen Y, Xing D. Operative versus non-operative treatment in complex proximal humeral fractures: a meta-analysis of randomized controlled trials. *Springerplus 2015;4:728.*

141. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med 2002;21-11:1539-58.*

142. West SL, Gartlehner G, Mansfield AJ, Poole C, Tant E, Lenfestey N, Lux LJ, Amoozegar J, Morton SC, Carey TC, Viswanathan M, Lohr KN. In: *Comparative Effectiveness Review Methods: Clinical Heterogeneity*. Rockville (MD), 2010.

143. Stanley K. Design of randomized controlled trials. *Circulation 2007;115-9:1164-9.*

144. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ 2009;339:b2535.*

145. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA, Cochrane Bias Methods G, Cochrane Statistical Methods G. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ 2011;343:d5928.*

146. Boons HW, Goosen JH, van Grinsven S, van Susante JL, van Loon CJ. Hemiarthroplasty for humeral four-part fractures for patients 65 years and older: a randomized controlled trial. *Clin Orthop Relat Res 2012;470-12:3483-91.*

147. Stableforth PG. Four-part fractures of the neck of the humerus. *J Bone Joint Surg Br 1984;66-1:104-8.*

148. Fjalestad T, Hole MO. Displaced proximal humeral fractures: operative versus non-operative treatment--a 2-year extension of a randomized controlled trial. *Eur J Orthop Surg Traumatol 2014;24-7:1067-73.*

149. Xu J, Zhang C, Wang T. Avascular necrosis in proximal humeral fractures in patients treated with operative fixation: a meta-analysis. *J Orthop Surg Res 2014;9:31.*

150. Patsopoulos NA. A pragmatic view on pragmatic trials. *Dialogues Clin Neurosci 2011;13-2:217-24.*

151. Wise J. Surgery is no better than a simple sling for displaced fracture of upper arm, study finds. *BMJ 2015;350:h1304.*

152. Foruria AM, de Gracia MM, Larson DR, Munuera L, Sanchez-Sotelo J. The pattern of the fracture and displacement of the fragments predict the outcome in proximal humeral fractures. *J Bone Joint Surg Br 2011;93-3:378-86.*

153. Bellomo R, Warrillow SJ, Reade MC. Why we should be wary of single-center trials. *Crit Care Med 2009;37-12:3114-9.*

154. Boutron I, Ravaud P, Nizard R. The design and assessment of prospective randomised, controlled trials in orthopaedic surgery. *J Bone Joint Surg Br 2007;89-7:858-63.*

155. Wylie JD, Beckmann JT, Granger E, Tashjian RZ. Functional outcomes assessment in shoulder surgery. *World J Orthop 2014;5-5:623-33.*

156. Haywood KL, Griffin XL, Achten J, Costa ML. Developing a core outcome set for hip fracture trials. *Bone Joint J 2014;96-B-8:1016-23.*

157. Gargon E, Williamson PR, Altman DG, Blazeby JM, Tunis S, Clarke M. The COMET Initiative database: progress and activities update (2015). *Trials 2017;18-1:54.*

158. Rangan A, Jefferson L, Baker P, Cook L. Clinical trial networks in orthopaedic surgery. *Bone Joint Res 2014;3-5:169-74.*

159. Higgins J, Green SP. *Cochrane handbook for systematic reviews of interventions.* Oxford: Wiley-Blackwell, 2008.

160. Higgins JP. Commentary: Heterogeneity in meta-analysis should be expected and appropriately quantified. *Int J Epidemiol 2008;37-5:1158-60.*

161. Jobin CM, Galdi B, Anakwenze OA, Ahmad CS, Levine WN. Reverse Shoulder Arthroplasty for the Management of Proximal Humerus Fractures. *J Am Acad Orthop Surg 2015;23-3:190-201.*

162. Cuff DJ, Pupello DR. Comparison of hemiarthroplasty and reverse shoulder arthroplasty for the treatment of proximal humeral fractures in elderly patients. *J Bone Joint Surg Am 2013;95-22:2050-5.*

163. Hush JM, Cameron K, Mackey M. Patient satisfaction with musculoskeletal physical therapy care: a systematic review. *Phys Ther 2011;91-1:25-36.*

164. Deshpande PR, Rajan S, Sudeepthi BL, Abdul Nazir CP. Patient-reported outcomes: A new era in clinical research. *Perspect Clin Res 2011;2-4:137-44.*

165. Parslow R, Patel A, Beasant L, Haywood K, Johnson D, Crawley E. What matters to children with CFS/ME? A conceptual model as the first stage in developing a PROM. *Arch Dis Child 2015;100-12:1141-7.*

166. Jones S, Hanchard N, Hamilton S, Rangan A. A qualitative study of patients' perceptions and priorities when living with primary frozen shoulder. *BMJ Open 2013;3-9:e003452.*

167. Braun V, Clarke V. What can "thematic analysis" offer health and wellbeing researchers? *Int J Qual Stud Health Well-being 2014;9:26152.*

168. Moore AJ, Blom AW, Whitehouse MR, Gooberman-Hill R. Deep prosthetic joint infection: a qualitative study of the impact on patients and their experiences of revision surgery. *BMJ Open 2015;5-12:e009495.*

169. Bardgett M, Lally J, Malviya A, Kleim B, Deehan D. Patient-reported factors influencing return to work after joint replacement. *Occup Med (Lond) 2015.*

170. Boyle MJ, Youn SM, Frampton CM, Ball CM. Functional outcomes of reverse shoulder arthroplasty compared with hemiarthroplasty for acute proximal humeral fractures. *J Shoulder Elbow Surg 2013;22-1:32-7.*

171. Schliemann B, Hartensuer R, Koch T, Theisen C, Raschke MJ, Kosters C, Weimann A. Treatment of proximal humerus fractures with a CFR-PEEK plate: 2-year results of a prospective study and comparison to fixation with a conventional locking plate. *J Shoulder Elbow Surg 2015;24-8:1282-8.*

172. Burdine JN, Felix MR, Abel AL, Wiltraut CJ, Musselman YJ. The SF-12 as a population health measure: an exploratory examination of potential for application. *Health Serv Res 2000;35-4:885-904.*

173. Blake P-L, Ali E, Reilly P, Emery R. To sleep, perchance to dream: ay, there's the rub. Shoulder and Elbow. 2012; 4-3;153-157

174. Reid KJ, Martinovich Z, Finkel S, Statsinger J, Golden R, Harter K, Zee PC. Sleep: a marker of physical and mental health in the elderly. *Am J Geriatr Psychiatry 2006;14-10:860-6.*

175. Shulman BS, Liporace FA, Davidovitch RI, Karia R, Egol KA. Sleep disturbance after fracture is related to emotional well-being rather than functional result. *J Orthop Trauma 2015;29-3:e146-50.*

176. Uchino BN, Cacioppo JT, Kiecolt-Glaser JK. The relationship between social support and physiological processes: a review with emphasis on underlying mechanisms and implications for health. *Psychol Bull 1996;119-3:488-531.*

177. Stewart MA. Effective physician-patient communication and health outcomes: a review. *CMAJ 1995;152-9:1423-33.*

178. Street RL, Jr., Makoul G, Arora NK, Epstein RM. How does communication heal? Pathways linking clinician-patient communication to health outcomes. *Patient Educ Couns 2009;74-3:295-301.*

179. AAOS. Patient-Physician Communication. *2011* http://www.aaos.org/CustomTemplates/Content.aspx?id=22278&ssopc=1. [Accessed: 1st July 2016]

180. Brorson S, Frich LH, Winther A, Hrobjartsson A. Locking plate osteosynthesis in displaced 4-part fractures of the proximal humerus. *Acta Orthop 2011;82-4:475-81.*

181. Dur M, Sadlonova M, Haider S, Binder A, Stoffer M, Coenen M, Smolen J, Dejaco C, Kautzky-Willer A, Fialka-Moser V, Moser G, Stamm TA. Health determining

concepts important to people with Crohn's disease and their coverage by patient-reported outcomes of health and wellbeing. *J Crohns Colitis 2014;8-1:45-55.*

182. Theiss MM, Ellison MW, Tea CG, Warner JF, Silver RM, Murphy VJ. The connection between strong social support and joint replacement outcomes. *Orthopedics 2011;34-5:357.*

183. Ziden L, Kreuter M, Frandin K. Long-term effects of home rehabilitation after hip fracture - 1-year follow-up of functioning, balance confidence, and health-related quality of life in elderly people. *Disabil Rehabil 2010;32-1:18-32.*

184. Tsouna-Hadjis E, Vemmos KN, Zakopoulos N, Stamatelopoulos S. First-stroke recovery process: the role of family social support. *Arch Phys Med Rehabil 2000;81-7:881-7.*

185. Baig AA, Benitez A, Quinn MT, Burnet DL. Family interventions to improve diabetes outcomes for adults. *Ann N Y Acad Sci 2015;1353-1:89-112.*

186. Raivio R, Jaaskelainen J, Holmberg-Marttila D, Mattila KJ. Decreasing trends in patient satisfaction, accessibility and continuity of care in Finnish primary health care - a 14-year follow-up questionnaire study. *BMC Fam Pract 2014;15:98.*

187. Arraras JI, Illarramendi JJ, Viudez A, Ibanez B, Lecumberri MJ, de la Cruz S, Hernandez B, Zarandona U, Cambra K, Martinez M, Salgado E, Lainez N, Vera R. Determinants of patient satisfaction with care in a Spanish oncology day hospital and its relationship with quality of life. *Psychooncology 2013;22-11:2454-61.*

188. Webster F, Bremner S, Katz J, Watt-Watson J, Kennedy D, Sawhney M, McCartney C. Patients' perceptions of joint replacement care in a changing healthcare system: a qualitative study. *Healthc Policy 2014;9-3:55-66.*

189. Germann G, Wind G, Harth A. [The DASH(Disability of Arm-Shoulder-Hand) Questionnaire--a new instrument for evaluating upper extremity treatment outcome]. *Handchir Mikrochir Plast Chir 1999;31-3:149-52.*

190. Hirschmann MT, Fallegger B, Amsler F, Regazzoni P, Gross T. Clinical longer-term results after internal fixation of proximal humerus fractures with a locking compression plate (PHILOS). *J Orthop Trauma 2011;25-5:286-93.*

191. Hosker H, Anstey K, Lowe D, Pearson M, Roberts CM. Variability in the organisation and management of hospital care for COPD exacerbations in the UK. *Respir Med 2007;101-4:754-61.*

192. Porter ME. What is value in health care? *N Engl J Med 2010;363-26:2477-81.*

193. Ford J. The NHS is facing a deepening financial crisis. *BMJ 2013;347:f4422.*

194. Nwachukwu BU, Bozic KJ, Schairer WW, Bernstein JL, Jevsevar DS, Marx RG, Padgett DE. Current status of cost utility analyses in total joint arthroplasty: a systematic review. *Clin Orthop Relat Res 2015;473-5:1815-27.*

195. Kuye IO, Jain NB, Warner L, Herndon JH, Warner JJ. Economic evaluations in shoulder pathologies: a systematic review of the literature. *J Shoulder Elbow Surg 2012;21-3:367-75.*

196. National Audit Office. Progress in making efficiency savings 2011. https://www.nao.org.uk/report/progress-in-making-nhs-efficiency-savings/[Accessed: 1st July 2016]

197. NHS England. The NHS Belongs to the people. 2013. https://www.england.nhs.uk/2013/07/call-to-action/[Accessed: 1st July 2016]

198. Briggs T. Getting it right first time. *Improving the quality of care within the NHS in England.* 2012. http://www.gettingitrightfirsttime.com/downloads/briggsreporta4_fin.pdf[Accessed: 1st July 2016]

199. AJ OC, Hanly P, Skally M, O'Neill C, Fitzpatrick P, Kapur K, Staines A, Sharp L. Cost comparisons and methodological heterogeneity in cost-of-illness studies: the example of colorectal cancer. *Med Care 2013;51-4:339-50.*

200. Spross C, Platz A, Rufibach K, Lattmann T, Forberger J, Dietrich M. The PHILOS plate for proximal humeral fractures--risk factors for complications at one year. *J Trauma Acute Care Surg 2012;72-3:783-92.*

201. Jain NB, Kuye I, Higgins LD, Warner JJ. Surgeon volume is associated with cost and variation in surgical treatment of proximal humeral fractures. *Clin Orthop Relat Res 2013;471-2:655-64.*

202. Steiner CA, Friedman B. Hospital Utilization, Costs, and Mortality for Adults With Multiple Chronic Conditions, Nationwide Inpatient Sample, 2009. *Preventing Chronic Disease 2013;10.*

203. The Kings Fund. The four UK health systems: Learning from each other. 2013. http://www.kingsfund.org.uk/sites/files/kf/field/field_publication_summary/four-uk-health-systems-jun13.pdf [Accessed: 1st July 2016]

204. Mould G, Bowers J, Ghattas M. The evolution of the pathway and its role in improving patient care. *Qual Saf Health Care 2010;19-5:e14.*

205. Mahoney FI, Barthel DW. Functional Evaluation: The Barthel Index. *Md State Med J 1965;14:61-5.*

206. Linstone HA, Turoff M. *The Delphi method : techniques and applications.* Reading, Mass. ; London: Addison-Wesley, 1975.

207. Yam CH, Wong EL, Cheung AW, Chan FW, Wong FY, Yeoh EK. Framework and components for effective discharge planning system: a Delphi methodology. *BMC Health Serv Res 2012;12:396.*

208. Keen DV, Fonseca S, Wintgens A. Selective mutism: a consensus based care pathway of good practice. *Arch Dis Child 2008;93-10:838-44.*

209. Schmitt J, Langan S, Stamm T, Williams HC. Core outcome domains for controlled trials and clinical recordkeeping in eczema: international multiperspective Delphi consensus process. *J Invest Dermatol 2011;131-3:623-30.*

210. Alexandrov AV, Pullicino PM, Meslin EM, Norris JW. Agreement on disease-specific criteria for do-not-resuscitate orders in acute stroke. Members of the Canadian and Western New York Stroke Consortiums. *Stroke 1996;27-2:232-7.*

211. NHS Careers. Agenda for change - pay rates. 2013. http://www.nhscareers.nhs.uk/working-in-the-nhs/pay-and-benefits/agenda-for-change-pay-rates/ [Accessed: 1st July 2016]

212. NHS Employers. Pay and Conditions (2014). 2014. http://www.nhsemployers.org/~/media/Employers/Publications/Pay[Accessed: 1st July 2016]

213. Ockert B, Siebenburger G, Kettler M, Braunstein V, Mutschler W. Long-term functional outcomes (median 10 years) after locked plating for displaced fractures of the proximal humerus. *J Shoulder Elbow Surg 2014;23-8:1223-31.*

214. NHS England. 2014/15 National Tariff Payment System. 2014. https://www.england.nhs.uk/resources/resources-for-ccgs/ccg-out-tool/ccg-ois/qual-prem/ [Accessed: 1st July 2016]

215. Fordyce A. Operating Theatre Efficiency Improvements using Operations Management Science. NHS Institute for Innovation and Improvement 2007.

216. The Kings Fund. The NHS under the coalition government. 2015. http://www.kingsfund.org.uk/publications/nhs-performance-under-coalition-government [Accessed: 1st July 2016]

217. Kaplan RS. Improving value with TDABC. *Healthc Financ Manage 2014;68-6:76-83.*

218. Basch E, Torda P, Adams K. Standards for patient-reported outcome-based performance measures. *JAMA 2013;310-2:139-40.*

219. Dawson J, Doll H, Boller I, Fitzpatrick R, Little C, Rees J, Jenkinson C, Carr AJ. The development and validation of a patient-reported questionnaire to assess outcomes of elbow surgery. *J Bone Joint Surg Br 2008;90-4:466-73.*

220. Suzuki M, Kurimoto S, Shinohara T, Tatebe M, Imaeda T, Hirata H. Development and validation of an illustrated questionnaire to evaluate disabilities of the upper limb. *J Bone Joint Surg Br 2010;92-7:963-9.*

221. Mahomed NN, Davis AM, Hawker G, Badley E, Davey JR, Syed KA, Coyte PC, Gandhi R, Wright JG. Inpatient compared with home-based rehabilitation following primary unilateral total hip or knee replacement: a randomized controlled trial. *J Bone Joint Surg Am 2008;90-8:1673-80.*

222. Jenkins PJ, Clement ND, Hamilton DF, Gaston P, Patton JT, Howie CR. Predicting the cost-effectiveness of total hip and knee replacement: a health economic analysis. *Bone Joint J 2013;95-B-1:115-21.*

223. NICE. Guide to the methods of technology appraisal. *2013.* http://www.nice.org.uk/article/pmg9/chapter/foreword [Accessed: 1st July 2016]

224. Hearnden A, Tennent D. The cost of shoulder arthroscopy: a comparison with national tariff. *Ann R Coll Surg Engl 2008;90-7:587-91.*

225. The Kings Fund. Emergency bed use: what the numbers tell us. 2011. http://www.kingsfund.org.uk/sites/files/kf/data-briefing-emergency-bed-use-what-the-numbers-tell-us-emmi-poteliakhoff-james-thompson-kings-fund-december-2011.pdf [Accessed: 1st July 2016]

226. Mason SE, Nicolay CR, Darzi A. The use of Lean and Six Sigma methodologies in surgery: A systematic review. *Surgeon 2014.*

227. Donovan CJ, Hopkins M, Kimmel BM, Koberna S, Montie CA. How Cleveland Clinic used TDABC to improve value. *Healthc Financ Manage 2014;68-6:84-8.*

228. Cram P. CORR Insights: Time-driven Activity-based Costing More Accurately Reflects Costs in Arthroplasty Surgery. *Clin Orthop Relat Res 2015.*

229. The Kings Fund. How is the NHS performing? *2015.* *http://qmr.kingsfund.org.uk/2015/16/* [Accessed: 1st July 2016]

230. Guy P, Slobogean GP, McCormack RG. Treatment preferences for displaced three- and four-part proximal humerus fractures. *J Orthop Trauma 2010;24-4:250-4.*

231. Bastian JD, Hertel R. Osteosynthesis and hemiarthroplasty of fractures of the proximal humerus: outcomes in a consecutive case series. *J Shoulder Elbow Surg 2009;18-2:216-9.*

232. Sebastia-Forcada E, Cebrian-Gomez R, Lizaur-Utrilla A, Gil-Guillen V. Reverse shoulder arthroplasty versus hemiarthroplasty for acute proximal humeral fractures. A blinded, randomized, controlled, prospective study. *J Shoulder Elbow Surg 2014;23-10:1419-26.*

233. National Joint Registry. National Joint Registry 13th Annual Report *2016.* http://www.njrcentre.org.uk/njrcentre/Reports,PublicationsandMinutes/Annualreports/tabid/86/Default.aspx [Accessed: 3rd March 2017]

234. Torjesen I. Two thirds of NHS trusts forecast a deficit this year, up from a quarter last year. *BMJ 2015;351:h3670.*

235. Wei DH, Hawker GA, Jevsevar DS, Bozic KJ. Improving Value in Musculoskeletal Care Delivery: AOA Critical Issues. *J Bone Joint Surg Am 2015;97-9:769-74.*

236. Murray DW, MacLennan GS, Breeman S, Dakin HA, Johnston L, Campbell MK, Gray AM, Fiddian N, Fitzpatrick R, Morris RW, Grant AM, group KAT. A

randomised controlled trial of the clinical effectiveness and cost-effectiveness of different knee prostheses: the Knee Arthroplasty Trial (KAT). *Health Technol Assess 2014;18-19:1-235, vii-viii.*

237. Ramsey S, Willke R, Briggs A, Brown R, Buxton M, Chawla A, Cook J, Glick H, Liljas B, Petitti D, Reed S. Good research practices for cost-effectiveness analysis alongside clinical trials: the ISPOR RCT-CEA Task Force report. *Value Health 2005;8-5:521-33.*

238. Edwards RT, Hounsome B, Linck P, Russell IT. Economic evaluation alongside pragmatic randomised trials: developing a standard operating procedure for clinical trials units. *Trials 2008;9:64.*

239. Theivendran K, Hassan S, Tambe A, Cresswell T, Clark DI. Not all patients with displaced proximal humerus fractures are suitable for sling treatment. *BMJ 2015;350:h1669.*

240. Commonwealth Fund. International profiles of health care systems, 2013 : Australia, Canada, Denmark, England, France, Germany, Italy, Japan, the Netherlands, New Zealand, Norway, Sweden, Switzerland and the United States. http://www.commonwealthfund.org/~/media/Files/Publications/Fund%20Report/2013/Nov/1717_Thomson_intl_profiles_hlt_care_sys_2013_v2.pdf [Accessed: 1st July 2016]

241. Philips Z, Bojke L, Sculpher M, Claxton K, Golder S. Good practice guidelines for decision-analytic modelling in health technology assessment: a review and consolidation of quality assessment. *Pharmacoeconomics 2006;24-4:355-71.*

242. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, Augustovski F, Briggs AH, Mauskopf J, Loder E, Force IHEEPG-CGRPT. Consolidated Health Economic Evaluation Reporting Standards (CHEERS)--explanation and elaboration: a report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force. *Value Health 2013;16-2:231-50.*

243. Neumann Jv, Morgenstern, Morgenstern O. *Theory of Games and Economic Behavior.* Princeton: Princeton University Press, 1944.

