MONASH University
Business and Economics

Centre for Health Economics

Research Paper 2006 (12)

Priority Setting in Osteoarthritis

A/Professor Leonie Segal
Deputy Director, Centre for Health Economics,
Monash University

Susan Day
Research Fellow,
Centre for Health Economics, Monash University

Adam Chapman
Public Health Trainee,
on placement at Centre for Health Economics,
Monash Universtiy

Richard Osborne
Research Fellow,
Centre for Health Economics, Monash University

November, 2004

ISSN 1833-1173

ISBN 1 921187 11 5

ACKNOWLEDGEMENTS

This project was supported by funding from the Population Health Division, Australian Government Department of Health and Ageing and Monash University Faculty of Business and Economics. It has also been supported by the Department of Human Services, through the Public Health Trainee Scheme. We would also like to acknowledge the support of the Advisory Panel.

The content of the Report remains the responsibility of the research team.

Contact:

A/Prof Leonie Segal

Deputy Director, Centre for Health Economics

E-mail: leonie.segal@buseco.monash.edu.au

Phone: 613 9905 0734

Advisory Panel members

Professor Nicholas Bellamy
Director, Centre of National Research on Disability and Rehabilitation Medicine, University of Queensland

Professor Nikolai Bogduk
Director, Newcastle Bone and Joint Institute, Royal Newcastle Hospital, Newcastle University

Professor Peter Brooks
National Coordinator of the Bone and Joint Decade, Faculty of Health Science, University of Queensland

Ms Helen Brown
Director Arthritis and Related Projects Section, Priorities and Quality Branch, Population Health Division, Department of Health and Ageing

Associate Professor Rachelle Buchbinder
Director of Clinical Epidemiology, Cabrini Hospital and Associate Professor, Department of Epidemiology and Preventive Medicine, Monash University

Professor Marc Cohen
Founding Head of Department, Department of Complementary Medicine, RMIT University

Associate Professor Julian Feller
Orthopaedic Surgeon, Austin and Repatriation Medical Centre and LaTrobe University Medical Centre

Professor Mary Galea
Professor of Clinical Physiotherapy, Austin and Repatriation Medical Centre, School of Physiotherapy, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne

Ms Susan Garner
Director Health Priorities and Outcomes Section, Population Health Division, Department Health and Ageing

Mr Brian Harrison
Director, Budget and Review Section, Strategic Planning Branch, Population Health Division, Department Health and Ageing

Mrs Julie Kelly
Community Representative

Ms Sue Kirsa
Senior Drug Usage Evaluation Pharmacist, Department of Pharmacy, Austin and Repatriation Medical Centre

Dr Daniel Lewis
Rheumatologist and Research Associate, Centre for Complementary Medicine, Monash University

Associate Professor Lyn March
Staff Specialist, University of Sydney, Department of Rheumatology, Royal North Shore Hospital

Associate Professor Geoff McColl
Department of Medicine, Royal Melbourne Hospital, The University of Melbourne

Ms Helen McNeil
General Manager, Education & Services, Arthritis Victoria

Mr Colin Sindall
Director, National Centre for Disease Control Department of Health and Ageing

Ms Christine Stone
Epidemiologist – Cancer and Genetics, Prevention and National Health Priorities, Public Health Division, Department of Human Services

Mr Peter Woodley
Director, Economics and Financial Analysis Section, Strategic Planning Branch, Population Health Division, Department Health and Ageing.

TABLE OF CONTENTS

ABSTRACT i

SECTION I INTRODUCTION

1 THE PRIORITY SETTING MODEL – METHODS 1
1.1 BACKGROUND 1
1.2 PRIORITY SETTING FRAMEWORK 2
1.3 RESEARCH APPROACH 3
ANNEXURE TO CHAPTER 1 8

2 SELECTION OF INTERVENTIONS 10
2.1 INTRODUCTION TO INTERVENTION OPTIONS 10
2.2 LITERATURE REVIEW - METHOD 10
2.3 SELECTION OF INTERVENTIONS 11

SECTION II COST-UTILITY ANALYSES

3 INTRODUCTION AND METHODS 16
3.1 INTRODUCTION 16
3.2 COLLATION OF EVIDENCE ON EFFECTIVENESS 16
3.3 TRANSLATION OF EFFECTIVENESS INTO A COMMON METRIC 17
3.4 COSTS 22
3.5 DEVELOPING COST-UTILITY ESTIMATES 22
ANNEXURE TO CHAPTER 3 - STATISTICAL TRANSFORMATION BETWEEN SELECTED HEALTH OUTCOME/HEALTH STATUS MEASURES AND QUALITY OF LIFE 24

4 PRIMARY PREVENTION 28
4.1 KEY DATA 28
4.2 ASSUMPTIONS 31
4.3 COST-UTILITY ANALYSES - COMPREHENSIVE MASS MEDIACAMPAIGN 38
4.4 COST-UTILITY ANALYSIS - SURGERY FOR WEIGHT LOSS 43
4.5 COST UTILITY ANALYSIS - INTENSIVE TELEPHONE-BASED GP/DIETICIAN INTERVENTION 47
4.6 COST UTILITY ANALYSIS -GP INTENSIVE DIET/BEHAVIOURAL PROGRAM FOR PERSONS WITH PREVIOUS KNEE INJURY 52
4.7 SUMMARY OF PERFORMANCE OF PRIMARY PREVENTION PROGRAMS 54

5 SELF MANAGEMENT/EDUCATION 56
5.1 INTRODUCTION 56
5.2 LAY LED COMMUNITY BASED - ARTHRITIS SELF MANAGEMENT PROGRAM (ASMP) 56
5.3 NURSE LED EDUCATION AND TELEPHONE SUPPORT 62
5.5 GP-BASED NURSE LED EDUCATION PROGRAM 64

6	**EXERCISE AND STRENGTH TRAINING**	**67**
	6.1 INTRODUCTION	67
	6.2 COSTS	68
	6.3 HOME-BASED INTERVENTIONS	68
	6.4 CLINIC-BASED INTERVENTIONS	73
	6.5 PERFORMANCE SUMMARY	77
	6.6 CONCLUSIONS	77
	ANNEXURE TO CHAPTER 6	80
7	**KNEE BRACING**	**82**
	7.1 INTRODUCTION	82
	7.2 THE EVIDENCE	82
	7.3 COSTS	82
	7.4 OUTCOMES	83
	7.5 PERFORMANCE	84
	7.6 CONCLUSIONS	85
8	**PHARMACOTHERAPIES**	**86**
	8.1 INTRODUCTION	86
	8.2 EFFICACY OF PRESCRIPTION, OVER-TH-COUNTER AND COMPLEMENTARY MEDICINES	87
	8.3 SIDE EFFECT PROFILE - NSAIDS	92
	8.4 SIDE EFFECTS ANALGESICS	96
	8.5 SIDE EFFECTS COMPLEMENTARY AND TOPICAL PHARMACOTHERAPIES	96
	8.6 COSTS	97
	8.7 COST-UTILITY MODEL	98
	8.8 RESULTS OF COST-UTILITY ANALYSIS	100
	8.9 CONCLUSIONS	102
	ANNEXURE TO CHAPTER 8	104
9	**HIP AND KNEE REPLACEMENT SURGERY**	**109**
	9.1 INTRODUCTION	109
	9.2 EVIDENCE OF EFFICACY	109
	9.3 KNEE REPLACEMENT SURGERY	112
	9.4 HIP REPLACEMENT SURGERY	114
	9..5 CONCLUSIONS	117
	ANNEXURE TO CHAPTER 9	118
10	**ARTHROSCOPIC SURGERY AND JOINT IRRIGATION**	**120**
	10.1 INTRODUCTION	120
	10.2 EVIDENCE	120
	10.3 COSTS AND VOLUMES	121
	10.4 CONCLUSIONS	122

SECTION III DISCUSSION AND CONCLUSIONS

11 RANKING OF INTERVENTIONS 123

11.1 INTRODUCTION 123
11.2 PERFORMANCE 125
11.3 OTHER OBJECTIVES 131
11.4 CONCLUSIONS – DESIRABLE RESOURCE SHIFTS AND RESEARCH AGENDA 131

12 PERFORMANCE OF THE HEALTH SECTOR WIDE (HsW) PRIORITY SETTING MODEL 134

12.1 INTRODUCTION – KEY ISSUES 134
12.2 IDENTIFICATION OF AND SELECTION OF INTERVENTIONS 134
12.3 ADOPTION/DEVELOPMENT OF SINGLE OUTCOME MEASURE 135
12.4 CAPACITY TO DEVELOP CONCLUSIONS 136
12.5 ROLE OF ADVISORY PANEL 136
12.6 OVERVIEW – SUCCESS OF THE HsW PRIORITY SETTING MODEL 137

REFERENCES 138

APPENDIX 1 - QUESTIONNAIRE 146

APPENDIX 2 - LITERATURE REVIEW 158

ABSTRACT

Background and aims

The Population Health Division of the Australian Government Department of Health and Ageing commissioned a research project into priority setting to be completed in two stages. The first stage involved a review of priority setting models by Segal and Chen[1]. The second stage involved case study of the application of the best performing Health Sector Wide Disease Based Model (HsW).

Osteoarthritis (OA) was chosen as a suitable case study for application and further refinement of the model. It is an extremely common condition, affecting 2.2 million Australians, and responsible for a substantial reduction in their quality of life. An estimated $1,000 million is spent each year on the management of OA, largely to address symptoms. The number of potential modalities for reducing disease burden in persons at risk and those with established disease is large, covering primary care, pharmacological interventions, physical therapies, surgical interventions and population health initiatives. The major focus of interventions is to enhance quality of life, largely to control pain and extend physical function, thus a priority setting exercise in OA provides a unique opportunity to explore methods for the measurement and comparison of quality of life outcomes.

Study approach

Application of the HsW priority-setting framework involves four distinct stages:

i) *A preliminary phase* to gain an understanding of OA and to establish an Advisory Panel of clinicians, health department officers and consumers/consumer organisations, to provide support and advice to the research team;

ii) *Selection of a comprehensive set of interventions for economic analysis* – identification of all potential intervention/service types to reduce disease burden and selection of a subset for economic analysis - based on defined criteria;

iii) *Conduct economic evaluations of the selected interventions* - drawing on the published evidence to establish costs and outcomes, defining outcomes in a way to facilitate comparison between modalities;

iv) *Comparison of performance* of interventions and development of conclusions about desirable resource shifts - reflecting both equity and efficiency objectives.

Twenty interventions were selected for economic evaluation following an exhaustive literature review. These are listed in Table E.1. These interventions, while comprehensive, represent a sub-set (albeit a large sub-set) of all the potential interventions for reducing disease burden from OA. A selection was necessary in view of resource limits on the research and gaps in reported trial data. The non-inclusion of a modality is not a statement on performance.

[1] Segal, L. and Chen, Y. (2001b) *Priority setting models for health. The role of priority setting and a critique of alternative models - full report*, Research Report 22, Health Economics Unit, Monash University, Melbourne

Table E.1 Interventions for the prevention and management of OA selected for economic evaluation

PRIMARY PREVENTION of OA through weight loss (4)

- Comprehensive media campaign
- Intensive primary care (GP/nurse) based diet and behavioural intervention for weight loss for a general overweight group
- Intensive primary care diet and behavioural program for persons with previous knee injury
- Surgery for obese persons.

PATIENT MANAGEMENT for persons with OA

Patient education (2)

- Lay led program
- GP/clinical nurse educator led

Physical therapies (1)

- Knee brace for persons with knee OA

Exercise/strength training (4)

- Home based basic program
- Home based intensive program
- Primary care clinic based intensive program
- Out-patient based intensive program

Pharmacotherapies – prescription /OTC medications (3)

- Standard NSAIDs – diclofenac and naproxen
- COX-2 specific NSAIDs - celecoxib

Pharmacotherapies – complementary medicines (3)

- Oral Glucosamine sulphate
- ASU (avocado soybean unsaponifiables)
- Topical capsaicin

Surgery (3)

- Total Knee replacement
- Total Hip replacement
- Knee arthroscope with lavage.

Evidence of effectiveness and program descriptions used for generating costings were based entirely on published studies. In the literature, effectiveness is reported using various disease specific and generic instruments. This means that results as reported, are not directly comparable across studies and across modalities. This presented a challenge: to establish a means for comparison of outcomes across trials.

In response to this challenge, a unique approach was developed for the translation of reported outcomes into utility values, which we have dubbed the “Transfer To Utility” technique or TTU. The technique involved the development of four regression equations that mapped scores from four instruments commonly used to measure clinical outcomes in OA intervention trials onto a utility score. The instruments mapped were the SF-36, the VAS (visual analogue scale) for pain, the WOMAC (Western Ontario and MacMaster Arthritis Index) and the Lesquesne arthritis index. The regression equations were derived from responses to a specially developed questionnaire, completed by a sample of 303 persons with OA.

This technique enabled reported trial outcome data to be translated into utility values. These values could then be combined with estimated time in various health states and with estimated mortality impact (where relevant) to calculate effectiveness in quality adjusted life years (QALYs). In this way, the performance of all interventions was measured in the same metric - cost/QALY and

directly compared. The development of the "Transfer To Utility" was central to the successful completion of the priority setting exercise.

Key study results

Cost per QALY was estimated for eighteen of the twenty interventions, (excluding two for which evidence of efficacy was not demonstrated). The level of certainty in calculated values depends on the quality of the trial evidence, the inherent variability in outcomes experienced in a patient population, and the sensitivity of results to key parameters for which there is no agreed value. Sensitivity to the selected rate for discounting future health gains or life years lost (through excess risks associated with some treatments) proved to be important.

The estimated gain in utility score per person treated, cost of treatment per person (per year where relevant) and the estimated cost/QALY are summarised in Table E.2. The key assumptions underpinning these results are presented in Table E.3.

In terms of management of symptoms, many interventions yield a similar level of utility gain compared to baseline - of around 0.08 to 0.12. This includes non-specific and COX-2 NSAIDS, intensive exercise and strength training, use of knee brace and complementary medicines. However, compared with placebo, the utility gain from pharmacotherapies are all around 0.05, while intensive exercise retains a benefit relative to controls of between 0.08 and 0.1. As noted below, hip and knee replacement surgery perform considerably better.

The most effective intervention by far is ***hip replacement surgery***. The estimated utility gain against baseline is 0.305, which is considerably higher than for any other intervention. As the benefits from surgery should continue for several years without further investment (except in a small proportion who require revision surgery, which has been factored into the analysis), total QALY gain per hip replacement is estimated at 3.52. (An expected operative mortality of 1/1000 has been factored in). ***Knee replacement surgery*** is also highly effective, confering benefits over many years, with an estimated QALY gain of 2.085 per total knee replacement. These interventions are also highest cost, at an estimated $16,000 to $17,000 per case. But, because of the high level of benefit, cost/QALY is most favourable at $4,500 to $7,000 for hip replacement and $7,700 to $11,700 for knee replacement surgery.

In terms of net QALY gain, ***nsNSAIDs*** (represented by naproxen and diclofenac) ***and COX-2 NSAIDs*** (represented by celexocib) perform less well, primarily because of a serious side effect profile. Excess risk of hospitalisation and death thus offsets in part at least health gain through symptom control. The QALY loss may, depending on the assumptions, be approximately equivalent to, slightly greater or slightly less than the QALY gain, resulting in either zero, negative or a small positive net QALY gain. In relation to the COX-2 NSAIDs the 'best estimate' of performance, based on mean values from seminal clinical trails and discounting future life years lost at 5% pa is $33,000/QALY, or a negative benefit (net QALY loss), if life years lost from current deaths are counted in full. In either case, COX-2 NSAIDS represented by celexocib is dominated by ***nsNSAIDs*** (represented by naproxen and diclofenac) – higher cost and no evidence of better performance or side effect profile. In relation to nsNSAIDs (naproxen and diclofenac), the 'best estimate' of performance, based on mean values from seminal clinical trails and discounting future life years lost is $15,000/QALY or also a negative benefit (net QALY loss), if life years lost from current deaths are counted in full The performance of other NSAIDS has not been studied, and cannot be commented upon.

Primary prevention via weight loss is potentially cost-effective, with estimated cost/QALY ranging from $2,000 to $48,000/QALY. This estimate is based on observational studies, relating over-weight and obesity to incidence of OA and the effectiveness of weight loss program on BMI. It has not been corroborated by direct evidence of weight loss programs on the incidence of OA. Such evidence would be difficult to gain, and require a lengthy follow-up period. The role for

primary prevention strategies targeted at other potentially modifiable risk factors for OA, such as recreational or work related injury, could not be established from the available literature. Research into these options is indicated.

The evidence concerning ***education*** is slight and of uneven quality with contradictory results emerging. Additional RCTs are desirable, especially in relation to the lay lead programs, which appear more promising. A direct comparison with an exercise program might be especially useful. The Lorig group program, run by professionally trained lay teachers, appears to yield important changes in behaviour and possibly some modest gain in quality of life, which if confirmed suggest a program that would be highly cost-effective. However, as the VAS pain result on which the estimated QoL gain was based, was not statistically significant, the reported improvement may be spurious. There is little objective evidence that the professionally led education programs in OA work, thus a cost-effectiveness estimate could not be calculated.

Knee bracing, for persons with knee OA using a specially fitted and made product is identified as highly cost-effective, at between $3,700 and $12,200/QALY. Performance is dependent on the typical period of use of the brace. Other physical therapies such as patella taping also appear to work are inexpensive. However, the nature of data did not allow a formal cost-utility analysis to be conducted.

Exercise/strength training when delivered via an intensive clinic based program, is estimated to be highly cost-effective, at $5,000/QALY for a primary care based program or $8,000/QALY for an outpatient based program, (range $3,000 to $15,000/QALY). These results are based on two good quality studies. Home based exercise, is less cost-effective, with the more intensive program performing better, at an estimated $14,500/QALY (range $10,000 to $34,000). However, under some assumptions the effectiveness of a more basic home-based program is in doubt.

The natural pharmacotherapies, ***topical capsaicin*** (for knee, hand, elbow and ankle OA) and ***glucosamine sulphate*** are identified as highly cost-effective at less than $5,000/QALY. These drugs demonstrate equivalent efficacy to NSAIDs in controlled trials, but with an apparently benign side effect profile. The performance of ***ASU*** is less clear with contradictory results from the available studies. Additional trial evidence would be desirable to corroborate these results.

Performance and society expectations

It is useful to compare the performance of interventions for the prevention and management of OA, not just with each other, but also with society standards. While, there is no agreement concerning what is an acceptable amount to 'pay for a life year' an indication is found in decisions by the PBAC in relation to the listing of pharmaceuticals on the Pharmaceutical Benefits Schedule. An analysis of these decisions by George, Harris and Mitchell (2000)[2] suggests a community norm of at least $40,000/QALY as an acceptable threshold for the funding of health interventions. George and colleagues found that the vast majority of drugs with a cost/QALY of less than $40,000 are recommended for listing 'at current price', while those in the $40,000 to $70,000 range are sometimes recommended for listing, whilst listing is rare at >$70,000/QALY or life year. Segal and McNeil (1999)[3], have also explored this question, and find that a figure of $40,000/life year is consistent with the value of life incorporated into decisions concerning road traffic initiatives.

The performance of many of the interventions for the management of OA is found to be exceedingly favourable against these norms, with many interventions costing less than $10,000/QALY.

[2] George, B., Harris, A. and Mitchell, A. (2001) "Cost-effectiveness analysis and the consistency of decision making: evidence from pharmaceutical reimbursement in Australia (1991-1996)", *Pharmacoeconomics*, **19**, pp. 1103-9.

[3] Segal, L. and McNeill, H. (2000) *Quality of life and obesity*, Research Report No. 17, Health Economics Unit, Centre for Health Program Evaluation, Monash University, Melbourne.

Results

The interventions have been classified into three groups on the basis of the cost-utility analyses, which are associated with specific policy recommendations:

1. ***Interventions that are highly cost effective (cost/QALY < $10,000) supported by strong evidence***
   - Intensive clinic based (out-patient or primary care-based) exercise/strength training programs.
   - Total hip replacement surgery.
   - Total knee replacement surgery.

   Policy Implications: Programs/services should be expanded to meet of all clinically indicated need.

2. ***Interventions that appear to be highly cost effective (cost/QALY < $10,000), but for which analysis is based on few studies***
   - Topical capsaicin.
   - Oral glucosamine sulphate.
   - Knee brace.

   Policy Implications*: Additional trial evidence should ideally be gathered, but some expansion to service delivery may be warranted in the interim.*

3. ***Interventions that may be highly cost effective (cost/QALY < $20,000), but where this is based on indirect evidence***
   - Primary prevention through weight loss – support to programs to address obesity, through any of the modalities studied - comprehensive community based media campaign, intensive primary care intervention, surgery for persons who are seriously obese.
   - Other approaches to primary prevention – such as avoidance/better management of knee injury.

   Policy Implications*:* A research program should be support to gather additional trial evidence; for example through a Pilot or Trial or well constructed observational study.

4. ***Interventions for which cost-effectiveness is uncertain/highly dependent on assumptions where parameter values are indeterminate or subject to debate.***
   - Non-specific NSAIDs.
   - Patient education – lay-based.

   Policy Implications: Analyse assumptions of the model and redirect services to those with greatest capacity to benefit and for NSAIDs less likelihood of side effects.

5. ***Efficacy not proven -*** Evidence of efficacy is equivocal or not proven relative to placebo or cheaper alternative.
   - COX-2 NSAIDS – Relative benefit of COX –2 NSAIDs (celecoxib) compared with nsNSAIDs (diclofenac and naproxen) yet to be demonstrated.
   - Patient education – professionally-based.
   - Arthroscopy

   Policy Implications: Services to be curtailed and resources redirected to areas with demonstrated effectiveness and cost-effectivness

Comment

The current allocation of resources for the prevention and management of OA may be sub-optimal and resource shifts towards interventions identified as highly cost-effective and away from those of dubious cost-effectiveness should enhance community health and wellbeing. While the evidence is

incomplete, some conclusions can confidently be drawn. For instance, it seems clear that community wellbeing can be enhanced by allocating additional resources to clinic-based exercise and strength training programs and to hip and knee replacement surgery, to ensure access by persons with OA for whom these treatments are clinically appropriate.

Facilitating access to topical capsaicin and oral glucosamine may also be desirable, although additional trial evidence on these treatments would be an advantage. The clinical evidence also suggests that the use of arthroscopy in the management of knee OA needs to be challenged.

Greater net benefits to society will be achieved by focussing nsNSAIDs on those with greatest capacity to benefit and who have a lower than average excess mortality risk (and/or on persons who value their current quality of life more highly than delaying death). The role for COX-2 NASIDs needs still to be revisited pending evidence of superior performance to nsNSAIDs. As noted this analysis is based entirely on naproxen, diclofenac and celexocib, as the products most commonly prescribed in Australia, and as the subject of the key clinical trials. These conclusions may not apply to other NSAIDs. Each formulation really requires specific investigation.

These conclusions, for example recommending additional resources to clinic-based exercise and strength training programs and hip and knee replacement surgery, presume that maximising health as measured by quality of life and longevity and summarised in the QALY is the primary objective of health care. Policy makers may also wish to consider other factors when allocating and redistributing resources, however, this will involve the loss of health benefits that may be considerable.

An important contribution of this priority setting exercise was the development of a robust approach to compare interventions where outcomes are reported in different units - the ‘TTU’ or ‘Transfer to Utility’ technique. This approach allowed the use of trial outcome data, measured through a variety of instruments, to be translated into a utility equivalent to create a common metric. Net utility gain was able to be calculated and combined with length of time in health state and estimated mortality, to calculate performance in terms of cost per QALY. This technique proved extremely powerful and may have wide application.

The Health Sector Wide (HsW) disease based priority setting model proved highly suitable providing a valid and workable approach to the establishment of priorities for reallocating resources to reduce the disease burden from OA. It has also enabled a research agenda to be identified to address critical data gaps. The inclusion of the Advisory Panel in this process worked well and was very valuable.

Further research to establish the policy implications and specifically the means to achieve the desired changes in behaviour that can underpin the recommended resource shifts is now needed.

Table E.2 Summary of cost-utility analyses for prevention and management of OA [1]

Program	Est. mean QALY gain per person (0% disc rate)	Estimated mean program cost $/person	$ Cost/QALY [2] Best estimate (Range)
PRIMARY PREVENTION – modelled over 20 years			
1. Comprehensive mass media program for weight loss		$4	$20,000 (3 - 48,000)
2. Intensive primary care GP/ dietitian weight loss program for overweight/obese persons	0.09	$720	$11,000 (7 - 13,000)
3. Surgery (stomach stapling) for obese persons	2.91	$15,000	$20,000 (13 -20,000)
MANAGEMENT			
Education - modelled over 2 years			
5. Lay led group education	0.072	$162	(2,400 to ∞)
6. Primary care – GP/ clinical nurse educator with phone support	Equivocal	$200 - $400	∞
Exercise/strength training - modelled over 1 year			
7. Home based exercise - basic	0.022	$ 400	$18,000 (9,000 - ∞)
8. Home based exercise - intensive	0.100	$1,420	$15,000 (10 -34,000)
9. Clinic based exercise - primary care	0.091	$ 480	$ 5,000
10. Clinic based exercise - outpatients	0.078	$ 590	$ 8,000 (3 -15,000)
Knee brace - modelled over 6 months to 3 years			
11. Specially fitted knee brace	0.12 to 0.355	$1,300	$ 6,000 (4 -12,000)
Pharmacotherapies[3] : Prescription / OTC medications			
12. Non specific NSAIDs - naproxen, diclofenac	Symptom control 0.043 Mortality loss - 0.027 to 0.044	Drug $104/yr Morbidity$ 70/yr	r =0 $15,000 (23,000 - ∞) r =5% ∞ (9,000 -70,000)
13. COX-2 NSAIDs - celecoxib	Symptom control 0.043 Mortality loss - 0.027 to 0.044	Drug $391/yr Morbidity$ 70/yr	r=0 ∞ (71,000 - ∞) r=5% $33,000 (21,400-84,000)
Complementary medicines			
14. Glucosamine Sulphate	0.052	$ 180	$3,000 (2 to 5,000)
15. ASU (avocado, soy, unsapofinables)	0.081	$ 333	$5,000 (4,000 to ∞)
16. Topical capsaicin	0.053	$ 236	$4,500
Surgery – modelled over 15 years			
17. Total Knee Replacement	QoL gain +2.085 Mortality -0.015	$16,500	$8,000 (8 - 12,000)
18. Total Hip Replacement	QoL gain +3.520 Mortality -0.015	$15,900 - $17,100	$5,000 (4 - 7,000)
19. Knee Arthroscopy with Lavage	none*	$ 3,500	∞

Notes:

a. Relative to placebo, or no intervention for THR and TKR surgery
b. Rounded to nearest $1000 – costs discounted at 5% pa.
c. r=0 future life years and QoL counted in full, r=5% future life years and QoL discounted at 5% pa.
∞ no evidence of net benefit
***** control group did better

Table E.3 Key assumptions underlying the modelling

Attribute and Modality	Key Assumptions
Duration of Benefits	
Primary prevention	20 years
Education/Self Management	2 years
Exercise	1 year
Knee Brace	18 months to 3 years
Total hip and knee replacement	15 years – adjusted for all-cause mortality (ABS mean death rates for a cohort commencing 69 years of age)
NSAIDs[1]	12 months (treatment contiguous with benefit)
Complementary pharmaco-therapies	12 months (treatment contiguous with benefit)
Discount Rates: all modalities	
Costs – incurred or cost savings	Beyond 12 months discounted at 5% per annum
QALY – gains or losses	0% (undiscounted) and 5% per annum
Morbidity	
NSAIDs	Rate of hospital admissions assumed the same across all NSAIDs[1] GI [2] admissions = 2.13/100 patient years CHF[3] admissions = 0.5 /100 patient years
Mortality	
NSAIDs	Death rate assumed the same across all NSAIDs[1] GI = 10% GI hospitalisation rate = 0.00231/ person year NSAID use CHF = 5% CHF hospitalisation rate = 0.00025 Deaths associated with mean loss of 18.5 years (= life expectancy at 65 years of age)
Total hip and knee replacement	Assumed death rate from surgery = 1/1000
Sensitivity analyses	
Common	Discount rate on QALYs 0% and 5% Clinical trial results: where available +/- 2 SD (95% confidence intervals) or +/- 1 SD for NSAIDs
Various	See Chapters 4 to 10

Notes:

1 NSAIDs – diclofenac, naproxen, celecxoib

2 Gastro-intestinal admissions – perforations, ulcers and bleeds

3 CHF chronic heart failure.

SECTION I INTRODUCTION

1. THE PRIORITY SETTING MODEL - METHODS

1.1 Background

Priority setting is a health-planning task concerned with achieving the optimal mix of health services for a population. The specific objective is to identify desirable resource shifts that will enhance net community welfare. The aim is to identify services that yield high benefit for resources allocated, to be expanded and others that yield low benefit for resources allocated, to be contracted. Given the large differentials in cost-effectiveness ratios that are observed for different health interventions (see Table A.1 in the annexure to this chapter), substantial benefits may be obtainable by the selective redirection of resources between programs and services. Large differences in cost-effectiveness ratios can emerge because of the nature of the health market, which prevents consumers from determining and giving effect to their needs, and prevents providers from responding to these needs in a flexible fashion.

This report is part of a larger project to adopt a formal priority setting model that can be used to identify and recommend desirable resource shifts to reduce burden of harm from selected conditions, in this case osteoarthritis. In achieving this aim this study focuses on technical and allocative efficiency using the QALY as the primary measure of outcome. Thus, provided health maximisation is the goal, the findings from this study will provide valid recommendations for resource redistribution. To the extent that other objectives are important, such as the reduction of health inequalities, optimal policy may depart from that implied by a simple analysis of relative cost/QALY. However, health remains the dominant, if not the only objective of health care, and thus understanding how to maximise health is of considerable importance.

This report is the fifth in a series that explores priority setting methods and the application of these methods in the Australian health care setting. The Population Health Division of the Australian Government Department of Health and Ageing commissioned this research project to be completed in two stages, with a potential third stage:

i) *Review of priority setting models:* The first stage of this research program involved reviewing the performance of alternative priority setting models, resulting in the recommendation of a preferred model for adoption by the Department. The review is reported in a Department document (Segal and Chen, 2000) and a CHPE research report (Segal and Chen, 2001b). The review recommended the adoption of the Health Sector Wide Disease Based Model (HsW-DBM) for priority setting.

ii) *Case study application*: The second stage of the research program involved the application of the HsW-DBM to a selected case study – osteoarthritis. The rationale for that selection is described in an earlier report (Segal and Chen, 2001b). Two other reports have been drafted arising from the case study: Osborne, Segal and Day (2001), containing a description of osteoarthritis, and Segal, Day, Chapman and Osborne (2002), in which the possible intervention options to reduce disease burden are described, and the set of interventions chosen for economic evaluation identified. Evidence on effectiveness has been collated and reported in some detail, and only some of this material is covered again here.

iii) *Policies to achieve recommended resource shifts:* A potential third stage of the research program involves the identification and exploration of policy options and strategies available to implement the recommended resource shifts to realise the theoretical benefits of the priority setting exercise.

The reasons for selection of osteoarthritis for case study application of the priority setting model were extensively discussed earlier (Osborne *et al*., 2002). As summarised below, they relate to

size of health burden, range of potential intervention options and capacity to focus on quality of life as the primary outcome.

i) *Size of health burden:* OA is an extremely common condition that has a substantial impact on the health of the community and the health system. Some 2.26 million people were affected by OA in 1996, and the cost of management was estimated in 1993-4 at $700 million (see Table A.2 in the annexure to this chapter). The estimated cost of management has been recalculated in Chapter 4.

ii) *Range of intervention opportunities:* There are a large number of interventions potentially available that may reduce the burden of OA. These cover the disease spectrum from the general community to the at-risk population and persons with mild and severe disease. They also cover a wide range of modalities, across the entire healthcare sector.

iii) *The role of quality of life/disability in disease burden:* OA is responsible for substantial loss in quality of life (see Chapter 3) and because interventions are targeted at quality of life not mortality it provides an imperative to explore the challenge of identifying and applying a consistent measure of quality of life (utility) across disease stages and treatment modalities.

iv) *Other criteria:* OA had not previously been subject to a priority setting exercise and there was a substantial literature (although with gaps) on interventions addressed at OA.

1.2 Priority setting framework

Various models of priority setting have been developed. The review, completed as the first stage of this research program for the Australian Government Department of Health and Ageing (Segal and Chen, 2001) recommended the adoption of the Health Sector Wide Disease Based Model (HsW-DBM). An acceptable alternative model is PBMA adjusted to make it more evidenced based (dubbed Evidenced Based Marginal Analysis EBMA). The HsW models has been successfully applied to NIDDM (Segal, 2000) and the EBMA to cancers (Carter *et al*., 2001). They are also applied to OA (current study), mental health and cardiac disease.

The key features of the HsW model are:

- a health sector wide disease-based framework;
- the adoption of comparative marginal cost-benefit ratios as the decision criteria (with definition of benefit to be determined);
- comprehensiveness in identification of possible intervention options, with classification of interventions into disease stage and by relevant target groups as appropriate;
- the use of an expert panel to assist in specification and selection of intervention options, definition of program objectives and to support possible adoption of recommendations; and
- the use of published evidence to establish cost-benefit ratios.

The logic of the HsW-DBM requires that all conceivable intervention options are identified and analysed and then ranked according to their marginal benefit-cost ratio. The aim is to identify the most and least cost-effective interventions. The research activities are: i) gain an understanding of the disease or health problem under question; ii) establish suitable outcome measure; iii) identify all possible intervention options for reducing disease burden; iv) conduct cost-effectiveness (or cost-utility) analyses of all interventions (or a selected sub-set), using published of costs and outcomes; v) compare interventions, based primarily on the cost-effectiveness analyses, but incorporating other criteria.