244. Ledley RS, Lusted LB. Reasoning foundations of medical diagnosis; symbolic logic, probability, and value theory aid our understanding of how physicians reason. *Science 1959;130-3366:9-21.*

245. Buxton MJ. Economic evaluation and decision making in the UK. *Pharmacoeconomics 2006;24-11:1133-42.*

246. Keith MW, Masear V, Amadio PC, Andary M, Barth RW, Graham B, Chung K, Maupin K, Watters WC, 3rd, Haralson RH, 3rd, Turkelson CM, Wies JL, McGowan R. Treatment of carpal tunnel syndrome. *J Am Acad Orthop Surg 2009;17-6:397-405.*

247. Hoen B, Bonnet F, Delaugerre C, Delobel P, Goujard C, L'Henaff M, Persiaux R, Rey D, Rouzioux C, Taburet AM, Morlat P, French HIVeg. French 2013 guidelines for antiretroviral therapy of HIV-1 infection in adults. *J Int AIDS Soc 2014;17:19034.*

248. NICE. Guide to the methods of technology appraisal 2013. https://www.nice.org.uk/article/pmg9/resources/non-guidance-guide-to-the-methods-of-technology-appraisal-2013-pdf [Accessed: 1st July 2016]

249. OCEBM. Explanation of the 2011 Oxford Centre for Evidence-Based Medicine (OCEBM) Levels of Evidence. http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009 [Accessed: 1st July 2016]

250. Besch L, Daniels-Wredenhagen M, Mueller M, Varoga D, Hilgert RE, Seekamp A. Hemiarthroplasty of the shoulder after four-part fracture of the humeral head: a long-term analysis of 34 cases. *J Trauma 2009;66-1:211-4.*

251. Torgerson DJ, Raftery J. Economic notes. Discounting. *BMJ 1999;319-7214:914-5.*

252. Cai M, Tao K, Yang C, Li S. Internal fixation versus shoulder hemiarthroplasty for displaced 4-part proximal humeral fractures in elderly patients. *Orthopedics 2012;35-9:e1340-6.*

253. Jost B, Spross C, Grehn H, Gerber C. Locking plate fixation of fractures of the proximal humerus: analysis of complications, revision strategies and outcome. *J Shoulder Elbow Surg 2013;22-4:542-9.*

254. Hussey MM, Hussey SE, Mighell MA. Reverse shoulder arthroplasty as a salvage procedure after failed internal fixation of fractures of the proximal humerus: outcomes and complications. *Bone Joint J 2015;97-B-7:967-72.*

255. Street A, Gutacker N, Bojke C, Devlin N, Daidone S. In: *Variations in outcome and costs among NHS providers for common surgical procedures: econometric analyses of routinely collected data*. Southampton (UK), 2014.

256. Whitehead SJ, Ali S. Health outcomes in economic evaluation: the QALY and utilities. *Br Med Bull 2010;96:5-21.*

257. Neumann PJ, Zinner DE, Wright JC. Are methods for estimating QALYs in cost-effectiveness analyses improving? *Med Decis Making 1997;17-4:402-8.*

258. Sprague S, Bhandari M. An economic evaluation of early versus delayed operative treatment in patients with closed tibial shaft fractures. *Arch Orthop Trauma Surg 2002;122-6:315-23.*

259. Coe MP, Greiwe RM, Joshi R, Snyder BM, Simpson L, Tosteson AN, Ahmad CS, Levine WN, Bell JE. The cost-effectiveness of reverse total shoulder arthroplasty compared with hemiarthroplasty for rotator cuff tear arthropathy. *J Shoulder Elbow Surg 2012;21-10:1278-88.*

260. Brauer CA, Rosen AB, Olchanski NV, Neumann PJ. Cost-utility analyses in orthopaedic surgery. *J Bone Joint Surg Am 2005;87-6:1253-9.*

261. Clement ND, Court-Brown CM. Oxford shoulder score in a normal population. *Int J Shoulder Surg 2014;8-1:10-4.*

262. Blomquist J, Solheim E, Liavaag S, Schroder CP, Espehaug B, Havelin LI. Shoulder instability surgery in Norway: the first report from a multicenter register, with 1-year follow-up. *Acta Orthop 2012;83-2:165-70.*

263. Stinnett AA, Mullahy J. Net health benefits: a new framework for the analysis of uncertainty in cost-effectiveness analysis. *Med Decis Making 1998;18-2 Suppl:S68-80.*

264. The NHS in England: blue sky aspirations and earthly tremors. *Lancet 2015;386-10001:1311.*

265. Chambers L, Dines JS, Lorich DG, Dines DM. Hemiarthroplasty for proximal humerus fractures. *Curr Rev Musculoskelet Med 2013;6-1:57-62.*

266. Ham C. The three crises facing the NHS in England. *BMJ 2015;351:h5495.*

267. Weintraub WS, Cohen DJ. The limits of cost-effectiveness analysis. *Circ Cardiovasc Qual Outcomes 2009;2-1:55-8.*

268. Byford S, Raftery J. Perspectives in economic evaluation. *BMJ 1998;316-7143:1529-30.*

269. Sabharwal S, Carter A, Darzi LA, Reilly P, Gupte CM. The methodological quality of health economic evaluations for the management of hip fractures: A systematic review of the literature. *Surgeon 2015;13-3:170-6.*

270. Brooks R. EuroQol: the current state of play. *Health Policy 1996;37-1:53-72.*

271. Sintonen H. The 15D instrument of health-related quality of life: properties and applications. *Ann Med 2001;33-5:328-36.*

272. Stavem K, Froland SS, Hellum KB. Comparison of preference-based utilities of the 15D, EQ-5D and SF-6D in patients with HIV/AIDS. *Qual Life Res 2005;14-4:971-80.*

273. Briggs A, Sculpher M. An introduction to Markov modelling for economic evaluation. *Pharmacoeconomics 1998;13-4:397-409.*

274. Stahl JE. Modelling methods for pharmacoeconomics and health technology assessment: an overview and guide. *Pharmacoeconomics 2008;26-2:131-48.*

275. Hayes B. First Links in the Markov Chain. *American Scientist 2013;101-2:92-7.*

276. Briggs AH, Claxton K, Sculpher MJ. *Decision modelling for health economic evaluation.* Oxford: Oxford University Press, 2006.

277. Brennan A, Chick SE, Davies R. A taxonomy of model structures for economic evaluation of health technologies. *Health Econ 2006;15-12:1295-310.*

278. Clarke A, Pulikottil-Jacob R, Grove A, Freeman K, Mistry H, Tsertsvadze A, Connock M, Court R, Kandala NB, Costa M, Suri G, Metcalfe D, Crowther M, Morrow S, Johnson S, Sutcliffe P. Total hip replacement and surface replacement for the treatment of pain and disability resulting from end-stage arthritis of the hip (review of technology appraisal guidance 2 and 44): systematic review and economic evaluation. *Health Technol Assess 2015;19-10:1-668, vii-viii.*

279. Vale L, Wyness L, McCormack K, McKenzie L, Brazzelli M, Stearns SC. A systematic review of the effectiveness and cost-effectiveness of metal-on-metal hip resurfacing arthroplasty for treatment of hip disease. *Health Technol Assess 2002;6-15:1-109.*

280. Spiegl UJ, Faucett SC, Horan MP, Warth RJ, Millett PJ. The role of arthroscopy in the management of glenohumeral osteoarthritis: a Markov decision model. *Arthroscopy 2014;30-11:1392-9.*

281. Weinstein MC, O'Brien B, Hornberger J, Jackson J, Johannesson M, McCabe C, Luce BR, Studies ITFoGRP--M. Principles of good practice for decision analytic modeling in health-care evaluation: report of the ISPOR Task Force on Good Research Practices--Modeling Studies. *Value Health 2003;6-1:9-17.*

282. Neuhaus V, Swellengrebel CHJ, Bossen JKJ, Ring D. What are the Factors Influencing Outcome Among Patients Admitted to a Hospital With a Proximal Humeral Fracture? *Clinical Orthopaedics and Related Research 2013;471-5:1698-706.*

283. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, Augustovski F, Briggs AH, Mauskopf J, Loder E, Force CT. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. *BMJ 2013;346:f1049.*

284. Timmins N. The four UK health systems. The Kings Fund, 2013. http://www.kingsfund.org.uk/publications/four-uk-health-systems-june-2013[Accessed: 1st July 2016]

285. World Bank. World Bank Indicators. 2015. http://blogs.worldbank.org/opendata/category/tags/news [Accessed: 1st July 2016]

286. Antuna SA, Sperling JW, Cofield RH. Shoulder hemiarthroplasty for acute fractures of the proximal humerus: a minimum five-year follow-up. *J Shoulder Elbow Surg 2008;17-2:202-9.*

287. Office for National Statistics. National Life Tables, United Kingdom, 2011-2013. 2014. http://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/lifeexpectancies/bulletins/nationallifetablesunitedkingdom/2014-09-25 [Accessed: 1st July 2016]

288. Park C, Jang S, Lee A, Kim HY, Lee YB, Kim TY, Ha YC. Incidence and mortality after proximal humerus fractures over 50 years of age in South Korea: national claim data from 2008 to 2012. *J Bone Metab 2015;22-1:17-21.*

289. Olsson C, Petersson C, Nordquist A. Increased mortality after fracture of the surgical neck of the humerus: a case-control study of 253 patients with a 12-year follow-up. *Acta Orthop Scand 2003;74-6:714-7.*

290. Public Health England. Recent Trends in Life Expectancy at Older Ages. 2015. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/403477/Recent_trends_in_life_expectancy_at_older_ages.pdf [Accessed: 1st July 2016]

291. The Kings Fund. Ageing Population. 2015. http://www.kingsfund.org.uk/time-to-think-differently/trends/demography/ageing-population [Accessed: 1st July 2016]

292. Knickman JR, Snell EK. The 2030 problem: caring for aging baby boomers. *Health Serv Res 2002;37-4:849-84.*

293. Ravi B, Jenkinson R, Austin PC, Croxford R, Wasserstein D, Escott B, Paterson JM, Kreder H, Hawker GA. Relation between surgeon volume and risk of complications after total hip arthroplasty: propensity score matched cohort study. *BMJ 2014;348:g3284.*

294. Khan SK, Weusten A, Bonczek S, Tate A, Port A. The Best Practice Tariff helps improve management of neck of femur fractures: a completed audit loop. *Br J Hosp Med (Lond) 2013;74-11:644-7.*

295. Rosas S, Law TY, Kurowicki J, Formaini N, Kalandiak SP, Levy JC. Trends in surgical management of proximal humeral fractures in the Medicare population: a nationwide study of records from 2009 to 2012. *J Shoulder Elbow Surg 2015.*

296. Wang J, Zhu Y, Zhang F, Chen W, Tian Y, Zhang Y. Meta-analysis suggests that reverse shoulder arthroplasty in proximal humerus fractures is a better option than hemiarthroplasty in the elderly. *Int Orthop 2015.*

297. Schairer WW, Nwachukwu BU, Lyman S, Craig EV, Gulotta LV. Reverse shoulder arthroplasty versus hemiarthroplasty for treatment of proximal humerus fractures. *J Shoulder Elbow Surg 2015;24-10:1560-6.*

298. The Kings Fund. The NHS Under the Coalition Government: Part Two. *2015. http://www.kingsfund.org.uk/sites/files/kf/field/field_publication_file/the-nhs-under-the-coalition-government-nhs-performance-kings-fund-mar15.pdf* [Accessed: 1st July 2016]

299. Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, Carpenter J, Rucker G, Harbord RM, Schmid CH, Tetzlaff J, Deeks JJ, Peters J, Macaskill P, Schwarzer G, Duval S, Altman DG, Moher D, Higgins JP. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ 2011;343:d4002.*

300. Schmid CH, Stark PC, Berlin JA, Landais P, Lau J. Meta-regression detected associations between heterogeneous treatment effects and study-level, but not patient-level, factors. *J Clin Epidemiol 2004;57-7:683-97.*

301. Robinson JC, Pozen A, Tseng S, Bozic KJ. Variability in costs associated with total hip and knee replacement implants. *J Bone Joint Surg Am 2012;94-18:1693-8.*

302. Birkmeyer JD, Finks JF, O'Reilly A, Oerline M, Carlin AM, Nunn AR, Dimick J, Banerjee M, Birkmeyer NJ, Michigan Bariatric Surgery C. Surgical skill and complication rates after bariatric surgery. *N Engl J Med 2013;369-15:1434-42.*

303. Guyatt G, Montori V, Devereaux PJ, Schunemann H, Bhandari M. Patients at the center: in our practice, and in our use of language. *ACP J Club 2004;140-1:A11-2.*

304. Sudkamp N, Bayer J, Hepp P, Voigt C, Oestern H, Kaab M, Luo C, Plecko M, Wendt K, Kostler W, Konrad G. Open reduction and internal fixation of proximal humeral fractures with use of the locking proximal humerus plate. Results of a prospective, multicenter, observational study. *J Bone Joint Surg Am 2009;91-6:1320-8.*

305. Robinson CM, Amin AK, Godley KC, Murray IR, White TO. Modern perspectives of open reduction and plate fixation of proximal humerus fractures. *J Orthop Trauma 2011;25-10:618-29.*

306. Ellwood S, Chambers N, Llewellyn S, Begkos C, Wood C. Debate: Achieving the benefits of patient-level costing-open book or can't look? *Public Money & Management 2015;35-1:69-70.*

307. Fjalestad T, Iversen P, Hole MO, Smedsrud M, Madsen JE. Clinical investigation for displaced proximal humeral fractures in the elderly: a randomized study of two surgical treatments: reverse total prosthetic replacement versus angular stable plate Philos (The DELPHI-trial). *BMC Musculoskelet Disord 2014;15:323.*

308. Pennington MW, Grieve R, van der Meulen JH. Lifetime cost effectiveness of different brands of prosthesis used for total hip arthroplasty: a study using the NJR dataset. *Bone Joint J 2015;97-B-6:762-70.*

309. Heintzbergen S, Kulin NA, Ijzerman MJ, Steuten LM, Werle J, Khong H, Marshall DA. Cost-utility of metal-on-metal hip resurfacing compared to conventional total hip replacement in young active patients with osteoarthritis. *Value Health 2013;16-6:942-52.*

Appendix 1:
Data Collection Sheets for Meta-Analytical Study

Study Number	1
Title	Surgical vs Nonsurgical Treatment of Adults With Displaced Fractures of the Proximal Humerus The PROFHER Randomized Clinical Trial
Authors	Rangan A, Handoll H, Brealey S, Jefferson L, Keding A, Martin BC, Goodchild L, Chuang LH, Hewitt C, Torgerson D; PROFHER Trial Collaborators.
Country	United Kingdom
Journal	Journal of the American Medical Association (JAMA)
Year	2015
DOI	10.1001/jama.2015.1629.
Design	RCT
Single/Multicentre	Multicentre
Methods	September 2008 – April 2011 (2.5 years) 32 acute NHS Trusts Power calculation based on a 5 point difference on OSS (**ES** 0.4 80% **P** 5% **SL**) – **moderate effect size** Randomisation with independent remote randomisation service. No blinding of participants, clinicians or assessors. Independent data entry, processing and analysis.. Loss to follow up 19
Fracture classification	Neer
Exclusion criteria	Dislocation, open fracture, insufficient mental capacity, co-morbidities precluding surgery, clear indication for surgery such as soft tissue compromise, multiple injuries, pathological fracture, terminal illness, not resident in catchment area.
Sample size	250
Participants	Patients > 16 years Fractures < 3 weeks old Displacement of fracture (not by Neer criteria)
Interventions	Surgical intervention: plate fixation or hemiarthroplasty Non-surgical intervention: sling for 3 weeks followed by physiotherapy Both groups received information leaflets for physiotherapy and inpatient, outpatient or community setting physiotherapy.
Outcomes	Primary outcome: Oxford Shoulder Score (OSS). Collected at 6, 12 and 24 months. Secondary outcomes: 1. SF-12 at 6, 12 , 24 months 2. Complications 3. Complications requiring reoperation 4. Medical complications 5. EuroQol at 3, 6, 12, 24 months

Results	Primary outcome **(OSS)** **6M S** 37.07 **NS** 35.59 **P** 0.06 **12M S** 39.23 **NS** 38.80 **P** 0.71 **24M S** 40.11 **NS** 40.40 **P** 0.80 Secondary Outcomes **SF 12 physical 24 months** **S** 45.68 **NS** 44.20 **P** 0.33 **SF 12 mental 24 months** **S** 49.30 **NS** 50.69 **P** 0.35
Notes/Complications	30/125 (24%) surgical patients had a complication 11/125 (8.8%) surgical patients had a revision procedure within 2 years 119/250 Neer 2 part 11/250 Neer 4 part 90/109 Plate and screws 10/109 Hemiarthroplasty 9/109 Other Mean age approximately 65 years.
Risk of bias	
Random sequence generation (selection bias)	Low risk. "…research associates randomly allocated patients to surgical or nonsurgical treatment using an independent remote randomization "service (telephone or online access) provided by the York Trials Unit (University of York). "Randomization was performed using a computer program with 1:1 allocation, stratifying by tuberosity involvement (yes or no) and using random block sizes of 4, 8, and 12."
Allocation concealment (Selection bias)	Low risk. See above.
Blinding of outcome assessment (Performance bias)	High risk. "There was no blinding of trial participants, clinicians, or assessment of outcomes"
Blinding of outcome assessment –PROMS, pain, clinical outcomes, complications(Detection bias)	High risk. See above
Blinding of outcomes –death, reoperation (Detection bias)	High risk. See above
Incomplete outcome data (Attrition bias)	Low risk. A full account of reasons for loss to follow up was provided and loss to follow up was less than 10%.
Incomplete outcome data (Attrition bias)	Low risk. See above.
Selective reporting (Reporting bias)	Low risk. The outcomes in the protocol were those presented in the trial results.
Other bias/study problems	The study sought to evaluate and compare surgical treatment of displaced proximal humerus fractures in adults. They adopted the Neer

	Classification, however stated that "The degree of displacement had to be sufficient for the treating surgeon to consider surgical intervention but did not have to meet the displacement criteria of Neer". The majority of fractures were 2/3 part. The majority of patients were elderly and the vast majority of surgery was fixation. Whether the studies should inform decision making on younger patients, more comminuted fractures/fractures that meet Neer's displacement criteria or hemiarthroplasty in the elderly remains unclear.
Study Number	**2**
Title	Hemiarthroplasty for Humeral Four-part Fractures for Patients 65 Years and Older
Authors	Boons HW, Goosen JH, van Grinsven S, van Susante JL, van Loon CJ.
Country	Netherlands
Journal	Clinical Orthopaedics and Related Research (CORR)
Year	2012
DOI	10.1007/s11999-012-2531-0
Design	RCT
Single/Multicentre	Single
Methods	June 2005 – June 2009 (5 years) hospital in The Netherlands Power calculation based on 15 point difference on CMS with 80% power and 5%SL **(Large effect size)** Computer generated randomisation system used No mention of patient, clinician or assessor blinding No mention of independent data entering, monitoring or analysis Loss to follow up 3 patients (2 unwell, 1 died unrelated causes)
Fracture classification	Neer
Exclusion criteria	Pre-existing mental health or cognitive problems, additional trauma to arm, pathological or open fracture, neurovascular injury, pre-existing contralateral shoulder problem, lack of fluency in dutch, unable to participate in rehab, ASA >2.
Sample size	50
Participants	Patients ≥65 Fracture < 1 week old Displaced 4 part proximal humerus fractures Displacement by Neer Criteria
Interventions	Surgical intervention: Hemiathroplasty (cemented) with suture fixation of tuberosities Non-surgical: Shoulder immobilizer for 6 weeks Both groups underwent the same rehabilitation protocol. Light passive ROM from 2 weeks. 45degress passive FF and ABD from 2 – 6 weeks. ER restricted for 6 weeks.
Outcomes	Primary outcome: Constant Murray Score (CMS): collected at 3 and 12 months

	Secondary outcomes (also at 3 and 12 months): 1. Shoulder Strength Test (STT) 2. Abduction strength 3. VAS for pain and disability 4. ROM *Data on complications and reoperation*
Results	Primary outcome (CMS) 3M S 48 NS 54 P 0.125 12M S 64 (15.8) NS 60 (17.6) P 0.413 Secondary outcomes VAS pain 3M S 19 NS 37 P 0.002 12M S 23 NS 25 P 0.725 SST 3M S 41 NS 48 P 0.209 12M S 25 NS 23 P 0.592 ABD Strength 3M S 20 NS 30 P 0.015 12M S24 NS 42 P 0.008
Notes/Complications	Non operative group: Osteonecrosis 2/23, 3/23 non-union, 1/23 had operation at 13 months for pain from non-union. Operative group: 1/24 had revision 1 week post-surgery due to head stem separation, mal-positioning of GT in 4/24, superior migration of GT in 5/24 at 12 months, 1/24 proximal migration of hemiarthroplasty, non-union in 2/24.
Risk of bias	
Random sequence generation (selection bias)	Low risk. "A computer-generated variable block schedule was used for randomization of the 50 patients to either hemiarthroplasty (n = 25) or nonoperative treatment (n = 25)."
Allocation concealment (Selection bias)	Low risk. "The randomization list was generated by an independent statistician and the resulting treatment allocations were stored in sealed opaque envelopes in the statistician's room"
Blinding of outcome assessment (Performance bias)	High risk. No mention of blinding.
Blinding of outcome assessment –PROMS, pain, clinical outcomes, complications (Detection bias)	High risk. No mention of blinding.
Blinding of outcomes –death, reoperation (Detection bias)	High risk. No mention of blinding.
Incomplete outcome data (Attrition bias)	Low risk. A full account of incomplete outcome data was described and it only accounts for 3/50 patients with 2 in intervention group and 1 in the control group.

Incomplete outcome data (Attrition bias)	Low risk. See above.
Selective reporting (Reporting bias)	Low risk. The authors investigated the outcomes described in the methods.
Other bias/study problems	1. The sample size is small and the study is only sufficiently powered to detect a larger effect size. The possibility of type II error for moderate-small effect size is present. 2. This is a single centre study. The question of institutional procedural performance and its effect on intervention outcomes arises. Moreover the authors describe 13/25 undesirable surgical outcomes in the intervention group.
Study Number	**3a**
Title	Surgical Treatment With an Angular Stable Plate for Complex Displaced Proximal Humeral Fractures in Elderly Patients: A Randomized Controlled Trial
Authors	Fjalestad T, Hole MØ, Hovden IA, Blücher J, Strømsøe K
Country	Norway
Journal	Journal of Orthopaedic Trauma
Year	2012
DOI	10.1097/BOT.0b013e31821c2e15
Design	Randomised controlled trial
Single/Multicentre	Single
Methods	May 2003 to May 2008 (5 years) at a hospital in Norway Power calculation "Constant score was used to calculate power and sample size with the software nQuery Advisor 4.0 (Statistical Solutions Ltd, Cork, UK). To detect a difference in mean Constant score of 26 points, with a 5% significance level and 25 patients in each group, resulted in a power of 72%". Randomization was from a computer program. No mention of clinician or patient blinding. Independent assessors were not blinded to treatment.
Fracture classification	Neer
Exclusion criteria	"1) younger than 60 years old; 2) history of injury or illness of the injured or contralateral shoulder; 3) injuries of other parts of the humerus or the contralateral upper extremity; 4) alcohol or drug abuse; 5) dementia; 6) neurologic diseases; or 7) severe cardiovascular diseases that would contraindicate surgery. Patients of non-Scandinavian ethnicity were also excluded to reduce possible bias from differences in bone mineral content given the high incidence of osteoporosis in Scandinavians"
Sample size	50
Participants	1. Patients ≥60 2. Type 3/4 Neer fracture 3. Displacement between shaft and head could be not more than 50% shaft diameter 4. Fracture age not specified however all patients had surgery within 1 week

Interventions	Surgical patients had a fixation with a fixed angle locking plate. Conservative patients – some actually had a closed reduction under GA if the shaft head displacement was > 50%. (23 patients – 2 died) Rehab: Surgical – passive rom after 3 days. Active rom after 3 weeks. Strengthening exercises after 6 weeks. (25 patients, 1 was ITT) Conservative – passive Rom after 2 weeks. Active ROM after 5 weeks. Strengthening exercises after 6 weeks.
Outcomes	Primary outcome measure: Constant Murray Score (CMS) at 3, 6 and 12 months Secondary outcome measures: 1. American Shoulder and Elbow Society (ASES) form at 6 and 12 months 2. Radiographic results at 2, 8, 26 and 52 weeks (authors created their own rating system)
Results	Primary outcome (CMS) 12 M S 52.3 (20.9) C 52.2 (18.3) P = 0.99 Secondary outcome ASES 12M S 14.8 C 15.5 P 0.71 Other Surgical 8/23 developed AVN Conservative 13/25 developed AVN (1 was ITT) Conservative 2/25 had non unions Surgical 1/23 need re-operation because of metal work failure at 6 months 1/25 conservative need surgery at 2 weeks because of further displacement
Notes/Complications	8/25 conservative patients had a closed reduction under GA
Risk of bias	
Random sequence generation (Selection bias)	Low risk. Computer programme used.
Allocation concealment (Selection bias)	Low risk. Selection and allocation from non-translucent envelopes.
Blinding of outcome assessment (Performance bias)	High risk. Not performed
Blinding of outcome assessment –PROMS, pain, clinical outcomes, complications (Detection bias)	High risk. Not performed
Blinding of outcomes –death, reoperation (Detection bias)	High risk. Not performed
Incomplete outcome data (Attrition bias)	Low risk. Loss of follow up or cross over described and intention to treat analysis performed.

Incomplete outcome data (Attrition bias)	Low risk. Loss of follow up or cross over described and intention to treat analysis performed.
Selective reporting (Reporting bias)	Low risk. The authors investigated the outcomes described in the methods.
Other bias/study problems	1. Single centre 2. Type II error risk; small sample size 3. Patients had a closed reduction under GA in conservative group
Study Number	**3b**
Title	Health and cost consequences of surgical versus conservative treatment for a comminuted proximal humeral fracture in elderly patients
Authors	Fjalestad T, Hole MØ, Jørgensen JJ, Strømsøe K, Kristiansen IS.
Country	Norway
Journal	Injury
Year	2010
DOI	10.1016/j.injury.2009.10.056
Design	RCT
Single/Multicentre	Single centre
Methods	May 2003 to May 2008 (5 years) at a hospital in Norway Power calculation "Constant score was used to calculate power and sample size with the software nQuery Advisor 4.0 (Statistical Solutions Ltd, Cork, UK). To detect a difference in mean Constant score of 26 points, with a 5% significance level and 25 patients in each group, resulted in a power of 72%". Randomization was from a computer program. No mention of clinician or patient blinding. Independent assessors were not blinded to treatment.
Fracture classification	Neer
Exclusion criteria	"1) younger than 60 years old; 2) history of injury or illness of the injured or contralateral shoulder; 3) injuries of other parts of the humerus or the contralateral upper extremity; 4) alcohol or drug abuse; 5) dementia; 6) neurologic diseases; or 7) severe cardiovascular diseases that would contraindicate surgery. Patients of non-Scandinavian ethnicity were also excluded to reduce possible bias from differences in bone mineral content given the high incidence of osteoporosis in Scandinavians"
Sample size	50
Participants	1. Patients ≥60 2. Type 3/4 Neer fracture 3. Displacement between shaft and head could be not more than 50% shaft diameter 4. Fracture age not specified however all patients had surgery within 1 week
Interventions	Surgical patients had a fixation with a fixed angle locking plate. Conservative patients – some actually had a closed reduction under GA if the shaft head displacement was > 50%. (23 patients – 2 died) Rehab: Surgical – passive rom after 3 days. Active rom after 3 weeks. Strengthening exercises after 6 weeks. (25 patients, 1 was ITT)

	Conservative – passive Rom after 2 weeks. Active ROM after 5 weeks. Strengthening exercises after 6 weeks.
Outcomes	Primary 15 D Instrument (HRQol) at baseline, 3, 6, 12 months Costs
Results	15D 3M S 0.814 (0.062) C 0.817 (0.074) 6M S 0.836 (0.083) C 0.817 (0.088) 12M S 0.841 (0.105) C 0.819 (0.083) p = 0.436
Notes/Complications	
Risk of bias	
Random sequence generation (Selection bias)	Low risk. Computer programme used.
Allocation concealment (Selection bias)	Low risk. Selection and allocation from non-translucent envelopes.
Blinding of outcome assessment (Performance bias)	High risk. Not performed
Blinding of outcome assessment –PROMS, pain, clinical outcomes, complications (Detection bias)	High risk. Not performed
Blinding of outcomes –death, reoperation (Detection bias)	High risk. Not performed
Incomplete outcome data (Attrition bias)	Low risk. Loss of follow up or cross over described and intention to treat analysis performed.
Incomplete outcome data (Attrition bias)	Low risk. Loss of follow up or cross over described and intention to treat analysis performed.
Selective reporting (Reporting bias)	Low risk. The authors investigated the outcomes described in the methods.
Other bias/study problems	1. Single centre 2. Type II error risk; small sample size 3. Patients had a closed reduction under GA in conservative group
Study Number	**4**
Title	Hemiarthroplasty versus nonoperative treatment of displaced 4-part proximal humeral fractures in elderly patients: a randomized controlled trial
Authors	Olerud P, Ahrengart L, Ponzer S, Saving J, Tidermark J.
Country	Sweden
Journal	Journal of Shoulder and Elbow Surgery
Year	2011
DOI	10.1016/j.jse.2011.04.016
Design	RCT

Single/Multicentre	Single
Methods	April 2003 and June 2008 (approximately 5 years) hospital in Sweden No sample size estimation performed Randomisation procedure not described Blinding not described for clinician, patient or assessor
Fracture classification	Neer
Exclusion criteria	1. High energy trauma 2.Previous ipisilateral shoulder problems 3.institutionlisation 4. Severe cognitive dysfunction
Sample size	55
Participants	1. ≥55 2. 4 part fractures 3. See exclusion criteria
Interventions	Surgery: Cemented hemiarthroplasty with suture fixation of tuberosities. Sling for 6 weeks. Pendular and passive ROM abduction to 90 from day. Free ROM from 6 weeks. Strengthening exercised from 3 months. post op. Conservative: Sling for 6 weeks. Pendular and passive ROM abduction at 2 weeks. Free active ROM from 6 weeks.
Outcomes	Primary outcome EuroQol-5D 4, 12 , 24 months Secondary outcomes 1. CMS 4, 12, 24 months 2. DASH 4, 12, 24 months Complications
Results	Primary outcome Eq-5D 4 M S 0.69 C 0.59 12M S 0.73 C 0.66 24M S 0.81 C 0.65 ($p < 0.05$) Secondary outcomes CMS 4 M S 36 C 41.4 P = 0.21 12M S 48.9 C 47.7 P = 0.76 24M S 48.3 C 49.6 P = 0.81 DASH 4M S 42.8 C 41.5 P 0.92 12M S 32 C 35 P 0.71 24M S 30.2 C 36.9 P 0.25
Notes/Complications	Complications In Surgical reoperation in 3/27 in surgical group within 2 years. 1 was a locking plate included as ITT. 1 had an acromioplasty and capsular release. 1 had a reduction and fixation of the GT. 0 infection/nerve injury

	In Conservative 1/28 had hemi after 1 month because of further displacement. 1/28 non union. 3/28 had AVN. 5/28 had post traumatic OA.
Risk of bias	
Random sequence generation (Selection bias)	High risk. Randomisation procedure not described.
Allocation concealment (Selection bias)	High risk. Randomisation procedure not described.
Blinding of outcome assessment (Performance bias)	High risk. Not performed.
Blinding of outcome assessment –PROMS, pain, clinical outcomes, complications(Detection bias)	High risk. Not performed.
Blinding of outcomes –death, reoperation (Detection bias)	High risk. Not performed.
Incomplete outcome data (Attrition bias)	Low risk. Loss of follow up described. Intention to treat analysis performed.
Incomplete outcome data (Attrition bias)	Low risk. Loss of follow up described. Intention to treat analysis performed.
Selective reporting (Reporting bias)	Low risk. Outcomes of interest in methods were reported.
Other bias/study problems	1. Single centre 2. Sample size not calculated 3. Randomisation not described
Study Number	**5**
Title	Internal fixation versus nonoperative treatment of displaced 3-part proximal humeral fractures in elderly patients: a randomized controlled trial
Authors	Olerud P, Ahrengart L, Ponzer S, Saving J, Tidermark J.
Country	Sweden
Journal	Journal of Shoulder and Elbow Surgery
Year	2011
DOI	10.1016/j.jse.2010.12.018
Design	RCT
Single/Multicentre	Single
Methods	April 2003 and March 2008 (5 years) one hospital in Sweden Sample size calculation not performed Randomisation procedure not described Blinding not described for clinician, patient or assessor
Fracture classification	Neer
Exclusion criteria	1.complete shaft head displacement 2.valgus impacted fracture

Sample size	60
Participants	1. ≥ 55 2. 3 part fracture 3. Low energy trauma 4. No previous shoulder problems 5. Independent living
Interventions	Surgery: Philos plate for all patients. Tuberosity fractures fixed with no absorbable suture. Post op sling for 4 weeks. Pendular exercises from day 1. Free active ROM from week 4. Conservative. Sling for 2 weeks. Pendular exercises after 2 weeks with passive elevation/abduction to 90. After 4 weeks free active ROM.
Outcomes	Primary Outcome EQ-5D (HRQol) (4,12,24 months) Secondary Outcome (4,12,24 months) 1. CMS 2. DASH Score Complications
Results	Primary Outcome (27 available at 2 years for surgery, 26 for conservative) EQ-5D 4M S 0.71(0.27) C 0.61(0.23) 12M S 0.74(0.24) C 0.65 (0.28) 24M S0.70 (0.34) C 24(0.35) Secondary Outcome CMS 4M S 52.3 (14.3) C 48.8 (16.3) P = 0.48 12M S 61.5(18.4) C 56.8 (16.8) P = 0.18 24M S61 (19.2) C 58.4(23.1) P = 0.64 DASH 4M S 36.2 (22.4) C 35.7 (20.1) P = 0.85 12M S 29.1 (23.3) C 35.1 (24.2) P = 0.32 24M S 26.4(25.2) C 35.0 (26.8) P = 0.19
Notes/Complications	Complications Surgery: AVN in 3 patients (3/27), 9/27 had reoperation at 2 years. Surgery for deep infection 2/9. Surgery for non union 1/9. Surgery for impingement 1/9. Surgery for stiffness 3/9. Surgery for AVN 2/9 Conservative: Non union 1/26. AVN 2/26. OA 1/26. Reoperation for impingement 1/26. Axillary nerve palsy 1/26 **Overall mortality rate at 2 years is 7%.**
Risk of bias	