While the model requires that all plausible intervention options are identified and subject to economic analysis, the size of this task may make it infeasible. An extremely large number of potential intervention options can invariably be identified to reduce disease burden. This reflects the great variety of ways in which programs/services can be delivered and the almost infinite variety of ways that therapies might be used in combination. Thus selection of a sub-set of

intervention options for economic evaluation will almost certainly be necessary. That is the goal of comprehensiveness is likely to be unrealisable. The importance of the documentation and selection of intervention options for comparison of performance cannot be overstated. Only for those interventions that are selected will performance be assessed and recommendations developed about expansion or contraction. There is an implicit assumption that interventions not studied are either so insignificant as to be of no consequence or that the current volume/level of delivery is about right.

That is, recommendations can only be derived in relation to the set of interventions studied. While this might seem obvious, commonly in economic evaluations a very restricted set of interventions is analysed at any one time. Unless the interventions are chosen with care, the analysis might result in recommendations that are inconsistent with the global optimum. The logic of the model is that over time, and progressively, all plausible intervention options will be subject to economic analysis using a consistent approach and a single outcome measure. Comparison across interventions will be facilitated by the use of consistent evaluation methods.

Priority setting is not, however, about developing a simple hierarchy of interventions, or league table ranked by cost-effectiveness or cost utility ratios. Rather, a priority setting process is designed to find that suit of interventions that warrant funding to a level consistent with best practice care and to identify those interventions from which funding should be withdrawn. A simple hierarchy of interventions would make sense where all interventions are substitutes for each other, where all interventions address the same population and where distributional issues are unimportant. In reality none of these conditions apply. Identifying the appropriate set of health services to be made available, to be used in isolation or in combination is the broad aim. Priority setting will ideally proceed in a complementary way with clinical guideline development, to determine when best practice care is also cost-effective and thus when funding to meet clinical guidelines is supported in the context of resource scarcity.

1.3 Research approach

The research program involves four broad research stages consistent with the HsW-DBM (Health Sector Wide Disease Based Model) outlined above.

Stage I: Gain an understanding of osteoarthritis

The research team sought to understand the aetiology of OA, the epidemiology – who is affected what are the risk factors, what is the nature of disease progression and the nature and severity of complications, and to understand the broad approaches to management and their expected impact on disease severity. This was achieved through access to relevant literature and discussion with clinicians and others on our Advisory Panel. The Advisory Panel was established to provide advice to the study team, and more broadly, to facilitate dialogue between researchers, clinicians, policy makers and consumer groups. Full membership details are listed in the Acknowledgements. The panel included three groups:

1. clinicians/researchers – selected to ensure coverage of all pertinent modalities of surgery, medicine, pharmacy, physiotherapy and complementary therapies;
2. officers from the Australian Government Department of Health and Ageing and the Department of Human Services Victoria, to facilitate information transfer between the project team and health officers;
3. consumer representation - through Arthritis Victoria and a person with osteoarthritis.

Advisory Panel members assisted in locating pertinent literature, contributed to the identification and consideration of potential intervention options, and provided valuable feedback on draft material: most importantly on our summary of the evidence concerning the effectiveness and side effect profile of alternative treatment modalities. Two Advisory Panel meetings were held in Melbourne. In addition, contact was made with individual panel members as required for advice on matters about which they were expert. Our understanding of the disease and the options for reducing disease burden are described in Chapter 2.

Stage II: Determine outcome measure

Determination of a suitable outcome measure incorporates two elements: consideration of the concept of benefit and adoption of a single outcome measure that can be applied across all interventions. The latter is a necessary requirement for comparison of performance.

Concept of benefit: The concept of benefit was discussed with the Advisory Panel and a decision made to focus, in the first instance, on standard health outcomes. Other potentially relevant attributes such as equity and access, size of benefit, contribution to community empowerment or attributes of the process of care were to be introduced, if feasible, as second stage criteria. That is, performance was to be determined initially in terms of cost per unit of health outcome, and then issues of equity and access etc., considered at a qualitative level, to establish whether some adjustment to the initial conclusions might be warranted.

Unit of health outcome: It was found that for the pertinent trials, four instruments were commonly used in addition to numerous investigator-developed tools. (See also discussion in Chapter 3.) Thus it was necessary to develop an approach to deriving a common health outcome unit. Because mortality was not the major focus of treatment, life years could not become the common metric. The options to consider were: i) one of the disease specific instruments; ii) a generic health status measure (such as the SF-36), or the Disability Adjusted Life Year (DALY); or iii) a utility instrument that will enable QALYs (Quality Adjusted Life Years) to be calculated. The disease specific measures are not easily interpreted or available for other studies. Thus even if we were able to obtain all outcomes in terms of the WOMAC (Western Ontario and McMaster Osteoarthritis scale, one of the most commonly applied OA-specific outcome instruments), it would have no meaning outside arthritis. Also, health status instruments encompass only quality of life, they cannot be directly combined with mortality. The ideal is an instrument that can incorporate both quality of life and mortality in a single measure. Even though OA is not a direct cause of death, some common treatments are associated with excess mortality, and interventions for prevention, (notably weight loss) are associated with reduced mortality. Thus interventions can affect mortality as well as morbidity.

Published disability weights for OA, for use in calculating DALYs, could not be used as only three distinct disability weights for osteoarthritis have been specified (see Table A1.3 in the annexure to this chapter). This is clearly insufficient to encapsulate trial results with any sensitivity. Moreover the nominated health states described for each disability weight bear no obvious relationship to health states at entry or follow-up in clinical trials. For these reasons, the DALY was an unsuitable outcome measure for this study. More broadly, published disability weights will be unsuitable where, as with OA, there are no clear categorical disease stages that persons with the condition can be classified into, nor to which interventions might be targeted to move people between. Rather OA is a condition in which there is a continuum of symptoms, for which symptom control is the major objective of treatment, and there is a poor concordance with observable pathology. DALYs are of most use in describing the broad health status of populations, or in estimating the possible benefits from disease prevention, the context in which the DALY was developed by the World Bank. Their application to cost-effectiveness analysis is not suited, expect in the unique circumstance of a disease with precisely defined disease stages which exhibit a narrow variation in quality of life.

A decision was thus made to explore the QALY as the common outcome metric, and to derive utility values for each intervention. There are several advantages in choosing utility and the QALY as the common outcome measure. Firstly, the impact on quality of life and mortality can be combined and taken together with time in designated health states to derive QALYs. These can be used to derive cost/QALYs as a standard for comparing performance; secondly the nature of the outcome – the QALY or quality of life (QoL) has a meaning that is widely understood; and finally comparisons across other interventions and disease states (outside OA) are possible.

It would be preferable to use utility values reported in published trials. However, utility instruments were rarely used in trials in OA. Thus, an alternative technique was devised specifically for this study. This involved the estimation of a utility value through a statistical transformation of reported outcome measures. As far as we are aware this technique has not been previously employed. The principle underlying the approach is that key instruments applied in OA intervention studies are seeking to establish the effect of the intervention on quality of life – either overall or for specific dimensions. The technique developed allows published trial results, as reported using a range of instruments, to be translated into a common value, a utility, through derived regression equations. While this constitutes a second best approach, in the absence of the widespread use of utility instruments in the conduct of clinical trials, it represents a potentially useful way forward. The strength of the relationship between instruments gives some confidence in the resulting transformations. Without recourse to such a technique, comparisons across interventions and modalities would need to await the more general adoption of utility instruments in the conduct of clinical trials, which is to be encouraged.

The procedure represents an extremely important conceptual and technical development. It provides a potential technique for the comparison of performance across a wide range of modalities/trials where outcomes are reported using several different instruments. Full details of the approach are reported in Chapter 3.

Stage III: Select options for review

The possible intervention options to reduce disease burden from OA were classified and described. There were over 12 major categories with numerous alternative models for delivery within each. Thus, selection of a subset of interventions for economic evaluation on which to conduct cost-utility analyses for comparison of performance was required. The selection proceeded according to pertinent criteria, but with the primary objective of ensuring coverage of a broad range of modalities and target populations.

This process is extremely important as it defines the scope of the study, and ultimately the interventions and services about which recommendations can be made about desirable resource shifts. The selection process requires a sound understanding of OA, and of the literature on intervention trials. This task is reported on in detail in the technical report by Segal *et al*. (2002) and summarised in Chapter 2. A total of 24 intervention options were selected for cost-utility analyses. Ultimately cost-utility analyses have been completed for 20 service types (reflecting access to relevant trial data), representing 14 broad treatment modalities.

Stage IV: Conduct cost-utility analyses and compare interventions

Economic analyses have been conducted for 20 selected interventions, most of these representing full cost-utility analyses. (The exceptions relate to interventions for which there were no evidence of effectiveness, meaning that cost-utility values could not be derived). The cost-utility analyses have represented the major task of the priority setting exercise. The results including detailed methods are reported below in Section II of this report in Chapters 4 through 10 as per Table 1.1.

Table 1.1 Reporting of cost-utility analyses

Chapter	Interventions modelled	Number of	
		Modalities	Service types
4	Primary prevention through weight management via: i) media/ community program to the general population, ii) surgery to seriously obese persons, and iii) primary care, to a general overweight population and overweight persons with previous knee injury). No other approaches to prevention such as avoiding injury were modelled due to absence of relevant intervention trials.	3	4
5	Patient Education through: i) lay lead group program and ii) professionally lead by GP/nurse (2 distinct programs).	2	3
6	Physiotherapy/exercise and strength training through: i) clinic based intensive, two distinct services; and ii) home based, intensive, home based basic.	2	4
7	Other Physical therapies: i) Knee Brace and ii) Patella taping (but C-U analysis not undertaken due to lack of suitable trial data)	1	1
8	Pharmacotherapies Prescription medicines: i) ns NSAIDs (naproxen and diclofenac - pooled), ii) COX 2 NSAID (rofecoxib) Complementary medicines: iii) oral glucosamine sulphate, iv) topical capsaicin, v) ASU (avocado soybean unsaponifiables)	3	5
9	Surgery (Arthroplasty): hip and knee replacement surgery	2	2
10	Arthroscopy: with lavage or debridement for knee OA.	1	1
		14	20

Stage V: Draw conclusions

The final task of the study is to draw conclusions about interventions for reducing disease burden in OA and also to comment on the success of the HsW-DBM in this application. These matters are reported on in Chapters 11 and 12 respectively, with some brief comments below.

Priority setting in osteoarthritis: The primary purpose in undertaking the priority setting exercise in OA is to assess the relative performance of the various interventions to enable conclusions to be drawn about desirable resource shifts that will make the greatest contribution to a reduction in disease burden from OA. Performance in this research program is defined by comparing estimates of incremental cost/QALY gain. Strength and quality of the evidence and the robustness of calculations is also important impinging on the confidence in the conclusions. Ideally other objectives, such as access and equity would also be considered. While the logic of the model is to generate a type of league table from high performing interventions (low cost/QALY gain) to poorly performing interventions (high cost/QALY gain), it needs also to be recognised that a mix of interventions will be required to meet the health needs of persons with OA. Clinical appropriateness must always be a prior consideration in deciding on service needs, before the issue of cost-effectiveness become relevant. Within a group of persons with a particular disease, in this case OA, there will be a wide range of situations in terms of disease severity (including an at-risk population) and capacity to respond to alternative treatments. Thus in translating the results of a priority setting program and cost-effectiveness analyses into a program plan for resource shifts, a further analysis is required. This would need to cover the nature of the population with the disease and at-risk, a description of the service system, the possible policy levers available to achieve resource shifts and other health system objectives.

Based on efficiency criteria alone, it is logical to recommend that services found to be highly cost-effective should be expanded to a level where all persons for whom they are clinically appropriate can access them in a timely, convenient and culturally appropriate manner. While and services found not to be cost-effective be contracted and targeted only at those with greatest capacity for net benefit.

Performance of the Health Sector Wide Disease based model: The performance of the Model is assessed in terms of the robustness of the framework for conducting a priority setting exercise, and specifically:

- the usefulness of the criteria for selecting a set of interventions for the conduct of economic evaluations;
- the capacity to develop a single outcome measure that will support comparisons across a wide range of modalities and health services;
- the capacity to develop cost-effectiveness estimates based on objective evidence as reported in the scientific literature; and
- the capacity to draw conclusions about desirable resource shifts.

The performance of the model is this to be analysed in the context of the application to OA, but also in relation to other potential applications.

ANNEXURE TO CHAPTER 1

Table A1.1 Observed variation in cost-effectiveness ratios

Type of intervention	Cost-effectiveness ratio
Australian studies: Drugs approved for listing on the PBAC [1]	 $5,000 to $69,000 per LY or QALY
Primary prevention of NIDDM - diet/behavioural approaches [2]	Cost saving to $2,400 per LY
Comprehensive diabetes care [2]	<$1,000/LY
Extend Victorians skin smart campaign [3]	<$500/DALY
2 yearly screening for colorectal cancer [3]	$12,000/DALY
Extend screening interval for cervical cancer [3]	$420,000/DALY
US studies of `life saving' interventions' [4]	
Childhood immunisation (6 studies), prenatal care (12 studies)	Cost saving
Drug & alcohol treatment (4 studies)	Cost saving
Arsenic, benzene control (42 studies), school bus safety (6 studies)	>US$1million/LY

Sources:

1 George *et al.,* 1999
2 Segal, 2000
3 Carter *et al*., 2001
4 Tengs *et al*., 1995

Notes: LY = life year; DALY = disability adjusted life year; QALY = quality adjusted life year.

Table A1.2 Burden of musculoskeletal disease and osteoarthritis

Disease		DALYs [1] 1996			Cost [2] 1993-4 $million	Numbers affected [3] `000
		Male	Female	Total		
Rheumatoid arthritis+		3,646	8,343	11,989	129	780
Osteoarthritis*		22,610	33,695	56,305	700	2,256
Back problems	Chronic back pain	2,089	1,927	4,016	294	783
	Slipped disc	2,301	1,574	3,875		
Osteoporosis		315	2,240	2,555	60	257
Other musculoskeletal disorders		3,574	7,602	7,727	1,561	
All musculoskeletal				89,916	3,002	4,780
Asthma				36,240	480	2,040
Diabetes				74,930	370	410
CVD				548,585	3,720	3,870
Cancers				478,580	1,900	380

Sources:

1 Mathers *et al.,* 1999b
2 Mathers and Penm, 1999a
3 ABS 1995 National Health Survey

Notes

\+ Rheumatoid arthritis and rheumatism
* Including osteoarthritis and arthritis nec,

Table A1.3 Disability weights used in the Australian Burden of Disease Study

Musculoskeletal condition	Disability weight	Source of weighting
Osteoarthritis		
Grade 2 (radiological) hip or knee (asympt.)	0.01	Dutch weight
Grade 2 symptomatic	0.14	Dutch weight
Grade 3-4 (radiological) hip or knee (asympt.)	0.14	Dutch weight
Grade 3-4 symptomatic	0.42	Dutch weight

Source: Mathers *et al*., 1999b

2. SELECTION OF INTERVENTIONS

2.1 Introduction to intervention options

Our research has identified an extremely wide range of intervention options for reducing disease burden from osteoarthritis. This list has been established through a comprehensive review of the literature and discussions with clinicians on the Advisory Panel. The identification and classification of interventions for reducing disease burden in OA reflects our understanding of the disease, its aetiology, and risk factors and of guidelines for its management (as reported by Pencharz *et al.,* 2001), together with a knowledge of common practice. The description of the disease and implications for possible ways of reducing disease burden is described fully in an earlier technical report, (Osborne *et al.*, 2001). The literature review has also been reported fully earlier in (Segal *et al*., 2002). The method adopted for the review is outlined below. Summaries of 53 key trials located from this review are contained in Appendix 2 of this report. These cover interventions for weight loss, patient education/telephone support, exercise and strength training, oral and topical pharmacotherapies, intra-articular agents, complementary therapies, total hip and knee replacement and arthroscopy. Some of this evidence is also contained within Chapters 4 to 10 when it is central to the economic evaluations. The set of interventions recommended for analysis, based on the literature review and application of the selection criteria, is described in Section 2.3 below.

2.2 Literature review - method

A comprehensive review of the literature has been completed to gain the information required to select the intervention options for analysis, and provide the evidence on outcomes and cost. The literature was interrogated for relevant articles using key words through the major databases, including Medline, PubMed, CINAHL, Cochrane database of Systematic Reviews, Database of Abstracts of Reviews of Effectiveness (DARE), Current Contents, AUSTHealth. Initially, systematic reviews were identified and collected. While such reviews provide a useful overview of the literature, in general they are inadequate for cost-effectiveness analysis or even identifying suitable interventions. This is because they rarely contain adequate descriptions of intervention options or precise information on effectiveness or program inputs (required for estimation of program costs). The summaries contained in review articles were also at times found to be erroneous when compared with the reports on which they were based. Reviews were thus mainly used to indicate the possible role for various modalities and to identify key studies, which were subsequently obtained. Information was collected from over 600 original reports.

Key studies were identified that met at least the following criteria:

- clear and precise description of the intervention; and
- clearly defined outcome measures and precise quantitative results.

Plus, ideally, the additional criteria of:

- long term follow-up (preferably 2+ years);
- randomised study design, incorporating suitable control group(s);
- ‘reasonable’ retention rate of trial participants;
- actual treatment close to intention to treat (or analyses reported both in terms of intention to treat and actual treatment);
- validated outcome scales were used, preferably the Western Ontario and McMaster University Osteoarthritis scale (WOMAC), the SF-36, LeQuesne Functional Index, a utility instrument, and/or a visual analogue pain scale; and
- a large sample size.

Very few trials met most of the criteria and we were thus forced to rely on the less demanding criteria of precise description of the intervention and defined outcome measures with clearly expressed quantitative results. Confidence in the results of the cost-utility analyses reflects in part the integrity of the trial data on which estimates are based.

Over 50 key trials were identified and directly interrogated for the following information:

- description of intervention – modality, delivery model, site of OA, timeframe;
- trial/study design;
- description of intervention and control cohorts – entry criteria, demography, health status;
- observations at baseline, trial end, follow-up for control and intervention cohorts; and
- other information as relevant.

As noted these summaries are contained in Appendix 2 of this report.

2.3 Selection of interventions

The evidence suggests that disease burden from OA may potentially be modified through both primary prevention - addressing modifiable risk factors through symptom management and disease modification. Sub-classification into levels of disease severity for those with established disease did not prove possible, as disease staging systems (eg radiographic evidence or symptoms) are poorly defined, with little correlation between radiographic evidence and the common symptoms of pain and loss of mobility.

Thus only two broad means for impacting on the population burden due to OA are described.

i) *Primary prevention:* aimed at reducing the incidence of OA by modifying the risk factors associated with its development, targeted either at the general population or at high risk groups; and

ii) *Management:* for those with established disease (defined by symptomatic OA with or without radiographic evidence of joint deterioration), with the primary aim of symptom control - reduction in pain and enhancement in activities of daily living, or, potentially, modification of the disease.

A framework for further categorising interventions has been developed to assist the process of selection of interventions to achieve comprehensiveness in modalities covered and presented in Table 2.1. Interventions are classified firstly by disease stage and target group, and then by modality and type of intervention. The purpose of the intervention is also noted – whether it is symptom management or disease modification. For some interventions, the target site (eg hip or knee) is also noted where relevant.

For each broad treatment modality there may be a number of specific program types that can be employed and most interventions can be implemented in a multitude of ways. (For instance patient education programs can be implemented via one-on-one provider/patient consultation or through groups; and be delivered by lay persons or professionals, who could be GPs or nurse educators; the education content could be delivered through face-to-face contact, phone or mail and employ various educational materials.) This potential variety creates an enormous number of potential intervention options. Thus choices have to be made in selecting interventions for detailed study. (However, it is desirable that ultimately all feasible intervention options are subject to analysis.)

Our research has revealed many interventions options for reducing disease burden in OA that would ideally be subject to comparative cost-utility analyses. Given a limited budget and time frame it was not possible to analyse all potentially relevant intervention options, although the model ideally requires this. Additional clinical evidence concerning benefits would need to be gathered for some interventions before it would be possible to conduct a cost-utility analysis. The selection of the interventions to be included in the current research program has been guided by the criteria noted below, with a particular concern to ensure comprehensiveness with respect to disease stage and modality and access to relevant evidence on efficacy.

Five criteria used to select intervention options for conduct of cost-effectiveness/cost-utility analyses are:

1. Comprehensiveness of coverage - particularly in terms of disease stage and modality of treatment.
2. Include commonly employed interventions and those that involve substantial resource use.
3. Include interventions that have the potential to reduce disease burden - based on disease aetiology and/or clinical evidence.
4. Preliminary evidence that a particular intervention may perform either particularly well or particularly poorly, that is, it may constitute a marginal program (one to be expanded or contracted).
5. Quality and availability of quantitative evidence on effectiveness and program description that can be used to derive costs.

The list of intervention options presented in Table 2.1 covers the broad categories, without specifying all the potential variation within each category. The interventions that have been selected for analysis are highlighted, also identifying those not to be reviewed at this stage. These cover both primary prevention and management of OA and all major modalities. The selected interventions and the section in the report where they are analysed are described in Table 2.2.
.

Table 2.1 Interventions for osteoarthritis

Stage Therapy Focus	Modality	Intervention Strategy	Recommended for Cost-Utility Analysis Current	Future
I PRIMARY PREVENTION				
Health Promotion Risk Factor modification for reduction of incidence of OA	Population based Media campaigns to adopt healthy life style	Focus on incidence of OA or broad non-communicable diseases eg with CVD.	✓	
		Modify environment to promote healthier life style		✓
	Primary care targeted to overweight adults	Behavioural: diet, exercise/physical activity; individual or group program		
		– To a general group of overweight adults	✓	
	Surgery	- To overweight adults with previous knee injury	✓	
		Surgery for seriously obese adults	✓	
	Quadriceps strengthening	Individual/group, home based/gym, physiotherapy.		✓
	Occupational injury and Recreational injury	Information-individual/group to citizens/providers		✓
		Regulation		✓
		Financial penalties/rewards		✓
		Improved management of injury		✓
II MANAGEMENT OF PERSONS WITH ESTABLISHED DISEASE				
Non-Pharmacological Symptom Management Risk Factor Reduction	Patient education	Self Management/Education/ Empowerment	✓	
		Social Support/Telephone Support		✓
	Physiotherapy / Physical Therapy	Exercise and strength training		
		- Home based intensive	✓	
		Brief	✓	
		- Clinic based	✓	
		Therapeutic Ultrasound		✓
		Knee bracing	✓	
		Ambulatory aids		✓
	Occupational Therapy	Aids to Activities of Daily Living		✓

Table 2.1 (Contd.)

Therapy	Modality	Intervention Strategy	Recommend for Cost-Utility Analysis	
			Current	Future
Pharmacological Symptom Management	Oral	Simple Analgesics - Paracetamol, aspirin		✓
		ns NSAIDs (non-specific non-steroidal anti-inflammatory drugs)	✓	
		COX-2 NSAIDs	✓	
		Opioids		✓
	Topical	NSAIDs		✓
	Intra-articular	Hyalurons		✓
		Corticosteroids		✓
Complementary & Alternative Symptom Management Disease Modification?	Oral	Glucosamine sulphate	✓	
		Chondroitin		✓
		Avocado/Soybean Unsaponifiables (ASU)	✓	
		Other herbal supplements		✓
		S-adenosylmethionine (SAMe)		✓
		Other micro-nutrients		✓
	Topical	Capsaicin	✓	
	Physical Therapy	Acupuncture		✓
		TENS		✓
Surgery Symptom Management Disease Modification	Joint modification Joint replacement	Arthroscopy (knee)	✓	
		Arthroplasty total hip replacement (THR)	✓	
		Arthroplasty total knee replacement (TKR)	✓	

Table 2.2 Selected interventions – description and location in report

PRIMARY PREVENTION		
1	Healthy life style for at-risk adults: Media/community - A high profile comprehensive and intensive population based media program, with extensive community based supportive elements	Chapter 4
2	Surgery, stomach stapling/banding for seriously obese adults	Chapter 4
3	Primary care via intensive GP/allied health worker diet/behavioural program for overweight or obese adults	Chapter 4
4	Primary care via intensive GP/allied health worker diet/behavioural program for overweight or obese adults with a previous knee injury	
MANAGEMENT OF PERSONS WITH ESTABLISHED DISEASE		
	Patient self-management, Patient education	Chapter 5
6	- Trained lay leaders for group based patient education – tightly scripted program of 6 x 2hr sessions	
7	- Patient education by health professionals – arthritis nurse specialist in patient education + telephone follow-up + feedback to physician	
8	- Nurse + GP 4x1hr group sessions by research nurse at GP surgery + home based assessment	
	Exercise and strength training	Chapter 6
	Home based	
9	- Booklet + 12 home visits over 16 weeks	
10	- Clinic assessment + home based daily strengthening exercises. 4 home visits by nurse metrologist	
	Clinic based	
11	- Physiotherapist-managed exercise regime delivered at GP surgery. 16 x ½ hr physio sessions per client over 12 weeks	
12	- Out-patient physio 2/wk sessions ~ 1hr each over 4 weeks of manual physical therapy from physical therapist for joint movement and muscle strengthening	
13	knee brace for knee OA – fitting and wearing of specialised knee brace	Chapter 7
	Prescription and over-the-counter oral medicines	Chapter 8
14	- Non-specific NSAIDs – diclofenac and naproxen	
15	- COX 2 specific NSAIDs - rofecoxib (paracetamol as comparator)	
	Complementary therapies	Chapter 8
16	- Oral Glucosamine sulphate	
17	- Topical capsaicin	
18	- Avocado/Soybean Unsaponifiables (ASU)	
	Surgery	Chapter 9
19	- Total knee replacement (TKR)	
20	- Total hip replacement (THR)	
	Surgery	Chapter 10
21	- Arthroscopy of the knee with debridement and/or lavage	

SECTION II COST-UTILITY ANALYSES

3. METHODS

3.1 Introduction

The cost-utility analyses of the selected interventions are reported in Chapters 4 to 10. In this chapter we explore some of the conceptual and technical issues involved in these analyses.

The primary tasks in completing the cost-utility analyses are:

- assemblage of quantitative evidence of effectiveness;
- development of a common measure of outcome to apply across all interventions to facilitate comparison;
- estimation of costs of the intervention and of possible adverse events; and
- assessment of downstream impacts, costs and outcomes where relevant – including application of a suitable discount rate.

The final task is to compare performance across all interventions, based primarily on cost/QALY, but ideally also incorporating other objectives of health care. The aim is to identify a set of interventions that warrant expansion to ensure access for all where this is clinically indicated and another set of interventions that should be contracted. The expectation is that the implied change in resource mix would achieve a reduction in the burden of OA on the community. This research program does not cover the matter of how recommended resource shifts might be achieved. That would ideally form part of a subsequent research program.

3.2 Collation of evidence on effectiveness

The evidence of effectiveness has been gathered for each intervention from the literature. The pertinent evidence is contained within the key studies as discussed in the literature review (see Appendix 2) and the prior report (Segal *et al.,* 2002). In the chapters on the various modalities, the key evidence on effectiveness is summarised, while the seminal studies, which are used to estimate program effectiveness and cost are described in some detail. The seminal studies were selected on the basis of precision of program description, quantitative specification of outcomes, longer-term follow up, sufficient sample size and quality of evaluation design (preferably an RCT).

In relation to primary prevention, as there are no intervention studies designed to reduce the incidence of OA the impact had to be modelled, based on the observed relationship between obesity (a modifiable risk factor) and incidence of OA. A relationship between BMI and incidence of OA was determined from an analysis of the ABS Health Survey. A mortality adjustment has also been applied reflecting evidence of the relationship between BMI and all cause mortality (Stevens *et al*., 1998). The method employed is described in Chapter 4.

A number of measures of effectiveness are used in intervention trials for OA. Instruments typically used are the WOMAC various scores/sub-scores, the SF-36 (eight component scores and two summary scores), various pain scales, the Lequesne Index and various investigator developed instruments.

3.3 Translation of effectiveness into a common metric

In order to compare performance across disparate interventions a common metric is necessary. This poses a major challenge. None of the disease specific or generic health status measures commonly used in OA lend themselves to becoming the 'universal unit'. Firstly, there is no simple interpretation of the results. That is, even if it were possible to translate all outcomes into WOMAC scores this would have no meaning outside arthritis. Secondly, the commonly applied health status measures cannot be combined with mortality. Even though arthritis is not a direct cause of death, common treatments have documented excess mortality, and interventions for prevention (through weight loss) are associated with reduced mortality. Only two choices are available that combine quality of life and life years – the DALY and the QALY.
However there are flaws with the DALY - specifically with the published disability weights – that undermine their use in cost-effectiveness analysis. The DALY (which combines disability weights with time in health states and lost life years) has been developed and used by the World Bank, as a broad health status measure. Disability weights - ranging from '0' for no disability/perfect health to '1' for total disablement have been derived for hundreds of objectively specified health states. The DALY has been used to describe the overall health-state of communities and to compare communities in terms of total disease burden.

Disability weights tend to be too insensitive for use in cost-effectiveness analysis. Only three disability weights are reported to cover the entire disease/health status spectrum for persons with OA, and the published disability weights attach to health states that do not relate to the health states/outcomes reported in clinical trials. The WHO/World Bank published disability weights are only suited to cost-effectiveness analysis for diseases with precisely defined disease stages that exhibit a narrow range of health outcomes, and where interventions are designed to move people between these stages. Osteoarthritis is not of this type thus disability weights and the DALY were not suitable for this priority setting exercise.

The utility score, the basic element of the QALY, has several advantages as a common measure of outcome.

i) A multi-attribute utility instrument can be used to estimate utility scores for a selected population/patient group. As discussed below this has been used to establish a data set from which to derive a statistical transformation between commonly applied instruments and a utility score.

ii) Utility instruments are occasionally applied in the context of clinical trials, with a trend towards their more widespread use; that is they will increasingly be reported as part of clinical trial results.

And in common with the DALY:

iii) The impact on quality of life and mortality can be combined and taken together with time in designated health states to derive QALYs.

iv) QALYs can be compared with costs to calculate cost/QALYs, a performance measure increasingly applied in the health sector known as cost-utility analysis - potentially enabling comparisons with other disease/health problem areas.

However utility values were rarely reported in trial outcomes, thus an alternative technique had to be devised specifically for this study.

'Transfer to Utility' technique

We developed an approach to derive utility values through a statistical transformation between the reported outcome measure and utility (0-1). The technique, which we have dubbed the TTU or 'Transfer to Utility' technique, is described in detail below. As far as we are aware the development of this technique, and its application, is entirely original.

The principle underlying the approach is that the various health status/health outcome instruments are all seeking to establish the effect of the intervention on quality of life – either overall or in relation to specific dimensions. The technique seeks to establish a statistical transformation between selected instruments and a utility value. The transformation would then be used to translate the outcomes of intervention trials, as reported, into a utility value. While a perfect transformation will not occur, the instruments will be measuring somewhat different constructs, it is postulated that there will be enough commonality to derive a transformation that is robust. While, this constitutes a second best approach, in the absence of the widespread use of utility instruments in the conduct of clinical trials it represents an extremely useful advance.

We explored two possible techniques for deriving the statistical transformations. The first technique involved the use of existing data sets that contain both a utility instrument and instruments commonly used in OA intervention trials. The South Australian Health Omnibus Survey, which contained both the AQoL utility instrument and the SF-36, a health status instrument commonly used in OA studies, also gathered information on disease state and was analysed to derive a transformation between the SF-36 and utility values. A strong relationship between the SF-36 and AQoL scores was observed, which was strengthened by limiting the analysis to persons with reported OA. The transformation of the SF-36 covered the full utility scale, unlike the method derived by Brazier, Usherwood, Harper and Thomas (1998) where utility values are effectively truncated at 0.4, an unsatisfactory outcome (Hawthorne, Richardson and Day, 2001). This application suggested the technique might well provide robust results. However using the SA study a transformation could only be derived for the SF-36. In order to derive transformations for a number of other instruments, a second method was employed.

The four most commonly used instruments in OA intervention trials were identified and a questionnaire was distributed to a sample of persons with OA containing these four instruments plus the AQoL, to gather data for this study. The four instruments chosen, based on our review of the literature were the SF-36, VAS pain scale, the WOMAC and the Lequesne Index (see Table A3.1 in the annexure to this chapter for more information on these instruments). Additional information was requested from participants on the site of their OA, age, gender, height, weight and common treatment modalities used. (The survey instrument is reproduced in Appendix 1.) This component of the study received ethics approval through the University of Melbourne.

Advisory Panel members provided critical support in locating a suitable sample of people with OA[4]. The sample was strategically selected to include the breadth of health states that occur in people with OA (those expected to have mild to moderate disease drawn from patients attending a rheumatologist, those with severe disease drawn from an orthopaedic waiting list, persons receiving rehabilitation after surgery, and a mixed group accessed through Arthritis Victoria). The survey was distributed by post and direct delivery and 324 were returned.

Quality of life of respondents

The mean utility score of respondents was 0.48, demonstrating a vastly poorer health-related quality of life of people with OA compared with the population norm of 0.83 (based on the South

[4] Persons with OA for the sample were identified by clinician members of the OA Priority Setting Advisory Panel; Assoc. Professor Rachelle Buchbinder, Dr Julian Feller, Dr Daniel Lewis, Assoc. Professor Geoff McColl and a community sample identified through Ms Helen McNeil at the Arthritis Foundation of Victoria.

Australian Health Omnibus survey). The distribution of AQoL scores was well spread over the range of the scale (see Figure A3.1 in the annexure to this chapter). As expected those on the orthopaedic waiting list had the lowest mean utility value at 0.37, while people receiving treatment reviews at a private rheumatology clinic had the highest mean utility score at 0.62 (see Table A3.2 in the annexure).

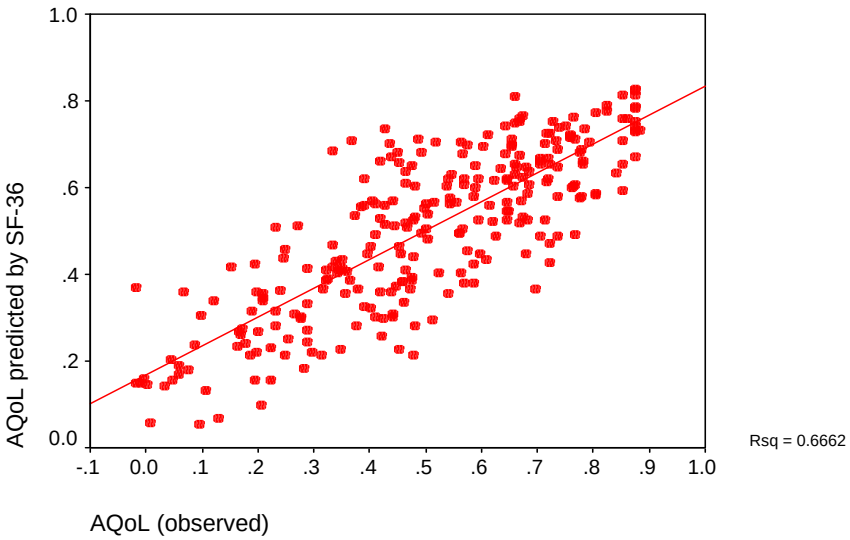
Statistical Methods

Linear regression equations were derived to describe the relationship between scores from the SF-36, the VAS Pain scale, the WOMAC and the AQoL. Various relationship forms were tried. As reported below, for each instrument, a strong linear relationship between the instrument and the AQoL was found, supporting use of this method. The derived equations and an illustrative application are provided below.

Conversion of SF-36 sub-scales to utility score

Three multiple linear regression models of AQoL (independent variable) against the SF-36 sub-scales were constructed. It was found that applying a quadratic to two of the eight sub-scales, Physical Function and Bodily Pain, improved the explanatory power[5]. All SF-36 subscales, including the two quadratic transformed scales, were entered into a multiple regression model and beta weights obtained. The model was a very good fit as evidenced by the strong relationship between the observed and predicted scores (see Figure 3.1) and the high adjusted R^2 of 0.66 ($p<0.001$). There was little evidence of multi-collinearity[6]. Separate disease specific weights were obtained for hip and knee OA each of which resulted in slightly different but excellent fitting models (R^2 = 70% and 63%, $p<0.001$ for hip and knee respectively). The parameters of the hip model are described below in Table 3.1.

Figure 3.1 Observed vs predicted utility using SF-36 subscales



Application of the regression equation to develop utility values for a cost-utility analysis is demonstrated in relation to a trial of 252 patients who underwent hip or knee replacement surgery, (reported by Bachmeier, March and Cross, 2001). Health status is reported at baseline and at 3, 6 and 12 months. These have been translated into utility scores, so that by simple subtraction the utility gain derived from surgery can be calculated. In this example the utility sore increased from a mean value of 0.464 at base line to 0.767 at 12 months, a mean gain of 0.304 utility gain (see

[5] For Physical function (PF) quadratic equation is: Y(est. AQoL) = 0.12964+(PF*0.01313)+(PF2*-0.000076),
For Bodily pain (BP) the quadratic equation is: Y(est. AQoL) =0.06443+(BP*0.01354)+(BP2*-0.0000648)

[6] The highest variance inflation factor value was 2.8 (approximate threshold = 5.0 suggests collinearity).

Table 3.2). This result can then be taken together with expected time for which benefit will be maintained to yield an estimated mean QALY gain from surgery.

Table 3.1 Illustration of application - Conversion of published SF-36 sub-scale scores to a utility estimate for hip replacement surgery

Hip only	**Regression Weights**	**SF-36 [(a)] Pre-surgery Score**	Quadratic Adjustment	**Utility Component**	**SF-36 [(a)] 12 mth post surgery**	Quadratic Adjustment	**Utility Component**
(Constant)	-0.1976						
Physical Function	0.4803	26.9	0.4661	0.224	66.6	0.7345	0.353
Role Physical	-0.0001	14.6		-0.002	58.7		-0.007
Bodily Pain	0.2438	32.9	0.4562	0.111	72.8	0.7486	0.182
General Health	0.0003	66.3		0.023	73.8		0.025
Vitality	0.0009	47.1		0.045	67.5		0.064
Social Function	0.0018	52.5		0.092	88.6		0.155
Role Emotion	-0.0003	60.0		-0.018	71.8		-0.022
Mental Health	0.0026	71.4		0.187	81.7		0.214
Est. Utility value				0.4635			0.7672
Utility change							0.3037

Source: (a) Bachmeier, March and Cross, 2001

Notes:

1. Each SF-36 sub-scale taken from published trials is multiplied by the subscale-specific regression weight (or beta value). For example, the reported value for the sub-scale Mental Health is 71.4. This is multiplied by the regression weight (beta = 0.002614) to obtain a 'utility component' score of 0.187. The utility component of each sub-scale is summed (with the constant) to obtain a total 'utility equivalent' score. The Physical Function and Bodily Pain scales undergo an initial transformation as these scales were not linearly related to the AQoL (see notes 2 and 3 below).

2 The reported Physical Function scale score (PF = 26.9) is first transformed via a quadratic adjustment: = 0.108164 + 0.01595 x 26.9 - 0.0000983 x 26.9^2 = 0.4661. This adjusted value is then multiplied by the multiple linear regression weight (beta = 0.480275) to obtain the final utility component (0.224) of the Physical Function scale.

3 The reported Bodily Pain scale score (BP = 32.9) is first transformed via a quadratic adjustment: = 0.061499 +0.014104 x 32.9 - 0.000064092 x 32.9^2 = 0.4562. This adjusted value is then multiplied by the multiple linear regression weight (beta = 0.24376) to obtain the final utility component (0.111) of the Bodily Pain scale.

Conversion of WOMAC subscales to utility score

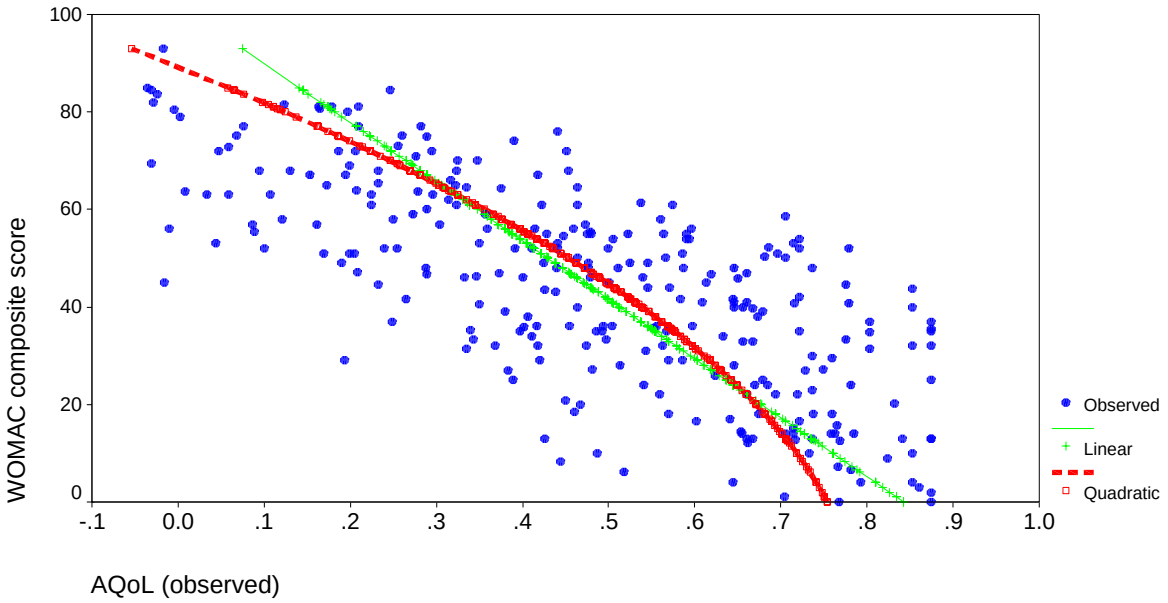
The WOMAC subscales were also converted to a utility score in a multiple regression analysis. For the WOMAC, several regression equations needed to be constructed because the instrument is scored in several different ways[7]. Conversions for each of the variants of the WOMAC were calculated. Each subscale was highly correlated with the AQoL.

[7] Published studies present WOMAC scores are reported as:

- raw scores for the 3 separate sub-scales, stiffness, pain, and bodily pain;
- summed raw scores range 0 to 96,
- sub-scores re-scaled to 0 to 100 each or alternative value, re-scaled subscores summed,
- a VAS version of the instrument, usually with sub-scales each of 0 to 100 mm..

The calculation of equivalence between the three WOMAC scales and the AQoL was completed using a multiple regression equation. Each sub-scale had a substantial linear relationship with the AQoL; the correlation was highest for Physical Function (Pearson's R = -0.72), lowest for Stiffness (R=-0.59) and intermediate for Pain (R = -0.66). Some multicollinearity appeared between the Function and Pain scales (variance inflation factor = 4.4 and 3.6 respectively), so these two scales were combined (equal weighting). A slightly better fitting model was obtained through use of the WOMAC summated scale (ie raw scale scores added) using a quadratic prediction (adjusted R2 = 0.53, p<0.001). This is indicative of a robust relationship given the use of individual data [8]

Figure 3.2 **Scatter plot of AQoL vs Predicted AQoL from composite WOMAC scale Linear line of best fit Adj R^2 = 0.52 Quadratic line of best fit Adj R^2 = 0.53**



Separate transformations were calculated for the whole dataset (any type of OA) and for knee and hip OA. Transformations were also calculated for the summated WOMAC scale. The regression weights for each are displayed in Table A3.4 in the annexure to this chapter. The relevant equations for a knee only OA conversion and the hip and knee group conversion are as follows:

- Estimated utility knee OA = 0.710039 – 0.00097 x W_{100} – 0.0000729 x $(W_{100})^2$
- Estimated utility hip and knee OA = 0.75369 – 0.00277 x W_{100} – 0.000057 x $(W_{100})^2$

Conversion of VAS pain to utility score

A linear regression model of the AQoL vs VAS pain scores was constructed. The VAS pain significantly predicted utility in a linear model; adjusted R^2=0.42, p<0.001, Pearson's correlation R=0.65. The beta weight was -0.006029 and the intercept was 0.771. Simple use of the regression equation (y=ßx+c) then provides a conversion between the VAS pain scale and utility.
Thus estimated utility = VAS pain score from published paper x -0.006029 + 0.771. A plot of the AQoL score versus VAS pain is shown in Figure A3.4 in the annexure. Quadratic and other non-linear models were explored but these did not result in a substantial increase in the amount of variance explained, hence the parsimonious linear model is adopted. The fit is not quite as good as with the SF-36 or the WOMAC, which is not surprising given the simple nature of the VAS pain scale. In applying the regression equations to yield a utility equivalent, where a trial has reported outcomes using several instruments, the instrument associated with the highest R^2 has been used.

[8] See Cohen, 1988

Hip and knee specific equations were estimated, which were used if the nature of the reported trial data allowed. A higher correlation between VAS pain and utility was found for persons with hip OA, with a quadratic model providing the best fit with an adjusted R^2 of 0.49, while for knee OA, a linear model was the best fit, but with only a modest correlation (adjusted R^2 = 37%):

- Estimated utility hip OA = (VAS x -0.002978) + (VAS^2 x -0.0000386) + 0.74858;
- Estimated utility knee OA = (VAS x -0.00595) + 0.7607.

Overview

A regression equation was not estimated for the Lequesne Index, as this proved unnecessary. All seminal studies used in the cost-utility analysis presented results in at least one of the SF-36, WOMAC or VAS pain instruments.

The development and application of the TTU technique was not envisaged in the original description of the study method, but was necessitated by the lack of an alternative means to compare performance across modalities. It represents an extremely important conceptual and technical development, as it provides a potential technique for the comparison of performance across a wide range of modalities and trials where outcomes are reported using different instruments.

3.4 Costs

Cost consists of the direct costs of the intervention or service for the management of OA plus any change in downstream costs. Downstream costs may include costs to treat adverse events or change in the costs of management costs (such as reduced use of NSAIDs). In relation to prevention, costs of the intervention are offset in part through avoidance of disease and associated costs of management. Costs are derived from program descriptions which have been used to establish typical inputs, to which are applied published unit costs (2002 A$) to generate current dollar values. In some cases where program costs are reported these have been translated into current Australian dollars – using an exchange rate adjustment and health price deflator.

The possible impact on downstream costs was estimated when reported. In relation to prevention, the costs of managing OA for Australia have been estimated and translated into an equivalent cost per patient year. This cost is presumed to be avoided through disease prevention.

Estimates of the morbidity and mortality associated with interventions have been derived from the literature. A serious side effect profile with associated health costs is identified for NSAIDs and COX-2 inhibitors. These are discussed in some detail in Chapter 8. In relation to surgery, a proportion of cases are presumed to be revisions of failed prosthesis, which is considerably more complex and thus more expensive than an original procedure. These are discussed in Chapter 9.

3.5 Developing cost-utility estimates

All of the data on costs and effectiveness have been drawn together to obtain cost-utility values for each intervention. Performance is expressed in terms of cost per QALY, where QALYs reflect identified quality of life gain (or loss) and time in health state. Where relevant this is combined with expected excess mortality. Limited sensitivity analyses have been performed, incorporating alternative values for key parameters. The level of uncertainty associated with particular estimates is discussed.

For management options variable time frames have been adopted to reflect the nature of the intervention and data available from clinical trials. Most reported outcomes of OA interventions reflect less than 1-year of follow-up, providing incomplete information on which to conduct modelling of downstream impacts. Hip and knee replacement surgery is the exception, with some data sets providing long term of 15+ years of follow-up. The primary outcome in this case is

failure/survival of prosthesis/need for revision surgery. Surgery is thus modelled over 15 years. All other interventions have only short-to medium-term follow-up. Medicines, prescription or complementary, are assumed to yield benefits only while they are being taken. Exercise programs are assumed to yield benefits for 12 months, and lay education for 2 years. Knee brace has been modelled for benefits derived for between one and two years. In relation to primary prevention, disease incidence, mortality and costs have been modelled over 20 years. While there is long term follow-up of obesity intervention trials of 5+ years, the implication for incidence of OA is based entirely on observational data. The utility differential associated with OA years avoided has been estimated from ABS Health survey data of QoL for persons with and without OA.

Discounting

The appropriate approach to the discounting of future health benefits to ensure an equivalence across time is unclear. In conformity with convention in economic evaluation, discounting is applied to costs at a rate of 5% pa. Discounting of benefits is more contentious. Discounting of benefits in effect involves an equity weighting in favour of health benefits today compared with health benefits in the future, which inherently involves different individuals. Whether this reflects community values has not been established. Both very high rates of discounting of future health benefits, as well as a positive weighting in favour of future health benefits can be seen in individual and societal behaviours. While resources can be invested today to yield greater value in the future, such that in a real sense $10,000 today is equivalent to $11,025 in 2 years time (assuming a 5% pa return on investment or a 5% pa discount rate). It is less clear that a death today, resulting in of loss of 5 years is equivalent to a loss of 3.9 life years now. The attitude to combining health benefits now and in the future may be quite divergent across society and circumstances. In the UK the standard protocol for the conduct of cost-utility analyses is to discount costs by 6% but benefits by 1.5% pa[9].

While sensitivity analyses allowing discount rates on health benefits to vary say between 0% and 5% can be applied, where this results in widely divergent performance, as measured by cost/QALY, this can be confusing rather than enlightening - the case in relation to ns and Cox-2 NSAIDs is one such example. Ideally some exploration of society values, pertinent to the treatment of future health benefits is thus required.

The results of each analysis are now reported in detail, with each chapter providing a description of the methods as well as the results.

[9] National Institute for Clinical Excellence http://www.nice.org.uk/2002

ANNEXURE TO CHAPTER 3

Additional information from the TTU (transfer to utility) sub-study

Table A3.1 Brief description of the four instruments that were the subject of the statistical transformation into a utility score

WOMAC

The Western Ontario and McMaster University Osteoarthritis Index (WOMAC) is probably the most common disease-specific instrument in use today. It was primarily developed and validated by Prof Nicholas Bellamy (University of Queensland) and has received extensive validation over the last twenty years (Bellamy, Kaloni, Pope, Coulter *et al*., 1998; Angst, Aeschlimann, Steiner and Stucki, 2001; Hawker, Melfi, Paul, Green *et al*., 1995; Sun, Sturmer, Gunther and Brenner, 1997). It consists of 24 questions; 5 pain (range 0-20), 2 stiffness (range 0-8), and 17 physical function (0-68). It takes 5 to 10 minutes to complete.

Lequesne Index of severity of Osteoarthritis

The Lequesne index was first developed in 1980 has is specific for hip and knee OA. In 1985 the EULAR recommend it as a measure for antirheumatic drug research. It has mostly been used in European studies. It has 15 questions with 3 components; pain or discomfort, maximum distance walked, and activities of daily living. It takes 5 to 10 minutes to complete.

SF-36

The SF-36 is a generic measure health status (Ware, 2000). The SF-36 is a widely used, extensively investigated and validated instrument. It comprises 36 questions in eight health dimensions: Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Function, Role Emotional and Mental Health. Each of the eight dimensions is separately scored, using item weighting and additive scaling. Summed data are transformed onto a 0–100 point scale. These eight dimensions can be combined into two key health status measures—Physical function (PCS index) and Mental health (MCS index). For computation of the PCS and MCS, each dimension score is weighted in a three-step process to produce a standardized T-score (where the population mean score is 50, sd = 10). It takes 10 to 15 minutes to complete.

VAS Pain

Clinical studies often include visual analogue scales (VAS) where respondents indicate on a 10cm line their present pain (on movement or at rest), stiffness, limitations etc. Each end of the line is labelled with ‘anchors’ such as 0 (no pain) and 100 (worst possible pain). VAS scores are commonly used in addition to other outcome measures (eg clinical changes) or are sometimes primary outcome measures. Three versions were included in the study questionnaire; average pain in last week, average pain in last week on resting and average restriction to daily activities.

AQoL Utility Instrument

The Assessment of Quality of Life (AQoL) instrument is an Australian generic utility instrument comprising five dimensions (Illness, Independent Living, Social Relationships, Physical Senses, and Psychological Wellbeing) of which the latter four are used in the calculation of utility scores (Hawthorne, Richardson and Day, 2001; Hawthorne, Richardson and Osborne, 1999). The utility score ranges from –0.04 (worst possible HRQoL state) to 0.00 (death equivalent HRQoL state) to 1.00 (full HRQoL).

Characteristics of study sample

Questionnaire responses were returned from 324 people with osteoarthritis, based on a sample derived from various clinical and community groups. The average age was 66 years (range 37 to 90) and the average body mass index was 28 (range 14 to 49), with 69% of the sample female. Subjects reported the location of their OA - 68% report knee OA, 52% back, 50% hands/wrists and 49% the hips; 75% report more than one site with OA and 32% report both hip and knee.

Figure A3.1 Distribution of Utility scores of sample

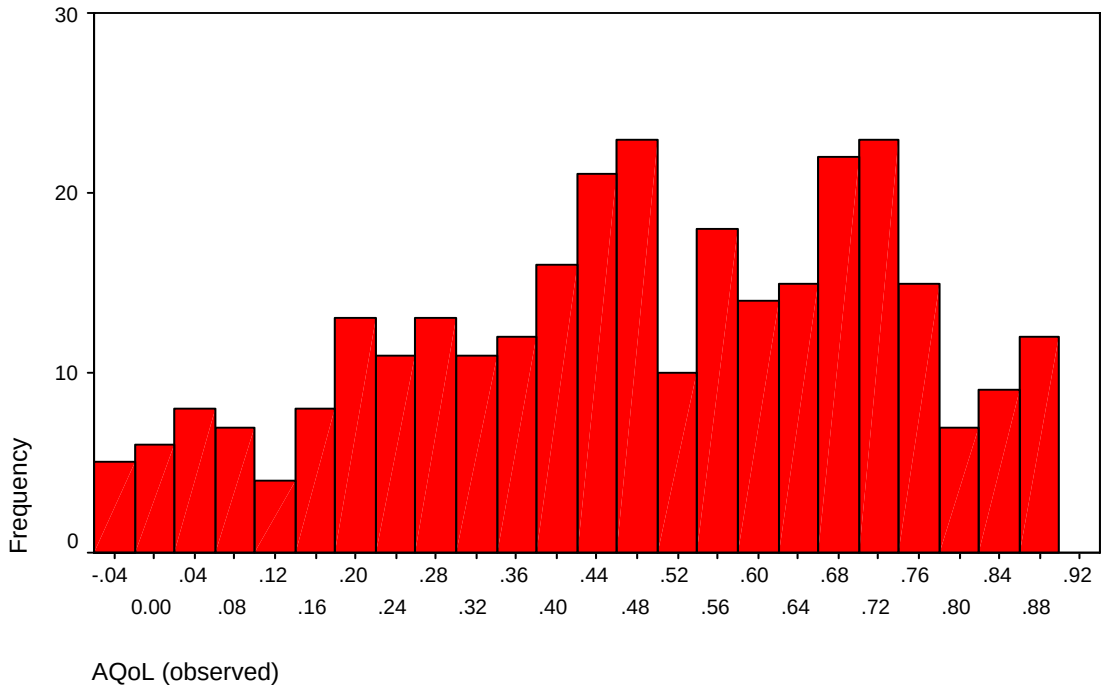


Table A3.2 AQoL scores for people with OA by recruitment source

	Count	Mean	SD	Minimum	Maximum
Rheumatology/Rehabilitation					
Cedar Court Rehabilitation Hospital	28	0.40	0.24	-0.04	0.86
Cabrini Private Hospital	20	0.62	0.23	0.10	0.87
RMH outpatients	24	0.44	0.21	-0.03	0.78
Orthopaedics					
RMH waiting list[1]	60	0.37	0.26	-0.02	0.87
ARMC	11	0.51	0.24	0.09	0.87
Community group					
Arthritis Foundation of Victoria	158	0.52	0.22	-0.03	0.88
Total	**303**	**0.48**	**0.24**	**-0.04**	**0.88**

Notes:

[1] Waiting list for knee or hip replacement surgery

Abbreviations:

RMH - Royal Melbourne Hospital, ARMC – Austin and Repatriation Medical Centre

Table A3.3 shows the mean, standard deviation and range of score for the comparator instruments. In a similar way to the AQoL, each scale was reasonably well distributed across the scale.

Table A3.3 Descriptive statistics for WOMAC, SF-36 and VAS

	N	Mean	SD	Minimum	Maximum
WOMAC					
Physical Function	300	30.9	15.3	0	67
Stiffness	315	4.0	1.8	0	8
Pain	303	8.8	4.6	0	20
SF-36					
Physical Function	320	41.2	25.2	0	100
Role Physical	305	30.2	38.9	0	100
Bodily Pain	323	41.6	20.9	0	100
General Health	310	57.5	22.8	0	100
Vitality	321	46.2	22.5	0	100
Social Function	323	65.3	28.7	0	100
Role Emotional	297	56.7	44.5	0	100
Mental Health	323	66.3	20.5	4	100
Visual analogue scales (VAS)					
Average pain over last week	318	47.2	25.3	1	96
Pain while resting over past week	313	29.9	23.7	0	96
Restriction in ADL over past week	313	40.5	27.5	0	96

Table A3.4 Conversion weights for WOMAC scale score (range 0 to 100)

	Regression weights[1]			
	Beta 1	**Beta 2**	**Constant**	**Adj R^2**
All[2]	-0.00277	-0.000057	0.753685	54%
Knee[3]	-0.00097	-0.000073	0.710039	49%

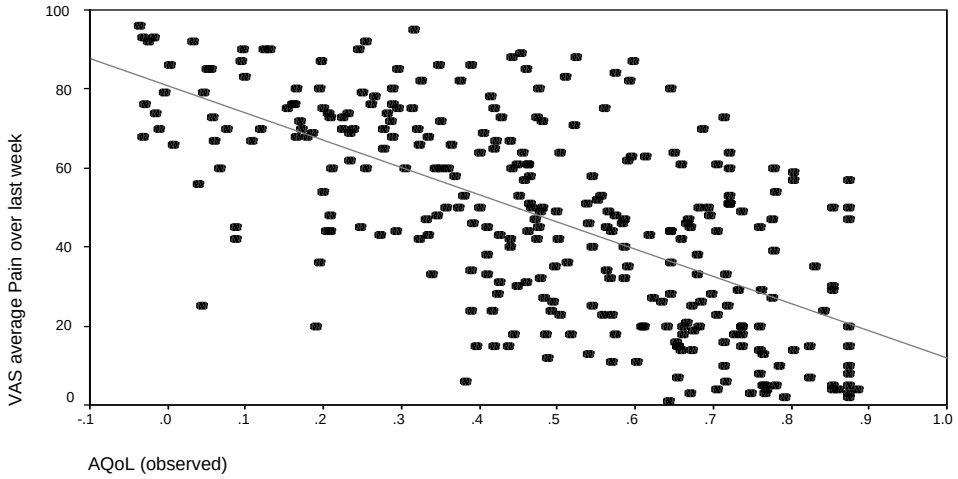
Notes:

1 Regression coefficients: 1 beta weight indicates linear, 2 indicates quadratic and 3 indicates cubic equations. All models $p<0.001$.

2 The composite score for a combined hip and knee sample was converted using a quadratic transformation. Say the reported composite score = 72.6. This value is then applied in a quadratic regression equation using the beta values shown to obtain a utility estimate: $(- 0.00277 \times 72.6) + (-0.000057 \times 72.6^2) + 0.753685 = 0.2498$.

3 The composite score for a knee only sample was converted using a quadratic transformation. Say the reported composite score is 72.6, this value is then applied in a quadratic regression equation using the beta values shown to obtain a utility estimate: $(-0.00097 \times 72.6) + (-0.000073 \times 72.6^2) + 0.710039 = 0.2556$.

Figure A3.4 Scatter plot of AQoL vs VAS average pain over the last week

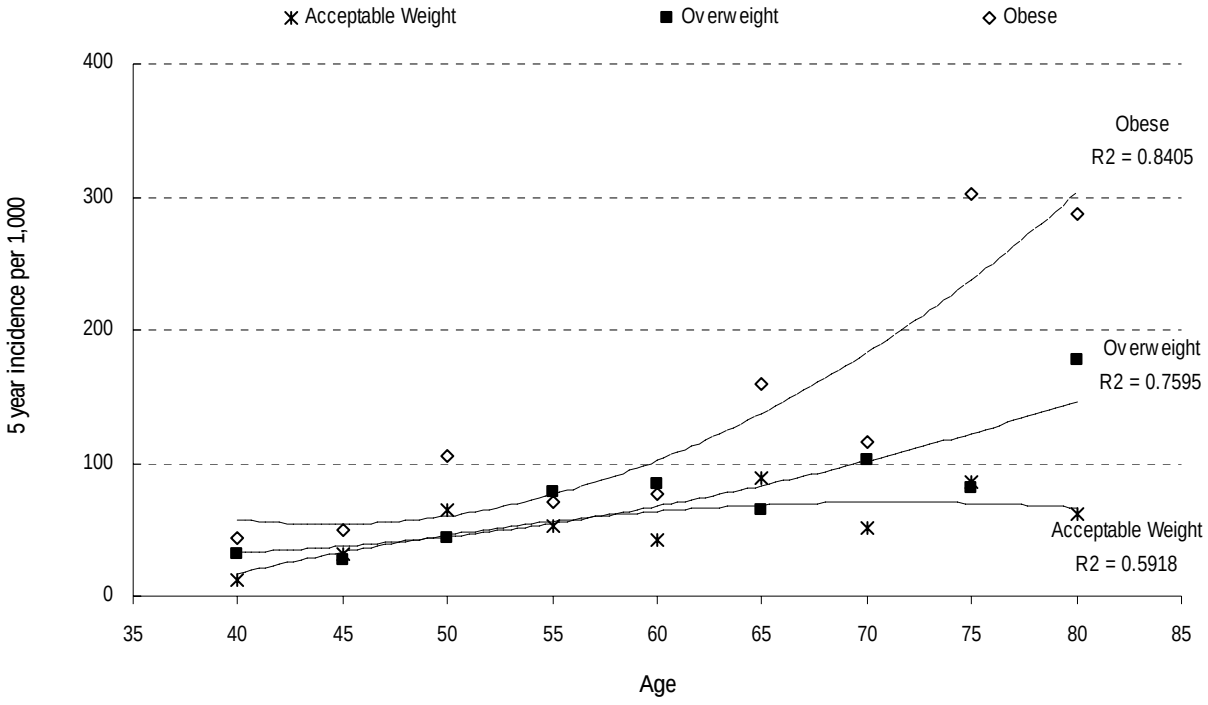


4. PRIMARY PREVENTION

4.1 Key data

The incidence of OA is related to age but also to potentially modifiable risk factors such as obesity and occupational and recreational injury. As reported earlier, the evidence is convincing, and modelling of data from the 1989 and 1995 National Health Surveys support this evidence, showing a strong correlation between obesity and the incidence of OA. Interestingly, the association with age only applies to obese and overweight persons (BMI $\geq$25 kg/m^2) (see Figure 4.1). The data is consistent with the Framingham longitudinal study, which indicated that high BMI was a predictor of the development of knee OA later in life (Felson, Anderson, Naimark, Walker *et al.*, 1988). There is, therefore, an *a priori* case for suggesting OA may be preventable, or at least that the incidence of OA may be reduced, through programs aimed at reducing weight.

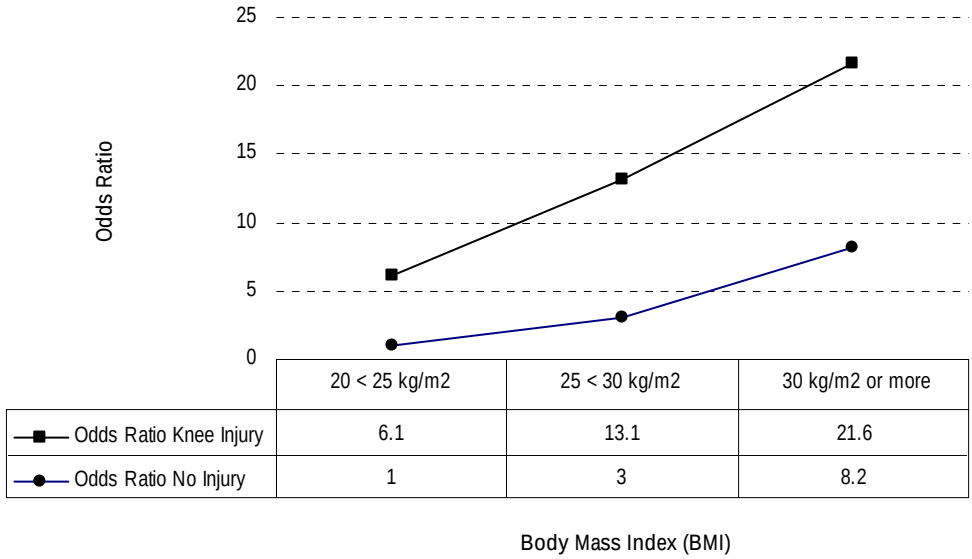
Figure 4.1 Osteoarthritis incidence rates based on the NHS 89 and 95 data



Source: Based on an analysis of the 1989 and 1995 Australian National Health Survey data.

Coggon, Reading, Croft, McLaren *et al*, (2001) report that the risk of developing knee OA is substantially increased with knee injury or surgery and that the risk is exacerbated by obesity. This is clearly demonstrated in Figure 4.2 derived from their study results. While the greatest effect on incidence could be achieved though avoiding knee injury, reduction of BMI for those who have suffered a knee injury and are also overweight or obese will also reduce the risk of developing OA. Unfortunately, we have not been able to locate studies suitable for modelling the prevention of knee injury – which is suggested as an area for research. It is clear however, that for people with a knee injury it is particularly important to reduce BMI to reduce their risk of developing OA.

Figure 4.2 Relative risk of developing OA by people who have suffered a knee injury by BMI



Source: Based on Coggon *et al.* (2001)

Four interventions have been used in modelling primary prevention of OA, targeted at several distinct populations. All interventions seek to reduce the prevalence of overweight and obesity:

- Mass media campaign
  - Targeted at the general population but specifically at persons who are overweight or obese.
- Surgery for obese persons who are overweight or obese
  - A general group.
- A GP/die titian intervention, for persons who are overweight or obese,
  - A general group
  - For persons with a previous knee injury.

Intervention studies were located from which to model the impact on weight and BMI. These results were used together with the observational data, as illustrated in Figures 4.1 and 4.2 to estimate the impact of the intervention on incidence of OA.