Random sequence generation (Selection bias)	High risk. Randomisation procedure not described.
Allocation concealment (Selection bias)	High risk. Randomisation procedure not described.
Blinding of outcome assessment (Performance bias)	High risk. Not performed.
Blinding of outcome assessment –PROMS, pain, clinical outcomes, complications(Detection bias)	High risk. Not performed.
Blinding of outcomes –death, reoperation (Detection bias)	High risk. Not performed.
Incomplete outcome data (Attrition bias)	Low risk.
Incomplete outcome data (Attrition bias)	Low risk. Loss of follow up described. Intention to treat analysis performed.
Selective reporting (Reporting bias)	Low risk. Loss of follow up described. Intention to treat analysis performed.
Other bias/study problems	1. Single centre 2. Sample size not calculated 3. Randomisation not described
Study Number	**6**
Title	Treatment of displaced proximal humeral fractures in elderly patients
Authors	Zyto K, Ahrengart L, Sperber A, Törnkvist H.
Country	Sweden
Journal	Journal of Bone and Joint Surgery (British Volume)
Year	1997
DOI	none
Design	RCT
Single/Multicentre	Single
Methods	Patients seen at the Huddinge University Hospital in Stockholm from April 1990 to February 1993 (3 years) Sample size calculation not performed Randomisation poorly described “randomised by sealed envelope into either a surgical or conservative treatment group” Blinding not described for clinician, patient or assessor
Fracture classification	Neer
Exclusion criteria	1. High energy trauma 2. Pathological fractures 3. < 30% contact between shaft and head 4. Other fractures 5. Concomitant disease likely to effect treatment

	6. Patient ability to cooperate
Sample size	40
Participants	1. All adult patients 2. ¾ part fractures
Interventions	Surgical: Tension band wiring procedure. Same post op physio as conservative Conservative: Sling for 7 – 10 days then physion
Outcomes	Primary outcome (follow up 3 – 5 years) CMS at 50 months Secondary outcomes Complications Subjective assessment
Results	CMS At 50 months S 60 (19) C 65 (15) Complications Surgery: AVN (1/14), Deep infection (1/14), non-union (1/14), OA (2/14), PE (1/14), K wire penetration 1/14 Conservative : OA (2/15),
Notes/Complications	As above
Risk of bias	
Random sequence generation (Selection bias)	High risk. Randomisation procedure poorly described.
Allocation concealment (Selection bias)	High Risk. Randomisation procedure poorly described
Blinding of outcome assessment (Performance bias)	High risk. Not performed
Blinding of outcome assessment –PROMS, pain, clinical outcomes, complications (Detection bias)	High risk. Not performed
Blinding of outcomes –death, reoperation (Detection bias)	High risk not performed.
Incomplete outcome data (Attrition bias)	High risk. 27.5 % of patients were lost to follow up.
Incomplete outcome data (Attrition bias)	High risk. 27.5 % of patients were lost to follow up.
Selective reporting (Reporting bias)	Low risk. Description of reasons for loss of follow up provided.
Other bias/study problems	1. Procedure not commonly performed 2. Small sample size and no power calculation

	3. Outcomes assessment was not at uniform times 4. Large proportion of patients lost to follow up 5. Single centre study
Study Number	**7 (EXCLUDED because of conservative management)**
Title	Transcutaneous reduction and external fixation of displaced fractures of the proximal humerus. A controlled clinical trial.
Authors	Kristiansen B, Kofoed H.
Country	Denmark
Journal	Journal of Bone and Joint Surgery (British Volume)
Year	1988
DOI	none
Design	RCT
Single/Multicentre	Single
Methods	Time frame not described Method of randomisation not described Sample size calculation not performed Blinding not described Loss to follow up 10/31
Fracture classification	Neer
Exclusion criteria	Not stated
Sample size	31
Participants	30 patients with 31 displaced 2-, 3- and 4-part proximal humeral fractures
Interventions	Surgery: Percutaneous reduction and external fixation Conservative: Closed manipulation under GA and sling
Outcomes	Primary Functional outcome with Neer score at 3, 6, 12 months Secondary Complications
Results	Primary Neer At 12 months S 60 C 79 Complications Surgery: Infection (1/15), Reoperation (1/15), Pseudoarthrosis (1/15) Conservative: Nonunion (4/16), refracture (1/16), AVN (2/16)
Notes/Complications	As above
Risk of bias	
Random sequence generation (Selection bias)	High risk. Not described.

Allocation concealment (Selection bias)	High risk. Not described.
Blinding of outcome assessment (Performance bias)	High risk. Not described.
Blinding of outcome assessment –PROMS, pain, clinical outcomes, complications (Detection bias)	High risk. Not described.
Blinding of outcomes –death, reoperation (Detection bias)	High risk. Not described.
Incomplete outcome data (Attrition bias)	High risk. Large loss to follow up.
Incomplete outcome data (Attrition bias)	High risk. Participant flow provided.
Selective reporting (Reporting bias)	Unclear risk.
Other bias/study problems	1. Small study 2. Outdated treatment technique 3. Single centre 4. Large loss of follow up 5. Randomisation poorly described
Study Number	**8**
Title	Four part fractures of the neck of the humerus
Authors	PG Stableforth
Country	United Kingdom
Journal	Journal of Bone and Joint Surgery (British volume)
Year	1984
DOI	none
Design	RCT
Single/Multicentre	Single
Methods	1970 to 1981 (11 years) at Bristol Royal Infirmary Method of randomisation not described Sample size calculation not performed Blinding not described
Fracture classification	Neer
Exclusion criteria	Impacted or minimally displaced
Sample size	32
Participants	All adult patients
Interventions	Surgery: Hemiarthroplasty with Neer Prosthesis Conservative: Closed manipulation Both wore sling and started physio after 2-3 days

Outcomes	Activities of daily living ROM Complications
Results	Surgery: Deep infection (1/16) , Revision (1/16)
Notes/Complications	
Risk of bias	
Random sequence generation (Selection bias)	High risk not described
Allocation concealment (Selection bias)	High risk not described
Blinding of outcome assessment (Performance bias)	High risk. Not blinded
Blinding of outcome assessment –PROMS, pain, clinical outcomes, complications (Detection bias)	High risk not blinded,
Blinding of outcomes –death, reoperation (Detection bias)	Unclear risk.
Incomplete outcome data (Attrition bias)	High risk large loss of follow up
Incomplete outcome data (Attrition bias)	Unclear risk
Selective reporting (Reporting bias)	Unclear risk
Other bias/study problems	Small study Randomisation not described Single centre PROMS not used

Appendix 2:
Qualitative Study Documentation

Ethics Approval Documentation

NHS
Health Research Authority

National Research Ethics Service

NRES Committee London - Hampstead
Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

Telephone: 0161 625 7815
Fax: 0161 625 7299

12 December 2014

Mr Sanjeeve Sabharwal
15 Bedford Road
Moor Park
HA6 2BA

Dear Mr Sabharwal

Study title:	**Exploring and contrasting the elderly patient's experience of care after surgical and non-surgical treatment for a proximal humerus fracture: a comparative-qualitative study.**
REC reference:	**14/LO/2191**
Protocol number:	**Version 1, 30.08.2014**
IRAS project ID:	**164392**

The Research Ethics Committee reviewed the above application at the meeting held on 10 December 2014. Thank you for attending to discuss the application.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager Dr Ashley Totenhofer, nrescommittee.london-hampstead@nhs.net.

Ethical opinion

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below. .

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on question 2 of the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS Sites

The favourable opinion applies to all NHS sites taking part in the study taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Summary of discussion at the meeting

Social or scientific value; scientific design and conduct of the study

The committee queried if the study would involve patients who have had an arm or shoulder fracture.

You stated they would have had a shoulder fracture; the proximal humerus refers to the part of the shoulder nearest to the arm.

The committee noted that the participants in this study would all be elderly patients and commented that may have memory or mobility issues and queried how this would be dealt with.

You stated the two consultants involved in the study would be responsible for their clinical care and they know these patients quite well as they attend fairly frequently. You are looking to cover a range of injuries and outcomes so will consider each patient before making a clinical decision whether they are capable of participating before inviting them.

The committee queried if the decision of surgery or not was through choice or random.

You stated it is down to the clinician's judgement; part of the aim of this study is to see why outcomes are what they are.

Favourable risk benefit ratio; anticipated benefit/risks for research participants (present and future)

The committee noted that the application referred to the fact that participants may become distressed by the interview and this is not an uncommon occurrence.

You stated that unfortunately quite a few patients will have had a bad experience and so may become distressed when they recall it.

The committee queried what would happen if a participant disclosed any situation where confidentiality may need to be broken such as harm to themselves or others or malpractice.

You stated if it involved harm to them and was an ongoing risk you would escalate it to your supervisors. You would only break confidentiality if it was necessary. If it involved any malpractice you would discuss this with the research team as it should be reported.

Other ethical issues were raised and resolved in preliminary discussion before your attendance at the meeting

The committee commented that it is very reassuring to see an orthopaedic surgeon who is interested in a holistic outcome for patients rather than just whether the bone is healed.

The committee noted that the researcher had answered their queries regarding the assessment of capacity, patient injuries and potential misconduct satisfactorily.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Arthur J Gallagher International]		21 July 2014
Interview schedules or topic guides for participants [Interview prompt sheet]	1	30 August 2014
Letter from sponsor [Imperial College]		17 November 2014
Letters of invitation to participant	1	30 August 2014
Other [Case report form]	1	30 August 2014
Participant consent form	1	30 August 2014
Participant information sheet (PIS)	1	30 August 2014
REC Application Form	3.5	18 November 2014
Research protocol or project proposal	1	30 August 2014
Summary CV for Chief Investigator (CI) [Sanjeeve Sabharwal]		17 November 2014
Summary CV for supervisor (student research) [Chimnay Gupte]		13 November 2014
Summary CV for supervisor (student research) [Peter Reilly]		10 November 2014
Summary CV for supervisor (student research) [Stephanie Archer]		10 November 2014

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

14/LO/2191	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

Signed on behalf of:
Miss Stephanie Ellis
Chair

E-mail: nrescommittee.london-hampstead@nhs.net

Enclosures:	*List of names and professions of members who were present at the meeting and those who submitted written comments*
	"After ethical review – guidance for researchers"
Copy to:	Ms Christine Buicke - AHSC Joint Research Compliance Office , Imperial College

Patient Information Letter

Imperial College Healthcare NHS Trust

Imperial College London

Mr Sanjeeve Sabharwal
Department of Orthopaedics
Ground Floor Salton House
South Wharf Road
St Mary's Hospital London
W2 1NY
Tel: 07939447204

Patient Information Sheet

Patient Perspectives After A Shoulder Fracture

Version 1 30.08.2015

Principal/Chief Investigator: Mr Sanjeeve Sabharwal

Co-Investigators: Mr Peter Reilly, Mr Chinmay Gupte, Mr Dylan Griffiths, Dr Stephanie Archer

Introduction

You are being invited to take part in a research study. Before you decide whether to participate it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish.

Part 1 tells you the purpose of this study and what will happen to you if you take part. **Part 2** gives you more detailed information about the conduct of the study

Please ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Part 1: Purpose of the study

The purpose of our study is to better understand how patients who have had a shoulder fracture treated with or without an operation felt about their treatment and recovery. Listening to and exploring your experiences will be helpful in better understanding how treatments are helping you and what difficulties you have had that doctors should try and help with in the future.

Part 2: Study Conduct

Why have I been chosen?

You have been chosen for this study because you are 65 years or older and had a shoulder fracture which was managed at Imperial College NHS Trust. We are interested in interviewing patients such as yourself a year after their injury to better understand their experience of care and recovery. There will be between 16 and 20 patients in the study.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. If you have taken part in the interview you can still withdraw from the study. The information collected during the interview will still be used for the research analysis, however no further information will be sought from you. A decision not to take part, will not affect the standard of care you receive to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive. If you wish to withdraw from the study please contact the principle investigator. Contact details are provided at the end of this information sheet.

What will happen to me if I take part?

Patients who have a shoulder fracture that are managed by Imperial College NHS Trust are often treated and followed up by the shoulder specialists at the trust, Mr Peter Reilly and Mr Dylan Griffiths. We commonly see patients for up to a year after the fracture has occurred in their clinics at St Mary's Hospital in Paddington. If you have an existing follow up appointment and are interested in participation in the study please contact our research team. We will arrange a time to sit down and discuss the study in more detail after your clinic appointment and answer any questions you may have. If you are willing to participate in the study we will ask you to sign a study consent form and proceed with the interview. You will be interviewed by the principle study investigator (Sanjeeve Sabharwal). The interview will last approximately 45 minutes and will be recorded on an audiotape. Notes will also be taken by the investigator during the interview. Much of the interview will involve open ended questions like 'tell me about your experience after the operation and how it made you feel?', however specific questions like ' did you have any trouble with sleep' may be also be asked by the interviewer. After the interview is completed you will be free to leave the clinic and your outpatients follow up with Mr Reilly or Griffiths will be organised if required.

In cases where you have already been discharged from outpatient care you invited back to the outpatient clinic at St Mary's Hospital t conduct the interview at a time that Mr Reilly or Griffiths is conducting their normal outpatient clinic. The interview process will be identical to that described above. If you have any existing concerns

related to your shoulder on the day of the interview, one of the consultants will be available to talk to you and organise appropriate clinical review if it is required.

What do I have to do?

You can eat, drink and take all medications normally during this study and as such there are no life style restrictions required. The only inconvenience to you is the time required to participate in the interview to better understand your experience of the injury and your recovery

What are the possible disadvantages and risks of taking part?

The only disadvantage of this study is the inconvenience of time required to participate in the interview after your clinic appointment or attend the hospital for the interview if you have already been discharged from outpatient follow up. There are no side effects of the study because there are no drugs, medical devices or other types of treatment being tested. You may become upset discussing or remembering your injury during the interview. If this happens the interview will be stopped and your clinical care team will speak to you and decide whether it is in your interest to continue in the study.

What are the benefits of taking part?

Your participation in the study may help us better understand a patients experience after suffering a shoulder fracture and as a result improve our treatment of this injury in the future. It is unlikely that there will be any direct benefit to you, however if there are any ongoing problems related to your injury that are reported by you at the time of the interview or identified by the investigator, we will discuss this with one of the shoulder specialists in the clinic and arrange appropriate care for you.

What happens if the research study stops?

If the research study stops unexpectedly we will inform you by letter of this. All data will be stored securely and if there is no expectation of the study restarting, then this data will be destroyed. Since no benefit to you will be derived directly from this study, we will not contact you any further beyond this, unless it is for routine hospital follow-up appointments.

What if something goes wrong?

Imperial College London holds insurance policies which apply to this study. If you experience serious and enduring harm or injury as a result of taking part in this study, you may be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation. If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator

(sanjeeve.sabharwal@imperial.nhs.uk). The normal National Health Service complaints mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial AHSC Joint Research Compliance Office.

Will my taking part in this study be kept confidential?

Only members of the research team who are involved in your clinical care will know of your participation in the study. These include Mr Peter Reilly or Mr Dylan Griffiths as well as their research registrar, Mr Sanjeeve Sabharwal. At the start of the interview you will be given a pseudonym which will be then be used to identify all the information gathered in the interview and used in subsequent analysis. This information will be stored on password protected NHS computers. Trust policy is to store this data for 10 years.

What will happen to the results of the research study?

This research will form part of the principal investigators post graduate research thesis. Our aim would be to publish the results of the study, but there would be no participant identifiable data in the publication.

Who is organising & funding the research?

The research is sponsored by Imperial College London. The study is being funded by one of the investigators, Mr Peter Reilly None of the researchers are being paid to perform this research.

What if new information becomes available?

If any new information becomes available during the study that may affect your condition or recovery you will be informed of this. You will be asked if you wish to continue in the study. I you wish to withdraw from the study this will not affect the care you are receiving for your injury.

Who has reviewed this study?

This study has been reviewed by the Joint Research Office based at Imperial College and Research Ethics Committee.

Contact for further information

The contact person for this study if you have any queries is myself the principal investigator in this study: Sanjeeve Sabharwal, orthopaedic registrar, contact 07939447204, sanjeeve.sabharwal@imperial.nhs.uk.

Other research team members

Mr Dylan Griffiths, Consultant Orthopaedic Surgeon, Imperial College NHS Trust

Mr Chinmay Gupte , Consultant Orthopaedic Surgeon, Imperial College NHS Trust

Dr Stephanie Archer, Postdoctoral Scientist and Chartered Psychologist, Imperial College

Mr Peter Reilly, Consultant Orthopaedic Surgeon, Imperial College NHS Trust

Thank you for taking part in this study. You will be given a copy of this patient information sheet and the signed consent form for the research

Patient Consent Form

Imperial College Healthcare NHS Trust

Imperial College London

Mr Sanjeeve Sabharwal
Department of Orthopaedics
Ground Floor Salton House
South Wharf Road
St Mary's Hospital London
W2 1NY
Tel: 07939447204

CONSENT FORM

Patient Perspectives After A Shoulder Fracture

Version 1, 30.08.2015

Study Identification Number for this trial:

Name of Researchers: Mr Sanjeeve Sabharwal, Mr Peter Reilly, Mr Chinmay Gupte, Mr Dylan Griffiths, Dr Stephanie Archer

Please initial each box to indicate you have read the statement:

1. I confirm that I have read and understand the Patient Information Sheet version 21 dated 30/08/2014 for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary, and that I am free to withdraw at any time without giving any reason without my medical care, education or legal rights being affected. ☐

3. I understand that any interview I take part in will be audio recorded. ☐

4. I understand that my personal data will be kept confidential and that all information collected for the research will be stored securely at Imperial College NHS Trust on a password protected database. Only the research team have access to this. ☐

5. I agree to take part in the above named study ☐

Name of subject	Date	Signature

Name of person taking consent	Date	Signature

Example of Transcripts Used For Analysis

Transcript: UM Patient 1
Date: 11 December 2015

PageSix
Transcription Services

[0:00:00]

Interviewer: So it's the 13 April 2014, so for the purpose of the study we need to allocate you a pseudonym, so a name that's not your name that we can refer to for the purpose of this dictation and refer back to it.

Respondent: Which will (inaudible 0:00:22).

Interviewer: Yeah what will be your preference in terms of what we could call you for the sake of this interview?

Respondent: Choose a name.

Interviewer: Shall we call you Mr U?

Respondent: Yes why not.

Interviewer: Mr U. Okay. So we've done the consent process, and I'm going to start with questions now, so tell me a bit about what happened to you.

Respondent: Well I was resulting the resort with my with my grandchildren skiing in Switzerland, and we left a cabin that we arrived down to the village and I asked them if I could carry the skis you see, and then I slipped on a piece of ice and then I went and luckily a huge piece of ice and it stopped me before going any further.

Interviewer: Yeah.

Respondent: So that was the case that helped me – saved me but made me this injury.

Interviewer: Okay.

Respondent: So I went straight away to see one of the doctors there, and was very – well its better not to mention anything and he told me that I had to straight and come back straight away to London, so to get that train and so on, and I did it the following morning, and then I came here and I was better treated than there of course, and...

Interviewer: That's (inaudible 0:01:52).

Respondent: Yes.

Interviewer: And...

Respondent: Like this.

Interviewer: Yeah because you're the one who's going to be speaking the most and I just make sure that we're getting everything you're saying. Okay carry on.

Respondent: Well and then I started your treatment, and then I saw (I don't know the name of the doctor) but a doctor, and then I felt alltight and I don't remember if I had – was I just with (what do they call it)...

Interviewer: Yeah this is the bandage.

Respondent: Well no maybe something else...

Interviewer: A sling.