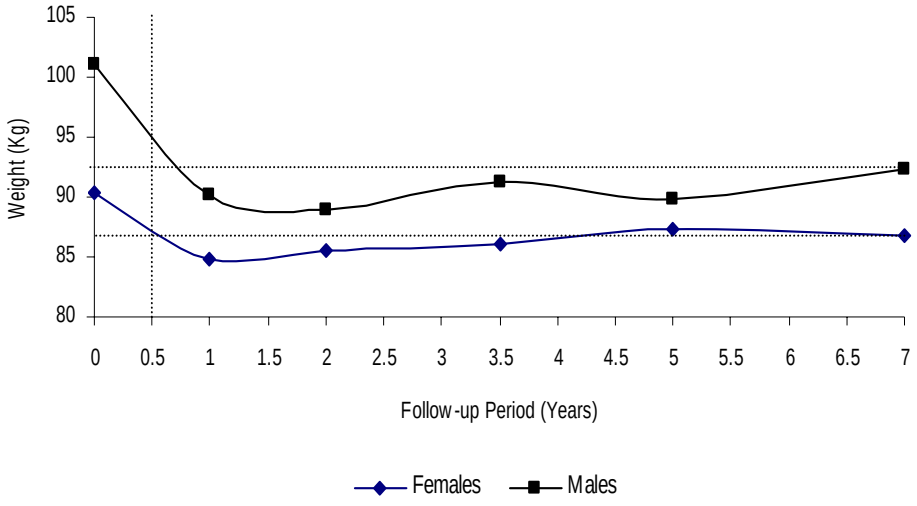
Ideally, the studies used for modelling would meet the following criteria:

- long term follow-up (preferably 2 or more years);
- a randomised study design incorporating suitable control groups;
- a 'reasonable' retention rate;
- analyses based on intention-to-treat (or reported both in terms of intention-to-treat and actual treatment);
- large sample size; and
- validated outcomes scales.

However, this ideal was not attainable and it has been necessary to rely on the less demanding criteria of a precise description of the intervention and defined outcome measures with clearly expressed quantitative results. In relation to the length of follow-up, studies relating to weight reduction were often of short/medium term duration (<12 months).

We thus relied on published data from an important long term trial (7 year follow-up) to assess likely long term impact. In this Finnish study, 117 obese subjects were randomised to the weight loss intervention and 126 to a control group. Of these 22 men and 71 women completed the six-week weight reduction course led by a trained public health nurse. They then met at regular intervals with their group leader over the remainder of the year. The weight reduction course was based on nutrition education and dietary counselling and included lectures by a physician, psychologist and physiotherapist. Eighty-five percent of the 93 participants who completed the intervention (17 men and 62 women) were followed for seven years. Their average weight loss at the end of the 12-month intervention was 10.9 kg for men and 5.4 kg for women. While some of the weight was regained at 7 years, their weight at the end of six months was a good approximation of their weight at seven years, (see Figure 4.3).

Figure 4.3 Seven-year weight loss - people completing weight reduction course in Finland



Source: Karvetti and Hakala (1992) p. 746

The four studies that have been used in the modelling are shown in Table 4.1. The follow-up periods were 6 months and 2 years and the average baseline BMI of the participants was >30 kg/m^2. The studies indicated that the interventions had some success in reducing BMI for some of the participants. These changes are used to estimate a reduction in incidence of OA and also death rates, which generates additional QALYs. This is made up of a gain in quality of life through the reduction in OA years and extra life years through reduced mortality attributable to weight reduction.

Table 4.1 Interventions included in the cost-utility analysis

	Mass Media Campaign	Bariatric Surgery	GP/Dietitian Intervention
Studies	Miles (2001); Wardle, Rapoport, Miles, Afuape *et al.* (2001)	Karlsson, Sjostrom and Sullivan (1998)	Bowerman, Bellman, Saltsman, Garvey *et al.* (2001)
Country	UK	Sweden	USA
Follow-up Period	5 months	2 years after surgery	6 months
Number completing follow-up	2,112		116
Average Baseline BMI	31.7 kg/m^2	41.8 kg/m^2	33.8 kg/m^2
Average change in BMI	1.5 kg/m^2	9.2 kg/m^2	1.9 kg/m^2
Average BMI at follow-up	30.2 kg/m^2	32.6 kg/m^2	31.9 kg/m^2
Statistical Significance	No comparison group but a not insignificant weight loss and large sample size indicate that this is a significant result	Within group comparisons of change between baseline and two year follow-up were significant in the surgical group ($p<0.000$) but not in the control group	No comparison group but a not insignificant weight loss and reasonable sample size indicate this is a significant result

4.2 Assumptions

There are a number of common assumptions used in the modelling of each of these interventions:

- the prevalence and incidence of OA – including the impact of previous knee injury;
- the adjustment of male and female death rates due to high BMI;
- the cost of managing of OA;
- the discount rate used to estimate the present value costs and benefits/outcomes; and
- the difference in quality of life between those with and without OA.

Each of these is considered in turn.

Prevalence and incidence of OA

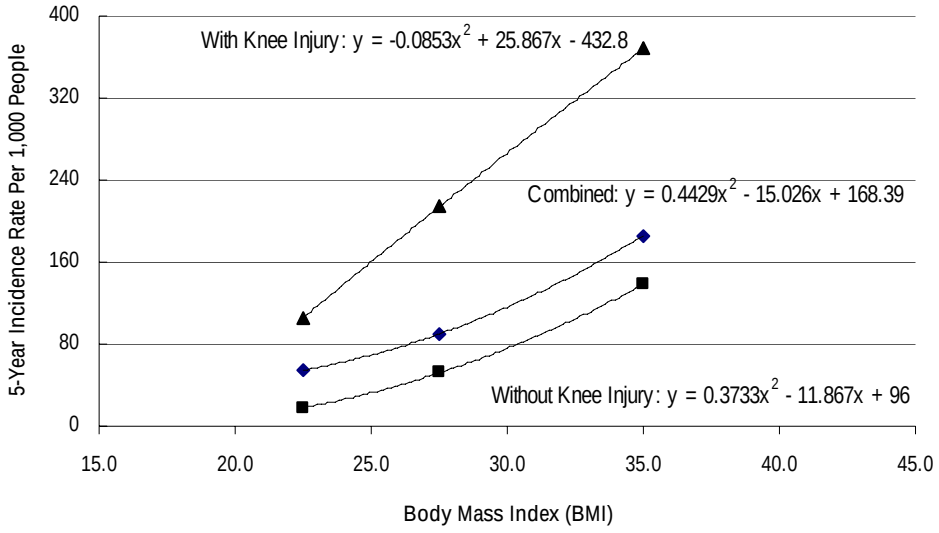
The 1995 National Health Survey data indicated that the prevalence of OA in the Australian population was ~11% and this has been used as the baseline prevalence of OA in each of the cohorts used in the models.

The Australian National Health Survey data for 1989 and 1995 were analysed to calculate an incidence rate for OA. In these surveys four levels of BMI are reported – below acceptable BMI <20 kg/m^2, acceptable 20< 25 kg/m^2, overweight 25 < 30 kg/m^2 and obese ≥30 kg/m^2. The age adjusted 5-year incidence rate per 1,000 people was calculated as 54.5 for normal weight, 90.1 for overweight people and 185 for obese people (taking account of the proportion of new cases in each age group). It was necessary to convert these estimates into a continuous relationship between BMI and incidence of OA, to enable application of the study results. This was done using polynomial regression to estimate the average incidence rates for the normal, overweight and obese BMI categories.

Separate incidence rates were also estimated for persons with and without knee injury. This was done by applying the relative risk ratios from Coggon *et al.* (2001) to the ABS incidence data – and also using estimates from Coggon *et al.* (2001) of the relative proportion of persons with OA who had a previous knee injury. While it would be preferable to base this analysis on a random sample,

in which history of knee injury in the prevalence of OA was specifically identified, this was not available. The resulting equations were used to estimate changes in the incidence rates for OA as a result of changes in BMI for people with and without a knee injury, as shown in Figure 4.4.

Figure 4.4 Five-year OA incidence rates per 1,000 people by BMI and history of knee injury



Notes: Calculation prepared for this study from ABS National Health Survey 1989 and 1995 and Coggon *et al.,* 2001

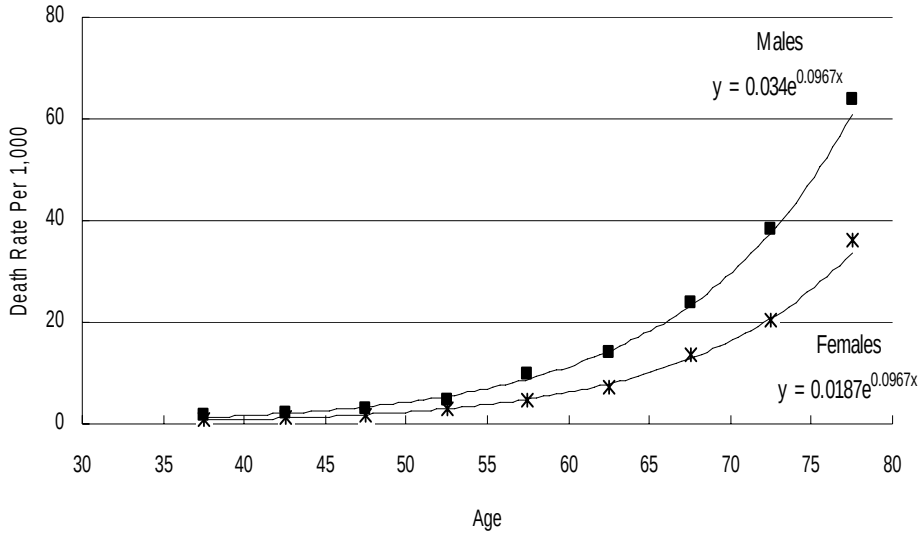
Death rates

An equation was also developed for the female and male death rates in relation to age (see Figure 4.5 – based on ABS death statistics) and BMI, developed from the work of Stevens, Cai, Pamuk, Williamson *et al.* (1998). The results were modelled assuming an initial cohort aged 50:

$$\text{Increased Risk} = 0.0014 \times \text{BMI}^2 - 0.016 \times \text{BMI} + 0.6751.$$

In the cost-utility analyses for primary prevention this increased risk has been assumed to apply at age 47, the age at which the modelling starts.

Figure 4.5 Death rates based on ABS data



Source: Australian Bureau of Statistics (1995)

Cost of managing OA

An estimate of mean patient costs per annum for managing OA is required as a potential cost saving associated with avoidance of OA. A total cost of managing OA has estimated using a combination of estimates from 1993-94 prepared by the Australian Institute of Health and Welfare, updated to current prices, using the health price index deflator adjustment, and bottom-up calculation for drug costs and surgery and physician and GP costs. The methods are described in the notes to Table 4.2. The current costs for managing OA across Australia were estimated to be $1,090 million. Based on National Health Survey 1995 data it was estimated that there were ~1.55 million people with OA in Australia (1.16 million with OA plus one third of those identified with 'arthritis nec'). Therefore the mean annual cost per patient for management of OA is estimated to be $1,100 million/1.55 million or $700 per OA person year.

Quality of life

An analysis of the SA Health Omnibus survey data indicated that the QoL for people with OA was 0.72 and the QoL for those without arthritis was 0.86. It has been assumed, therefore, that on average having OA results in a reduction of QoL of 0.14.

Discount rates

The discount rate used to calculate the present value of future expenditures (avoided) is 5%. The discount rates used to calculate the present value of future savings in QALYs are 0% and 5%.

Table 4.2 Costs of managing OA

	1993-4 $ million	Current 2001 $ million
Hospital Inpatients	266.5	597[1]
Public	131.7	
Private	134.8	
Non-inpatients	34.3	39[2]
Nursing Homes	117.2	135[2]
GPs	35.8	68[3]
Specialists	44.2	84[3]
Prescriptions	37.5	65[4]
Over-the-counter drugs	20.5	24[2]
Allied Health	35.9	41[2]
Research	5.4	6[2]
Other	26.7	31[2]
TOTAL[5]	**624**	**1090**

Notes:

1 Calculated on total costs for hip and knee replacements for 2000-2001 x 0.9 (given ~ 90 % of these operations are assumed to be for OA).

2 Prices calculated based on 1993-4 costs x total inflation cost of 15% (93/94-2001) (ABS health price deflator).

3 Calculated from Bettering the Evaluation and Care of Health (BEACH) study data, showing OA as a problem managed in 2.5/100 patient encounters with GPs. Although multiple conditions can be managed per patient encounter, related factors associated with OA such as dyspepsia, ulceration, and hypertension through NSAID consumption, and other problems caused or linked with OA are not included. In 1997-98, non-specialist (ie GP and other medical practitioners) expenditure =$2,279 million (an increase of 12.1% from 1993-4 totals). 1997-98 specialist expenditure = $4,752 million (an increase of 23.4% from 1993-4 totals). 2.5% x total cost of GP visits = 2.5% x $2,729 = $68.2 million. Assuming a similar increase in specialist expenditure related to OA gives $84.2 million.

4 Total PBS (government reimbursement) NSAID prescription costs for the year 2001 was $231 million. Patients' copayments have been assumed to represent a further 15% in costs ($35 million), giving a total cost of $266 million. BEACH data shows that 20.6% of all NSAIDs (including COX-2s) prescribed in GP encounters were for OA. Therefore costs of NSAIDs for OA are calculated as: $266 x 0.206 = $56 million. PBS costs of paracetamol and aspirin (alone or combinations) is estimated at ~$9million, using information from the 1995 NHS survey. Therefore total prescription drug costs for OA = $65 million.

5 Other costs not included: according to BEACH data, OA was the problem for which imaging tests were the third most frequently ordered, while shoulder syndromes (incl. Arthritis and OA) was the tenth. 13.3% of all GP contacts for OA generated an order for an imaging test. These costs have not been included.

Table 4.3 Summary of the key assumptions

QoL utility values[1]	With OA	0.72
	Without Arthritis	0.86
	Difference	0.14
Current costs of managing OA[2]		$700 per OA year
Mean prevalence of OA in the adult community[3]		11%
5 year OA incidence rate per 1,000 people[4]		
Without knee injury		$0.3733xBMI^2 - 11.867xBMI + 96$
With knee injury		$-0.08533xBMI^2 + 25.867xBMI – 432.8$
Combined		$0.4429xBMI^2 – 15.026xBMI + 168.39$
Mortality rates[5]	Males	$0.034e^{0.0967*AGE}$
	Females	$0.0187e^{0.0967*AGE}$
Adjustment for mortality rates for obesity[6]	Age 47	$0.0014*BMI^2-0.016*BMI+0.6751$
	Age 60	$0.008*BMI^2+0.0052*BMI+0.5564$
Discount rate		5% for costs, 0% and 5% for benefits/outcomes
Modelling period		20 years

Notes:

1 Based on SA Health Omnibus survey. Ideally utility weights would reflect the change in quality of life associated with the combined impact of a fall in BMI and avoidance of OA. This adjustment could be addressed in a refinement of the model.

2 See Table 4.2

3 ABS Health survey 1995

4 See Figure 4.4 – based on ABS Health Survey and Coggon *et al.* (2001)

5 Australian Bureau of Statistics Catalogue No. 3302.0

6 Based on Stevens *et al.* (1998)

4.3 Cost-utility analyses - comprehensive mass media campaign

Background

In 1998, the World Health Organisation commented that the mass media has a role to play in reducing obesity by promoting a healthy diet and exercise (WHO, 1998). However, while some mass media campaigns have targeted factors that contribute to obesity (diet and sedentary lifestyle) their main focus has been on the reduction of other risk factors, such as smoking, sun exposure and motor vehicle accident. Few media campaigns target obesity. It has also been shown that mass-media campaigns can increase knowledge and awareness of health-related issues and potentially change behaviours, especially where supported by community level interventions (eg Buchbinder, Jolley and Wyatt, 2001; Buchbinder, Jolley and Wyatt, 2001b; Wimbush, 1998).

Program description

The economic modelling for the media campaign has been based on the BBC's Fighting Fat, Fighting Fit (FFFF) campaign, which ran in the United Kingdom in 1999. The campaign ran for seven weeks and involved peak and daytime programs on BBC One and Two, BBC radio 2 and local BBC radio. This was supported by a Website, Ceefax pages, a book, a video, the Radio Times and telephone lines for further information. It was targeted at groups with a high prevalence of obesity and was designed to inform these groups about the risk, and the role for a healthy diet and physical activity.

People could actively respond to, and join, the campaign by writing or telephoning for a registration pack, which cost £2. The pack included a self-help guide for lifestyle change (22 pages) and three

registration cards to return over a 5-month period to chart progress in weight loss, activity levels and eating habits. Those sending back the second registration card received a voucher for a free exercise session in a participating fitness centre. Participants who showed the greatest improvement in eating and activity habits over the 6-month period had a chance to win prizes, such as a year's supply of fruit and vegetables or a home visit by a health and fitness expert (Miles, 2001; Wardle *et al*., 2001).

Wardle *et al.* (2001) undertook an evaluation of the campaign's success in terms of public awareness. Data was collected as part of a monthly omnibus survey conducted by the Office for National Statistics, in March 1999. It involved a stratified probability sample of adults across Great Britain. Within each household, one person over the age of 16 was interviewed. From a target sample of 2,690 eligible addresses, 1,894 (70%) were interviewed, (583 refused and 213 were unable to be contacted). The results indicated that 57% of responders were aware of the campaign, that 1.3% of overweight and obese people requested a registration pack and 0.2% actually registered. However, when this estimate was extrapolated to the target group and compared with the number who actually sent for a registration pack and the number who registered, the actual proportions were approximately half those anticipated on the basis of the survey.

Miles (2001) also evaluated the campaign using a random sample of the 33,474 actual registrants who had returned their first registration card within one month of the campaign starting. Of the 6,000 registrants sampled, 3,661 (61%) agreed to participate and returned the first questionnaire and 2,112 (35%) completed a final questionnaire five months later. Average baseline BMI was 31.7 kg/m^2. Most registrants (76%) were female, as were those who participated in the evaluation (86%). Mean age of completers was 47 years. Mean weight loss reported after five months was 1.5 kg/m^2. The data are summarised in Table 4.4 and provide the basis for the values used in the cost-effectiveness analysis.

Table 4.4 Registrants and evaluation participants in the FFFF campaign

	All Registrants (N=33,474)	**Participants in the Evaluation sample (N=3,661)**	**Evaluation Completers (N=2,112)**
Average Age	43 years	45 years	47 years
Average Baseline BMI	30.5 kg/m^2	32.2 kg/m^2	31.7 kg/m^2
Average Change in BMI	Unknown	Unknown	1.5 kg/m^2 decrease
% Female	79%	86%	86%

Source: Miles (2001)

Target group

The cost-effectiveness analysis was based on a campaign targeted to a regional population the size of Victoria, and specifically to overweight and obese adults (BMI≥25 kg/m^2). It is estimated that this group comprises about 1.5 million people, mean age 47 years, mean BMI 28.7 kg/m^2 and 41% female (Table 4.5).

Table 4.5 Target group for the model – overweight and obese adult Victorians

	Overweight			Obese			Total		
	Female	**Male**	**Total**	**Female**	**Male**	**Total**	**Female**	**Male**	**Total**
Persons[1]	417,375	695,625	1,113,000	205,979	203,522	409,500	623,354	899,147	**1,522,500**
%	37.5%	62.5%	100%	49.7%	50.3%	100%	40.9%	59.1%	100%
Mean Age[2]	46.6 years			46.9 years			46.7 years		
Mean BMI[2]	27.1 kg/m^2			33.2 kg/m^2			28.7 kg/m^2		

Notes:

1 1996 Census data 3.5 million Victorians > 15 years of age. NHS 1995 data, 42% of Australians over the age of 15 years overweight or obese

2 Estimated from 1995 National Health Survey data

Costs

We were unable to obtain costs for the UK FFFF campaign, and even if they were obtained it can be difficult to translate into an Australian setting. However the Transport Accident Commission spent $6m in Victoria in 1994/5 on a media campaign (Segal, 2000) and the Victorian WorkCover Authority's statewide media campaign 'Back Pain – don't take it lying down' which began in 1997 cost $5.8 m in its first year, $2.8m in the second and $2m in the third year[10]. While more modest campaigns such as the 2-fruit-5-veg campaign in Victoria, cost less than $500,000 (Segal and Chen, 2001).

Costs for a FFFF campaign in Australia that is short term but quite intensive have been assumed to be $5.8 million dollars – equivalent to the first year cost of the WorkCover campaign. This is equivalent to $3.90 per person in the target group.

Modelling

Outcomes are considered in terms of the percentage of the target group who actively engaged with the campaign, and the mean weight loss achieved in this subgroup. Based on the work of Wardle *et al* (2001) and Miles (2001), we have assumed engagement rates of 1%, 0.3% and 0.1% of the target population and a mean reduction in BMI of 1.5 kg/m^2 (see Table 4.6). Results have also been modelled assuming firstly 86% of those responding to the campaign were female (as per the UK FFFF experience) or alternatively that the gender mix is as per the ratios is that of the Victorian population given that there is no precedence in the Australian setting.

Table 4.6 Number of persons assumed to respond to media campaign and achieve mean reduction in BMI of 1.5 kg/m^2 – target population 1.5 million overweight obese adults.

	Overweight (N=1,113,000)	**Obese (N=409,500)**	**Total (N=1,522,500)**
1.0% response	11,130	4,095	15,225
0.3% response	3,339	1,229	4,568
0.1% response	1,113	410	1,522

10 Private communication from Dr Rachelle Buchbinder, 2002

The modelling was undertaken for a period of 20 years starting at age 47. It was assumed that 11% of the target group had OA at the start of the period and the cost of managing OA was $700 per OA person year. Based on these assumed values and those as outlined in Table 4.3 we calculated total OA years that would be incurred with and without the intervention, at the 3 assumed levels of success. We also calculated life years lost over 20 years. This was adopted as a relatively conservative assumption. In reality benefits could be expected to accrue over the full life of a patient, the maintenance of weight loss over extended periods is not known. Neither has any account been taken of the 'extra' benefits that may accrue from a reduction in risk factors for other diseases (eg diabetes, cardiovascular disease) due to the reduction in BMI.

Performance

These results were used to calculate OA years avoided and life years saved and these were combined into QALY equivalents using the estimated mean utility loss associated with OA. Cost savings from reduction in costs of managing OA were offset against campaign costs. These were used to estimate net cost/QALY for the media program at the three levels of success and at discount rates of 0% and 5% for the QALY benefits. As shown in Table 4.7 (undiscounted QALYs) and Table 4.8 (discounted QALYs), the cost per QALY was found to be very modest at $1,968-$3,104 if 1% of the target group lose weight (success), $9,386-$14,803 for 0.3% success, up to $30,582-$48,231 for 0.1% success.

A second model was used to explore the impact of the campaign if the gender distribution in the proportion of people responding was similar to the distribution in the overweight and obese target groups. Outcomes and performance have been recalculated as shown in Table 4.9 (undiscounted QALYs) and Table 4.10 (discounted QALYs). Under this scenario, net cost/QALY gain would improve slightly to $1,755-$2,715 at 1% success, $8,225–$12,723 at 0.3% success and $26,710-$41,317 at 0.1% success.

Conclusion

A comprehensive large-scale media campaign for weight loss, similar to the FFFF campaign in the UK is indicated to be highly cost-effective, in terms of cost per QALY as a means to reduce burden from OA. These results are based on an intensive campaign able to achieve considerable behaviour change in a small percent of the target, which still represent a large number of persons. It also assumes that weight loss achieved will be maintained. It should be noted also that the relative risk of OA in those who are overweight may have been underestimated. The relative risks derived from the ABS Health survey are less than that suggested by the literature (Coggon, Croft, Kellingray, Barrett *et al.*, 2000; Felson and Zhang, 1998). A bias in the ABS estimate is probable, given the recognised misreporting of height and weight based on self-report which will tend to include overweight people in the acceptable weight group, thus distorting the 'base' value.

Table 4.7 Cost-utility analysis for mass media campaign: 86% of people successfully losing weight are female (QALYs not discounted)

TARGET GROUP					
Number of Persons[1]		1,522,500			
% Female		41%			
Average Age		47 years			
Average Baseline BMI		28.7 kg/m^2			
Average Change in BMI by Successful[2]		1.5 kg/m^2			
ANALYSIS (over 20 years)		Comparator No Change in BMI	1% Engage (Lose weight)	0.3% Engage (Lose weight)	0.1% Engage (Lose weight)
OUTCOMES		C	I_1	I_2	I_3
A Total OA Years[3]	(Disc @ 0% pa)	7,792,189	7,786,596	7,790,511	7,791,630
B Life Years Lost	(Disc @ 0% pa)	2,206,947	2,205,905	2,206,634	2,206,842
C OA Years Avoided	(AC – AI)		5,594	1,678	559
D Life Years gained	(BC - BI)		1,041	312	104
E Difference in Utility Non OA c/w OA[4]			0.140	0.140	0.140
F Difference in QoL	(C x E)		783	235	78
G Gains in QALYs	(D + F)		1,824	547	182
COSTS					
H Program Cost Per Person			$3.81	$3.81	$3.81
I Gross Program Costs			$5,800,000	$5,800,000	$5,800,000
J Savings in Present Value Cost of Managing OA	(Cx$700 disc @ 5% pa)		$2,210,072	$ 663,022	$ 221,007
K Net Program Costs	(I -J)		$3,589,928	$5,136,978	$5,578,993
PERFORMANCE					
L Gross Cost Per OA Year Avoided	(I / C)		$ 1,037	$ 3,456	$ 10,369
M Net Cost Per OA Year Avoided	(K / C)		$ 642	$ 3,061	$ 9,974
N Net Cost Per Life Year Gained	(K / D)		$ 3,448	$ 16,446	$ 53,582
O Net Cost Per QALY Gained	**(K / G)**		**$ 1,968**	**$ 9,386**	**$ 30,582**

Notes:

1 The demographic and anthropometric data for the target group was based on the 1996 Census data and 1995 NHS data.

2 Based on the average change in BMI reported by Miles (2001).

3 Assumed 11% of the target group have OA at baseline.

4 Based on 1998 South Australian Health Omnibus Survey data.

Table 4.8 Cost-utility analysis for mass media campaign: 86% of people successfully losing weight are female (QALYs discounted @ 5%)

TARGET GROUP					
Number of Persons[1]		1,522,500			
% Female[2]		41%			
Average Age[3]		47 years			
Average Baseline BMI[4]		28.7 kg/m^2			
Average Change in BMI by Successful[5]		1.5 kg/m^2			
ANALYSIS (over 20 years)		Comparator No Change in BMI	1% Engage (Lose weight)	0.3% Engage (Lose weight)	0.1% Engage (Lose weight)
OUTCOMES		C	I_1	I_2	I_3
A Total OA Years[3]	(Disc @ 5% pa)	4,626,787	4,623,630	4,625,840	4,626,471
B Life Years Lost	(Disc @ 5% pa)	1,481,970	1,481,256	1,481,756	1,481,899
C OA Years Saved	(AC – AI)		3,157	947	316
D Life Years Saved	(BC - BI)		715	214	71
E Difference in Utility Non OA c/w OA[4]			0.140	0.140	0.140
F Difference in QoL	(C x E)		442	133	44
G Gains in QALYs	(D + F)		1,157	347	116
COSTS					
H Program Cost Per Person			$ 3.81	$ 3.81	$ 3.81
I Gross Program Costs[8]			$ 5,800,000	$ 5,800,000	$ 5,800,000
J Savings in Present Value Cost of Managing OS	(Cx$700 disc @ 5%)		$ 2,210,072	$ 663,022	$ 221,007
K Net Program Costs	(I - J)		$ 3,589,928	$ 5,136,978	$ 5,578,993
PERFORMANCE					
L Gross Cost Per OA Year Avoided	(I / C)		$ 1,837	$ 6,123	$ 18,370
M Net Cost Per OA Year Avoided	(K / C)		$ 1,137	$ 5,423	$ 17,670
N Net Cost Per Life Year Gained	(K / D)		$ 5,023	$ 23,958	$ 78,060
O Net Cost Per QALY Gained	**(K / G)**		**$ 3,104**	**$ 14,803**	**$ 48,231**

Notes:

1 The demographic and anthropometric data for the target group was based on the 1996 Census data and 1995 NHS data.

2 Based on the average change in BMI reported by Miles (2001).

3 Assumed 11% of the target group have OA at baseline.

4 Based on 1998 South Australian Health Omnibus Survey data.

Table 4.9 Cost-utility analysis mass media campaign: % females and males same as in the target group (QALYs not discounted)

TARGET GROUP					
Number of Persons[1]			1,522,500		
% Female			41%		
Average Age			47 years		
Average Baseline BMI			28.7 kg/m^2		
Average Change in BMI by Successful[2]			1.5 kg/m^2		
ANALYSIS (over 20 years)			Comparator No Change in BMI	1% Engage (Lose weight)	0.3% Engage (Lose weight)	0.1% Engage (Lose weight)
OUTCOMES			C	I_1	I_2	I_3
A	Total OA Years[3]	(Disc @ 0% pa)	7,792,189	7,786,835	7,790,583	7,791,654
B	Life Years Lost	(Disc @ 0% pa)	2,206,947	2,205,604	2,206,544	2,206,812
C	OA Years avoided	(AC - AI)		5,354	1,606	535
D	Life Years gained	(BC - BI)		1,342	403	134
E	Difference in Utility Non OA c/w OA[4]			0.140	0.140	0.140
F	Difference in QoL	(C x E)		750	225	75
G	Gains in QALYs	(D + F)		2,092	628	209
COSTS						
H	Program Cost Per Person			$3.81	$3.81	$3.81
I	Gross Program Costs			$5,800,000	$5,800,000	$5,800,000
J	Savings in Present Value Cost of Managing OA	(Cx$700 disc @ 5% pa)		$2,128,744	$ 638,623	$ 212,874
K	Net Program Costs	(I - J)		$3,671,256	$5,161,377	$5,587,126
PERFORMANCE						
L	Gross Cost Per OA Year Avoided	(I / C)		$ 1,083	$ 3,611	$ 10,832
M	Net Cost Per OA Year Avoided	(K / C)		$ 686	$ 3,213	$ 10,435
N	Net Cost Per Life Year Gained	(K / D)		$ 2,735	$ 12,819	$ 41,628
O	**Net Cost Per QALY Gained**	**(K / G)**		**$ 1,755**	**$ 8,225**	**$ 26,710**

Notes:

1 The demographic and anthropometric data for the target group was based on the 1996 Census data and 1995 NHS data.

2 Based on the average change in BMI reported by Miles (2001).

3 Assumed 11% of the target group have OA at baseline.

4 Based on 1998 South Australian Health Omnibus Survey data.

Table 4.10 Cost-utility analysis mass media campaign: % females and males same as in the target group (QALYs discounted @ 5% pa)

TARGET GROUP					
Number of Persons[1]		1,522,500			
% Female[2]		41%			
Average Age[3]		47 years			
Average Baseline BMI[4]		28.7 kg/m^2			
Average Change in BMI by Successful[5]		1.5 kg/m^2			
ANALYSIS (over 20 years)		Comparator No Change in BMI	1% Engage (Lose weight)	0.3% Engage (Lose weight)	0.1% Engage (Lose weight)
OUTCOMES		C	I_1	I_2	I_3
A Total OA Years[3]	(Disc @ 5% pa)	4,626,787	4,623,746	4,625,875	4,626,483
B Life Years Lost	(Disc @ 5% pa)	1,481,970	1,481,044	1,481,692	1,481,878
C OA Years Saved	(AC – AI)		3,041	912	304
D Life Years Saved	(BC - BI)		927	278	93
E Difference in Utility Non OA c/w OA[4]			0.140	0.140	0.140
F Difference in QoL	(C x E)		426	128	43
G Gains in QALYs	(D + F)		1,352	406	135
COSTS					
H Program Cost Per Person			$ 3.81	$ 3.81	$ 3.81
I Gross Program Costs			$ 5,800,000	$ 5,800,000	$ 5,800,000
J Savings in Present Value Cost of Managing OA	(Cx$700 disc @ 5% pa)		$ 2,128,744	$ 638,623	$ 212,874
K Net Program Costs	(I - J)		$ 3,671,256	$ 5,161,377	$ 5,587,126
PERFORMANCE					
L Gross Cost Per OA Year Avoided	(I / C)		$ 1,907	$ 6,357	$ 19,072
M Net Cost Per OA Year Avoided	(K / C)		$ 1,207	$ 5,657	$ 18,372
N Net Cost Per Life Year Gained	(K / D)		$ 3,962	$ 18,569	$ 60,303
O Net Cost Per QALY Gained	**(K / G)**		**$ 2,715**	**$ 12,723**	**$ 41,317**

Notes:

1 The demographic and anthropometric data for the target group was based on the 1996 Census data and 1995 NHS data.

2 Based on the average change in BMI reported by Miles (2001).

3 Assumed 11% of the target group have OA at baseline.

4 Based on 1998 South Australian Health Omnibus Survey data.

4.4 Cost-utility analysis - Surgery for weight loss

Program description

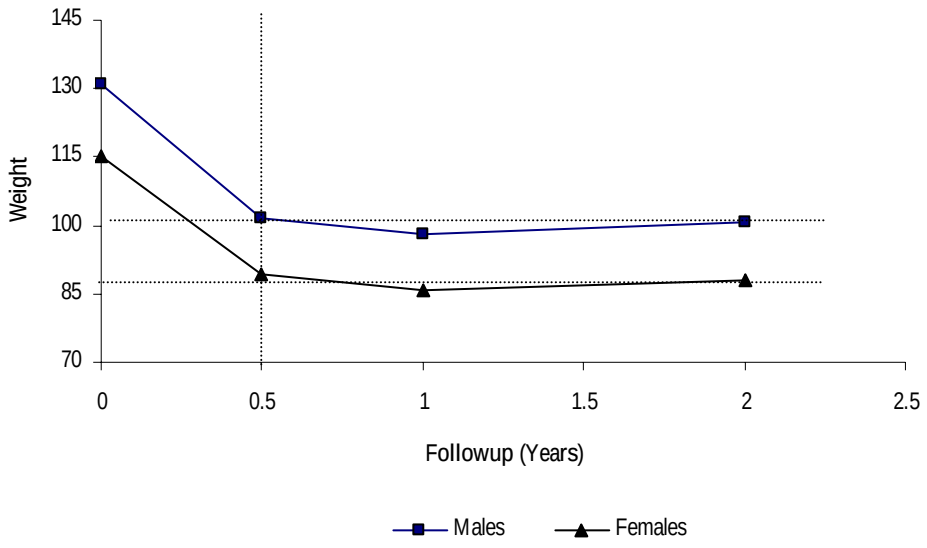
The modelling of surgical procedures for obesity is based on the intervention trial reported by Karlsson, Sjostrom and Sullivan (1998). In this trial, people on the registry of the Swedish Obesity Study (SOS) and waiting lists at surgical departments were recruited to undergo bariatric surgery. The inclusion criteria were, age 37-60 years and BMI for males ≥34 kg/m^2 and for females ≥38 kg/m^2. The surgical procedures involved gastric banding, vertical banded gastroplasty and gastric bypass, with 487 participants undergoing surgery, all of whom received a comprehensive pre-operative evaluation. All patients were given instruction on nutrition and returned regularly for complete medical check-ups. Mean age of the participants was 47 years, mean BMI was 42 kg/m^2.

Outcomes

Surgery for weight loss is found to be highly successful. Over 90% of those who have surgery achieve more than 50% reduction in excess weight. For the study group, the mean loss in BMI at the two-year follow-up was 9.3 kg/m^2 for males and 9.8 kg/m^2 for females. The loss in BMI was achieved in the first six months after the surgery and maintained for the period of follow-up (see Figure 4.6).

The potential target group for surgery is large. For instance an estimated 38,500 Victorians meet the demographic and BMI characteristics described above. Their mean BMI is slightly lower than that of Karlsson *et al*. (1998) study group at 41.2 kg/m^2 for women, and 36.2 kg/m^2 for men.

Figure 4.6 Weight loss by subjects undergoing surgery in Swedish Obesity Study (SOS)



Source: Karlsson, Sjostrom and Sullivan (1998)

Costs

The cost of the intervention is estimated to be A$15,000 as reported in Segal (2000). This covers counselling/assessment prior to acceptance for surgery (4 visits), pre-surgery pathology tests, in-patient procedure, including immediate post-operative care, on-going behavioural nutrition support – 15 sessions over 5 years, plus management of comorbidities. Downstream cost savings, based on cost of managing OA of $700 per person year, have been discounted at 5% per annum.

Cohort

The cohort is assumed to be 100 obese individuals, with characteristics based on Karlsson *et al.* (1998): mean age 47 years, mean baseline BMI is 41.8 kg/m^2 (42.3 kg/m2 for females and 40.8 kg/m2 for males), 11% of cohort with OA. It is assumed that 69% are female.

Modelling

The modelling was undertaken for a period of 20 years, starting at age 47. It was assumed that 11% of the cohort had OA at baseline. Benefits (QALYs) have been discounted at 0% and 5% per annum.

Performance

Based on these assumptions and those previously outlined, for a cohort of 100 obese persons having bariatric surgery, this is estimated to result in 173-291 fewer OA years, (1.2-2.9 per person), and an extra 45-64 life years (0.45-0.64 per person). Given a program cost of $15,000 per person, net cost/QALY allowing for some downstream cost savings is estimated at $13,107-$19,938 - see Table 4.11 (undiscounted QALYs) and Table 4.12 (discounted QALYs).

Table 4.11 Cost-utility analysis for surgery (QALYs not discounted)

COHORT			
Number of Persons		100	
% Female[1]		67%	
Average Age		47	
Average Baseline BMI		41.8 kg/m^2	
Average Change in BMI by Successful[2]		9.6 kg/m^2	
ANALYSIS		No Intervention	Surgical Intervention
OUTCOMES			
A Total OA Years[3]		902	610
B Total life Years Lost		208	143
C OA Years Avoided	(AC - AI)		291
D Life Years Gained	(BC - BI)		64
E Difference in Utility Non OA c/w OA[4]			0.140
F Difference in QoL	(0.14[4] x C)		41.0
G Gain in QALYs	(D + F)		105
COSTS			
H Program Cost Per Person			$ 15,000
I Gross Program Costs			$1,500,000
J Savings in Present Value Cost of Managing OA	(Cx$700 disc @5% pa)		$ 121,050
K Net Program Costs	(I - J)		$1,378,950
PERFORMANCE			
L Gross Cost Per OA Year Avoided	(I / C)		$ 5,147
M Net Cost Per OA Year Avoided	(K / C)		$ 4,732
N Net Cost Per Life Year Gained	(K / D)		$21,411
0 Net Cost Per QALY Gained	**(K / G)**		**$13,107**

Notes:

1 The demographic and anthropometric data for the target group was based on the 1996 Census data and 1995 NHS data.

2 Based on the average change in BMI reported by Karlsson *et al* (1998).

3 Assumed 11% of the target group have OA at baseline.

4 Based on 1998 South Australian Health Omnibus Survey data.

Table 4.12 Cost-utility analysis for surgery (QALYs discounted @ 5% pa)

COHORT			
Number of Persons		100	
% Female		67%	
Average Age[1]		47	
Average Baseline BMI		41.8 kg/m^2	
Average Change in BMI[2]		9.6 kg/m^2	
ANALYSIS (over 20 years)		No Intervention	Surgical Intervention
OUTCOMES			
A Total OA Years[3]	(Disc @ 5% pa)	532	359
B Life Years Lost	(Disc @ 5% pa)	141	96
C OA Years Saved	(AC – AI)		173
D Life Years Saved	(BC - BI)		45
E Difference in Utility Non OA c/w OA[4]			0.140
F Difference in QoL	(C x E)		24
G Gains in QALYs	(D + F)		69
COSTS			
H Program Cost Per Person			$ 15,000
I Gross Program Costs[8]			$ 1,500,000
J Savings in Present Value Cost of Managing OA	(Cx$700 disc @ 5% pa)		$ 121,050
K Net Program Costs	(I - J)		$ 1,378,950
PERFORMANCE			
L Gross Cost Per OA Year Avoided	(I / C)		$ 8,647
M Net Cost Per OA Year Avoided	(K / C)		$ 7,974
N Net Cost Per Life Year Gained	(K / D)		$ 30,675
O Net Cost Per QALY Gained	**(K / G)**		**$ 19,938**

Notes:

1 The demographic and anthropometric data for the target group was based on the 1996 Census data and 1995 NHS data.

2 Based on the average change in BMI reported by Karlsson *et al* (1998).

3 Assumed 11% of the target group have OA at baseline.

4 Based on 1998 South Australian Health Omnibus Survey data.

4.5 Cost utility analysis - Intensive telephone-based GP and dietician intervention

Background

An estimated 82% of the population visit their GP annually (Bridges-Webb (1992) unsighted but quoted in Segal (2000)). Bowerman *et al.* (2001) reported that, in a one day review of patients attending 20 medical practices in Southern California, 33% of patients visiting the clinics had a BMI of 25<30 kg/m^2, 23% had a BMI 30<40 kg/m^2 and 4% had a BMI $\geq$ 40 kg/m^2. They noted that the findings were similar to other reports and are higher than the incidences reported in population-based surveys. It seems therefore, that GPs are well placed to intervene to engage in weight reduction interventions with their patients but their reluctance to do so has been well documented. The reasons given for this reluctance have included lack of time, patient non-compliance, inadequate teaching materials, lack of counselling training, inadequate reimbursement, and low GP confidence (see for example Ashley, St Jeor, Schrage, Perumean-Chaney *et al.* (2001); Bowerman *et al.* (2001)).

Program description

The modelling for the GP-based interventions was based on the study reported by Bowerman *et al.* (2001). This intervention was developed by at the Center for Human Nutrition, University of California and was designed as an intervention implemented by doctors in a primary care setting. Doctors interested in participating were provided with implementation guidelines, patient handouts and a Bioelectrical Impedance Analyser (BIA) to accurately measure BMI.

During the first six months, the intervention protocol included four or five visits to the doctor, two pathology assessments to test for comorbidities and 15 telephone calls from a dietician (weekly for the first 12 weeks and monthly for the next three months).

Doctors offered the program to their patients. Completed enrolment forms were faxed to a centrally located, registered dietician. The dietician provided support, guidance, and encouragement to the patients, answered dietary questions, and gathered information about the patient's weight, diet, medication and exercise compliance, and use of meal replacements. Physicians were faxed a monthly report from the dietician summarizing the results of all telephone contacts with enrolled patients.

Outcomes

Mean reduction in weight at 6 months for those still in the program was 8.6 kg for women and 7 kg for men. This is equivalent to a reduction in BMI at 6 months, for those who completed, of 3.09 kg/m^2 (3.36 kg/m^2 for females and 2.16 kg/m^2 for males). This is equivalent to a mean reduction in BMI of 0.93 kg/m^2 for the entire cohort, assuming that those who dropped out lost no weight. As per Bowerman *et al* (2001), 62% of participants remained in the study at 3 months, and 48% at 6 months.

Costs

The costs for the intervention are estimated at A$719 per participant, using the components described in the study by Bowerman *et al* (2001), and applying Australian costs, including local estimates of the costs of recruiting GPs into life style interventions (see Table 4.13).

Table 4.13 Costs of intervention for 252 participants recruited by 18 GPs

COSTS[1]	A$2002
Telephone System and Calls[2]	$ 1,891
Recruitment and training of GPs[3]	$ 11,700
Production and distribution of intervention materials[4]	$ 6,300
Program Management[5]	$ 43,750
Bioelectrical Impedance Analyser[6]	$ 63,000
GP Consultations[7]	$ 26,395
Dietitian[8]	$ 16,463
Pathology Assessments[9]	$ 11,599
TOTAL	$181,098
Cost Per Participant	$ 719

Notes:

1 Based on program implemented by Bowerman *et al.* (2001) involving 252 participants

2 Automated system $367 plus 3,402 calls @ $0.45/call

3 18 GPs @ $650 per GP (based on Segal (2000))

4 252 participants @ $25 per participant

5 Six months @ $70,000 pa plus 25% on-costs

6 One for each of 18 GPs @ $3,500 per unit

7 Assumed 5 consultations for those who complete 3 for those who did not. Costed at MBS Item 23 ($26.45)

8 Grade 1 Level 6 full-time for 12 weeks and 1 week per month for 3 months = 15 weeks @ $878 + 25% on-costs

9 Two assessments for completers, one for non-completers. Costed at MBS Items 66521 and 66542 ($11.40 + $19.70)

Cohort

The cohort is assumed to reflect those participants that were enrolled in the Bowerman *et al* (2000) study. In this study, 252 patients were recruited, referred by 18 GPs, average age of 47 years, and mean baseline BMI 33.8 kg/m^2, with 80% of participants female (see Table 4.14).

Table 4.14 Summary of attributes patient cohort and outcomes

Attribute		Females	Males	All
Enrolled		202	50	252
Baseline Weight		90.7 kg	107.5 kg	94.0 kg
Baseline BMI		34.0 kg/m^2	33 kg/m^2	33.8 kg/m^2
Completed Six Months	N	94	26	120
	%	47%	52%	48%
Mean weight Loss By Completers		8.6 kg	7 kg	8.3 kg
Mean weight loss intention to treat[1]		4.04kg	3.64 kg	4.0 kg
Mean BMI Loss By Completers[2]		3.36 kg/m^2	2.16 kg/m^2	3.09 kg/m^2
Mean BMI Loss intention to treat[3]		1.58 kg/m^2	1.12 kg/m^2	1.48 kg/m^2
Intermediate estimate of mean BMI Loss[3]				1.9 kg/m^2

Source: Bowerman *et al.* (2001)

Notes:

1 Assuming those who dropped out lost no weight

2 Height assumed to be 1.6m for females and 1.8m for males

3 Assuming those who were lost to follow-up achieved 30% of the weight loss of those who completed.

Modelling

The modelling was undertaken for a period of 20 years starting at age 47. It was assumed that 11% of the cohort group had OA at the start of the period, the cost of managing OA was $700 per annum per person with OA and the discount rate for the purposes of working out present value costs was 5% per annum. Benefits (QALYs) were discounted at 0% and 5% per annum.

Performance

Table 4.15 (undiscounted QALYs) and Table 4.16 (discounted QALYs) show that, if the weight loss reported is maintained, a reduction in all-cause mortality of 3-4 life years over 20 years is estimated, based on an illustrative cohort of 100 persons (ie 0.03-0.04 life years per participant). There would be 17-29 fewer OA years (a mean reduction of 0.2-0.3 OA years per participant). This is associated with a gain in quality of life of an estimated 5-9 QALYs (0.05-0.09 per person). At a mean program cost/participant of $719 (or $599 allowing for expected cost saving), this amounts to a net program cost of $2,438-$4,209 per OA year avoided, $13,409-$21,015 per life year gained and $6,971-$11,431 per QALY gain.

This result is reliant on the program outcomes as reported – which represents a substantial weight loss - and the maintenance of that weight loss over the long term. If this is not achieved then clearly the performance will be poorer.

Table 4.15 Cost-utility analysis for GP/Dietician intervention (QALYs not discounted)

COHORT				
Number of Persons			100	
% Female			80%	
Average Age			47 years	
Average Baseline BMI			Females = 34 kg/m^2 Males = 33 kg/m^2	
ANALYSIS (over 20 years)			Comparator No change in BMI	Intervention Mean BMI loss 1.94 kg/m^2 [1]
OUTCOMES			C	I_I
A	Total OA Years[2]		668	639
B	Life Years Lost		133	128
C	OA Years avoided	(AC - AI)		29
D	Life Years gained	(BC - BI)		4
E	Difference in Utility Non OA c/w OA[3]			0.140
F	Difference in QoL	(C x E)		4
G	Gains in QALYs	(D + F)		9
COSTS				
H	Program Cost Per Person			$ 719
I	Gross Program Costs			$71,864
J	Savings in Present Value Cost of Managing OA	(Cx$700 disc @ 5% pa)		$11,951
K	Net Program Costs	(I - J)		$59,913
PERFORMANCE				
L	Gross Cost Per OA Year Avoided	(I / C)		$ 2,438
M	Net Cost Per OA Year Avoided	(K / C)		$ 2,033
N	Net Cost Per Life Year Gained	(K / D)		$13,409
O	**Net Cost Per QALY Gained**	**(K / G)**		**$ 6,971**

Notes:

1 47% females completed six months with reduction in BMI of 1.9 kg/m, 52% males completed six months with reduction in BMI of 2.1 kg/m^2, average change for 48% completing six months 1.94 kg/m^2.

2 Assumed 11% of cohort has OA at baseline.

3 Based on analysis of 1998 South Australian Omnibus Survey data.

Table 4.16 Cost-utility analysis for GP/Dietitian intervention (QALYs discounted @ 5% pa)

COHORT			
Number of Persons		100	
% Female		80%	
Average Age		47 years	
Average Baseline BMI		Females = 34 kg/m^2 ; Males = 33 kg/m^2	
ANALYSIS (over 20 years)		Comparator No Change in BMI	Intervention Mean BMI loss 1.94 kg/m^2 [1]
OUTCOMES		C	I
A Total OA Years[2]	(Disc @ 5% pa)	392	375
B Life Years Lost	(Disc @ 5% pa)	87	84
C OA Years Saved	(AC - AI)		17
D Life Years Saved	(BC - BI)		3
E Difference in Utility Non OA c/w OA[3]			0.140
F Difference in QoL	(C x E)		2
G Gains in QALYs	(D + F)		5
COSTS			
H Program Cost Per Person			$719
I Gross Program Costs[5]			$71,864
J Savings in Present Value Cost of Managing OA	(Cx$700 disc @ 5% pa)		$11,952
K Net Program Costs	(I - J)		$59,913
PERFORMANCE			
L Gross Cost Per OA Year Avoided	(I / C)		$ 4,209
M Net Cost Per OA Year Avoided	(K / C)		$ 3,507
N Net Cost Per Life Year Gained	(K / D)		$ 21,015
O Net Cost Per QALY Gained	**(K / G)**		**$ 11,431**

Notes:

1 47% females completed six months with reduction in BMI of 1.9 kg/m, 52% males completed six months with reduction in BMI of 2.1 kg/m^2, average change for 48% completing six months 1.94 kg/m^2.

2 Assumed 11% of cohort has OA at baseline.

3 Based on analysis of 1998South Australian Omnibus Survey.

4.6 Cost utility analysis - GP intensive diet/behavioural program for persons with previous knee injury.

As discussed, previous knee injury is associated with substantially excess risk of OA, which is compounded by overweight. The relative risk of OA in a person who is obese and has had a previous knee injury is estimated to be 21 times that of a person within the acceptable weight range and without such an injury. The major benefit would be achieved through avoidance of the knee injury (or possibly by alternative management of that injury). We were, however, unable to identify any relevant trials for modelling such an intervention. We have thus modelled the effect of weight loss for persons who are overweight or obese and who have had a previous knee injury, using the intensive GP/dietician intervention reported in Section 4.5.

Key program attributes were assumed to be the same; mean weight loss achieved and program cost. However the incidence of OA of participants with and without the intervention has been modelled using the relative risk reported by Coggon *et al.* (2001). These relative risks were applied to incidence rates derived from the ABS Health surveys to yield annual incidence of OA for persons with/without previous knee injury as a function of BMI, as shown in Figure 4.4 above.

The results of the cost-utility analysis of an intensive GP/dietician intervention if targeted at persons with previous knee injury are reported in Table 4.18 (undiscounted QALYs) and Table 4.19 (discounted QALYs). The results are similar to that for the general overweight group. The reason for this is that, even though the absolute risk of OA is far higher for persons with previous knee injury, the impact of excess weight on the incidence of OA is similar, (especially for those who are obese). This means that the impact of weight reduction on incidence is similar. For example, in terms of non-discounted QALYs, total estimated OA years for this group is far higher at 995 (9.95/person), compared with 668 (6.67/person) for a general overweight group (Table 4.15) and the effect of weight loss is to reduce the OA years by 28 to 967 for the knee injury group and 29 to 639 for the knee injury group. Estimated cost per life year was ~$13,400 for the general group and ~$15,800 for the knee injury group. The costs per QALY are estimated to be ~$7,000 for the general group and ~$8,400 for the knee injury general group. Discounting the QALYs increased the cost per QALY to ~$11,400 for the general group and ~$13,400 for those with a knee injury.

Again the key assumption is that the reported weight loss of program participants of 8.7 kg for women and 7.0 kg for men for the 48% of completers is achieved, with those lost to follow-up achieving 30% of this result. It is also assumed that the weight loss is maintained for 20 years. This might be considered quite optimistic compared with other primary care based weight loss programs.

Table 4.17 Cost-utility analysis for GP/Dietitian intervention for people with a knee injury (QALYs not discounted)

COHORT				
	Number of Persons		100	
	% Female		80%	
	Average Age		47 years	
	Average Baseline BMI[1]		Females = 34 kg/m^2 ;Males = 33 kg/m^2	
ANALYSIS (over 20 years)			Comparator No change in BMI	Intervention Mean BMI loss 1.94 kg/m^2 [1]
OUTCOMES			C	I
A	Total OA Years[2]		995	967
B	Life Years Lost		133	128
C	OA Years avoided	(AC - AI$_i$)		28
D	Life Years gained	(BC - BI$_i$)		4
E	Difference in Utility Non OA c/w OA[3]			0.140
F	Difference in QoL	(C x E)		4
G	Gains in QALYs	(D + F)		8
COSTS				
H	Program Cost Per Person			$ 719
I	Gross Program Costs			$71,864
J	Savings in Present Value Cost of Managing OA	(Cx$700 disc @ 5% pa)		$ 1,211
K	Net Program Costs	(I - J)		$70,653
PERFORMANCE				
L	Gross Cost Per OA Year Avoided	(I / C)		$ 2,564
M	Net Cost Per OA Year Avoided	(K / C)		$ 2,521
N	Net Cost Per Life Year Gained	(K / D)		$ 15,813
O	**Net Cost Per QALY Gained**	**(K / G)**		**$ 8,420**

Notes:

1 47% females completed six months with reduction in BMI of 1.9 kg/m, 52% males completed six months with reduction in BMI of 2.1 kg/m^2, average change for 48% completing six months 1.94 kg/m^2.

2 Assumed 11% of cohort has OA at baseline.

3 Based on analysis of 1998 South Australian Omnibus Survey data.

Table 4.18 Cost-utility analysis for GP/Dietitian intervention for people with a knee injury (QALYs discounted @ 5% pa)

COHORT			
Number of Persons		1,000	
% Female		80%	
Average Age		47 years	
Average Baseline BMI[1]		Females = 34 kg/m^2 ; Males = 33 kg/m^2	
ANALYSIS (over 20 years)		Comparator No Change in BMI	Intervention Mean BMI loss 1.94 kg/m^2 [1]
OUTCOMES		C	I
A Total OA Years[2]	(Disc @ 5% pa)	584	565
B Life Years Lost	(Disc @ 5% pa)	87	84
C OA Years Saved	(AC - AI)		17
D Life Years Saved	(BC - BI)		3
E Difference in Utility Non OA c/w OA[3]			0.140
F Difference in QoL	(C x E)		2
G Gains in QALYs	(D + F)		5
COSTS			
H Program Cost Per Person			$ 719
I Gross Program Costs[5]			$ 71,864
J Savings in Present Value Costs of Managing OA	(Cx$700 disc @ 5% pa)		$ 1,211
K Net Program Costs	(I - J)		$ 70,653
PERFORMANCE			
L Gross Cost Per OA Year Avoided	(I / C)		$ 4,154
M Net Cost Per OA Year Avoided	(K / C)		$ 4,084
N Net Cost Per Life Year Gained	(K / D)		$ 24,783
O Net Cost Per QALY Gained	**(K / G)**		**$ 13,399**

Notes:

1 47% females completed six months with reduction in BMI of 1.9 kg/m, 52% males completed six months with reduction in BMI of 2.1 kg/m^2, average change for 48% completing six months 1.94 kg/m^2.

2 Assumed 11% of cohort has OA at baseline.

3 Based on analysis of 1998 South Australian Omnibus Survey data.

4.7 Summary of performance of primary prevention programs

A summary of the results of the analyses is shown in Table 4.19.

Table 4.19 Summary of cost-utility analysis for primary prevention of OA

	Media/community			Intensive Primary care GP/dietician	Surgery for weight loss
Cohort or Target group					
Target group/size of intervention	Regional/national population of 1.5 million overweight/obese persons			Cohort of 1,000 overweight or obese adults	Cohort of 1,000 seriously obese persons
Mean age	47 years			47 years	47 years
Mean baseline weight BMI (kg)	28.7kg/m^2			male 33.2kg/m^2 (107.5kg) female 34.0kg/m^2 (90.7kg)	BMI=41.8kg/m^2
Outcomes – trial data					
Mean weight change 'completers' BMI (kg)	BMI= -1.5kg/m^2			male -3.48kg/m^2 (-7.0kg) female -2.2kg/m^2 (-8.6kg)	-9.6 kg/m^2
responders/completers	0.1%	0.3%	1.0%	Male 52%, females 47%	
Mean weight change intention to treat				male -1.1kg/m^2 (-3.6kg) female -1.6kg/m^2 (-4.0kg)	-9.6 kg/m^2
Outcomes - modelled					
Reduction in OA years	559	1,678	5,594	295	2,914
Life years gained	104	312	1041	4.5	644
QALY gain (a)					
@ 0 disc rate	182	547	1,824	90	1051
@ 5% disc rate	116	347	1,157	50	690
Costs $					
Intervention cost/person	4			719	15,000
Cost of intervention for entire cohort	5,800,000			719,000	15,000,000
Est. savings in PV cost for managing OA	221,000	663,000	2,210,000	121,000	1,211,000
Program cost less downstream cost savings	5,579,000	5,137,000	3,590,000	598,000	13,789,000
Performance (QALYs not discounted) $					
Cost of intervention per OA year avoided	10,400	3,500	1,000	2,400	5,100
Cost of intervention per QALY gain	31,900	10,600	3,180	8,000	14,300
Cost per QALY gain adjusted for estimated downstream cost savings	30,600	9,400	2,000	6,640	13,100
Performance (QALYs discounted @5% pa) $					
Cost of intervention per QALY gain	**50,000**	**16,700**	**5,000**	**14,400**	**21,700**
Cost per QALY gain adjusted for down-stream cost savings	**48100**	**14,800**	**3,200**	**12,000**	**20,000**

Notes:

a) OA years avoided valued at 0.14 QALY, LY valued at 1.0 QALY ; eg est. QALY gain from surgery at 0 disc rate = 2914 x 0.14 = 408 + 644 = 1051 for a cohort of 1000 seriously obese persons.

* Most costs rounded to nearest $100

5. SELF MANAGEMENT/EDUCATION

5.1 Introduction

It was concluded in the review of the literature on self-management and education, that interpretation of the results of these interventions is difficult because of the generally poor quality of the trials and the use of a diverse set of outcome measures, some of which were investigator-developed. Overall, the effect of education/self management is at best modest, but clearly equivocal. But, given the importance of these interventions within the Australian context (underscored by budget initiatives for the support of chronic disease self-management programs including arthritis) it is important that they are incorporated into the cost-utility analysis. The programs selected for inclusion in the modelling are:

- the Arthritis Self Management Program (ASMP) developed at Stanford University;
- a nurse-led telephone based intervention; and
- a nurse-led, GP based intervention. (See Table 5.1)

Table 5.1 Studies used for modelling self management and education interventions

	Lay led Community based	**Nurse led Telephone based**	**Nurse led GP based**
Studies	Lorig, Lubeck, Kraines, Seleznick *et al.* (1985); Lorig (1989)	Mazzuca, Brandt, Katz, Chambers *et al.* (1997) Mazzuca, Brandt, Katz, Hanna *et al.* (1999)	Lord, Victor, Littlejohns, Ross *et al.* (1999)
Country	USA	USA	UK
Recruitment	Community	Outpatient clinics	GP clinics
Type of Study	RCT and cohort	Observational	Cluster Randomisation Trial
Number of Participants	190	211	170
% Female	83%	85%	73%
Average Age	67 years	62 years	63 years
Diagnosis of OA	77%	100%	100%

5.2 Lay led community based - Arthritis Self Management Program (ASMP)

Program description

The ASMP trial reported by Lorig *et al.* (1985) commenced in 1984. It consisted of 24 courses run in community settings by 20 trained leaders. Each course consisted of 6 two-hour sessions run over four months with 15-20 participants in each course. Family members could also participate. Participants were recruited through the mass media, a community clinic, and senior citizens centres, and were required to have their diagnosis of arthritis confirmed by their doctor and their doctor's consent to participate. Each course was taught by two lay-leaders, each of whom received 20 hours of instruction and a teaching manual.

A total of 286 people participated in the trial, mean age 67, with 77% diagnosed with OA, and 83% were female. Participants were randomised to receive the intervention either immediately, or to the control group to receive the intervention after four months. However, baseline data was only collected on 199 participants, to allow the effects of the pre-tests on outcome to be studied (on the other 87).

Of the 199 from whom baseline data was collected, 5 dropped out of the intervention group and 4 out of the control group in the first four months. No data was reported for those who dropped out, so the cost utility analysis is based on the 190 who remained in the trial at four months (see Table 5.2).

Table 5.2 Intervention and control group participants and times of data collection from baseline

		Baseline	4 Months	8 Months	20 Months
Intervention	n =	134	129	124	115
Control	n =	65	61	Offered Intervention	
Total	n =	199	190		

Source: Lorig *et al.*, 1985

A battery of instruments was used to collect the baseline and follow-up data relating to:

- *Knowledge of arthritis* – instrument developed at Stanford containing 10 multiple choice questions primarily concerned with arthritis self-help knowledge.
- *Practice of exercise, relaxation and walking* – self report of the monthly frequency.
- *Pain* – 10 cm VAS (0 = no pain) and an ordinal scale with patients asked to rank pain as mild, moderate or severe.
- *Disability* – Stanford Health Assessment Questionnaire (HAQ).
- *Locus of control* – Wallston Health Locus of Control scale.
- *Number of visits to a physician for treatment of arthritis* – self report.

At baseline, there was a statistically significant difference between the control and intervention group in terms of the pain they experienced as measured by the 10 cm visual analogue scale (VAS). Those in the intervention group reported less pain than those in the control group (see Table 5.3).

Table 5.3 Comparison of baseline characteristics of control and intervention group

	Control (n=61)		Intervention (n=129)		P Value[1]
	Mean	+/- SD	Mean	+/- SD	
Knowledge (0-10 scale)	4.11	1.92	4.69	1.81	0.06
Arthritis Exercise (times/month)	13.80	18.78	12.18	15.13	0.55
Relaxation (times/month)	10.37	17.84	6.62	11.98	0.13
Pain (VAS 0-10)	3.58	2.39	4.43	2.17	0.03
Pain (Ordinal Scale 0-3)	1.96	0.85	2.18	0.66	0.10
Disability (0-3 scale)	0.53	0.53	0.62	0.55	0.23
Physician Visits previous 4 mnths	2.02	3.06	1.33	1.82	0.29

Source: Lorig *et al.*, 1985
Notes:
[1] Wilcoxon rank sum test (non-parametric test based on differences of medians which corrects for outliers)

Outcomes – Randomised Control Trial

At four months, the intervention group recorded statistically significant increases in knowledge, exercise and relaxation ($p<0.0001$), compared to the control group and statistically significant decreases in the pain reported on both pain scales (see Table 5.4). But when a regression analysis was undertaken to control for the difference in pain scores at baseline, the mean difference in pain

as measured by the VAS was not significantly different (p=0.40) but the improvement on the ordinal scale remained significant (p=0.01) (Lorig *et al.*, 1985)[11].

Table 5.4 Changes in outcome measures control and intervention groups at 4 months

	Score changes from baseline				P Value[1]
	Control (n=61)		Intervention (n=129)		
	Mean	+/- SD	Mean	+/- SD	
Knowledge (0 - 10 scale)	0.10	1.48	1.39	2.00	< 0.0001
Arthritis Exercise (times/month)	-4.23	18.82	12.85	25.36	< 0.0001
Relaxation (times/month)	-5.21	15.96	4.63	15.10	< 0.0001
Pain (VAS 0 - 10) [2]	-0.43	1.68	-1.04	2.11	0.04
Pain (Ordinal Scale 0 - 3) [2]	-0.02	0.80	-0.45	0.77	0.002
Disability (0 - 3 scale)	-0.02	0.24	-0.06	0.34	0.45
Physician visit previous 4 months	-0.26	3.07	-0.46	1.98	0.61

Source: Lorig *et al.*, 1985

Notes:

1 Wilcoxon rank sum test

2 A higher scored denotes worse pain

Outcomes - Longitudinal Study

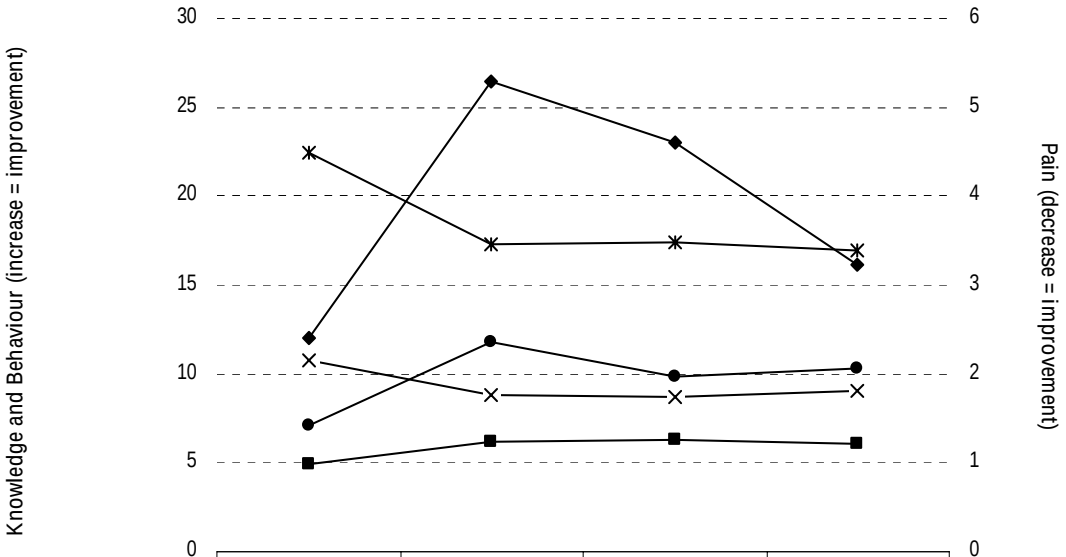
Follow-up was completed on 115 of the original intervention participants at 8 and 20 months from baseline. For these participants there were no significant changes in the use of medications or doctor's visits, however:

- knowledge of self-management and self-management behaviours declined over time but remained significantly above baseline levels at 20 months; and
- pain remained relatively stable at the levels achieved at 4 months and was still significantly below baseline levels at 20 months. (See Figure 5.1)

In 1989, Lorig undertook a study to test the hypothesis that reinforcement given approximately one year after the original ASMP intervention would either maintain or strengthen the effects of that intervention. Twelve months after participating in the ASMP, 589 subjects were randomly allocated to one of three groups: reinforcement of the original learning by participation in an Arthritis Reinforcement Course (ASC), reinforcement by receipt of a bi-monthly newsletter, and no reinforcement. Five hundred and forty-three (92%) completed the study. The results for the 543 participants for whom there was complete data indicated that reinforcement at 12 months did not enhance the effects of the original ASMP intervention (Lorig and Holman, 1989).