Respondent: A sling or something, but it hurt at the beginning with the exercises that I had and I went downstairs to the gym to do the treatment they had in there, and I still do a few exercises that they told me to do

every day, and now I am feeling fine accept that I had problems in writing, and before I used to be able to touch my fingers, but not anymore.

[0:03:06]

Interviewer: So you could reach behind your back?

Respondent: Yes maybe because ....

Interviewer: And is that something that troubles you very much, or is that something...?

Respondent: Well you get used to it. You have to accept it. — feels a need to accept condition

Interviewer: So you were seen oversees whilst you was on holiday and then you came back here and you was seen here?

Respondent: Yes straight away because the way it was treated in Switzerland and can you believe in Switzerland.

Interviewer: Yeah. ↳ disbelief at poor care

Respondent: It's not as you imagine anyway when this happens, and also I had to pay a lot of money because they wouldn't see me otherwise. — disbelief that care was based on money

Interviewer: Okay, and when you came here what was the experience of the decision making process?

Respondent: Well it seemed, and there was a younger blonde doctor and she was very kind, and she gave me strength to accept it the problem I had, and then it came once a week or so, and then went back to normal. Satisfaction with appearance — Satisfaction with behaviour

↳ she gave me strength - happy with supportive role

Interviewer: Okay.

Respondent: 80% let's say or 90.

Interviewer: And in the immediate days and weeks after you had that injury in Switzerland what was the thoughts that was going through your mind, and what were the experiences that you found were difficult for you.

Respondent: Well I was thinking to be more careful in the future because it was getting – I think it was eight years ago or something – no eight or seven, and never again going to ski or whatever. — anxiety, need to be careful — need to be careful anxiety.

Interviewer: And how do you feel that you've responded to the treatment so far?

Respondent: Fine.

Interviewer: Yeah you're happy with it?

Respondent: Yes. And the treatment was very good and I'm very pleased, and the way they treated me. ? fucking/ behaviour attitude.

Interviewer: Good. And what about the sort of rehab, the physiotherapy and what was the positives and negatives to take away from that?

Respondent: Everything positive.

Interviewer: Yes?

Respondent: Yes, oh yes.

Interviewer: No difficulties at all with the exercises?

[0:05:13]

Respondent: Well of course but then became better and better every day it was passing by.

Interviewer: And how are you now, tell me about the shoulder and the difficulties?

Respondent: I'm aware of what happened and I'll just have to be careful not to carry heavy weight with this arm, but I'm doing okay.

Interviewer: What, if anything, troubles you the most about your shoulder at the moment?

Respondent: Nothing else.

Interviewer: You feel fine?

Respondent: Yeah.

Interviewer: Okay. In terms of pain in the immediate aftermath of your injury, so in Switzerland tell me a bit about that pain?

Respondent: Well I couldn't sleep because of the pain in the first two or three days that is, and also when I came here I felt better mentally as well because I realised that I was treated the proper way and then that helped to accept the pain.

Interviewer: And how long did you experience the pain for after the injury?

Respondent: I can't remember - It's not on the system?

Interviewer: No that's fine, we're just trying to get as much from you as possible, but that's okay.

Respondent: Few weeks.

Interviewer: Okay a few weeks, and what about use of the arm what were your experiences in the immediate aftermath, so the first few weeks of things that you couldn't do that troubled you?

Respondent: Well luckily I had my wife who helps me and helped me quite well, and that solved the problem.

Interviewer: Were there any particular things such as dressing yourself?

Respondent: Oh yes of course, and to be careful not to make the wrong movements and so on.

Interviewer: And what about sleep was you waking up at all during the night?

Respondent: Occasionally because also I had a problem with the heart, and my consultant here is at this hospital, and he suggested that I should sleep on this side, and when I sleep for quite a long time I feel a little bit, so I had to go on the other side, but otherwise it's okay.

Interviewer: Okay.

Respondent: Do you feel it yourself occasionally if you sleep on this?

Interviewer: I don't to be honest, but that doesn't that you don't feel it and that's perfectly fine. And do you think that you had any problems with your mood at all, and were you feeling particularly low or do you think that you (inaudible 0:07:52).

Respondent: No, because I trust the people – your colleagues and so on, and that helps a lot in my case.

Interviewer: And what factors do you think inspired that trust and why is it that you felt that we were more trusted?

Respondent: Because they welcomed the first time. Like this very jolly young doctor, and as I explained what happened, and as I explained to you about the way I was treated in Switzerland and then it helped me along to carry on and to accept what I was going through.

Interviewer: What were the particular difficulties that you've had since the fall if you don't mind me asking?

Respondent: Well the attitude you see of this doctor, and they treated you just like you were the next one, and in the line.

Interviewer: So you felt like you were a product rather than a person?

Respondent: Yes, but also before seeing me he wanted me to pay, and that upset me quite a lot. The sooner the better and I walked out on him and we left there straight away the following morning, and then everything happened.

Interviewer: And when you come here and everything had been explained to you, did you have any concerns about the long-term affect that that injury would have on your quality of life or things that you like doing?

Respondent: Well I accepted it at my age as I'm 78, so it's fine for me.

Interviewer: So you're quite pragmatic and realised that it didn't matter that much. Okay.

Respondent: As (Socrates says it had to happen, so we had to accept it.

Interviewer: And were you working at the time of the injury at all?

Respondent: When was it – no I retired in 2002, and just a consultant.

Interviewer: Yeah.

Respondent: Where I was.

Interviewer: So there wasn't a concern about money or employment or anything like that?

Respondent: No.

Interviewer: And in the year after you had the injury, the entire year, did you need a lot of help or do you think it was only for a few weeks that you needed some help?

Respondent: I'd been having my wife who was very helpful.

Interviewer: Yeah what sort of things was she doing for you?

Respondent: Well just happily to do everything that I couldn't do.

Interviewer: If you can remember tell me about a normal day that you would have in the weeks and months after the injury, and how you'd wake-up and what you'd go through and what sort of things, so just a few things that she would do for you?

Respondent: Like normal things, and she helped me to wash when I couldn't wash and maybe having a shower or a bath, and put a jacket on in the proper way because it was all – I couldn't move this part of the body, but life went on because luckily we didn't go to work and we had plenty of time to organise ourselves.

Interviewer: What about eating and feeding was that okay?

[0:10:57]

Respondent: Well she helped me to cut because I couldn't use the left hand.

Interviewer: Okay.

Respondent: It didn't make an exception on my life.

Interviewer: Were you worried about going out at all or did you have any difficulty going out or going on the bus?

Respondent: No. Well I got used to it. Well taking more care of course, and afraid of falling but otherwise life went on.

Interviewer: And did you have any particular activities at all and any things that you like doing that...?

Respondent: Like reading and listening to music and walking.

Interviewer: So there wasn't that much of an effect on you?

Respondent: No.

Interviewer: And you said you still have some difficult with writing is that right?

Respondent: Yes. Well I don't know why but I have to do it like this because...

Interviewer: So you have to adjust in some holding?

Respondent: Yes, and sometimes I get...

Interviewer: Tremor?

Respondent: Yes.

Interviewer: Okay.

Respondent: But of course maybe it's my age or something. Like it's something on the way. Nothing to be sure now since.

Interviewer: And if I was to say to you that if you had this injury again and there was a choice between having an operation and not having an operation, and the difference was slight.

Respondent: I wouldn't have it.

Interviewer: You wouldn't have an operation?

Respondent: No. I would accept what happened.

Interviewer: Yeah.

Respondent: I will adjust myself.

Interviewer: So if you think of your normal activities at home, so the things you normally do, what things if I said, 'Those things would stop if you didn't have an operation' what things would you value the most and saying okay I'll have an operation?

Respondent: Don't you give me a list?

Interviewer: No this is from your own – so think about your life and think about...

[0:13:07]

Respondent: The problem is I don't drive any longer.

Interviewer: And you haven't driven since the injury?

Respondent: No.

Interviewer: A long time?

Respondent: About 10 years or so because I don't it when I'm here, and when I go abroad I have somebody else who takes care of me.

Interviewer: So at the moment you have recovered very well, and it's...

Respondent: Well I'm quite happy except as I mentioned when I had to write or I have to remember not to carry heavy things and that's fine.

Interviewer: Okay, and is there anything else that you think you want to mention about the injury or your recovery that you think was a bit different from your perspective or you think is worse?

Respondent: No I just said that I put a trust in you as this girl she gave me and all the others followed her, and I don't remember the name of the Head of the Department who saw me first and then he passed me on to the other and very kind people, and they were fond of inter-Milan and so it gave me somebody to talk about soccer even if I don't, as I'm a rugby man, but that helps to be friendly and take care of the patients.

Interviewer: Having an inter-personal connection.

Respondent: Yeah that's very important.

Interviewer: Okay.

Respondent: Well it helps and in my case and to make it stronger or something, and it helps to recover.

Interviewer: That's excellent and I think we've got mostly everything.

Respondent: And what about others like my case, have they gone through the same thing?

Interviewer: We've been through what patients experience and the sort of things that people highlight are things like getting dressed, feeding themselves.

Respondent: Well in the beginning of course for the first few, but I don't know how many weeks I had to (inaudible 0:15:07) and the years to come, and as they say making exercises down in the basement, and I know if you hear somewhere how further along.

Interviewer: I think it's here actually there's a physiotherapy department downstairs.

Respondent: Downstairs maybe yes. So there you had a good people. Very young, but they do their job properly.

Interviewer: And I think the other thing that people complained about a lot is sleep, sleep is a big problem for a lot of patients in the months after the injury, and a lot of people have been...

Respondent: Not as much.

Interviewer: Not as much for you. Everyone is different. Everyone's response and it's about understanding that spectrum of people.

welcoming staff
appearance of staff

Respondent: They've helped you (inaudible 0:15:47), but a welcome is very important. In my case the welcome I had here when I came and I met this young and she was a very nice blonde doctor, and that helped me, and I think a way of getting all of the others to follow, and they helped to recover in the proper way.

[0:16:10]

Interviewer: Okay that's interesting, so in terms of your treatment and your recovery you valued the inter-personal relationship you had with the doctors and the department, and that was a measure of how you felt about how you were doing?

Respondent: Yes.

Interviewer: Okay.

Respondent: If you consider that we think in Switzerland it's good... they have got their hand in every accident and find out, and I hope not. Have you ever been there?

Interviewer: No I haven't, but someone was trying to sell a chalet and ended up going on holiday there.

Respondent: They are just trying to grab at your money and nothing else.

Interviewer: Okay I'll stop that.

[End of Transcript]

1. initially avoiding criticism.
2. perception of treatment as better
3. accepting disability.
4. disbelief at poor care
5. perception of staff and satisfaction based on appearance
6. " " " " " " " behaviour
7. " " " " " " being supportive
8. need to be more careful
9. percpn of staff based on welcoming / behaviour
10. help from family important
11. getting worked.
12. getting read
13. pain
14. sleep.
15. feels lucky

Appendix 3:
Cost Analysis Documents and Data

Questionnaire used for staff interviews

Professional job description:
Name:
Date:
Assessment in emergency room
1. Are you routinely involved in this care component?
2. If so what is your function?
3. Please estimate your time commitment to this function.
4. Please list expected consumables you would require to provide care.
5. Please make any additional comments you would like regarding this care component.
Patient arrives in ward
1. Are you routinely involved in this care component?
2. If so what is your function?
3. Please estimate your time commitment to this function.
4. Please list expected consumables you would require to provide care.
5. Please make any additional comments you would like regarding this care component.
Patient awaiting surgery
1. Are you routinely involved in this care component?
2. If so what is your function?
3. Please estimate your time commitment to this function.

4. Please list expected consumables you would require to provide care.
5. Please make any additional comments you would like regarding this care component.
Transfer to theatre, anaesthetic room, operating room, recovery bay in theatre
1. Are you routinely involved in this care component?
2. If so what is your function?
3. Please estimate your time commitment to this function.
4. Please list expected consumables you would require to provide care.
5. Please make any additional comments you would like regarding this care component.
Post operative 24 hours.
1. Are you routinely involved in this care component?
2. If so what is your function?
3. Please estimate your time commitment to this function.
4. Please list expected consumables you would require to provide care.
5. Please make any additional comments you would like regarding this care component.
Day 2 post op – patient awaiting discharge
1. Are you routinely involved in this care component?
2. If so what is your function?

3. Please estimate your time commitment to this function.
4. Please list expected consumables you would require to provide care.
5. Please make any additional comments you would like regarding this care component.
Outpatient physiotherapy
1. Are you routinely involved in this care component?
2. If so what is your function?
3. Please estimate your time commitment to this function.
4. Please list expected consumables you would require to provide care.
5. Please make any additional comments you would like regarding this care component.
Outpatient follow up and discharge
1. Are you routinely involved in this care component?
2. If so what is your function?
3. Please estimate your time commitment to this function.
4. Please list expected consumables you would require to provide care.
5. Please make any additional comments you would like regarding this care component.

Final Delphi Evaluation Results

1. Accident and emergency admission (Day 1 afternoon)								
Personnel Activity	**Estimate of time commitment**	**Strongly Disagree**	**Mildly disagree**	**Neutral**	**Mildly agree**	**Strongly Agree**	**Previous round feedback**	**Round 2 Results**
1.1 Arrival by ambulance: triage nurse assessment	**Round 2 : 8 – 12 min** (Round 1: 10 – 15 min)	☐	☐	☐	☐	☐	Most common response is mildly agree. 7/13 respondents mildly or strongly agree. **Previous feedback: "is this a bit long?"**	**Most common response mildly agree (9/13). 13/13 agree CONSENSUS REACHED**
1.2 Triage nurse booking in with receptionist	**Round 2: 10 – 15 min** (Round 1: 5-10min)	☐	☐	☐	☐	☐	Most common response is mildly agree. 7/13 respondents mildly or strongly agree. **Previous comments " 10 – 15 minutes at least "**	**Most common response mildly agree (10/13). 13/13 agree CONSENSUS REACHED**
1.3 A/E middle grade assessment in A/E majors before x-ray is taken	**Round 2: 8 - 20 min** (Round 1 : 10 – 15 min)	☐	☐	☐	☐	☐	Most common response is mildly agree. 7/13 respondents mildly or strongly agree. **Previous comments "more often than not it is a junior grade assessment, in which case it will take 30-60 mins" & "is this too long"** **Moderator response: the assumption in the model is a middle grade review. There is a lack of consensus whether the review time is too long or short. The range has been expanded to accommodate a range of opinions**	**Most common response mildly agree (7/13). 10/13 agree CONSENSUS REACHED**
1.4 X-ray department for shoulder XR	10 – 20min	☐	☐	☐	☐	☐	Most common response is mildly agree. 7/13 respondents mildly or strongly agree. **Previous comments - multiple " does this include waiting times"** **Moderator response: waiting times are not included in any step. This includes patient positioning for x-ray, taking the x-ray and uploading it to PACS"**	**Most common response mildly agree (9/13). 12/13 agree CONSENSUS REACHED**

1.5 A/E middle grade assessment after XR. Referral to orthopaedics.	10-15 min	☐	☐	☐	☐	☐	**Most common response is mildly agree. 9/13 respondents mildly or strongly agree. CONSENSUS REACHED**	
1.6 Orthopaedic SHO assessment. Decision to admit to ward.	20 – 30 minutes	☐	☐	☐	☐	☐	**Most common response is mildly agree. 9/13 respondents mildly or strongly agree. CONSENSUS REACHED**	
1.7 Ongoing nursing assessment in A/E	30-40 minutes	☐	☐	☐	☐	☐	**Most common response is mildly agree. 9/13 respondents mildly or strongly agree. CONSENSUS REACHED**	
1.8 Nursing organisation of orthopaedic bed with bed manager	10-15 minutes	☐	☐	☐	☐	☐	**Most common response is mildly agree. 9/13 respondents mildly or strongly agree. CONSENSUS REACHED**	
1.9 Nursing transfer to ward with porter and hand-over to ward nurses	**Round 2: 20 – 40 min** (Round 1 :30-40 minutes)	☐	☐	☐	☐	☐	Most common response is mildly agree. 7/13 respondents mildly or strongly agree. **Previous comments "does this include waiting for a porter?"** **Moderator response: feedback despite a lack of consensus, was poor. Waiting times are not included in the model. This includes nurse and porter taking the patient from A/E to the ward and nurse to nurse handover on the ward. The range has been modified to accommodate a range of opinions or possible scenarios (complex/straight forward handover)**	**Most common response mildly agree (7/13). 13/13 agree CONSENSUS REACHED**
2. Admission to ward (Day 1 evening)								
Personnel Activity	**Estimate of time commitment**	**Strongly Disagree**	**Mildly disagree**	**Neutral**	**Mildly agree**	**Strongly Agree**	**Previous round feedback**	**Round 2 Comments**
2.1 Patient arrives on ward	15-20 min	☐	☐	☐	☐	☐	**Most common response is mildly agree.**	

and nurse receives hand over							9/13 respondents mildly or strongly agree CONSENSUS REACHED	
2.2 Nursing admission: includes observations, MRSA swabs and documentation.	40-60min	☐	☐	☐	☐	☐	Most common response is mildly agree. 12/13 respondents mildly or strongly agree. CONSESUS REACHED	
2.3 Orthopaedic middle grade assessment	15–30 min	☐	☐	☐	☐	☐	Most common response is mildly agree. 9/13 respondents mildly or strongly agree. CONSESUS REACHED	
2.4 Nursing care overnight: includes analgesia and observations	**Round 2: 15 – 35 min** Round 1 : 20-30 min	☐	☐	☐	☐	☐	Most common response is mildly agree. 8/13 respondents mildly or strongly agree. Previous comments " if controlled drugs this will take longer" vs " probably only takes 10 minutes" Moderator response: The range has been increased to take into consideration controlled drugs which are often given for this injury (but not likely to be administered more than once overnight). Have also acknowledge opinion that this can often take less time.	**Most common response is mildly agree (9/13.) 12/13 agree CONSENSUS REACHED**

3. Patient awaiting surgery (Day 2)								
Personnel Activity	**Estimate of time commitment**	**Strongly Disagree**	**Mildly disagree**	**Neutral**	**Mildly agree**	**Strongly Agree**	**Previous round feedback**	**Round 2 Comments**
3.1 Discussion of case at trauma meeting	5-10 min	☐	☐	☐	☐	☐	**Most common response mildly/strongly agree. 12/13 respondents mildly or strongly agree. CONSENSUS REACHED.**	
3.2 Organisation of equipment for theatre	5-15 min	☐	☐	☐	☐	☐	**Most common response mildly agree. 9/13 respondents mildly or strongly agree. CONSENSUS REACHED**	
3.3 Consultant led post-take ward round	5-10min	☐	☐	☐	☐	☐	**Most common response mildly agree. 11/13 respondents mildly or strongly agree. CONSENSUS REACHED.**	
3.4 Organisation of CT scan	**Round 2 : 5 – 15 min** Round 1: 5 – 10min	☐	☐	☐	☐	☐	Most common response mildly agree. 8/13 respondents mildly or strongly agree. **Moderator response: There was no feedback in for this response despite a lack of agreement or consensus. This activity includes booking the CT on the computer and discussing it with a radiologist. The upper limit of time has been increased to 15 minutes as the assumption is that disagreement was because this activity can take more time than previously stated.**	**Most common response is mildly agree 10/13.) 13/13 agree CONSENSUS REACHED**