11 The results for the regression analysis were not included in the original articles, only the discussion as reported above

Figure 5.1 Changes in knowledge, behaviour, pain at 20 months - intervention participants



	Baseline	4 Months	8 Months	20 Months
Knowledge (Scale 0-10)	4.94	6.19	6.34	6.02
Exercise (Times/Month)	12.08	26.41	22.96	16.17
Relaxation (Times/Month)	7.12	11.76	9.9	10.36
Pain (VAS 0-10)	4.48	3.45	3.47	3.39
Pain (Ordinal 0-3)	2.15	1.76	1.73	1.81

Source: Lorig *et al.*, 1985

Costs

Total program cost is estimated at A$162/participant. Costs have been calculated based on the detailed program description provided by Lorig, applied to current Australian unit costs. It is important to presume inputs as per Lorig *et al.,* the outcomes are taken from that study, and presumably related to inputs applied. Each course is assumed to consist of 6 sessions with 15 participants in each course (in Australia the average persons for similar courses is closer to 10). Cost estimates include the cost of training of lay leaders, recruitment of participants, payment of lay leaders, materials, room hire and overall management of the program (see Table 5.5).

Table 5.5 Estimated ASMP program costs

Item	Per Course (6 sessions)	Per Participant (n=15)
Training of two leaders (20 hours each plus manual) [1]	$ 103	$ 7
Recruitment of participants for course	$ 350	$ 23
Management and organisation by leaders for each course [2]	$ 500	$ 33
Leaders 6 sessions x 3 hours (including 1 hr preparation) [3]	$ 900	$ 60
Leader travel	$ 50	$ 3
Room hire (6 sessions @ 3 hours per session) [4]	$ 450	$ 30
Consumables (manual for participants)	$ 75	$ 5
Total	**$ 2,428**	**$ 162**

Notes:

1 40 hours at A$60/hr +$80 for the manual = A$2,480. Assuming that the lay leaders run a total of 6 courses per year for 4 years then the cost per course would be ~A$103 per course

2 20 hours at $25/hour

3 18 hours at A$25/hour

4 6 sessions at A$75/session

Performance

Several outcome measures were used to assess the impact of the patient self-education program. Three of these were intermediate outcomes, related to knowledge, exercise and relaxation. All of these were substantially and significantly enhanced in the intervention group and these changes were maintained over time. This suggests that a lay based patient education program does change knowledge and behaviours. What however is less clear is the relationship between knowledge and behaviours and quality of life and utility. A reduction in pain in the intervention group between commencement and end point of the RCT at 4 months is observed and maintained for the 20 months of follow-up, based on both the VAS pain scale and an ordinal pain measure (see Table 5.6). However, as stated, a regression analysis controlling for differences between the baseline scores of the control and intervention groups, found the difference in the VAS pain result was no longer statistically significant (p=0.40), although the improvement in the ordinal pain measure was still statistically significant. It is thus possible, although not certain, that this (and similar) lay based education programs result in a net improvement quality of life.

A cost utility analysis has been undertaken for the program, using the VAS pain results to measure improvement, but the results should be interpreted with caution, and ideally corroborated with other studies. Using the transformation developed between the VAS pain and the AQoL, an estimate of the utility gain from the education program has been derived. Improvements in VAS scores at 4 months for the intervention group equates to an estimated utility gain of 0.062, which compares with a gain of 0.026 in the control group, a net difference of 0.036. This is a small net gain. (See Figure 5.2)

As this small improvement in quality of life is maintained in the intervention group at the 20 month follow-up, a net QALY benefit has been calculated over a 2 year period. As shown in Table 5.6 this is estimated at 0.0716 or 0.0696, depending on whether QALY gain in the second year is discounted. When this estimated QALY gain is related to estimated program cost of $162 per participant (see Table 5.5), this is equivalent to a cost/QALY of $2,363 (or $2,376). Performance is dependent on how long the benefits from the program last, but an assumption of 2 years seems reasonable given the result at 20-month follow-up (24 months from baseline).

Figure 5.2 Modeled utility change (---assumed) (Lorig et al., 1985)

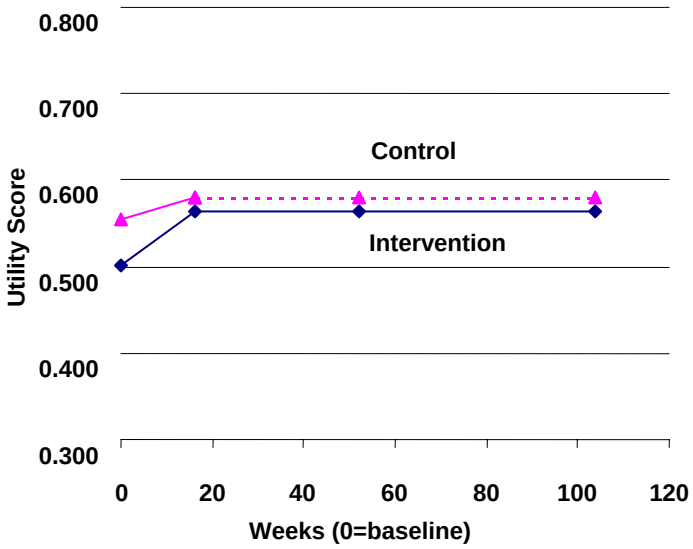


Table 5.6 Cost-utility analysis lay based patient education

Attribute	Control group	Intervention group	Difference net gain intervent vs control
Utility = - 0.06029 x VAS score (10 cm scale) + 0.77104			
Baseline	U = 0.555 (VAS = 3.58)[1]	U = 0.501 (VAS = 4.48)	
4 months	U = 0.581 (VAS = 3.15)[1]	U = 0.563 (VAS = 3.45)	
Diff. baseline to 4 months	U = 0.026	U = 0.062	U = 0.036[2]
20 months	U = 0.581 (VAS = 3.15)[2]	U = 0.567 (VAS = 3.39)	
QALY gain			
Baseline to 4 months [4]	0.0032 (0.026 x 0.5 x 0.25)	0.00775 (0.062 x 0.5 x 0.25)	0.0046
4 to 12 months	0.0195 (0.026 x 0.75)	0.0465 (0.062 x 0.75)	0.0270
12 to 24 months 0 disc	0.0260 (0.026 x 1.0)	0.0660 (0.567 – 0.501)	0.040
@ 5% disc	0.0247 (0.26 x 0.95)	0.0627 (0.066 x 0.95)	0.038
Total net QALY gain to 24 months	**0 disc rate**		**0.0716**
	@ 5% disc rate		**0.0696**
Cost per QALY[3]	**0 disc rate**		**$2,263**
	@ 5% disc rate		**$2,376**

Notes:

1 Results reported by Lorig *et al.,* 1985

2 Assumes quality of life remains at 4 month level for control group until 24 months.

3 Cost-utility analysis conducted as if difference between control and intervention groups represents a genuine gain. This has not really been established. Results need to be confirmed by other studies.

4 Assumes gain in quality of life occurs evenly over the first four months.

The conclusions that can be drawn about this type of program are somewhat uncertain, given the failure of the difference in the improvement in the VAS pain scale between the control and intervention group to reach significance. However as the program has undoubtedly achieved an improvement in knowledge and desirable changes in behaviour including greater levels of exercise, which as noted in Chapter 6 is an effective strategy for pain reduction, the observed improvements may well be real, rather than simply attributable to chance. If this is the case, because lay-based patient education programs are relatively inexpensive to run, although quite intensive, they may well be highly cost-effective. Thus lay-based patient education is potentially a program that yields modest benefits but at relatively low cost. None-the-less, confirmation of the effectiveness of lay-based patient education through other randomised control trials is desirable, ideally incorporating research into the most effective patient education models in the Australian context[12].

5.3 Nurse led education and telephone support

Program description

The modelling for this type of intervention, involving an arthritis nurse specialist in patient education - through intensive patient education sessions plus regular telephone contact and feedback to the physician about the patient - is based on the US study reported by Mazzuca *et al*., in 1997. The education intervention was delivered by an experienced arthritis nurse, under the supervision of a rheumatologist. It consisted of one session (30-60 minutes) of individualized arthritis self-care instruction, based on the needs of the patient. At the end of the session, participants were given a copy of the Arthritis Foundation Information Series pamphlet *Osteoarthritis* and a printed set of instructions for isometric quadriceps exercises. The nurse telephoned participants at one week and one month after the initial session to assess compliance with the self-care recommendations, to reinforce the recommendations, clarify any misconception and encourage continued participation in the trial.

Patients in the attention-control group reviewed a 20 minute audio visual presentation designed for the general public with the primary purposes of defining common types of arthritis in adults and encouraging those who think they may have arthritis to seek medical care. They received a current issue of a *Musculoskeletal Diseases Newsletter* that did not contain articles relevant to OA or RA self-care and exercise programs. Brief follow-up telephone calls were made to participants in this group at one week and one month to reinforce continued participation in the study. Baseline assessment consisted of:

- a general and OA-specific medical history;
- the disability and discomfort Scales of the Health Assessment Questionnaire (HAQ);
- measurement of pain when walking and at rest using 10cm visual analog scales (VAS);
- a utility score, using the Quality of Well-Being scale (QWB); and
- diagnostic assessment of arthritis self-care knowledge and skills (not reported).

The study recruited 211 outpatients with radiographically confirmed knee OA. They were assigned to the intervention group or an attention-control group. Assignment was not random but Mazzuca *et al* (1997) described it as ‘arbitrary and unbiased’ with respect to the study. The two groups were similar with respect to their demographic and clinical profiles, mean age was 62 years, symptoms had been evident for approximately 14 years, they had 1 to 2 comorbid conditions, and 85% were female.

[12] This is the primary focus of research by Dr Michael Battersby, Director, Coordinated Care Training Unit, Flinders University, South Australia.

Outcomes

Of the 211 subjects enrolled in the study, 165 (81%) completed the 12-month assessment-providing complete data (26 dropped out between 0 and 4 months, 11 between 4 and 8 months, 3 in the last four months). The attrition rates were similar in both groups (18% and 20 % respectively). The results for the HAQ disability and pain, VAS and QWB scales are shown in Table 5.7. Generally there were no significant differences between the groups in terms of changes from baseline. The HAQ disability performed most consistently over the 12 month, suggesting some improvement in the education group relative to the control. The VAS pain scores at rest and walking, while tending to show higher levels of improvement in the intervention compared to the control group, were somewhat erratic across the three data points. The QWB scale suggests an equivalence in utility scores and overall quality of life between the control and intervention groups at each data point. That is, based on the outcome data, it is not possible to conclude that the program had any significant impact on quality of life. It can be noted that the intervention was very modest involving only one individual session with the arthritis nurse specialist, plus two follow-up phone calls.

Table 5.7 Changes in pain and disability at 4, 8 and 12 months

		Baseline Adjusted Least Square Means		P Value Comparisons
		Attention Control (n=83)	Education Intervention (n=82)	
HAQ Disability Score[1]				
Baseline		1.07	1.21	
Adjusted Group Means	4 Months	1.332	1.150	0.009
	8 Months	1.357	1.194	0.035
	12 Months	1.338	1.216	0.135
HAQ Pain [1]				
Baseline		6.46	5.87	
Adjusted Group Means	4 Months	6.048	5.918	0.757
	8 Months	5.992	5.933	0.889
	12 Months	6.676	5.938	0.100
VAS Pain When Walking[2]				
Baseline		6.28	5.68	
Adjusted Group Means	4 Months	5.796	5.393	0.397
	8 Months	6.320	5.689	0.202
	12 Months	6.079	5.880	0.694
VAS Pain At Rest[2]				
Baseline		4.51	3.96	
Adjusted Group Means	4 Months	4.385	3.825	0.234
	8 Months	4.679	4.586	0.851
	12 Months	5.331	3.857	0.004
QWB Scale (General Health Status)[3]				
Baseline		0.58	0.58	
Adjusted Group Means	4 Months	0.571	0.572	0.967
	8 months	0.560	0.565	0.600
	12 Months	0.569	0.562	0.569

Source: Mazzuca *et al.,* 1997, p. 1470

Notes:

1 Health Assessment Questionnaire (HAQ) is a 4-point scale ranging from 0 (function without difficulty) to 3 (unable to function).

2 10 cm VAS, 0 (no pain) 10 (extreme pain).

3 Quality of Well-Being (QWB) utility instrument with a score ranging from 0 (death) to 1 (ideal health).

Costs

Mazzuca *et al.* (1999) estimated that the cost of delivering the self-care education intervention was US$6,163 in total or US$58.70 per patient in 1996. In 2002 A$ this would be equivalent to $126 per participant. As these costs do not include any cost for program set up, a further $43/person has been added making the cost $167/person. Alternatively, based on inputs identified: 30 mins to 1 hr for clinical nurse educator for education sessions, plus 2 follow-up phone calls, and a booklet, plus 15 minutes of physician time, direct costs would amount to some A$102 per person, (wages, wage on-costs, overheads). If we also want to factor in some costs for program management the total cost might be around A$132/participant, similar to reported cost.

Table 5.8 Costs of the nurse led, telephone based intervention - derived from US costs

Item	Cost/program		A$ Per Participant	Based on Australian unit costs
	US$ 1996	A$ 2002	(n=105)	$A/head
Senior Arthritis Nurse Educator	$5,871	$ 12,565	$ 120	$ 60
Printed Handouts for Participants	$ 14	$ 30	$ 0	$ 2
Overheads for Nurse Educator	$ 278	$ 595	$ 6	$ 20
Clinician time			Not included	$ 20
Est. Trial Setup and Management		$ 20,164 [1]	$ 41	$ 30
Total Including Trial Management	**$6,163**	**$ 35,778**	**$ 167**	**$132**

Notes:

[1] Not included in Mazzuca *et al.* (1997). Estimated at Nurse Manager for six months @ $69,040 AUD 2002 pa plus 20% on-costs. Assume in real clinical setting would apply to 500 participants

[2] Inflation rate of 1.14, source http://woodrow.mpls.frb.fed.us/economy/calc/cpihome.html accessed 24/05/02

[3] Based on the average exchange rate for Jan-May 2002 of 1.877386. Sources: http://www.x-rates.com/d/AUD/USD/hist2002.html accessed 24/05/02

Performance

Because there is no clear evidence of program benefit, it is not possible or appropriate to calculate a cost/QALY. Rather the conclusion must be that this type of program is of uncertain value.

5.5 GP-based nurse led education program

Program description

A GP-based, nurse led education program is modelled based on the OAK study, as presented by Lord *et al.* (1999). In this study, GP practices in a particular area were invited to take part and those that agreed were randomised to either an intervention or control group (cluster randomisation). GPs in the practices then recruited patients to take part in the study. To be included in the trial patients needed to have radiographic evidence of knee OA. The intervention consisted of four one-hour group sessions (up to 6 patients) at weekly intervals, led by a research nurse and held at GP surgeries. An initial assessment was undertaken in the home of the intervention group patients before the first session and each patient was given a diary to complete. Patients in the control group were offered the intervention after 12 months. Each practice participating in the study was visited by a GP or a consultant member of the project team and a research nurse and given an hour of professional development training on knee OA.

The primary outcome measure was the WOMAC but a range of other data was also collected. The first assessment was undertaken by a trained interviewer, in the participant's home. The assessment covered: i) demographic and socio-economic data, ii) history of disease and comorbidity, iii) satisfaction with GP care, iv) social activity and support sections of AIMS2, v) sources of information and knowledge of OA management and outcomes (a scale developed for the study), vi) self-efficacy in arthritis management - Arthritis Helplessness Index (AHI); vii) wellbeing through the SF-36, psychological well-being through the General Health Questionnaire (GHQ), and viii) medical, health and social service utilisation - using questions from the General Household Survey. Subsequent outcome data was collected by mailed questionnaire at 1, 3, 6 and 12 months. The postal questionnaires contained a subset of the questions asked at baseline, including the knowledge scale, AHI, WOMAC, SF-36 and GHQ. If participants refused to complete the one-year outcome questionnaire, or if they had failed to respond after one month, they were sent a reminder with a scaled down questionnaire comprising the WOMAC.

One hundred and seventy patients took part in the trial (65 control, 105 intervention), mean age was 63 years and 71% were female. There were statistically significant differences between the two groups at baseline. The intervention group were less likely to be living along (25% vs 46%), less likely to be non-white (48 vs 80%), and had a lower score on the physical dimension of the SF-36 (55 vs 65).

Outcomes

Lord *et al.* (1999) concluded that the study had 'failed to demonstrate improvements in knowledge, self-efficacy in arthritis management or health outcomes after one year. Not only were the differences not statistically significant, they were not consistent in direction.' (see Table 5.9). However, the authors did note that there were limitations to the study including 'a lack of statistical power', 'differences in patient and practice characteristics after randomisation' and 'evidence of selective loss to follow-up'. They concluded that further research was needed before firm conclusions relating to the impact of this type of intervention on the management of knee OA could be drawn.

Table 5.9 Results baseline and one year follow-up control and intervention group

	Baseline			12 Months		
	Control	**Intervention**	**P Value[1]**	**Baseline**	**12 mnths**	**P Value[2]**
Knowledge	78	74	0.14	77	77	0.65
AHI	61	59	0.23	61	63	0.25
WOMAC						
Pain	64	62	0.59	60	62	0.32
Stiffness	57	57	0.99	53	59	0.10
Disability	67	67	0.94	61	64	0.65
SF-36						
Physical	65	55	0.008	52	50	0.28
Role Physical	52	47	0.48	48	45	0.86
Role Emotional	78	72	0.31	57	56	0.78
Social	81	78	0.43	79	71	0.27
Pain	57	52	0.15	58	51	0.58
Mental	76	75	0.80	77	75	0.79
Vitality	57	57	0.90	54	53	0.85
General Health	65	58	0.10	64	59	0.90
GHQ	87	83	0.24	80	81	0.63

Source: Lord *et al.*, 1999

Notes:

[1] Logistic regression of dependent variable on dummy study group variable

[2] Linear regression of 1-year outcome variable on dummy study group variable and baseline value of outcome variable

We have generated a utility score from the SF-36 for the control and intervention group at baseline and at 12 months, using the transformation developed from the data-base gathered for this study. These calculations are summarised in Table 5.10 and suggest an almost equal reduction in quality of life in both groups, over the study period, of –0.0282 in the control group and – 0.0249 in the intervention group. This is not surprising given the conclusion of the authors that the study did not demonstrate improvements in the intervention cohort.

Table 5.10 Calculated mean utility values – GP-based, nurse led education program

	Control	Intervention
Baseline	0.6644	0.6238
Follow-up	0.6362	0.5989
Difference	-0.0282	-0.0249

Costs

Program cost is based on estimates reported by Lord, translated into current A$. Cost is estimated to be $422/particant plus development costs (see Table 5.11).

Table 5.11 Cost – GP-based, nurse led education (assuming recruitment from 20 GP practices, 38 groups, 174 patients)

COST ITEM	UK£ 1997	A$ 2002[2]	Per Participant A$ 2002
Training	1,230	$ 3,752	$ 22
Visits to GPs for prof develop	1,740	$ 5,308	$ 31
Organising sessions	4,674	$ 14,258	$ 82
Visits to patients	2,610	$ 7,962	$ 46
Running sessions	9,348	$ 28,515	$ 164
Room hire GP surgery	608	$ 1,855	$ 11
Consumables	3,480	$ 10,615	$ 61
Nurse travel	400	$ 1,220	$ 7
Total without development costs	24,090	$ 73,484	$ 422
Development costs			$ 317
Total with development costs			$ 739

Source: Lord *et al.*, 1999

Notes:

[1] Inflation rate of 1.12

[2] Exchange rate of one British pound = 2.723564 AUD (average of January to May 2002). Source http://www.x-rates.com/d/AUD/GBP/hist2002.html accessed 27/05/02

Performance

As with the previous intervention, because there is no clear evidence of program benefit, it is not possible or appropriate to calculate a cost/QALY. Rather the conclusion must be that this program has not been effective in the management of knee OA, and thus cannot be cost-effective.

6. EXERCISE AND STRENGTH TRAINING

6.1 Introduction

The Framingham study found that knee OA accounted for more dependency in relation to tasks such as walking and stair climbing than any other disease, especially in the elderly (Guccione, Felson, Anderson, Anthony *et al.*, 1994). There is evidence that increasing muscle strength, and aerobic capacity through exercise has the potential to reduce disability related to the symptoms of OA, particularly OA of the knee (Taylor, Fortmann, Flora, Kayman *et al.*, 1991). Exercise as an intervention in OA may work at a number of different levels. It can assist in weight reduction, an established factor in the incidence and progression of OA. Appropriate exercise can also strengthen the quadriceps muscles, which play an important role in supporting the knee. The Bristol OA knee study found that quadriceps strength was the greatest single predictor of lower limb functional limitation, exceeding that of knee pain (McAlindon, Cooper, Kirwan and Dieppe, 1993).

Only a small number of randomised studies of exercise as an intervention for management of OA were identified. Most have focussed on knee OA. A systematic review of exercise programs in OA (van Baar, Assendelft, Dekker, Oostendorp *et al.*, 1999) concluded that only two trials had sufficient validity and power to draw any firm conclusions (van Baar, Dekker, Oostendorp, Bijl *et al.*, 1998; Ettinger, Burns, Messier, Applegate *et al.*, 1997). The effect sizes of both these trials indicate small to moderate beneficial effects of exercise therapy on pain, a small beneficial effect on disability and moderate to great benefit based on patient global assessment. Only one of these two studies provided outcome measures which could be fitted to our modelling (van Baar *et al*., 1998). Three additional studies, which provide suitable outcome measures, were also selected for modelling. Each of these studies has been published since the systematic review (see Table 6.1).

Table 6.1 Studies used for modelling exercise and strength training interventions

	Home-Based		**Clinic-Based**	
	Intensive Strength Training	**Less Intensive Exercise**	**Primary Care Physiotherapy + GP Care**	**Outpatients**
Studies	Baker, Nelson, Felson, Layne *et al*. (2001)	O'Reilly, Muir and Hoherty (1999)	van Baar, Dekker, Oostendorp, Bijl *et al.* (1998)	Deyle, Henderson, Matekel, Ryder *et al.* (2000)
Type of Study	RCT	RCT	RCT	RCT
Control	Nutrition Education	No Intervention	GP Care Only	Placebo
Participants Randomised	46	191	201	83
Country	USA	UK	Netherlands	USA
Recruitment	Community	GP Clinic	GP Clinic	Outpatient Clinic
Percent Completing	82%	94%	96%	83%
% Female	78%	65%	80%	59%
Average Age	68 years	61 years	68 years	61 years
BMI/Weight	31 kg/m^2	76 kg	Not Reported	31 kg/m^2
Diagnosis	Knee OA	Knee OA	60% Knee, 40% Hip	Knee OA
Outcome Measures	SF-36	SF-36	VAS	WOMAC

6.2 Costs

There is a wide range of program types that fall under the broad category of exercise and strength training. Thus it is not possible to provide a typical cost, but rather we have attempted to determine the costs of these four seminal studies (in current Australian dollars). Any adjustment to cost and resourcing is problematic, as it will be uncertain how a change in resourcing would impact on outcomes. It seems clear from the literature that exercise and strength training programs which involve more regular contact time with primary care clinicians such as physiotherapists or specialist nurses appear to have better outcomes than those with fewer contact hours. This has implications for cost as well as effectiveness, as contact time with the primary care clinician contributes the bulk and in some cases the entirety of costs of the intervention. Only one of the three studies required any form of equipment (ankle weights in Baker *et al*. 2001).

Modelling utility estimates

Results from all studies were modelled over a one-year period. For three studies (Baker *et al*., 2001; O'Reilly *et al*., 1999; van Baar *et al.*, 1998) the outcome scores at the end of the evaluation period were extended through to 1 year. The Deyle *et al*. (2000) study reported a decline in utility between the end of the intervention and 12 months and this decline was used in the modelling.

The regression relationships derived between the VAS 100 m pain scores and the AQoL, the SF-36 and the AQoL and the WOMAC and the AQoL, have been used to translate outcomes reported based on these instruments into a common measure – a change in utility score. (See the annexure to this chapter for the transformation of the raw scores to utility scores.) Where 95% confidence intervals were reported at follow-up for the intervention group, these have been used to conduct sensitivity analyses.

6.3 Home-based interventions

Intensive strength training

Program description

In this intervention reported by Baker *et al*. (2001), 46 patients with OA of the knee were recruited from the local community, 23 were randomised to receive a home-based exercise program, and 23 to a nutrition control arm. The mean age of participants was 68, mean BMI was 31 kg/m^2 and 78% were female. Exercise patients received a booklet on exercises and a set of ankle-weights, and were visited at home 2 times per week for the first 3 weeks, once in week 4 and once every 2 weeks thereafter, for a total of 12 visits in 16 weeks. Control patients received a booklet on nutrition and received 7 visits over the 4 months. Thirty-eight participants (19 intervention and 19 control) completed the program.

Costs

Based on the information supplied by Baker *et al.* (2001), the cost per person for the intervention group has been estimated at $1,420 and the cost per person for the control group $770 (see Table 6.2). The incremental cost of the intervention is therefore estimated to be $650 per person.

Table 6.2 Estimated costs for the home-based intensive strength training program (16 weeks)

Item	Intervention arm		Control arm	
	No x unit cost[1]	Cost/Person	No x unit cost	Cost/Person
Booklet	1 @ $30	$ 30	1 @ $20	$ 20
Ankle Weights	1 set @$150	$ 150		
Nurse home visit	12 x 2hr @$50/hr	$1,200	7x2 hr @$50/hr	$700
Program admin/ management	Allow	$ 50		$ 50
Total		**$1,420**		**$770**

Source: Baker *et al.*, 2001

Notes

1 Including salary on-costs and 20% overhead costs.

Outcomes

The participants in the intervention group who completed the exercise program scored higher on all of the SF-36 subscales at follow-up compared to baseline. The scores for those in the nutrition control arm who completed the program improved on only one scale. There were statistically significant differences between the control and intervention group in mean change from baseline to follow-up on four of the SF-36 scales: Physical Function, Role Physical, Social and Mental (see Table 6. 3).

Table 6.3 Change in SF-36 outcomes[1] and estimated utility for intensive strength training exercise intervention (completers only = 83%)

	Control Group (n=19)			Intervention Group (n=19)			P value
	Baseline mean score	Follow-up mean score	Mean Change ΔC	Baseline mean score	Follow-up mean score (95% CI)	Mean Change ΔI	ΔC c/w ΔI
Physical Function	56.6	60.8	4.2	46.8	63.4 (50.5 – 76.3)	16.6	0.010
Role Physical	64.5	52.6	-11.8	42.1	75.0 (57.5 – 92.5)	33.0	0.009
Bodily Pain	59.5	56.3	-3.2	48.0	59.6 (48.7 – 70.6)	11.7	0.060
General Health	69.4	70.8	1.4	74.7	77.5 (66.7 – 88.4)	2.8	0.617
Vitality	55.5	55.3	-0.3	56.8	60.8 (49.7 –72.0)	4.0	0.264
Social	81.6	75.7	-5.9	78.3	90.8 (79.5 – 100)	12.6	0.012
Role Emotional	77.2	73.7	-3.5	73.7	77.2 (58.6 – 95.8)	3.5	0.636
Mental	80.4	77.3	-3.2	80.4	88.6 (82.6 – 94.6)	8.2	$\leq$0.001
Estimated Utility[2]	0.529	0.517	-0.012	0.483	0.5886 (0.5199-0.63940)	0.1058	

Source: Baker *et al.,* 2001, p. 1661

Notes:

1 A higher score is better

2 See Table A6.1 in the annexure to this chapter

Performance

Results from the study by Baker *et al.* were reported as SF-36 scores, at baseline and at 4 months. These show a greater improvement in most SF-36 sub-scales in the intervention arm compared to the control arm. Assuming that the changes in utility seen at 4 months continue for 1 year (Figure 6.1), the improvement in SF-36 scores in the exercise group equated to an increase in utility of 0.089 (range 0.031 to 0.132). This compares with a loss of utility of 0.010 in the control group. The net difference in utility at 1 year is 0.100 (range 0.042 – 0.143). This equates to a cost / QALY of $6,624 (range $15,892 - $4,628) (see Table 6.4).

Figure 6.1 Modeled utility change (---assumed) (Baker et al., 2001)

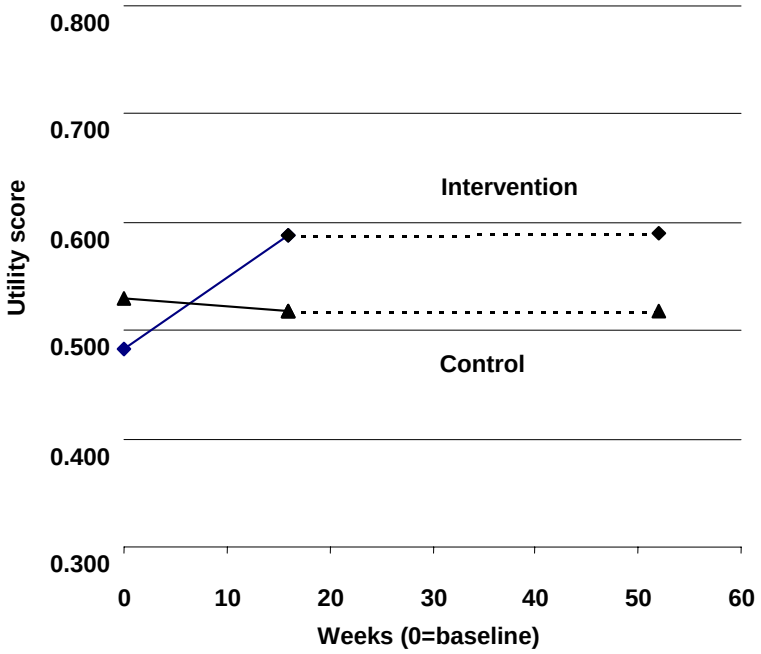


Table 6.4 QALY gains and cost / QALY for the home-based intensive strength training ntervention

	Utility at Baseline	Utility at follow-up [1]	Difference	QALY gain over 12 months[1, 2]	Cost/QALY[3] $
Intervention Group	0.483	0.589	+ 0.106	0.0895 (0.031 – 0.132)	$6,524 ($4,560 - $15,650)
Control group	**0.529**	**0.517**	**- 0.012**	**-0.0102 (0.042 – 0.143)**	

Notes:

1 Area under the graph – assuming pattern of utility over 12 months as shown in figure 6.1

2. Range based on upper and lower bounds of the 95% CI

3 Net utility gain = 0.0895 – (- 0.0102) = 0.0996 → Cost/QALY = $650/0.0996 = $6,524

Less intensive exercise program

Description

The less intensive program was designed to improve quadriceps strength and have a positive impact on knee pain and disability (O'Reilly *et al.*, 1999). Participants were recruited via telephone from among knee OA patients registered at two general practices in the UK. Those meeting initial criteria were asked to attend their local surgery for further assessment, including radiographs of both knees. Of the 191 participants recruited, 113 were randomised to receive an exercise intervention consisting of a series of home-based daily strengthening exercises taught by a nurse metrologist, with the remaining 78 (control) receiving no intervention. Eleven participants did not complete the program. The mean age of those who did complete was 61, mean weight was 76 kg, and 65% were female.

The intervention group received four home-visits by the nurse metrologist at study commencement, weeks 2, 6, and 12. Baseline and 6 month evaluations were performed on all participants at local surgeries. The outcome measures included VAS knee pain when walking on a flat surface and on stairs and the SF-36 (O'Reilly *et al.*, 1999). The SF-36 subscale scores have been used to model changes in utility.

Costs

The costs of the intervention have been calculated as $400, based on eight hours of nurse time (see Table 6.5).

Table 6.5 Estimated costs for the less intensive home-based exercise program (26 weeks)

Item	Intervention arm		Control arm	
	No x unit cost[1]	Cost/Person	No x unit cost	Cost/Person
Nurse home visit	4 x 2 hr @ $50/hr	$ 400	Not applicable	$0

Notes:

[1] Including salary on-costs and 20% overhead costs

Outcomes

O'Reilly *et al.* (1999) reported that there was a 'trend' towards improved outcomes on 7 of the 8 SF-36 scales for the intervention group participants who completed the program and on 4 scales for the completing participants in the control group (see Table 6.5). No significance tests were reported in the study therefore it is not clear if the differences between the groups are statistically significant. However, this study has been included in the modelling because there were statistically significant differences in VAS outcomes.

Table 6.6 Change in SF-36 outcomes and estimated utility for less intensive exercise program (completers only)

	Control Group (n=72)			Intervention Group (n=108)			
	Baseline Average	Follow-up Average	Mean Change	Baseline Average	Follow-up Average	(Range)[1]	Mean Change
Physical Function	52.6	51.0	-1.63	57.0	59.7	(56.6 – 62.8)	2.68
Role Physical	43.4	35.8	-7.59	50.6	53.8	(46.8 – 60.8)	3.19
Bodily Pain	53.3	53.5	0.16	55.2	60.2	(55.9 – 64.5)	4.97
General Health	53.9	53.2	-0.70	58.5	60.4	(57.7 – 63.1)	1.93
Vitality	46.7	47.2	0.56	53.7	56.2	(53.1 – 59.3)	2.47
Social	67.9	69.8	1.90	78.8	80.6	(75.9 – 85.4)	1.89
Role Emotional	68.6	69.1	0.48	68.5	70.4	(61.9 – 78.9)	1.85
Mental	74.6	71.7	-2.91	70.0	69.8	(67.2 – 72.3)	-0.21
Estimated Utility[2]	0.5907	0.5800	-0.0107	0.6047	0.6229	(0.5922-0.6257)	0.0182

Notes:

1 Based on the 95% CI for the change scores

2 See Table A6.2 in the annexure to this chapter

Performance

In the O'Reilly *et al.* study, there was a trend towards improvements on all but one of the SF-36 subscales for the intervention group and a decrease on five of the subscales for the control group. Assuming that the changes in utility seen at six months continue for 1 year (see Figure 6.2), the improvements in SF-36 scores in the intervention group equated to an increase in utility of 0.014 (range -0.009 - 0.036). This compares with a loss in utility of –0.008 in the control group. The net difference in utility at 1 year is 0.022 (range –0.001 to 0.044). This equates to an average cost / QALY of $18,439 (range n/a - $9,084). The cost/QALY of the lower utility bound was not calculated because there was a less than zero improvement for some participants (see Table 6.7).