3.5 Transfer to and from CT scan (portering time)	15 – 30 min	☐	☐	☐	☐	☐	Most common response mildly agree. 8/13 respondents mildly or strongly agree. **Previous comments "should the transfer not include portering" & "longer"** **Moderator response: The activity has been corrected – this is simply the time it takes the porter to take the patient to CT and bring them back up again. No waiting times.**	**Most common response is mildly agree (7/13.) 13/13 agree CONSENSUS REACHED**
3.5 CT scan duration (positioning, scanning and uploading CT images)	**Round 2 : 15 – 30 min** Round 1: 10-20min	☐	☐	☐	☐	☐	Most common response mildly disagree. 4/13 respondents mildly or strongly disagree. **Previous comments "longer" & " much longer " & " often patient away for ages"** **Moderator response: the activity time has been increased – this is the time the patient is in the CT suite and the time it takes the radiographer to upload the CT to PACS**	**Most common response is mildly agree (9/13.) 12/13 agree CONSENSUS REACHED**
3.6 Nursing ward round (2 per day)	10-20min	☐	☐	☐	☐	☐	**Most common response mildly agree. 10/13 respondents mildly or strongly agree. CONSENSUS REACHED**	

3.7 Nursing drug ward round (4 per day)	**Round 2: 10 – 30 min** Round 1 : 10-20min	☐	☐	☐	☐	☐	Most common response mildly agree. 8/13 respondents mildly or strongly agree **Moderator response: no feedback despite lack of consensus or agreement. This is the time it takes a nurse to do 4 drug ward rounds for 1 patient in a day. The upper limit has been increased to accommodate for the administration of controlled drugs.**	**Most common response is mildly agree (9/13.) 13/13 agree CONSENSUS REACHED**
3.8 HCA observations ward rounds (4 per day)	10-20min	☐	☐	☐	☐	☐	**Most common response mildly agree. 11/13 respondents mildly or strongly agree. CONSENSUS REACHED.**	
3.9 Trauma coordinator liaison with CT, theatre and ward staff	15-30min	☐	☐	☐	☐	☐	**Most common response mildly agree. 10/13 respondents mildly or strongly agree. CONSENSUS REACHED.**	
3.10 Ward Clerk organises notes and request old notes	**Round 2 : 5 – 20 min** Round 1: 5-10min	☐	☐	☐	☐	☐	Most common response mildly agree. 7/13 respondents mildly or strongly agree. **Previous comments "Does this actually happen at all anymore? Takes them 15-20 minutes anyway"** **Moderator response: Only 1 comment despite lack of agreement. It is possible that some respondents are not sure that this activity actually occurs. Assume**	**Most common response is mildly agree 10/13.) 12/13 agree CONSENSUS REACHED**

							that it does – in an ideal/safe patient pathway the medical team should access to a complete and organised set of notes. The upper limit has been increased to 20 min to accommodate the previous respondent's suggestion.	
3.11 Pharmacist reviews drug history	**Round 2: 5 – 10 min** Round 1: 10-15min	☐	☐	☐	☐	☐	Most common response mildly agree. 8/13 respondents mildly or strongly agree. **Previous comments "no idea"** **Moderator response: lack of response or opinion. The activity relates to a daily ward round done by pharmacists who review each patient's drug history and contact the GP if required for patients with an incomplete drug history.** **Minimum range has been reduced to 5 min for respondents who may feel this takes less time for patients that are not particularly frail.**	**Most common response is mildly agree (8/13.)** **11/13 agree** **CONSENSUS REACHED**

3.12 Anaesthetist review	**Round 1: 10 – 15 min**	☐	☐	☐	☐	☐	**Most common response mildly agree. 11/13 respondents mildly or strongly agree. CONSENSUS REACHED.**	
4. Patient arrives in operating theatre (Day 2)								
Personnel Activity	**Estimate of time commitment**	**Strongly Disagree**	**Mildly disagree**	**Neutral**	**Mildly agree**	**Strongly Agree**	**Previous round feedback**	
4.1 Transfer from ward to anaesthetic room including check in.	**Round 2: 15 – 30 min** Round 1 : 10-15 min	☐	☐	☐	☐	☐	5 respondents mildly or strongly agree with this. **Respondent feedback "longer", "much longer" & "sadly much longer".** **Moderator feedback: time range changed from 10 – 15 min to 15 – 30 min.**	**Most common response mildly agree (7/13) 11/13 agree CONCENSUS REACHED**
4.2 Anaesthetist and ODP: equipment check, drug preparation and administer anaesthetic (GA and regional block)	20-40min	☐	☐	☐	☐	☐	**Most respondents strongly agree. 11/13 respondents mildly or strongly agree. CONSENSUS REACHED**	
4.2 Surgeons check equipment, implant and review x-rays.	**Round 2: 5 – 15 min** Round 1: 10-15 min	☐	☐	☐	☒	☐	Most respondents strongly agree. 8/13 respondents mildly or strongly agree. **Respondent feedback " usually takes 5 min"** **Moderator feedback: Only 1 response despite a lack of agreement. The lower limit has been modified to 5 min to**	**Most common response mildly agree (9/13) 12/13 agree CONCENSUS REACHED**

							accommodate the scenario that all the kit is available/complete and easily assessable. The upper limit relates to time taken finding misplaced implants or equipment.	
4.3 Transfer to theatre: positioning, checklist and re-application of monitoring equipment	10-15min	☐	☐	☐	☐	☐	Most respondents mildly agree. 9/13 respondents mildly or strongly agree. CONSENSUS REACHED	
4.4 Operating procedure: including draping, surgery, application of dressings and safe transfer to bed.	90 – 150min	☐	☐	☐	☐	☐	Most respondents strongly agree. 11/13 respondents mildly or strongly agree. CONSENSUS REACHED	
4.5 Emergence from anaesthesia in theatre	5-10min	☐	☐	☐	☐	☐	Most respondents mildly agree. 11/13 respondents mildly or strongly agree. CONSENSUS REACHED	
4.6 Transfer to recover and handover to recover nurse	5-10min	☐	☐	☐	☐	☐	Most respondents mildly agree. 11/13 respondents mildly or strongly agree. CONSENSUS REACHED	
4.7 Recovery time nursing	60- 90 min	☐	☐	☐	☐	☐	Most respondents strongly agree. 11/13 respondents mildly or strongly agree. CONSENSUS REACHED	

4.7 Consultant review of patient in recovery	2-5 min	☐	☐	☐	☐	☐	**Most respondents strongly agree.** **11/13 respondents mildly or strongly agree.** **CONSENSUS REACHED**	
4.8 Handover to ward nurses and transfer back to ward	**Round 2: 20 – 35 min** Round 1: 15-25min	☐	☐	☐	☐	☐	Most common response mildly agree. 8/13 respondents mildly or strongly agree. **Responder feedback "longer including portering" & " no idea" & " occasionally much longer"** **Moderator feedback: range increased from 15 – 25 min to 20 – 35 min**	**Most common response mildly agree (11/13)** **13/13 agree** **CONCENSUS REACHED**
5. Day 1 post surgery (Day3)								
Personnel Activity	**Estimate of time commitment**	**Strongly Disagree**	**Mildly disagree**	**Neutral**	**Mildly agree**	**Strongly Agree**	**Previous round feedback**	
5.1 Consultant led ward round	5-10min	☐	☐	☐	☐	☐	**10/13 respondents mildly or strongly agree.** **CONSENSUS REACHED**	
5.2 Nursing ward round (2 per day)	10-30min	☐	☐	☐	☐	☐	**10/13 respondents mildly or strongly agree.** **CONSENSUS REACHED**	
5.3 Nursing drug ward round (4 per day)	10-20min	☐	☐	☐	☐	☐	**10/13 respondents mildly or strongly agree.** **CONSENSUS REACHED**	
5.3 HCA observations ward round (4 per day)	10-20min	☐	☐	☐	☐	☐	**11/13 respondents mildly or strongly agree.** **CONSENSUS REACHED**	
5.4 Transfer to and from X-ray (Post op films)	**Round 2 : 20 – 40 min**	☐	☐	☐	☐	☐	Most respondents mildly agree. 8/13 respondents mildly or strongly agree.	**Most common response mildly agree (8/13).** **13/13 agree.**

	Round 1: 15-30min						**Respondent feedback "? Includes transfer" & "60min" & "longer"** **Moderator feedback: This is portering time to and from x-ray. Range increased from 15 – 30 min to 20 – 40 min**	**CONSENCUS REACHED**
5.5 Radiographer performs x-ray	**Round 2 : 8 – 12 min** Round 1 : 5-10min	☐	☐	☐	☐	☐	Most common response is mildly agree. 7/13 respondents mildly or strongly agree. **Responder feedback: " longer" & "including transfer takes longer"** **Moderator feedback: this is patient positioning, taking the x-ray and uploading to PACS. Increased from 5 – 10 min to 8 – 12 m**	**Most common response mildly agree (9/13). 11/13 agree.** **CONSENCUS REACHED**
5.6 Inpatient physiotherapist review	20-30min	☐	☐	☐	☐	☐	**10/13 respondents mildly or strongly agree. CONSENSUS REACHED**	
5.7 Inpatient occupational therapist review	20-30min	☐	☐	☐	☐	☐	**9/13 respondents mildly or strongly agree. CONSENSUS REACHED**	
5.8 Phlebotomist takes blood	10-15 min	☐	☐	☐	☐	☐	**9/13 respondents mildly or strongly agree. CONSENSUS REACHED**	
5.9 Kitchen staff provide meals (3 per day)	**Round 2: 10 – 20min** Round 1: 6 - 12min	☐	☐	☐	☐	☐	Most common response strongly agree. 8/13 respondents strongly or mildly agree. **Responder feedback "Needs to include visit for menu request, preparation and meals and clearing up."** **Moderator feedback: only 1 comment despite lack of**	**Most common response mildly agree (8/13). 12/13 agree.** **CONSENCUS REACHED**

							agreement. Activity increased from 6 – 12 minutes for 3 meals in a day to 10 – 20 min per patient including serving and clearing. Food preparation not included.	
5.10 Junior doctor re-assessment of patient and investigations performed	10-20min	☐	☐	☐	☐	☐	**11/13 respondents mildly or strongly agree. CONSENSUS REACHED**	
5.11 Middle grade orthopaedic surgeon reviews x-rays	1-2min	☐	☐	☐	☐	☐	**10/13 respondents mildly or strongly agree. CONSENSUS REACHED**	
6. Day of discharge – discharge at 2pm (Day4)								**7.**
Personnel Activity	**Estimate of time commitment**	**Strongly Disagree**	**Mildly disagree**	**Neutral**	**Mildly agree**	**Strongly Agree**	**Previous round feedback**	
6.1 Middle grade orthopaedic ward round	2-5min	☐	☐	☐	☐	☐	**Most respondents mildly agree. 10/13 respondents mildly or strongly agree. CONSENSUS REACHED**	
6.2 Junior doctor completes discharge summary	10-15min	☐	☐	☐	☐	☐	**Most respondents mildly agree. 12/13 respondents mildly or strongly agree. CONSENSUS REACHED**	
6.3 Physiotherapy review	10-15min	☐	☐	☐	☐	☐	**Most respondents mildly agree. 11/13 respondents mildly or strongly agree. CONSENSUS REACHED**	
6.4 Nursing ward round (1)	5-10min	☐	☐	☐	☐	☐	**Most respondents mildly agree. 9/13 respondents mildly or strongly agree.**	

							CONSENSUS REACHED	
6.5 Nursing drug ward round (2)	5-10min	☐	☐	☐	☐	☐	Most respondents mildly agree. 10/13 respondents mildly or strongly agree. CONSENSUS REACHED	
6.6 HCA observations ward round (2)	5-10min	☐	☐	☐	☐	☐	Most respondents mildly agree. 12/13 respondents mildly or strongly agree. CONSENSUS REACHED	
6.7 Kitchen staff provides meal (2)	4-6min	☐	☐	☐	☐	☐	Most respondents mildly agree. 9/13 respondents mildly or strongly agree. CONSENSUS REACHED	
6.8 Nurse dispenses and checks analgesia from ward	10-15min	☐	☐	☐	☐	☐	Most respondents mildly agree. 12/13 respondents mildly or strongly agree. CONSENSUS REACHED	
6.9 Nursing discharge	20-30min	☐	☐	☐	☐	☐	Most respondents mildly agree. 10/13 respondents mildly or strongly agree. CONSENSUS REACHED	
6.10 Nurse organised clinic follow up with ward clerk	5-10min	☐	☐	☐	☐	☐	Most respondents mildly agree. 9/13 respondents mildly or strongly agree. CONSENSUS REACHED	
8. Orthopaedic outpatient clinic								**9.**
Personnel Activity	**Estimate of time commitment**	**Strongly Disagree**	**Mildly disagree**	**Neutral**	**Mildly agree**	**Strongly Agree**	**Comments**	
7.1 Patient checks in at reception	2-4min	☐	☐	☐	☐	☐	Most common response mildly agree. 12/13 patients mildly or strongly agree. CONSENSUS REACHED	

7.2 Clinic nurse organises notes and x-rays with middle grade doctor	4-6min	☐	☐	☐	☐	☐	**Most common response mildly agree. 10/13 patients mildly or strongly agree. CONSENSUS REACHED**	
7.3 Radiographer performs x-ray	**Round 2: 5 – 10 min** Round 1 : 4-8min	☐	☐	☐	☒	☐	Most common response mildly agree. 7/13 respondents mildly or strongly agree. **Respondent feedback " longer" & " usually long wait"** **Moderator feedback: this does not include waiting time. This is the time it takes to position the patient, take the x-ray and upload it to PACS. Previous estimate 4 – 8 min updated to 5 – 10 min.**	**Most common response mildly agree (8/13). 10/13 respondents agree. CONSENSUS REACHED**
7.4 Orthopaedic consultant review, documentation and dictation	10-15min	☐	☐	☐	☐	☐	**Most common response mildly agree. 12/13 patients mildly or strongly agree. CONSENSUS REACHED**	
7.5 Patient books follow up appointment with receptionist	2-4min	☐	☐	☐	☐	☐	**Most common response mildly agree. 10/13 patients mildly or strongly agree. CONSENSUS REACHED**	
10. Physiotherapy outpatient clinic								**11.**
Personnel Activity	**Estimate of time commitment**	**Strongly Disagree**	**Mildly disagree**	**Neutral**	**Mildly agree**	**Strongly Agree**	**Comments**	
8.1 Patient checks in at reception	2-4min	☐	☐	☐	☐	☐	**Most common response mildly agree. 9/13 patients mildly or strongly agree. CONSENSUS REACHED**	

8.2 Clinic nurse organises notes	2-3min	☐	☐	☐	☐	☐	6/13 respondents mildly or strongly agree. **Respondent feedback suggests no nurse allocated to this clinic so activity cancelled.**	
8.3 Physiotherapist assessment (standardised time slot)	30-45min	☐	☐	☐	☐	☐	**Most common response strongly agree.** **9/13 patients mildly or strongly agree.** **CONSENSUS REACHED**	
8.4 Patient books follow up with receptionist	2-4min	☐	☐	☐	☐	☐	8/13 respondents strongly or mildly agree. **Respondent feedback " neutral so don't really know"** **Moderator feedback: consider this activity to be similar if not the same to how long it takes the patient to book a follow up appointment in the orthopaedic clinic.**	**Most common response is mildly agree 8/13.** **12/13 agree.** **CONSENSUS REACHED**

Staff capacity cost estimates

(Based on NHS/Agenda for Change Pay scale. Adapted with market force factors)

	Minimum pay rate (£/min)	Maximum pay rate (£/min)	Mean pay rate (£/min)
Consultant	0.83	1.35	1.09
SpR	0.36	0.51	0.43
SHO	0.32	0.36	0.34
ED Nurse	0.23	0.34	0.28
Ward Nurse	0.23	0.34	0.28
Theatre Nurse (Scrub)	0.23	0.34	0.28
Theatre Nurse (Recovery)	0.23	0.39	0.31
Clinic Nurse	0.23	0.28	0.25
ODP	0.23	0.39	0.31
Receptionist/Ward Clerk	0.16	0.20	0.18
Physiotherapist	0.23	0.39	0.31
Occupational therapist	0.23	0.39	0.31
Porter	0.16	0.16	0.16
Phlebotomist	0.16	0.18	0.17
Kitchen staff/domestic services	0.16	0.16	0.16
Pharmacist	0.23	0.39	0.31
HCA	0.16	0.20	0.18
Bed manager	0.26	0.39	0.33
Trauma coordinator	0.26	0.39	0.33

Appendix 4:
Supplementary Data and Methods in Economic Analysis

Outcome Probabilities

1. Conservative management probability of a complication

Author	Study type	Number of cases	% of complications	% of cases requiring revision
Fjalestad et al[148]	RCT(Level I)	25	64% 16 (13 AVN, 2 non-unions, 1 acute displacement)	4% 1(ORIF for early displacement)
Olreud et al[69]	RCT (Level I)	26	37.5% 6(1 non-union, 2 AVN, 1 OA, 1 impingement, 1 axillary nerve palsy)	3.8% 1(SAD for impingement)
Olreud et al[30]	RCT(Level I)	28	35.7% 10 (1 further displacement, 1 non-union, 3 AVN, 5 OA)	3.6% 1(hemi for acute displacement)

2. Number of different secondary surgical procedures after complications following conservative management

Secondary procedure	Indication	Number (Total N = 3)
ORIF	Acute displacement	1
SAD	Impingement	1
Hemiarthroplasty	Acute displacement	1

3. Internal fixation (IF) probability of complication

Author	Study type	Number of IF cases	% of complications	% of cases requiring revision
Fjalestad et al [148]	RCT (Level I)	23	**69.6%** 16 (1 plate pull out, 7 screw penetrations into joint, 8 cases of AVN)	**17.4%** 4 (1 re-plating for plate pull out at 6 months,3 plate removals following screw penetration)
Cai et al [252]	RCT(Level I)	12	**25%** 3 (1 nonunion, 2 fixation failure)	**25%** 3 (1 nonunion treated with re-fixation, 2 fixation failures treated with plate removal)
Olreud et al [69]	RCT (Level I)	30	**33.3%** 10 (2 deep infection cases;1 treated with wound revision, repeated lavage, extraction of plate and spacer. 1 treated with wound revision and extraction of plate when wound healed; 1 non-union treated with re-plating + bone graft;2 cases of impingement – plate extraction and plate removal each; 3 stiffness – plate removal, 3 AVN – plate removal, hemi and non op treatment)	**30%** 9 (2 deep infection cases;1 treated with wound revision, repeated lavage, extraction of plate and spacer. 1 treated with wound revision and extraction of plate when wound healed; 1 non-union treated with re-plating + bone graft;2 cases of impingement – plate extraction and plate removal each; 3 stiffness – plate removal, 2 AVN – plate removal and hemi each)