Figure 6.2 Modelled utility change (---assumed) (O'Reilly et al., 2001)

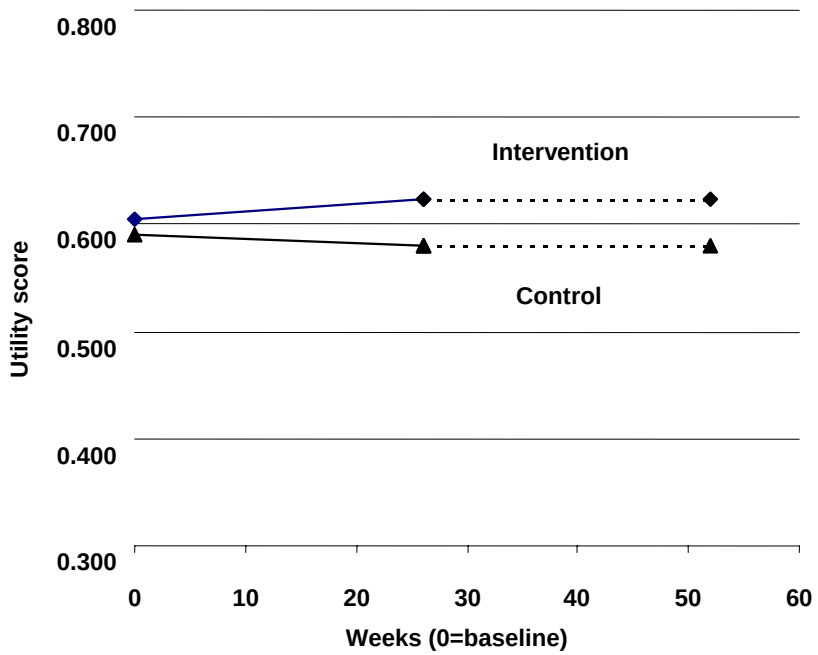


Table 6.7 QALY gains and cost/QALY for the less intensive home-based intervention

	Control Group	Intervention Group Average (Range)[1]	Cost / QALY (Cost / Person $400)
Change in utility (over 12 months)	-0.008	0.014 (-0.009 – 0.036)	
Net difference at 1 year		**0.022 (-0.001 – 0.044)**	**$18,439 (N/A[2] - $9,084)**

Notes:

1 Estimated using upper and lower bounds of the 95% CI for the change scores at 6 months

2 Not applicable, no QALY gain

6.4 Clinic-based programs

Primary care

Program description

In the primary care based program reported by van Baar *et al.* (1999), 201 patients with hip or knee OA were selected to participate through their GPs and randomised to receive either a physiotherapist-managed exercise regime in a primary care setting (n=99) or conservative treatment (n=102) (standard GP based treatment). Mean age of participants was 68 and 80% were female. Approximately 60% had knee OA and 40% hip OA.

Those in the exercise group were provided with individual exercise therapy sessions with a physiotherapist who followed an exercise protocol developed for the study. A mean 16 x ½ hour physiotherapy visits per patient occurred over the 12 week intervention period. No data was provided on weight or BMI. One hundred and ninety-one participants completed the program.

Costs

The costs for the exercise intervention provided by the physiotherapists has been estimated to be $480 (see Table 6.8).

Table 6.8 Costs for the primary care based exercise intervention

Item	Intervention arm		Control arm	
	No x unit cost[1]	Cost / Person	No x unit cost	Cost/Person
Physiotherapy Visits	~16x0.5hr @ $60/hr[2]	$ 480	Not applicable	$0

Notes:

1 Including salary on-costs and 20% overhead costs.

2 Assumes a combination of physiotherapist and exercise consultant and mean 2 sessions per week for 12 weeks,

Outcomes

Although both groups experienced a decrease in ‘pain during the last week’ as measured by a 100mm VAS pain scale, the decrease for the intervention group was four times that of the control group, and this difference was statistically significant (see Table 6.8).

Table 6.9 VAS pain and estimated utility scores for the primary care based intervention (completers only)

	Control Group (n=93)		Intervention Group (n=98)	
	VAS 100 mm	Estimated Utility	VAS 100 mm	Estimated Utility
Baseline	43.1	0.511	46.9	0.488
12 weeks	37.4	0.546	24.1	0.626
Change[1, 2]	-5.7	0.035	-22.8	0.138

Source: van Baar *et al.,* 1998, pp. 2436-2437

Notes:

[1] p value < 0.01 for change in intervention group compared with control group

[2] Utility = -0.006029 x VAS + 0.77104

Performance

Results from the study by van Baar *et al.* (1998) were reported estimates of 'pain last week' on a VAS 100 mm scale, with 0 indicating no pain and 100 the most severe pain. For persons in the intervention group, the average score at the 12 week follow-up went from 46.9 to 24.1 compared with 43.1 to 37.4 in the control group. Assuming that the changes in utility seen at 12 weeks continue for 1 year (see Figure 6.3), the improvements in the VAS scores for the intervention group equated to an increase in utility of 0.122. This compares with an increase in utility 0.030 in the control group. The net difference in undiscounted utility at 1 year is 0.091. This equated to a cost/QALY of $5,263 (see Table 6.10).

Figure 6.3 Utility change modelled on pain in last week (--- assumed) (van Baar et al., 1998)

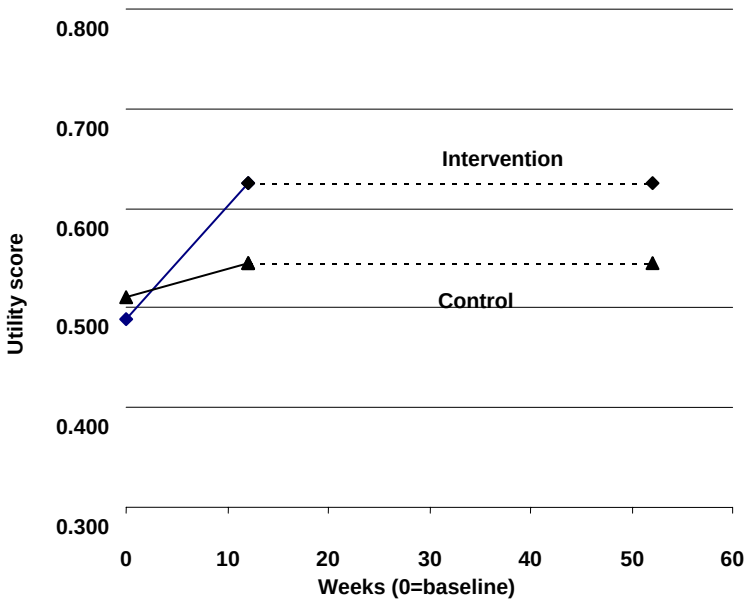


Table 6.10 QALY gains and cost/QALY for the

	Control Group	Intervention Group Average[1]	Cost / QALY (Cost / Person = $480)
Change in utility (over 12 months)	0.030	0.122	
Net difference at 1 year		**0.091**	**$5,263**

Notes:

1 No sensitivity analyses conducted as neither 95% CIs nor SDs reported

6.4.2 Outpatients based manual physical therapy and exercise

Program description

In the study by Deyle *et al.* (2000), 83 patients with knee OA were randomly assigned to receive manual physical therapy and exercise at an outpatient physical therapy department (n=42) or a 'placebo' treatment (n=41). Mean age of the participants was 61 and 59% female. The intervention group received two treatment sessions per week sessions over 4 weeks. Each session included:

i) manual physical therapy treatment from a physical therapist - consisting of passive physiologic and accessory joint movements, muscle stretching and soft-tissue mobilization, applied primarily to the knee, but also to the lumbar spine, hip or ankle if these areas showed limitation in active or passive movement, were symptomatic or were contributing to overall lower limb dysfunction; and

ii) a closely supervised standardized knee exercise program - muscle strengthening exercises, muscle stretching and riding a stationary bike.

The placebo group received treatment from a physical therapist, consisting of sub-therapeutic ultrasound for 10 minutes to the area of the knee symptoms. The amount of time spent per session with the physical therapist was approximately 30 minutes for both groups, with the exercise group requiring an additional 30-45 minutes to perform their exercises in the clinic. Intervention group patients were also provided with a detailed exercise instruction handout and were instructed by the therapist on undertaking their exercises at home on days where they were not seen at the clinic. Patients in the placebo group were instructed to continue their normal daily activities.

Costs

As shown in Table 6.12 the Costs of the intervention arm were estimated to be $590 per person and the cost for the control arm $300 per person.

Table 6.11 Cost estimates for the outpatients based manual therapy and exercise program (8 weeks)

Item	Intervention arm		Control arm	
	No x unit cost[1]	Cost/Person	No x unit cost[1]	Cost/Person
Physical therapist	8 x 0.5 hrs @ $75/ hr	$300	8 x 0.5 hrs @ $75/ hr	$300
Exercise instructor	8 x 1 hr @ $35 / hr	$280		
Booklet	1 @ $10	$ 10		
Total		**$590**		**$300**

Source: Deyle *et al* ., 2000

Notes:

1 Including salary on-costs and 20% overhead costs.

Outcomes

As shown in Table 6.11, the mean WOMAC scores decreased for both the intervention and the control group during the intervention (baseline –8 weeks) and then increased slightly during the period 8 weeks to 12 months. However, the WOMAC scores at 12 months were still lower than at baseline and the decrease was greater for the intervention group compared to the control group (-435.8, -116.9).

Table 6.12 Outcomes for outpatients based manual therapy and exercise intervention (completers only)

	Control Group (n= 36)		Intervention Group (n= 33)	
	WOMAC[1]	Estimated Utility[2]	WOMAC[1] (95% CI)	Estimated Utility[2]
Baseline	1093.5	0.515	1046.7	0.529
4 weeks	921.2	0.565	505.2 (572.4 –438.0)	0.657
8 weeks	934.3	0.562	462.4 (611.9 –312.9)	0.664
12 months	976.6	0.550	610.9 (884.2 –498.8)	0.638

Source: Deyle *et al.,* 2000

Notes:

1 Composite score out of 2400

2 See Table A6.3 in the annexure to this chapter

Performance

Deyle *et al*. (2002) provide aggregate WOMAC scores as outcome measures. The WOMAC version they used scored each of the 24 elements of the WOMAC questionnaire on a VAS 100mm scale, with the aggregate WOMAC score ranging from 0 to 2400mm (lower scores are better). Although the treatment period was 8 weeks, after only 4 weeks of treatment substantial improvement in WOMAC scores for the intervention group were noted. There was an additional small increase in this over the remaining 4 weeks of the treatment. Significant gain was still observed at 12 months for the treatment group.

The estimated gain in utility for the exercise group was 0.118 (range 0.079 - 0.137) and 0.041 for the control group, a difference of 0.078 (0.038 – 0.097) . This equates to a cost per QALY of $3,734 (range $7,622 - $3,001) (see Table 6.13).

Figure 6.4 Utility change modelled on WOMAC scores (Deyle et al., 2000)

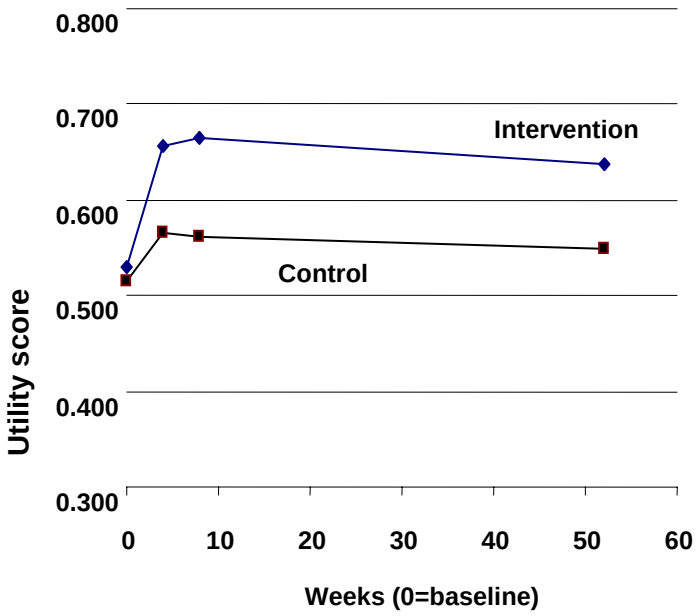


Table 6.13 Change in QALYs and Cost / QALY for the outpatients intervention

	Control Group	Intervention Group Average (Range)[1]	Cost / QALY (Cost / Person = $300)
Change in utility (over 12 months)	0.041	0.118 (0.079 – 0.137)	
Net difference		**0.078 (0.038 – 0.097)**	**$3,734 ($7,622 - $3,001)**

Notes:

[1] Based on upper and lower bounds of 95% CI

The improvement from baseline utility in the Deyle *et al.* study exercise group is larger than that observed in the other three exercise studies modelled. Importantly however, in this study participants were re-evaluated at 12 months and it was found that WOMAC scores were still significantly improved in the intervention group compared to the study baseline levels, whereas the control group showed no significant change from baseline. Additionally, at 12 months distance able to be walked in 6 minutes was almost unchanged from 8 weeks in both groups - an increase of 170m over baseline in the intervention group, but no substantial change over baseline in the control group.

6.5 Performance summary

Estimated costs and utility gain from the four exercise programs have been brought together to assess the performance of exercise and strength training as an intervention for OA. The results are presented in Table 6.14. All outcomes were modelled over a one year period.

For the three studies that did not evaluate participant outcomes over periods longer than 6 months, the model assumed outcomes at study end were retained for at least for one year. It is both possible that benefits might dissipate, but also that for some participants at least, benefits will continue well beyond 12 months. Studies involving longer term follow-up would be valuable to establish whether lasting changes are achieved in patient behaviour, improvement in OA symptoms and quality of life.

Present value utility was calculated as area-under-the-line gain in utility compared to baseline utility for both exercise and control groups. Present value utility was calculated for both control and intervention groups, and cost/QALY calculated for the difference in utility gain (change) between these two groups. The differential cost between control and intervention groups is the relevant cost concept for this analysis. On average, the cost per QALY for exercise/strength training interventions are estimated to fall between $3,000 and $18,500. The least intensive program was that described and evaluated by O'Reilly et al. (1999). It was also the least effective and the least cost-effective. The most effective and cost-effective programs tend to be more intensive and also involve specific strength training.

6.6 Conclusions

These studies indicate that a managed exercise/strength training program over the medium term (3-6 months) can lead to improvements in OA symptoms of the knee, and possibly the hip (van Baar *et al*. 1998). Regular patient-health practitioner contact and specific strength training elements may be important in determining the success of exercise as an intervention for OA. The three more rigorous and structured programs (Baker *et a.,* Deyle *et al* and van Baar *et al*) all show substantial and significant benefit. As the majority of costs in each of these studies relates to health practitioner contact time, the study with the most contact time was also the most expensive (Baker *et al*). Baker *et al* was a home-based study, so a cost for travel time was added which doubled the overall cost of the study. In comparison, the cost of health professional contact time in van Baar *et al* was reduced as all physiotherapist appointments took place at local primary care institutions.

Although it is uncertain whether participants will continue to follow exercise regimens without follow-up, and hence whether medium term changes are durable, the study by Deyle *et al* followed-up participants at 12 months and found sustained improvements among those who had received the intervention. These included significant improvements in WOMAC score compared to baseline, a sustained improvement in distance walked over 6 minutes, and fewer participants having knee arthroplasty (5%) compared with control (20%). Differences in the cost of other interventions have not been taken into account in this analysis. Given evidence that exercise may reduce other costs of management, exercise may well be more cost-effective than calculated here.

Although from the analysis here exercise appears both effective and cost-effective, the current level of provision and costs of exercise programs for persons with OA in Australia is not known. Various groups such as the Arthritis Foundation run a series of programs in areas such as self-management and water exercise, as do public hospitals and community health centres. It was not possible to collate data on these activities for this study. Our survey of 220 persons with OA found that 70% had tried exercise as part of their OA management. Most reported some success, with 55% of those who had tried exercise identifying it as moderately or extremely helpful.

In short, this analysis suggests exercise can improve quality of life for persons with OA (especially of the knee and hip) and at reasonable costs for benefits gained. Even if cost per patient for the exercise programs analysed were doubled, for instance to provide additional sessions, cost/QALY is still modest at between $7,500 - $37,000.

Table 6.14 Summary of cost-utility modelling of exercise studies

	Home -Based								Clinic-based					
	Intensive strength training and exercise Baker *et al* (2001)				Less intensive exercise O'Reilly *et al*. (1999)				Primary Care van Baar *et al.* (1998)		Outpatient Clinic Deyle *et al* (2000)			
	Control	Intervention			Control	Intervention			Control	Intervention	Control	Intervention		
	Average	Average	Lower	Upper	Average	Average	Lower	Upper	Average	Average	Average	Average	Lower	Upper
Utility Scores														
Baseline	0.529	0.483			0.591	0.605			0.511	0.488	0.515	0.529		
Study End	0.517	0.589	0.520	0.639	0.580	0.623	0.592	0.653	0.546	0.626	0.550	0.638	0.658	0.575
Change	-0.012	0.106	0.037	0.157	-0.011	0.018	-0.013	0.048	0.034	0.137	0.035	0.109	0.129	0.046
Est. QALY gain over 1 year	-0.010	0.089	0.031	0.132	-0.008	0.014	-0.009	0.036	0.030	0.122	0.041	0.118	0.079	0.137
Difference Intervention - control		0.100	0.042	0.143		0.022	-0.001	0.044		0.091		0.078	0.038	0.097
Cost														
Cost/Person	$770	$1,420	$1,420	$1,420	$0	$400	$400	$400	$0	$480	$300	$590	$590	$590
Diff. Cost/Person		$ 650	$ 650	$650		$400	$400	$400		$480		$290	$290	$290
Performance														
Gross Cost/QALY		$14,525	$34,192	$9,957		$18,439	N/A[3]	$9,084		$5,263		$7,597	$15,508	$6,106
Differential Cost/QALY		$ 6,524	$15,651	$4,558		$18,439	N/A[3]	$9,084		$5,263		$3,734	$ 7,622	$3,001

Notes:

[1] At 4 months for Baker *et al.*, 6 months for O'Reilly *et al.,* 3 months for van Baar *et al.*, 12 months for Deyle *et al.*

[2] Calculated as area under the line, from baseline to 1 year

[3] No QALY gain for lower bound

ANNEXURE TO CHAPTER 6

Table A6.1 Utility transformation of SF-36 scores Baker *et al.* (2001)

	AQoL Constant & Coefficients	Control				Intervention			
		Baseline		4 Months		Baseline		4 Months	
		SF-36	AQoL	SF-36	AQoL	SF-36	AQoL	SF-36	AQoL
Constant	-0.199829		-0.1998		-0.1998		-0.1998		-0.1998
Physical Function[1]	0.488052	0.61	0.2995	0.62	0.3048	0.58	0.2804	0.63	0.3071
Role Physical	0.000047	64.5	0.0030	52.6	0.0025	42.1	0.0020	75.0	0.0035
BodilyPain	0.002406	59.5	0.1432	56.3	0.1355	48.0	0.1155	59.6	0.1434
General Health	0.000000	69.4	0.0000	70.8	0.0000	74.7	0.0000	77.5	0.0000
Vitality	0.000669	55.5	0.0371	55.3	0.0370	56.8	0.0380	60.8	0.0607
Social	-0.000212	81.6	-0.0173	75.7	-0.0160	78.3	-0.0166	90.8	-0.0164
Role Emotional	-0.000041	77.2	-0.0032	73.7	-0.0030	73.7	-0.0030	77.2	-0.0036
Mental	0.003314	80.4	0.2664	77.3	0.2562	80.4	0.2664	88.6	0.2936
Utility Scores			**0.5290**		**0.5170**		**0.4828**		**0.5886**

Notes:

[1] Physical function raw scores converted using the quadratic adjustment for knees [0.000103(Physical Function SF-36)^2 + 0.01465(Physical Function SF-36) + 0.114479] before multiplied by the AQoL coefficient

Table A6.2 Utility transformation of SF-36 scores O'Reilly *et al.* (1999)

	AQoL Constant & Coefficients	Control Group				Intervention Group			
		SF-36		AQoL		SF-36		AQoL	
		Baseline	6 Mths	Baseline	6 Mths	Baseline	6 Mths	Baseline	6 Mths
Constant	-0.19983			-0.1998	-0.1998			-0.1998	-0.1998
Physical Function[1]	0.48805	0.60	0.59	0.2928	0.2897	0.61	0.62	0.3001	0.3036
Role Physical	0.00005	43.4	35.8	0.0021	0.0017	50.6	53.8	0.0024	0.0025
BodilyPain	0.00241	53.3	53.5	0.1283	0.1287	55.2	60.2	0.1328	0.1448
General Health	0.00067	53.8	53.1	0.0360	0.0356	58.5	60.4	0.0392	0.0404
Vitality	-0.00021	46.7	47.2	-0.0099	-0.0100	53.7	56.2	-0.0114	-0.0119
Social	0.00143	67.9	69.8	0.0967	0.0994	78.8	80.6	0.1122	0.1149
Role Emotional	-0.00004	68.6	69.1	-0.0028	-0.0029	68.5	70.4	-0.0028	-0.0029
Mental	0.00331	74.6	71.7	0.2473	0.2376	70.0	69.8	0.2320	0.2313
Utility Scores				0.5907	0.5800			0.6047	0.6229

Notes:

[1] Physical function raw scores converted using the quadratic adjustment for knees [0.000103(Physical Function SF-36)^2 + 0.01465(Physical Function SF-36) + 0.114479] before multiplied by the AQoL coefficient

Table A6.3 Utility transformation of WOMAC scores for Deyle *et al*. (2002)

	WOMAC Scores								Utility Scores[1]			
	Composite out of 2400				Out of 100							
	Base	4 Wks	8 Wks	12 Mths	Base	4 Wks	8 Wks	12 Mths	Base	4 Wks	8 Wks	12 Mths
Intervention	1046.7	505.2	462.4	610.9	43.61	21.05	19.27	25.45	0.529	0.657	0.664	0.638
Control	1093.5	921.2	934.3	976.6	45.56	38.38	38.93	40.69	0.515	0.565	0.562	0.550

Notes:

[1] Utility = $-0.0000729 \times (WOMAC_{100})^2 + -0.00097 \times WOMAC_{100} + 0.710039$

7. Knee bracing

7.1 Introduction

The knee is the most common weight bearing joint to be affected by OA, and varus deformity is the most common malalignment of the knee associated with OA (Kirkley, Webster-Bogaert, Litchfield, Amendola *et al.*, 1999). Malalignment of the knee in either a varus or valgus position increases the medial and lateral load on the knee respectively, placing more stress on these compartments of the knee and increasing the likelihood of progression of OA in these compartments. Knee malalignment has been estimated to increase risk of developing OA by 4-5 times (Sharma, Song, Felson, Cahue *et al.*, 2001). Bracing of the knee to re-align load has been demonstrated in studies to provide pain relief and reduce disability in patients with advanced knee OA. Additionally, in patients with OA of the patellofemoral joint, it is thought that patella malalignment may be an important cause of pain. Knee bracing can be undertaken in a number of ways, from simple taping of the patella to pull it into a medial position in patients with patellofemoral OA (Cushnaghan, McCarthy and Dieppe, 1994) a basic sport-style neoprene sleeve, to cast-fitted mechanical braces which can be adjusted to increase the angle of valgus/varus or shift the load direction through the knee.

7.2 The evidence

Most of the published studies on the use of knee braces in OA report biomechanical outcomes relating to changes in joint movement and posture, with only a small number of studies identified which report patient-derived outcomes that can be used in calculating utility values. Of those reporting patient-derived outcomes, many are underpowered to detect differences between study arms, and only one randomised study could be identified which had sufficient numbers of participants per arm to provide statistically robust results (Kirkley *et al.*, 1999). However, the results from this study, which show significantly reduced pain in those wearing the knee brace, are generally supported by smaller studies. Matsuno, Kadowaki and Tsuji (1997) recruited 20 patients with severe medial compartment OA to wear a brace for 12 months. At 12 months, none of the patients reported an exacerbation in pain, and 19/20 reported pain relief. In addition, quadriceps muscle strength increased in 17/20 patients. A study in the UK by Draper, Cable, Sanchez-Ballester, *et al.* (2000), which recruited 30 patients with medial compartment OA to wear a brace for 3 months, found similar results. Hewett, Noyes, Barber-Westin and Heckmann (1998) reported that walking time prior to pain more than doubled in 18 patients recruited to wear a knee brace for 7 hours per day over a year, with these results noted by week 9. Significant reductions in pain for activities of daily living were also found. Similar results are reported by Lindenfeld, Hewett, Andriacchi (1997).

Only one randomised study could be found in the area of patella taping for OA. Cushnaghan, McCarthy and Dieppe (1994) randomised 14 patients with OA of the patellofemoral and tibiofemoral compartments into a crossover study with three taping arms – neutral (tape directly over patella), medial (tape pulled patella medially) and lateral (tape pulled patella laterally). Diary VAS pain scores during 4 days of wear showed statistically significant improvements in pain for medial taping compared to lateral or neutral taping, (a mean improvement in VAS pain of 12mm).

7.3 Costs

Diagnosis and fitting of a knee brace will generally take place by a physiotherapist. It is possible to determine quite accurate costs given the simplicity of the procedure.

The brace used by (Kirkley *et al.*, 1999) is the 'Generation II valgus-producing functional knee brace'. The current (2002) cost of this brace for private patients in Australia is $1,170. In addition to this, we have been advised that three physiotherapy appointments would be required, one to diagnose if the underlying condition could be well treated with a knee brace, followed by making a cast of the joint. The second to fit the brace, and a third follow-up appointment to determine how well

the brace is functioning, and if adjustment is required. The cost of each appointment has been estimated at $50, giving a total cost of $1,320.

7.4 Outcomes

Modelling was undertaken using results from the study by Kirkley *et al.* (1999). In this study 122 patients were recruited and randomised to be professionally fitted for a brace (n=41), to a conservative medical management control (n=40) or an alternative over the counter orthotic. The results for first two groups are reported here. (There was no significant difference between the latter group and the control).

The primary outcome measures were the WOMAC and VAS 100mm pain following a six minute walk, and a 30 seconds of stair climbing. Mean VAS pain scores and WOMAC scores were reported at baseline, 6 weeks, 3 months and 6 months, with the baseline and 6 month results reported in Table 7.1.

Substantial improvement in VAS pain and WOMAC is reported at 6 months in the brace group on both VAS scales and the composite WOMAC score (0-2400), but a slight worsening of pain for the conservative medical management group. (The higher the score the worse the pain). The differences are statistically significant ($p<0.05$). As discussed below these scores have been translated into utility values as reported in table 7.1.

Table 7.1 Reported 100mm VAS pain and WOMAC scores at baseline and 6 months and utility transformation

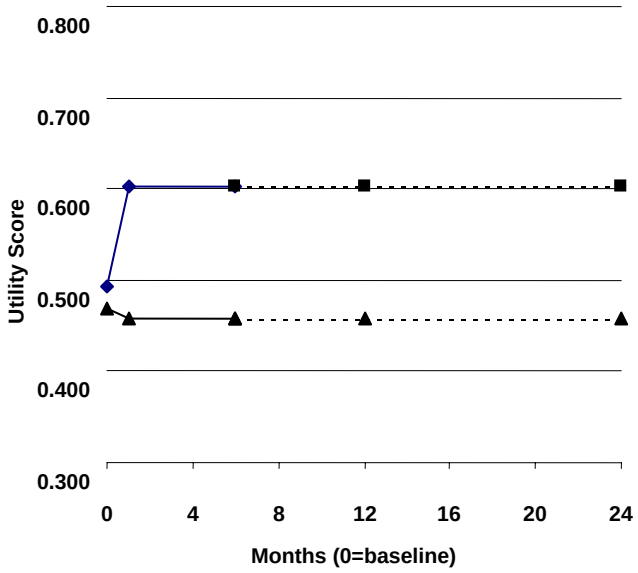
Attribute	Conservative Medical Management		Specially Fitted Knee Brace	
	Baseline	6 months	Baseline	6 months
VAS				
VAS Pain (walk) (a)	48	50.6	44	27.7
VAS Pain (stairs) (a)	50	51.1	46	25.6
VAS transformation: U= 0.76065 - 0.005951 x mean VAS pain).	0.469 (0.7605 - .005951 x 49)	0.458 (0.7605 –.005951x50.85)	0.493 (0.7605 – .005951x45)	0.602 (0.7605 – .005951x26.65)
WOMAC				
WOMAC 2400 (WOMAC 100) [(a)]	938 (39.08)	965 (41.84)	863 (35.95)	633 (26.38)
Womac transformation: U=0.71004 - 0.00097 x W_{100} – 0.000073 x W_{100}^2	0.561	0.541	0.581	0.634
Difference in utility score: b/ween baseline & 6 mths:				
VAS transformation		**- 0.011**		**+ 0.109**
WOMAC transformation.		**- 0.020**		**+ 0.053**
Net gain in utility:				
VAS transformation				**+ 0.120**
WOMAC transformation.				**+ 0.073**

Source: (a) Kirkley *et al.*, 1999

Two VAS scores, (walking and stairs) have been averaged to yield a mean VAS score. This has been used to calculate a utility score at baseline and 6 months, for the brace group and for conservative management, using the transformation developed between the VAS pain and the AQoL (utility score = 0.76065 - 0.005951 x mean VAS pain). A utility score has also been estimated by transforming the WOMAC composite score (see Table 7.1). It is clear that the specially fitted brace group experienced a modest to large improvement in utility of between 0.11 based on the VAS pain and 0.053 based on the WOMAC score. While the conservative management group experienced a

small reduction in utility of 0.01 to 0.02. The differential impact of the brace is thus estimated at between 0.07 and 0.12. The utility results based on the VAS pain are illustrated in Figure 7.1.

Figure 7.1 Modeled utility change (---assumed) (Kirkley et al., 1999)



7.5 Performance

A QALY gain can be estimated by assuming a time frame over which the health gain is achieved. Discussions with orthotists who specialise in this field suggest however that such a brace is typically worn for several years while continuing to yield substantial benefit. We have conservatively assumed use to vary between 6 months and two years.

The studies of the knee brace suggest full benefits are realised at between 1 and 2 months. It is more difficult to anticipate the pattern for utility benefit beyond 6 months. Few studies have measured outcomes from knee bracing up to 12 months, (or longer). Hewett *et al.* (1998) report that pain parameters measured at 9 weeks were further reduced at 12 months, although the majority of this benefit had been realised by 9 weeks. In contrast, the same authors noted that although walking-time-until-pain was significantly increased at both time points compared to baseline, it was less at 12 months than 9 weeks. A further factor is the possible increase in quadriceps strength through wearing of the brace, as noted at 12 months by Matsuno *et al.* (1997). The severity of an individual's symptoms at baseline, and the degree to which these symptoms are caused by a pathology which can be corrected via a brace, will also have a great effect on the magnitude of outcomes and how rapidly these can be achieved.

We have assumed that full benefit is obtained from 1 month and maintained for the period the brace is worn, assumed to vary from 6 months to 3 years. Benefits beyond 12 months are either discounted at
5% pa or undiscounted. Cost is as calculated earlier at $1320/patient. The results of the cost utility analysis, showing estimated QALY gains and cost/QALY under the various assumptions are reported in Table 7.2. Based on these assumptions cost/QALY for knee brace is estimated at between $3,900 and $38,800. The most significant impact on this result is the period for which the brace is used. Provided it is worn for at least 18 months on average, then cost/QALY is low at between $3,900 and $12,400.

While some studies suggest a reduction in pain and consequent use of NSAIDS and analgesics, expected cost savings and reduction in morbidity have not been included – lacking specific data on which to base such calculations.

Table 7.2 Cost utility analysis and cost/QALY of specially fitted knee brace for persons with knee OA

Time over which brace worn [1]		Utility gain in QALY [2]		$Cost /QALY [3]	
		Low	High	Low	High
6 months		0.038	0.055	$38,800	$24,000
18 months	0 disc rate	0.120	0.175	$12,200	$ 7,500
	@ 5% disc rate pa	0.119	0.172	$12,400	$ 7,700
36 months	0 disc rate	0.243	0.355	$ 6,000	$ 3,700
	@ 5% disc rate pa	0.240	0.337	$ 6,100	$ 3,900

Notes:
1 Assuming max improvement in quality of life occurs at 1 month which is retained
2 Low based on net utility gain of 0.074, high based on net utility gain of 0.12 (see text)
3 Cost per fitted brace = $1,320

7.6 Conclusions

Knee bracing and taping can provide substantial benefit to patients with patellofemoral OA. Knee braces are less expensive than surgery and non-invasive (although they may be cumbersome) and if well fitted are not likely to be associated with any negative side-effects. Patella taping is a cheap and discrete intervention and less cumbersome than wearing of a knee brace. Further research is warranted in this area, however it is expected that as an inexpensive intervention with apparent success and is thus likely to be highly cost-effective. In which case its use where clinically appropriate should be supported.

The duration of the knee brace will doubtless vary from individual to individual. However as a short to medium term option that may provide relatively rapid and substantial pain relief it appears attractive. A specially fitted knee brace appears to be cost-effective and could be recommended for all suitable patients. This might include in particular patients awaiting surgery for knee OA and for those for whom the risks from standard pharmacotherapies are especially high. Further research is warranted in these areas. The current level of use of knee brace including the time for which a brace is typically used and the opportunity to expand this modality of therapy is not known. This is a suitable matter for study.