4. Number of different secondary surgical procedures after complications following IF

Secondary procedure	Indication	Number (Total N = 16)
Re-plating	Plate pull out, non-union	2
Removal of plate	Screw penetration, failure of fixation, impingement, AVN, shoulder stiffness	11
Wound revision and removal of plate	Infection	1
Wound revision, removal of plate and spacer	Infection	1
Revision of IF to hemi	AVN	1

5. Hemiarthoplasty (HA) probability of complication

Author	Study type	Number of HA cases	% of complications	% of complications requiring revision
Cai et al [252]	RCT (Level I)	18	**16.6%** 3 (1 dislocation – hemiarthroplasty revision, 1 infection – wound revision, 1 prosthesis loosening – hemiarthroplasty revision)	**16.6%** 3 (1 dislocation – hemiarthroplasty revision, 1 infection – wound revision, 1 prosthesis loosening – hemiarthroplasty revision)
Sebastia-Forcada et al [232]	RCT (Level I)	30	**30%** 9 (1 intraoperative fracture treated with cerclage wire, 1 MUA for stiffness, 6 revisions to reverse for implant failure/loosening. Migration, 1 superficial infection needing antibiotics)	**26%** 8 (1 intraoperative fracture treated with cerclage wire, 1 MUA for stiffness, 6 revisions to reverse for implant failure/loosening. Migration)
Olreud et al [30]	RCT (Level I)	24	**8.3%** 2 (1 patient had acromioplasty and release of adhesions and 1 patient had refixation of greater tubercle)	**8.3%** 2 (1 patient had acromioplasty and release of adhesions and 1 patient had refixation of greater tubercle)

6. Incidence of different secondary surgical procedures after complications following HA

Secondary procedure	Indication	Number (Total N = 13)
Revision to other hemiarthroplasty	Instability, Prosthesis loosening	2
Wound washout	Infection	1
Intra-operative fracture treated with cerclage wire	Fracture	1
MUA	Stiffness	1
Revision to reverse implant	Implant failure, loosening, migration	6
Acromioplasty and release of adhesions	Stiffness/Impingement	1
Re-fixation of greater tuberosity	Loss of fixation	1

7. Overall complications HA versus IF versus conservative

	Total cases	Total complications	Mean probability of a complication	Probability range for a complication
IF	65	29	0.446	0.25 – 0.696
HA	72	14	0.194	0.083– 0.3
Conservative	78	32	0.410	0.357 – 0.64

8. Overall revision procedures for HA versus IF versus conservative

	Total cases	Total revisions	Mean probability for revision procedure	Probability range for revision procedure
IF	65	16	0.246	0.174 – 0.30
HA	72	13	0.181	0.083 – 0.26
Conservative	78	3	0.0385	0.036-0.04

9. Overall secondary surgery rate for complications HA versus IF versus conservative

	Total complications	Total number of secondary operations	Probability of complication requiring secondary surgery	Probability range for complications requiring secondary surgery
IF	29	16	0.551	0.25 – 1
HA	14	13	0.928	0.889 – 1
Conservative	32	3	0.094	0.0625 – 0.167

Outcome Costs (Institutional Perspective – adapted from Chapter 3)

Procedure	Cost (£)
Locking plate with inpatient stay	3113.63
Hemiarthroplasty with inpatient stay	4679.31
Clinic appointment	27.58
Re-plating for failed ORIF	4197.08
Plate removal	1381
Surgical revision –removal of plate	2974.08
Surgical revision – removal of plate + spacer	3074.08
Revision ORIF to Hemi	5253.93
Revision Hemi to Hemi	5469.93
Revision Hemi to Reverse	6469.93
Wound Revision Hemi	3079
Hemiarthroplasty with cerclage wire	5373.69
MUA	338
Acromioplasty and release of adhesions (hemi)	676
Fixation of tuberosity Hemi	796

Health Related Quality of Life (Health Utilities)

A literature review was performed to identify 2-year health utilities for patients that underwent surgical fixation, hemiarthroplasty and conservative management. The health utilities for successful interventions were based on the mean health utilities reported for

patients at 2 year follow up. A review of the literature revealed that health utilities for patients with complications or patients undergoing secondary surgery were not available. After consultation within the research group, estimates of health utilities were decided to be adapted from the existing studies. Standard deviation data was used to estimate the lower range of health utilities within each intervention. The following formula was used to calculate health utilities for patients with complications in each group: Mean Health Utility at 2 years – mean SD of 2-year Health Utility. Health utilities were converted to Quality Adjusted Life Years (QALYs) using the Area Under the Curve (AUC) method[256].

1. Published 2 year health utilities in the literature

Author	Pre-injury Health Utility	24 month Health Utility	SD value for 24 month
Fjalestad et al[148] (fixation)	0.87	0.849	Not reported (adapted as mean values)
Fjalestad et al[148] (conservative)	0.83	0.825	Not reported (adapted as mean values)
Olreud et al[69](fixation)	0.85	0.70	0.34
Olreud et al[69](conservative)	0.85	0.59	0.35
Olreud et al[30](hemiarthroplasty)	0.88	0.81	0.12
Olreud et al[30](conservative)	0.87	0.65	0.27
Cai et al [252] (fixation)	0.85	0.74	0.24
Cai et al [252] (hemiarthroplasty)	0.85	0.81	0.17

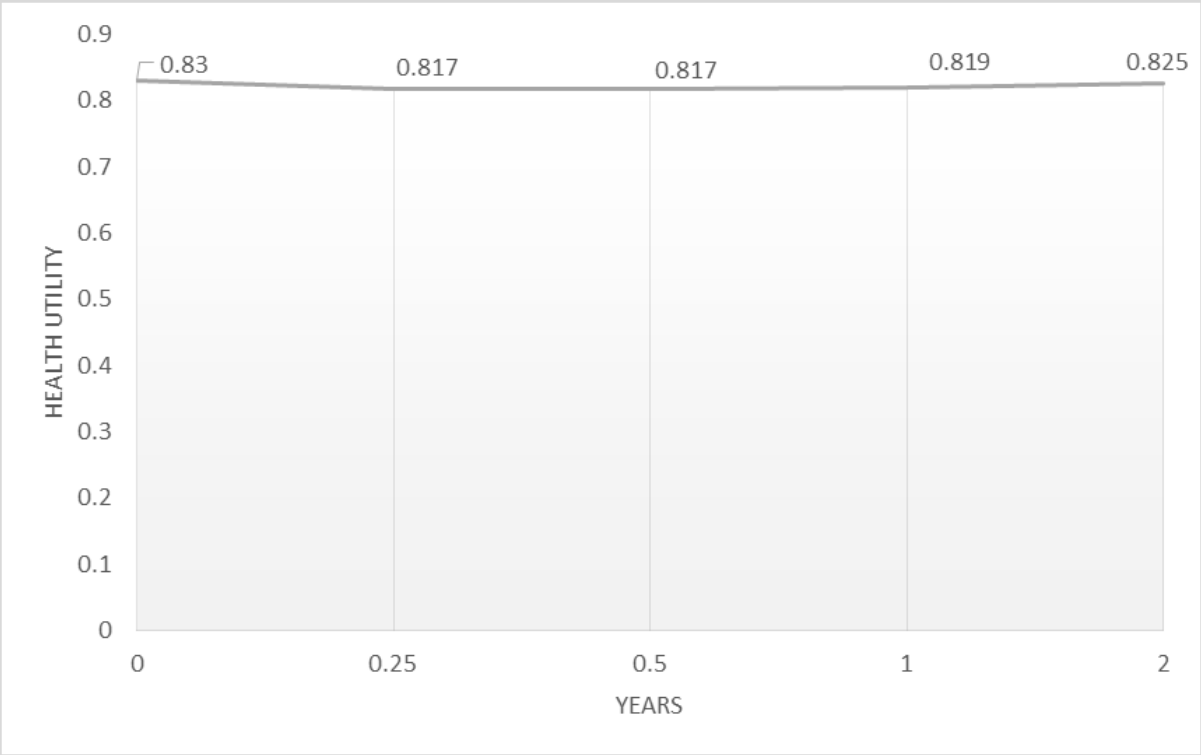
2. Conversion of health utilities to QALYs

For each trial containing health utility outcomes at 2 years, the relevant data was used in an AUC calculation to obtain QUALYs. For an uncomplicated outcome, the mean health utility as two years was selected for each trial. The mean QALYs of the trials were used for cost effectiveness outcomes for patients with uncomplicated treatment. For all patients who had a complication QALYs were estimated using the AUC calculation with a 2 year health utility generated from mean health utilities from all the trials which were subjected to devaluation

using the mean SD values (as described above). AUC calculations were performed in Microsoft Excel using the equation:

$$\int_{0}^{2} f(x)dx$$

An example is provided for AUC calculations for QALYs for patients managed conservatively from the trial of Fjalestad et al[148] = 1.641125



$$\int_{0}^{2} f(x)dx = 1.641125$$

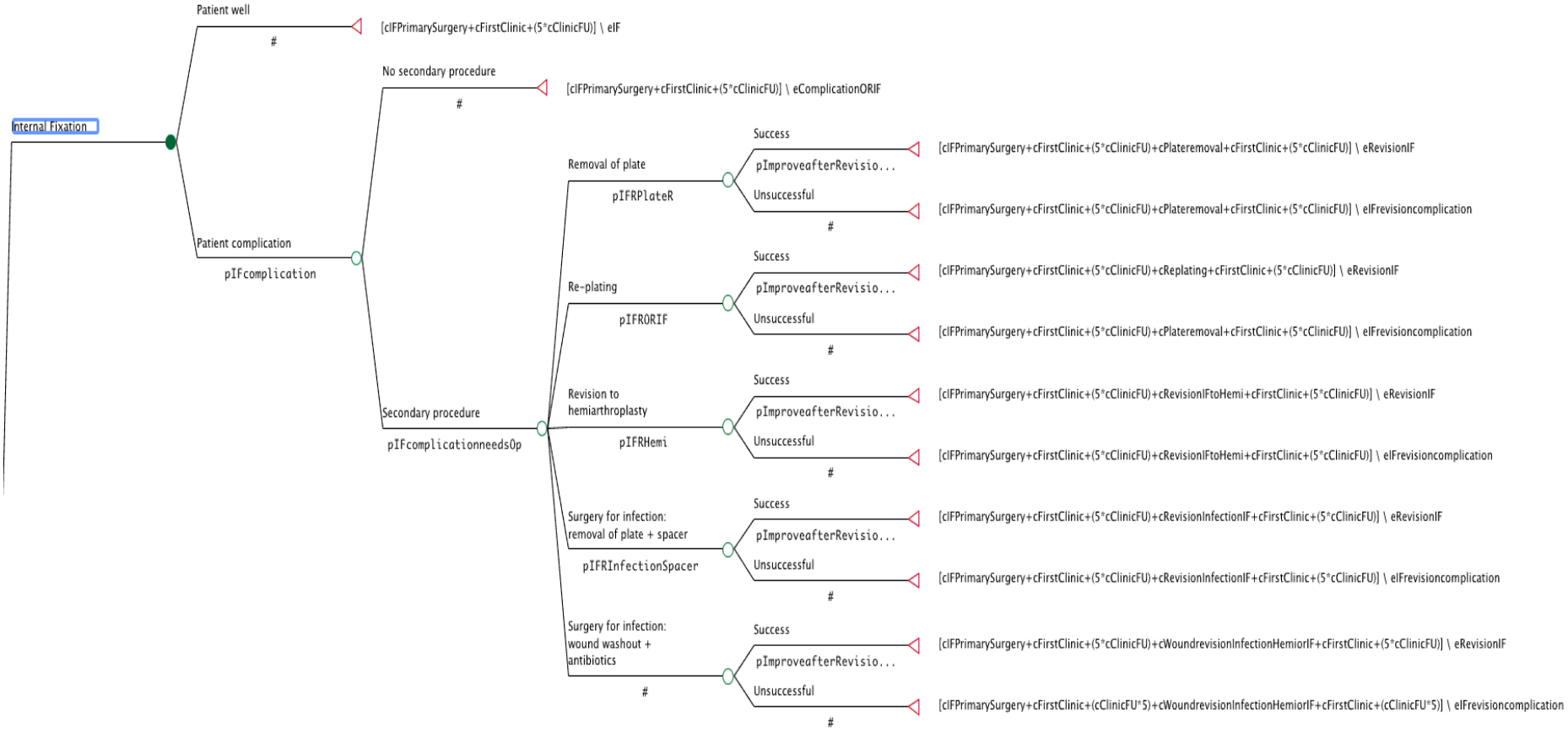
For patients that had successful surgery an additional 0.5 standard deviations were incorporated into the input values to derive a QALY of 1.719.

For patients with a complication a subtraction of 1 standard deviation was incorporated into the input values to derive a QALY of 1.486.

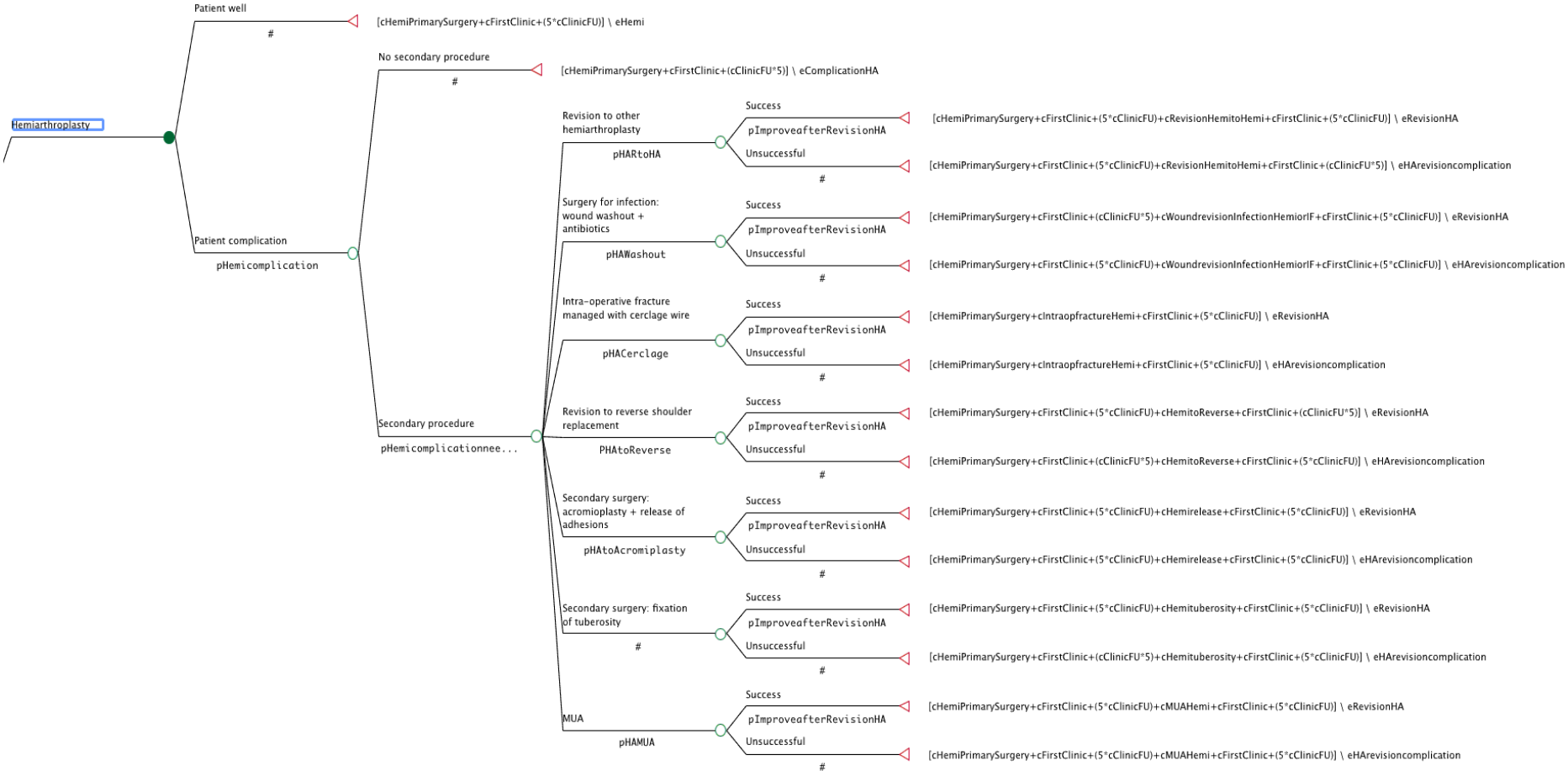
Patients who had a successful revision procedure were assumed to be halfway between the well and complicated state; QALY of 1.6025.

Patients who had a complication after revision surgery had a QALY which was taken as a ratio of the primary well and complication states applied to the successful revision state; QALY of 0.95104

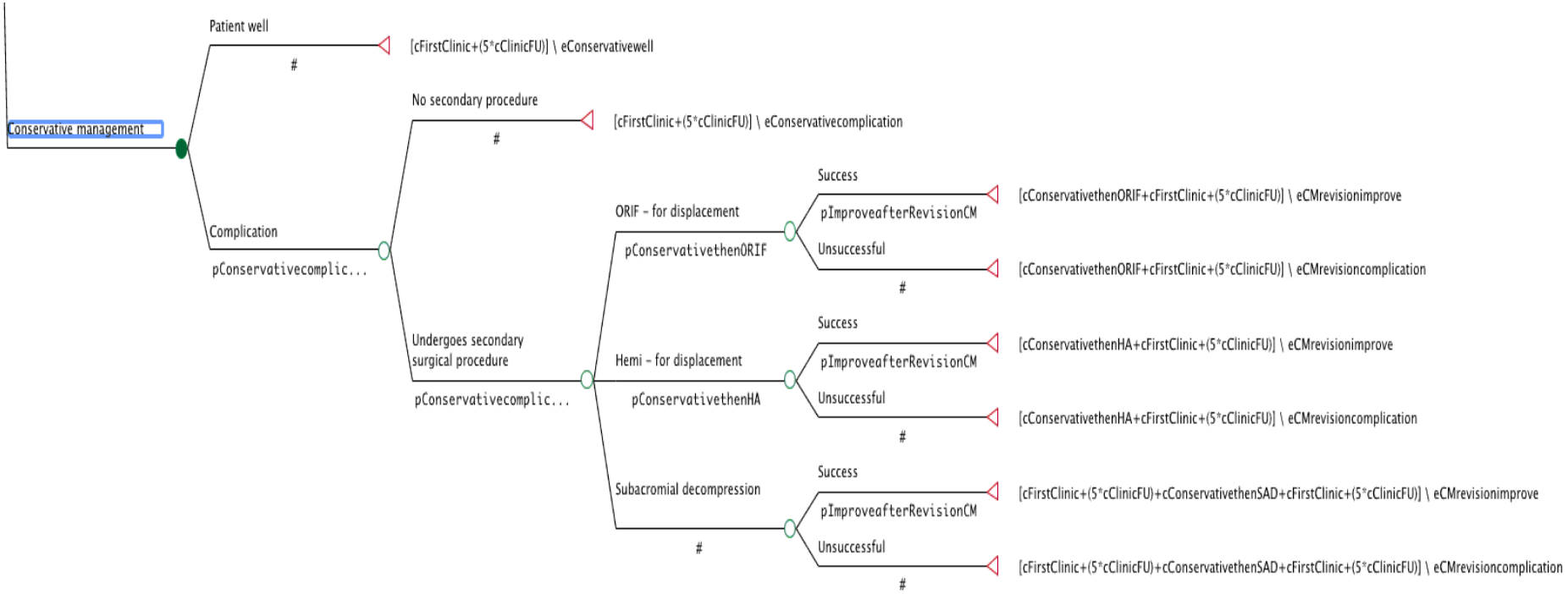
Decision Tree: Internal Fixation sub-tree



Decision Tree: Hemiarthroplasty sub-tree

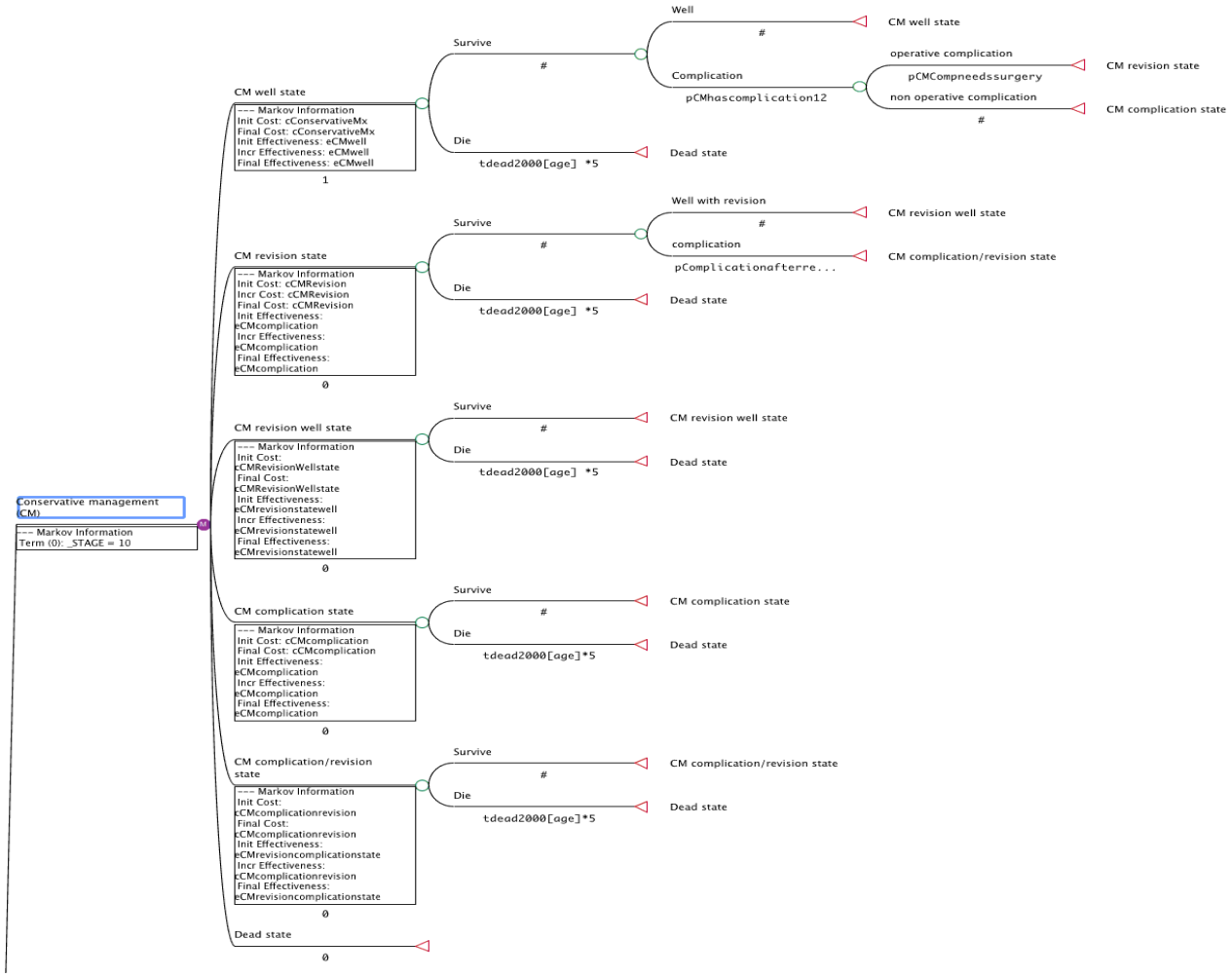


Decision Tree: Conservative Management sub-tree

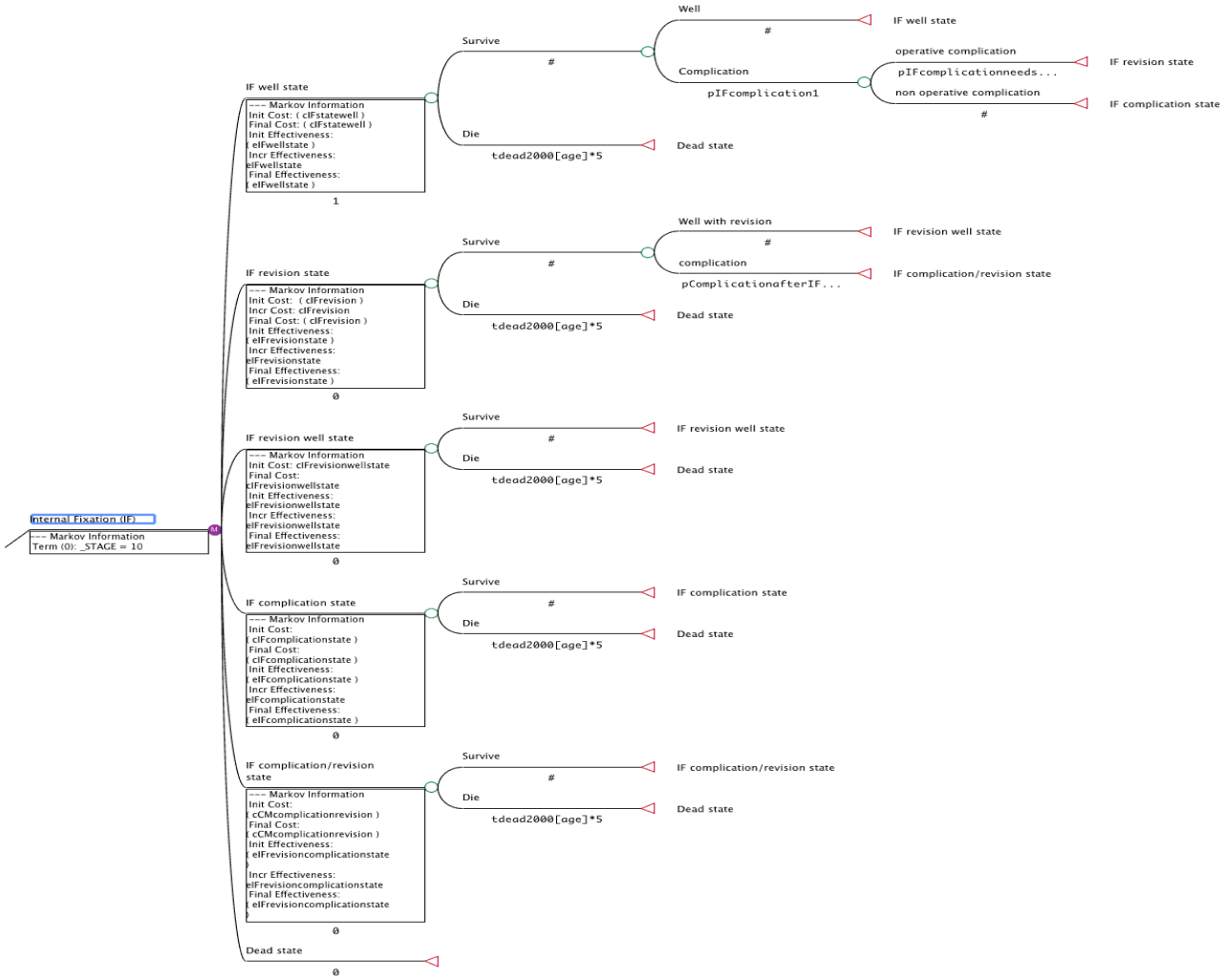


Appendix 5:
Supplementary Data and Methods in Markov Economic Analysis

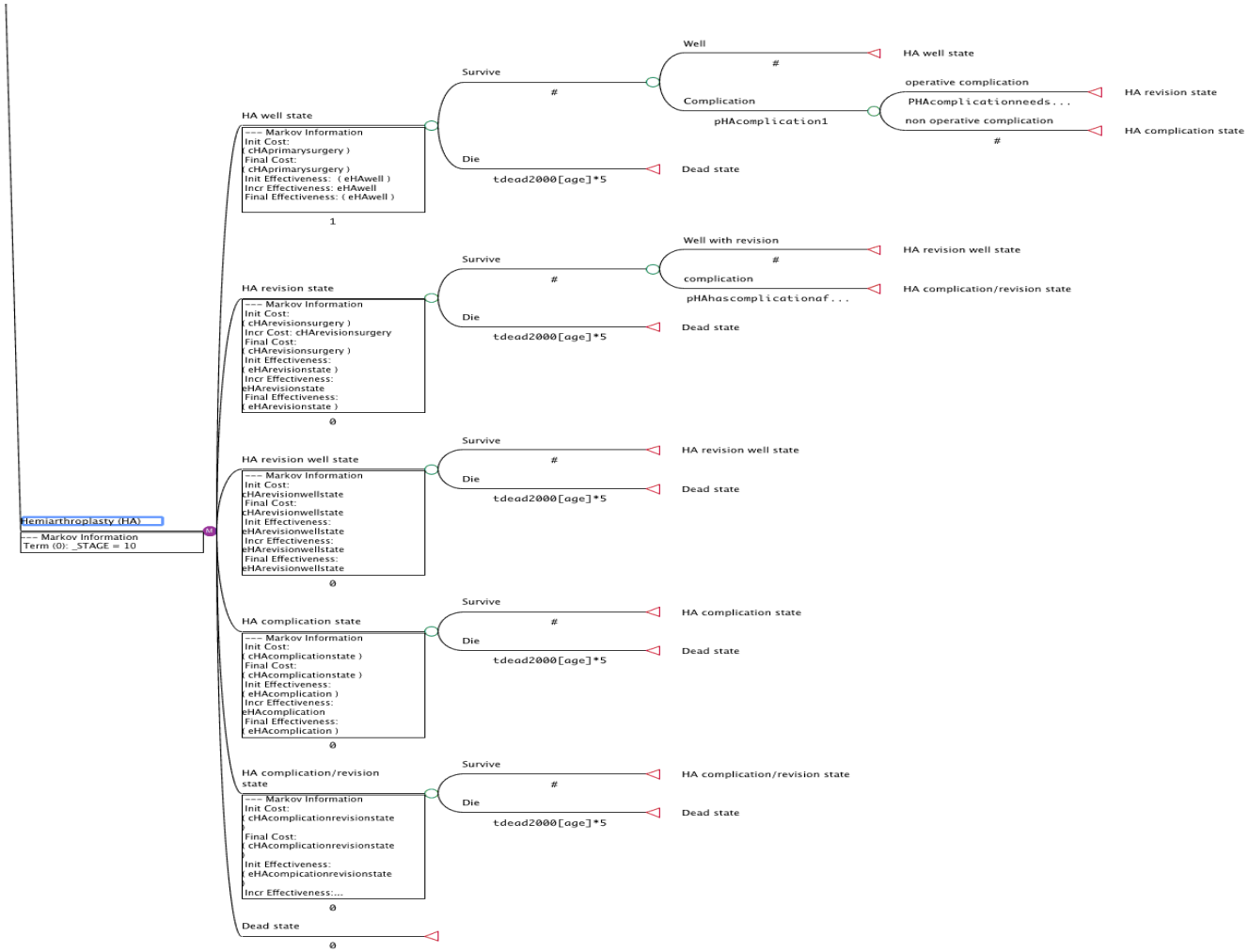
1. Markov tree: conservative management sub-tree



2. Markov tree: locking plate sub-tree



3. Markov tree: hemiarthroplasty sub-tree



Micro-costing estimates used for secondary analysis

Markov Health State	Cost (£)
Conservative Well State	165.48
Hemiarthroplasty Well State	4679.31
Locking Plate Well State	3113.63
Conservative Revision State	2716.67
Hemi Revision State	4260.80
Locking Plate Revision State	2175.42

Appendix 6:
Copyright and Permissions for inclusion of my own published research, as well as figures and tables from other authors.

Dear Sanjeeve

Thank you for your inquiry. Please find below our permission statement. This permission relates exclusively to this request:

Murray IR, Amin AK, White TO, Robinson CM. Proximal humeral fractures: current concepts in classification, treatment and outcomes. *J Bone Joint Surg [Br]* 2011;93-B:1-11. (Fig 1)

Thank you for your permission request. We are pleased to grant permission for you to reproduce figure 1 from the aforementioned article, *provided full and correct acknowledgement of source is given*. On this occasion the permission is granted free of charge as permission is for inclusion in your doctoral thesis and therefore falls under the category of academic purposes, and *is not for widespread or commercial publication or distribution*, but please note that our fees are usually £110 *per* page or £55 *per* table or figure.

Our standard acknowledgement is as follows below (***please ensure you cite the paper as shown above***)**:**

'Reproduced with permission and copyright © of the British Editorial Society of Bone and Joint Surgery [citation].'

Please note that *as a courtesy* it is normally necessary to seek, or make all reasonable attempts to seek, the author's permission in each case. The most recent address can be found on the paper's title page. The most recent email address we have for corresponding author, Mr Robinson, is as per the paper: c.mike.robinson@ed.ac.uk

If you have any further questions, please do not hesitate to contact me.

Kind regards,
Deborah

==========

Deborah Gray (Miss)
Production Management Assistant
The British Editorial Society of Bone and Joint Surgery
22 Buckingham Street, London WC2N 6ET
t: +44 (0)20 7782 0010 | f: + 44 (0)20 7839 9777
e: d.gray@boneandjoint.org.uk | www.bjj.boneandjoint.org.uk

==========

Visit us www.boneandjoint.org.uk | **Like us** www.facebook.com/BoneJointJournal | **Follow us** @BoneJointJ | **Join us** www.linkedin.com/groups/Bone-Joint-Journal

Dear Sanjeeve

We would be happy to provide you with permission to reproduce the *unedited, pre-publication* version of your paper 36255, in its entirety, in your thesis. You must clearly state in your thesis that this is the unedited, pre-publication version. I regret that we would not permit reproduction of the published version of the paper, which would constitute dual publication and therefore a breach of copyright. This policy relates to any author requesting to use such material in this way.

Please find our permission statement below. This permission relates exclusively to this request:

Sabharwal S, Carter AW, Rashid A, et al. Cost analysis of the surgical treatment of fractures of the proximal humerus. *Bone Joint J* 2016;98-B:249-259. [in press]

Please ensure the paper is correctly cited, as shown above, and ***is clearly identified as the unedited, pre-publication draft***. On this occasion the permission is granted free of charge as you are one of the authors of the original article and permission is for inclusion in your thesis and therefore falls under the category of academic purposes, and is not for widespread or commercial publication or distribution, but please note that our fees are usually £110 per page or £55 per table or figure.

Our standard acknowledgement is as follows (please ensure you cite the paper as shown above):
'Reproduced with permission and copyright © of the British Editorial Society of Bone and Joint Surgery [citation].'

Kind regards
Deborah

==========

Deborah Gray (Miss)
Production Management Assistant
The British Editorial Society of Bone and Joint Surgery
22 Buckingham Street, London WC2N 6ET
t: +44 (0)20 7782 0010 | **f:** + 44 (0)20 7839 9777
e: d.gray@boneandjoint.org.uk | www.bjj.boneandjoint.org.uk

==========

Please ensure the paper is correctly cited, as shown above, and ***is clearly identified as the unedited, pre-publication draft***. On this occasion the permission is granted free of charge as you are one of the authors of the original article and permission is for inclusion in your thesis and therefore falls under the category of academic purposes, and is not for widespread or

Deborah Gray (Miss)

Question	Answer
Name	Mr Sanjeeve Sabharwal
Institution/Company Name	Imperial College London
Street Address	15 Bedford Road
City	Northwood
State or Province	MIddlesex
Postal Code	HA6 2BA
Country	United Kingdom
E-mail	sanjeeve.sabharwal@ic.ac.uk
Phone Number	+447939447204
I am...	Academic/Educational
Journal Name	Journal of Bone and Joint Surgery
ISSN	1535-1386
Volume	52
Issue	6
Article Title	Displaced proximal humeral fractures. I. Classification and evaluation
Article Author(s)	Charles Neer
Number of Pages in Article	13
Article Date	01-09-1970
Type of Reuse	Figure/Table/Illustration
Content Requested [Provide specific figures, tables, excerpt needed for permission]	Figure 3
Do you have additionalpermissions to request?	No, I am ready to proceed
Are you the author of the requested Wolters Kluwer material?	No
Is the author a part of the new project?	No
How Will Our Content Be Used?	Thesis/Dissertation
Please provide details:	Thesis entitled The health and economic outcomes of managing complex proximal humerus fractures in the elderly”
Where do you attend university?	Imperial College London
Will this be posted to your university website?	Yes
Is the website password protected	Yes
Additional languages (other than English)	No

RightsLink

Copyright Clearance Center

Thank You For Your Order!

Dear Mr. Sanjeeve Sabharwal,

Thank you for placing your order through Copyright Clearance Center's RightsLink service. BMJ Publishing Group Ltd. has partnered with RightsLink to license its content. This notice is a confirmation that your order was successful.

Your order details and publisher terms and conditions are available by clicking the link below:
http://s100.copyright.com/CustomerAdmin/PLF.jsp?ref=eb227e3d-f72b-4a64-9b88-065d4fdf0646

Order Details
Licensee: Sanjeeve Sabharwal
License Date: Jan 25, 2016
License Number: 3795880171673
Publication: The BMJ
Title: Cemented, cementless, and hybrid prostheses for total hip replacement: cost effectiveness analysis
Type Of Use: Dissertation/Thesis
Total: 0.00 GBP

To access your account, please visit https://myaccount.copyright.com.

Please note: Online payments are charged immediately after order confirmation; invoices are issued daily and are payable immediately upon receipt.

To ensure that we are continuously improving our services, please take a moment to complete our customer satisfaction survey.

B.1:v4.2



+1-855-239-3415 / Tel: +1-978-646-2777
customercare@copyright.com
http://www.copyright.com