8. PHARMACOTHERAPIES

8.1 Introduction

A wide range of drugs are used in the management of OA, both prescription and over-the-counter medications and including drugs that might classed as 'complementary medicines'. These are used largely to control symptoms of pain, although some may modify disease state. The most commonly used prescription drugs for the treatment of OA are non-steroidal anti-inflammatory drugs (NSAIDS - both non-selective and COX-2 selective classes), analgesics such as paracetamol and compound analgesics such as paracetamol+codeine. In addition, it is widely accepted that a large proportion of people with OA will try a range of complementary pharmacotherapies to manage their symptoms.

The possible role of pharmacotherapies was assessed through a comprehensive study of the literature covering the evidence of efficacy and side effects and the nature of current use. The results of this review can be found in an earlier report to the Australian Government Department of Health and Ageing, *Osteoarthritis: Selecting the Interventions* (Segal, Day, Chapman and Osborne, 2002) Based on that review of the range of pharmacotherapies identified as potentially relevant in the management of OA, several were selected for economic analysis. These are:

i) NSAIDs
   - *Non-selective NSAIDs (nsNSAIDs)* - The most commonly prescribed nsNSAIDs in Australia in this class are diclofenac, naproxen and ibuprofen. These are also typically the nsNSAIDs used as comparators in efficacy trials and are generally regarded as having a more benign side effect profile than other nsNSAIDs.
   - *COX-2 selective NSAIDs* - This class is represented by celecoxib and rofecoxib, the two COX-2s prescribed in Australia and for which clinical trial data are available.

ii) Analgesics
   - A basic analgesic (paracetamol), commonly prescribed for OA and often reported in clinical trials (usually as comparator), and a compound analgesic (paracetamol/codeine).

iii) 'Complementary' pharmacotherapies
   - oral glucosamine sulphate;
   - avocado/soybean unsaponifiables (ASU); and
   - topical capsaicin.

   For each of the above complementary drugs, there is an established trial literature from which to draw evidence of effectiveness. Glucosamine sulphate is widely used in Australia, and ASU, while not available in Australia is widely used in continental Europe. While other complementary medicines are sometimes used in the management of OA, it was not possible within the budget constraint for the study to undertake economic analyses of all potentially effective pharmacotherapies.

Efficacy of these pharmacotherapies in the management of OA is discussed below in Section 8.2, followed by a discussion of the side effect profiles in Sections 8.3 to 8.5.

8.2 Efficacy of prescription, over-the-counter and Complementary medicines

Paracetamol is indicated as the first choice of drug treatment for OA in a number of international guidelines (American College of Rheumatology, 2000; Eccles, Freemantle and Mason, 1998; Manek, 2001). For patients with pain refractory to paracetamol, NSAIDs are commonly prescribed.
Two influential and frequently cited studies comparing paracetamol and nsNSAIDs found no significant differences in efficacy between these two drug classes in treating OA pain over the short term (4 weeks) (Bradley, Brandt, Katz, *et al.*, 1991), or longer term (2 years) (Williams, Ward, Egger *et al.*, 1993). However more recent studies have shown small but significant improvements in pain relief from nsNSAIDs compared with paracetamol over 4-6 weeks (Scott, Berry, Capell, *et al.*, 2000; Pincus, Koch, Sokka, *et al.*, 2001). In general, longer-term studies have not been able to show the significant efficacy differences between nsNSAIDs and paracetamol seen over the short term.

In contrast to paracetamol alone, paracetamol in combination with codeine (eg panadeine) has demonstrated improved efficacy in treating OA over either paracetamol alone (Peloso, Bellamy, Bensen, *et al.*, 2000) or NSAIDs alone (Quiding, Grimstad, Rusten, *et al.*, 1992). Compound analgesics containing opioids may offer improved benefits over NSAIDs, but as with NSAIDs, they are not well tolerated by all patients. There is however a dearth of trials that compare the efficacy of common compound analgesics such as paracetamol + codeine with nsNSAIDs or COX-2 NSAIDs. Given this gap in the evidence a decision was made not to conduct a cost-utility analysis of paracetamol alone or with codeine. The common use of paracetamol as a 'rescue medication' in placebo control trials also confounds the modelling of its cost-effectiveness.

No significant differences in efficacy between COX-2 NSAIDs and nsNSAIDs have been found in clinical trials comparing the two drugs in the management of patients with OA (eg Cannon *et al.,* 2000; Bensen *et al.,* 1999), although studies comparing COX-2s to paracetamol have reported greater efficacy of COX-2s over paracetamol at up to 6 weeks (Geba *et al*., 2002; Ehrich *et al.,* 1999).

Randomised control trials of glucosamine sulphate and capsaicin have demonstrated these drugs' superiority to placebo in the treatment of OA. Glucosamine has been found in clinical trials to be equivalent or superior in efficacy to NSAIDs and paracetamol (Towheed, Anastassiades, Shea, *et al.*, 2001; Reginster, Deroisy, Rovati, *et al.*, 2001), while capsaicin (0.025%) has been demonstrated in a number of trials to significantly reduce OA pain and tenderness compared to placebo (Altman, Aven, Holmburg, *et al.*, 1994; Deal, Schnitzer, Lipstein, Seibold *et al.*, 1991). Four recent trials of ASU have been published – three found significant benefits from ASU compared to placebo (Appelboom, Schuermans, Verbruggen *et al.*, 2001; Blotman, Maheu, Wulwik *et al.*, 1997; Maheu, Mazieres, Valat *et al.,* 1998), while one found no benefits (Lequesne, Maheu, Cadet *et al., 2*002).

Key outcomes reported from twelve seminal trials of pharmacotherapies in the management of OA, mainly knee or hip are reported in Table 8.1. Only randomised and blinded studies are included. These cover many of the studies referred to above. The subject of this table is comparative efficacy in the management of symptoms of OA. For instance the results of 3 key trials in which celecoxib has been compared - one with naproxen (3), one with rofecoxib and paracetamol (6) and one with placebo (7) - are reported. In each of the three trials, the primary outcome measure reported here is the WOMAC, with the mean scores at baseline and study endpoint, (or change) shown in the table. Other primary outcome measures reported are the VAS pain and the Lequesne Functional Index.

In interpreting the results a number of factors make comparison across studies problematic. It has been possible to address only some of these concerns, as discussed below.

i) *Use of different outcome measures* - No single outcome measure used across all trials. For this reason the 'Transfer to Utility Technique' has been developed as described in Chapter 3.

ii) *Reporting results* – The reporting of results is always partial and using various formats, for instance sometimes quoting only percentage changes from baseline scores.

iii) *Use of different comparators* - Three alternative nsNSAIDs are commonly used as the ns NSAID comparator: viz. diclofenac, naproxen, and ibuprofen.

iv) *Absence of a placebo arm* - A strong placebo effect has been shown in randomised, blinded studies in patients with OA, but the size of the effect can vary. Where a placebo arm is not included in a study, it may not be possible to determine the 'true' effect size of the intervention.

v) *Different follow-up periods/actual treatment received* - The studies listed have different follow-up periods ranging from 6 weeks to 3 years. Outcomes may be reported only at study commencement and end-point, or also at various intermediate points. Drop-outs as well as departure from study medications can be a confounding factor. This will particularly be an issue for longer-term studies. The use of intention to treat analysis does not really resolve the potential confusion. Conversely, short term studies may not be able to adequately distinguish real effect size differences between treatment arms if there is not an appropriate washout period from previous treatments.

vi) *Different principal joints* – Trials enrol different clinical populations, notably in terms of site affected, commonly hip and/or knee. Pharmacotherapies may have differential efficacy, depending on the joint affected. If, for instance, the impact of inflammatory factors is more pertinent in knee than hip OA, it may be expected that NSAIDs would perform better in a cohort of patients with knee OA than one which was entirely (or largely) hip OA.

vii) *Different baseline ages and scores* - Differences in baseline scores, due to severity of OA or age of cohort may confound comparisons across studies.

viii) *Different concomitant/rescue medications permitted* - Most studies permit enrolled patients to use selected 'rescue' or concomitant medications for the duration of the study, especially in placebo controlled trials. But these can differ across trials.

ix) *'Flares'/entrance criteria* - Patients with OA are known to have flare-ups of their condition, causing increased pain and associated disability. Where studies select patients on the basis of symptom severity, a larger proportion of patients may be experiencing a 'flare up' of their condition, rather than their 'chronic state'. Improvement will then in part reflect normal history, which should be largely addressed through a randomised placebo control.

x) *Sub-group analysis*- Studies in general report mean effects for all participants. However the effect in sub-groups of patients may differ. Especially where there are strong theoretical reasons for distinguishing sub-populations, this can be a valid element in study design and influence observed outcomes. In translating trial results into a clinical setting, it needs to be recognised that there is considerable variation between individuals in their response to different pharmacotherapies, (as demonstrated in N-of-1 studies, reported by March, Irwig, Schwarz, Simpson *et al.*, 1994).

Table 8.1. Comparative efficacy data from published pharmacotherapy trials in OA

Study	No enrolled	OA Site	Outcome instrument	NsNSAID D=diclofenac N=napraxen I=ibuprofen	COX-2 NSAIDs C= Celecoxib R= Rofecoxib	Paracetamol	Glucosamine Sulphate	ASU	Capsaicin Topical	Placebo
(1) Cannon *et al.,* 2000	784	hip and knee	Baseline VAS walking pain	75.8 D	77.5 R					
			12 month VAS change	-38 D	-36.5 R					
(2) Pincus *et al.,* 2001	227	hip and knee	Baseline WOMAC	42.5 D		44.8				
			6 week change	-12.2 D		-6.6				
(3) Bensen *et al.,* 1999	1003	knee	Baseline WOMAC	52.9 N	50.5 C					51.7
			12 week WOMAC change	-11.9 N	-13.3 C					-6.1
(4) Saag *et al.,* 2000	693	hip and knee	12 month VAS walking pain change	-37.3 I	-33.8 R					
(5) Ehrich *et al.,* 1999	219	knee	Baseline VAS pain		75.4 R					75.0
			6 week VAS pain		39.4 R					59.6
(6) Geba *et al.,* 2002	382	knee	6 week change in WOMAC		- 27.2 C - 33.4 R	-22				
(7) Williams *et al.,* 2001	718	knee	Baseline WOMAC		51.0 C					52.8
			6 week WOMAC		37.6 C					44.0
(8) Reginster *et al.,* 2001	212	knee	3 year change in WOMAC				-11.7%			+9.8%
			3 year change in WOMAC				-24.3%			+9.8%
(9) Muller-Fasbender *et al.,* 1994	199	knee	Baseline Lequesne Index	15.8			15.9			
			4 week Lequesne Index	9.6			9.6			
(10) Appelboom *et al.,*2001	260	knee	Baseline VAS (D=30)					41.9		46.7
			8 week VAS (D=90)					24.2		42.4
(11) Lequesne *et al.,* 2002	163	hip	Baseline VAS pain					49.9		50.5
			12 month VAS					31.8		30.8
(12) Altman *et al.,* 1994	113	knee, wrist, ankle, elbow, shoulder	Baseline VAS pain						54	56
			Week 12 % VAS change						25	34

Notes: **see next page**

Notes to Table 8.1

(1) Patients were randomised to 1 of 3 treatment groups - diclofenac 50mg x 3 daily, rofecoxib 12.5mg daily or rofecoxib 25mg daily. Primary outcome measure was pain when walking on a flat surface, 100mm VAS (WOMAC, question 1). No statistically significant difference between diclofenac and rofecoxib was found.

(2) Patients were randomised to 1 of 2 arms – (75mg diclofenac + 200ug misoprostol) x 2 daily or 1000mg paracetamol x 4 daily. A statistically significant difference between diclofenac + misoprostol and paracetamol was found for the cited outcome measures. As efficacy is the outcome measure of interest, use of misoprostol should not confound this outcome.

(3) Patients were randomised to 1 of 5 treatment groups – celecoxib 50, 100 or 200mg daily, naproxen 500mg x 2 daily or placebo. Celecoxib and naproxen were equally efficacious. Both were statistically significantly more efficacious than paracetamol.

(4) Patients were randomised to 12.5mg or 25mg rofecoxib daily or 800mg ibuprofen x 3 daily. Primary outcome measure was pain when walking on a flat surface, 100mm VAS (WOMAC, question 1). No statistically significant difference between ibuprofen and rofecoxib was found for this outcome. Baseline results were not reported.

(5) Patients were randomised to 1 of 3 treatment groups – rofecoxib 25 mg daily, rofecoxib 125 mg daily or placebo daily. Both doses of rofecoxib were statistically significantly more efficacious than placebo for all outcome measures. VAS 100mm pain outcomes for “Patient assessment of arthritic pain”. It is not clear which particular VAS pain measure this relates to.

(6) Patients were randomised to 1 of 4 treatment groups – rofecoxib 12.5mg daily, rofecoxib 25mg daily, celecoxib 200mg daily or paracetamol 4000mg daily. Change in WOMAC subscale scores after 6 weeks of treatment are provided, but no baseline WOMAC scores. No statistically significant differences between celecoxib, rofecoxib 12.5mg and paracetamol were noted for change scores on any of the three WOMAC subscales, however change in all subscales was significantly greater for rofecoxib 25mg daily than paracetamol, and for the pain and stiffness subscales compared to celecoxib.

(7) Patients were randomised to 1 of 3 treatment groups – celecoxib 100mg x 2 daily, celecoxib 200mg x 4 daily or placebo. All celecoxib scores for each WOMAC subscale were statistically significantly better than placebo ($p<0.005$)

(8) Patients were randomised to 1 of 2 treatment groups – glucosamine sulphate 1500mg daily or placebo daily. Results presented as % improvement in composite WOMAC scores at 3 years, separately for intention-to-treat and for study completers-only. Both analyses showed statistically significant improvements in WOMAC scores at 3 years for glucosamine compared to placebo.

(9) Patients were randomised to 1 of 2 treatment groups – glucosamine sulphate 500mg x 3 daily or ibuprofen 400mg x 3 daily. A modified Lequesne Functional Index was used as primary efficacy endpoint, with a possible score range from 0-34. (No regression analyses was undertaken to translate the Lequesne Index into utility scores). There was no significant difference between Lequesne scores between the two groups, although ibuprofen appeared to improve symptoms more quickly in the first week. From week 1 on, no difference was noted.

(10) Patients were randomised to 1 of 3 treatment groups – ASU 300mg or 600mg daily, or placebo. Improvement in pain was a secondary study endpoint. From day 60 onwards of ASU 300mg, and from day 30 onwards for ASU 600mg, there was a statistically significant improvement in VAS 100mm pain (spontaneous pain) compared to placebo. nsNSAID use was the primary outcome measure, and this was significantly reduced for both ASU doses from day 30 on compared to placebo.

(11) Patients were randomised to 1 of 2 treatment groups – ASU 300mg daily or placebo. Overall spontaneous VAS 100mm pain was a secondary outcome measure. Although substantial improvements from baseline VAS scores were noted in both groups, there was no statistical difference between the two.

(12) Patients were randomised to 1 of 2 treatment groups – topical capsaicin or placebo, both applied 4 x daily. Primary outcomes included VAS 100mm average pain experienced in the last week. Significant differences were noted between capsaicin and placebo from 4 weeks.

8.3 Side effect profile - NSAIDs

The most commonly studied side-effects of pharmacotherapies for OA are those related to NSAIDs. These include gastrointestinal perforation, ulceration and bleeding (PUBs) and congestive heart failure (CHF). It has been estimated that nsNSAID consumption increases the risk of PUBs by 2-5 times that of non-nsNSAID users, and that the mortality rate associated with hospitalisation for PUBs is approximately 10% (Hernandez-Diaz and Rodriguez, 2002; Straus and Ofman, 2001). While all oral NSAIDs increase the risk of PUBs, the relative risk profile of COX-2 selective NSAIDs and nsNSAIDs is the subject of several important studies.

Cardiac risks

The excess risk of hospital admission for CHF among NSAID-users is estimated at 0.5/100 patient years (a rate approximately double that of non-users). The excess risk increases dramatically in patients with a history of heart disease (Page and Henry, 2000). The mortality burden from hospitalisation for CHF is approximately 5%. In this report, the increased risk for CHF is assumed to be the same across all NSAIDs.

Gastrointestinal (GI) risks

Overview

The risk of PUBS associated with different nsNSAIDs has been the subject of a number of influential studies (Henry *et al*., 1993; Henry *et al*., 1996; Wolfe *et al*., 1999), which have demonstrated that certain nsNSAIDs appear to have a relative risk of causing PUBS up to 4-5 times that of others. It has only been in recent years that large scale clinical trials of NSAIDs with GI safety as the primary outcome have been attempted. These trials, undertaken by the manufacturers of the new COX-2s, were designed to compare the GI safety of COX-2 specific NSAIDs with commonly used nsNSAIDs. The two most important of these are:

- the CLASS trial (Celecoxib Long-term Arthritis Safety Study) comparing celecoxib with diclofenac and ibuprofen in patients with OA and rheumatoid arthritis, reported by Silverstein *et al.,* 2000, and with extensive re-evaluation and commentary by the US Food and Drug Administration and comment by others (eg Juni *et al.*, 2002); and
- the VIGOR trial (Bombardier *et al.,* 2000) – comparing rofecoxib and naproxen in patients with rheumatoid arthritis (RA) alone.

Both studies report significantly improved GI safety profiles for the respective COX-2s compared to nsNSAIDs (Silverstein *et al.,* 2000 and Bombardier *et al.,* 2000). However subsequent to publication, FDA analyses of the CLASS trial data were undertaken, showing substantially different results. Given the importance of the CLASS study in establishing the GI safety of celecoxib compared to nsNSAIDs these results are considered below in detail. Further analysis of the VIGOR study has not been included here, as that study was undertaken only in patients with RA.

CLASS – results published by Silverstein et al., 2000

The CLASS study was a double-blind, randomized controlled trial which took place at 386 sites in the USA and Canada between September 1998 and March 2000. Just over eight thousand patients (8,059) with OA or RA were enrolled, with 4,573 of these receiving treatment for at least 6 months.

Patients were assigned to receive either celecoxib 400mg x 2 daily, ibuprofen 800mg x 3 daily or diclofenac 75mg x 2 daily. Aspirin use for cardiovascular prophylaxis was permitted.

An initial report of the trial was made by Silverstein and colleagues in JAMA in 2000. The primary outcomes reported in this paper were symptomatic GI ulcers and ulcer complications

(perforations, bleeding, obstructions) that occurred during the 6 month treatment period. Using this definition of outcome and time frame, a significantly lower rate of upper GI (UGI) complications combined with symptomatic ulcers was reported for those taking celecoxib compared to the two nsNSAID groups (combined). For patients not taking aspirin (~90% of the study population), there was a significantly lower rate of UGI complications alone, or combined with symptomatic ulcers in the celecoxib group compared with the nsNSAID groups (combined). For patients taking aspirin, no difference was noted between the groups for these endpoints. In conclusion, the authors stated that 'celecoxib at dosages greater than those indicated clinically, was associated with a significantly lower incidence of symptomatic ulcers and ulcer complications compared to nsNSAIDs at standard dosages' (Silverstein *et al.,* 2000).

CLASS – FDA analyses[13]

The FDA report highlights a number of issues in the reporting of the study results by Silverstein and colleagues. The main issues relate to the failure to report the comparison between celexocib and diclofenac and ibuprofen separately, the failure to report the 12 month data and concerns about the specific measure of gastric toxicity. As noted by Juni *et al*. (2002) in an editorial in the BMJ all these concerns represent important departures from the study protocol.

The CLASS study was composed of two distinct arms, one comparing celecoxib to diclofenac, and the other comparing celecoxib to ibuprofen. The design provided for the data to be pooled, and if significant differences in primary study endpoints was shown between celecoxib and nsNSAIDs combined, then a second set of analyses comparing celecoxib to each nsNSAID separately was to be undertaken. As noted in the FDA Statistical Review, 'Celebrex *[celecoxib]* will be claimed to be different from an NSAID if both overall and pairwise comparisons of celebrex vs. that NSAID are significant' (page 1). The treatment period for both studies was defined as 52 weeks, with a primary endpoint based on pre-defined clinically significant upper gastrointestinal adverse events (CSUGIEs). Table 8.2 summarises the primary endpoint for the full study period for the total study population and for non-aspirin users. Figure 1 shows a Kaplan-Meier plot of gastric events. It can be seen that thee gastric events continue to accrue in the celecoxib group at a generally steady rate through to the end of the 12-month period, while in the diclofenac and ibuprofen groups, almost all events occurred in the first 6 months. This was expected. Over the 12 month period across all patients, there is no significant difference in adverse events between the celexocib group and those on diclofenac or ibuprofen, taken together or separately.

[13] Three FDA reports were used in this analysis:

1. Medical Officer's Report, www.fda.gov/ohrms/dockets/ac/01/ briefing/3677b1_03_med.pdf

2. Statistical Review Briefing Document for the Advisory Committee www.fda.gov/ohrms/dockets/ac/01/briefing/3677b2_04_stats.pdf

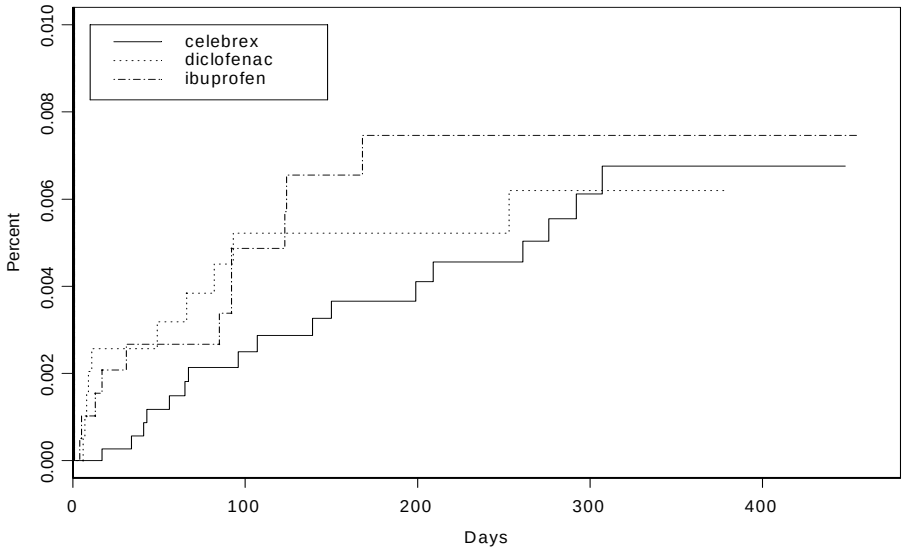
3. Medical Officer's Gastroenterology Advisory Committee Briefing Document http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b1_05_gi.pdf

Table 8.2 Primary study end-point CSUGIE incidence – 12 month (intention-to-treat)

	Celecoxib 400 mg BID	Diclofenac 75 mg BID	Ibuprofen 800 mg TID	Log-rank P values for Celecoxib vs Diclofenac	Ibuprofen	Both
All Patients	*n = 3,987*	*n = 1,996*	*n = 1,985*			
No. of CSUGIEs	17	10	11			
Week 52 crude rate	0.43%	0.50%	0.55%	0.640	0.414	0.450
No. per 100 patient yrs	0.73	0.93	0.98			
Patients not Taking Aspirin	*n = 3,105*	*n = 1,551*	*n = 1,602*			
No. of CSUGIE	8	4	10			
Week 52 crude rate	0.26%	0.26%	0.62%	0.972	0.037	0.185
No. per 100 patient yrs	0.44	0.48	1.14			

Source: www.fda.gov/ohrms/dockets/ac/01/ briefing/3677b1_03_med.pdf (page 35)
[Results not reported in Silverstein *et al*., 2000]

Figure 8.1 Kaplan-Meier Estimator for C SUGIE Incidence



Other analyses were also undertaken based on an expanded endpoint, to include also gastroduodenal ulcers (CSUGIEs/ GDUs), and for the entire study population and non-aspirin users. These results are reported below in Table 8.3.

An analysis at 6 month reported by Silverstein *et al.,* (2000), which is only part way through the nominated follow-up period is reported in the annexure to this chapter, in Tables A8.1 and A8.2, including a sub-analysis of aspirin users.

Table 8.3 CSGUIE/GDU incidence – 12 month (intention-to-treat)

	Celecoxib 400 mg BID	Diclofenac 75 mg BID	Ibuprofen 800 mg TID	Log-Rank P Values for Celecoxib vs. Diclofenac	Ibuprofen	Both
All Patients	*n = 3,987*	*n = 1,996*	*n = 1,985*			
No. of CSUGIE/GDUs	43	26	36			
Week 52 crude rate	1.05%	1.30%	1.76%	0.296	0.017	0.040
No. per 100 patient yrs	1.85	2.41	3.21			
Patients not Taking Aspirin	*n = 3,105*	*n = 1,551*	*n = 1,573*			
No. of CSUGIE/GDUs	21	10	28			
Week 52 crude rate	0.68%	0.64%	1.72%	0.992	<0.001	0.020
No. per 100 patient yrs	1.16	1.19	3.20			

Source: www.fda.gov/ohrms/dockets/ac/01/ briefing/3677b1_03_med.pdf (page 46)

Conclusions - side effect profile NSAIDs

The FDA analyses concludes that celecoxib 400mg x 2 daily did not show a statistically significant reduction for any measured endpoint, at any time in the study, compared to diclofenac. Celecoxib also failed to show significantly fewer endpoint events compared to ibuprofen for CSUGIEs at either 6 or 12 months (entire study population). Only when the expanded endpoint was used (CSUGIEs/GDUs), or when non-aspirin users were analysed separately was celecoxib found to be significantly better than ibuprofen, but not diclofenac. A different side-effect profile has not been established between celecoxib and diclofenac.

Presumed mortality associated with use of NSAIDs

Mortality from taking NSAIDs is a combination of excess deaths from gastrointestinal (GI) side effects, plus cardiac risks. In relation to the GI side effects morbidity from NSAIDs defined as perforations, ulcerations and bleeds (PUBs), the mean incidence rate of CSUGIE/GDU over 12 months as reported in the CLASS study for celecoxib (1.85/100 patient years, Table 8.3) and diclofenac (2.41/100 patient years, Table 8.3) of 2.13/100 patient years is taken as the estimated incident cases from 12 months NSAID use. To this a mortality rate of 10% is applied reported in relation to hospitalisation for PUBs (Day *et al*., 1999). A life expectancy of 18.5 years is presumed [14] yielding an estimated expected loss of life years from GI of 0.0394 (0.0213 x 0.1 x 18.5).

In relation to Congestive Heart Failure (CHF), as noted above, based on Page and Henry (2000) the excess risk of hospitalisation for CHF in those taking NSAIDs is 5/1000 per year compared to non-NSAID users. The mortality rate for those hospitalised for CHF is taken to be 5%[15]. It is also estimated that for persons on NSAIDs the mean life expectancy is approximately 18.5 years, (as above). This suggests a mortality rate from CHF of 0.005x.0.05 = 0.00025, which represents approximately 0.0046 life years lost (0.00025 x 18.5) per patient year on NSAIDs.

It is also assumed that PUBs and CHF are independent of each other, yielding an estimated 0.238 deaths per 100 patient years of NSAID use, equivalent to an estimated loss of **0.044** life years per patient year of use (2.38 x 18.5).

Minor side-effects NSAIDs

[14] In 1996-98, mean life expectancy at age 65 was 16.3 years for men and 20.0 years for women

[15] From *Heart, Stroke and Vascular Diseases*, National Centre for Monitoring Cardiovascular Disease, April 2001

Both selective and non-selective NSAIDs cause dyspeptic GI adverse events such as nausea and stomach ache. Over a 6 month period, between 5-15% of patients are reported to discontinue nsNSAID therapy because of NSAID-related dyspepsia (National Prescribing Service, 2000). Many patients taking NSAIDs also take concomitant gastrointestinal medication to counter these effects (Hogan, Campbell, Crutcher, Jennett *et al.*, 1994). Due to the difficulty in assigning costs to such events, and their non-serious nature, costs for dyspeptic-related adverse events have not been included in the modelling.

8.4 Side effect profile - analgesics

Acute or chronic side-effects associated with paracetamol consumption at the dosages used to provide pain relief for OA are rare. Common side effects associated with compound analgesics containing opioids, include nausea, vomiting and constipation or diarrhoea. It has been estimated that this may result in 10-25% of people stopping treatment with drugs containing codeine (Peloso, 2001). Where doses of codeine >120mg/day are taken, the discontinuation rate may rise to more than 50%. These side-effects cease when drug consumption stops, with no systemic or chronic effects observed. As a consequence, no morbidity costs have been included for paracetamol alone or in combination with codeine.

8.5 Side effect profile- complementary and topical pharmacotherapies

Glucosamine sulphate

This has been sold for many years in Europe as a treatment for OA. Periodic safety updates from the manufacturer (Rotta Research) covering over 13 million patient months of data from 1995-1999, indicate a mild side-effect profile. Additionally, published clinical trial data show a rate of adverse events from glucosamine which is comparable to placebo (Reginster *et al.,* 2001). There is no indication from the available data that glucosamine is associated with any serious morbidities or any fatalities. Despite some suggestion that glucosamine consumption may be associated with insulin resistance in animals, no such effects have been observed in long-term studies in humans (Reginster *et al.*, 2001).

Avocado/Soybean Unsaponifiables (ASU)

The efficacy and side effect profile of ASU in OA has been studied in 4 recent trials, resulting in key publications, (Blotman *et al.*, 1997; Maheu *et al.*, 1998; Appelboom *et al.*, 2001; Lequesne *et al.*, 2002). Although ASU was reported to have a side-effect profile comparable to placebo across all these studies, due to limits in the duration of treatment and the size of the cohorts treated, it may not be possible to conclude that ASU is safe in relation to infrequent or rare adverse events.

Capsaicin

This is a topical preparation with no reported serious morbidities. The only side effect listed in the MIMs Annual is a mild to moderate temporary burning sensation after application, which in a small percentage of patients may be such as to result in a discontinuation of treatment.

Conclusion

As there is no indication that any of these three complementary treatments cause serious morbidities, morbidity costs in the modelling are taken to be zero. Additional evidence derived from very large trials is desirable to confirm or contradict this conclusion.

8.6 Costs

Drug Costs

Where available, drug costs have been taken from the Pharmaceutical Benefits Schedule book (March 2002). While, for drugs not listed on the PBS, drug cost was based on market prices obtained from pharmacies or the manufacturer. In each case we identify total costs, which include both cost to government and cost to the patient. Usage per patient year was calculated from defined daily dosage (DDD) as described in the Australian Statistics on Medicines 1998 – DHAC, or where this was not available it was based on doses typically used in published clinical trials in patients with OA. Mean drug cost per patient year was simply the product of these two items. The mean drug costs per person year of treatment as used in the modelling are reported in Table 8.4 below. This shows estimated annual per patient cost of treatment varying from a low of $104 for naproxen and $136 for ibuprofen to a high of $521 for rofecoxib.

These costs represent total costs – to the patient and the government (taxpayers). The relative contribution of patient and taxpayer varies considerably between drugs. In relation to drugs listed on the PBS, notably ns and Cox-2 NSAIDs, patient co-payments will meet only a small part of total costs, with the majority of cost being met by government. This applies especially to the more expensive Cox2 NSAIDs drugs. In contrast, for medicines not listed in the PBS, patients will meet the full cost. In relation to complementary medicines, the patient also contributes to government revenue through the GST.

Table 8.4 Estimated mean cost per patient year for selected drugs used in the management of OA (dollars)

Drug	Estimated cost/ patient year
Diclofenac	**$ 175**
Ibuprofen	**$ 136**
Naproxen	**$ 104**
Celecoxib	**$ 391**
Rofecoxib	**$ 521**
ASU	**$ 333**
Capsaicin (topical)	**$ 236**
Glucosamine	**$ 180**
Paracetamol	**$ 224**
Paracetamol + codeine	**$ 388**

Morbidity Costs

The evidence supports a causal link between NSAID consumption and upper gastrointestinal perforation, ulceration and bleeding (PUBS) and congestive health failure (CHF). There are costs associated with these conditions - in terms of excess mortality, loss in quality of life and additional health services cost for management. The differential mortality impact has been modeled (see Section 8.7), based on evidence as described in Section 8.3. The extra health service costs of managing these conditions has been estimated and included in the cost calculations.

The impact of excess morbidity on quality of life has been ignored, at this stage, not because it is unimportant, but simply due to a lack of research resources that could be applied to the task. This

means the QALY burden from side effects is restricted to the mortality impact, thus understating this burden. As there is no evidence to link serious morbidities to the usage of the other pharmacological agents modeled, a morbidity cost has only been estimated for NSAIDs (non-specific and COX-2s).

Health service costs have been limited to hospital costs and estimated from the Australian Refined Diagnostic Related Group (AR-DRG) costs for the calendar year 2000-2001.

- *Upper gastrointestinal complications* - These were deemed to include the following ICD-10 codes – K25, K26, K27. The associated AR-DRG codes used to calculate costs for PUBs are: A06Z, G03B, G03C, G11A, G11B, G40A, G40B, G42A, G42B, G61A, G61B, G62Z, G63Z.
- *Congestive heart failure* – This is coded as I50.0 in ICD-10. The AR-DRG codes included in costing CHF are: A06Z, F12Z, F40Z, F42A, F62A, F62B.

Public and private hospital cases have been included in the cost calculations. Same-day and non-same day separations were added to generate a mean cost per separation. Public sector unit costs were used in calculating the total value of public and private sector separations, as private sector AR-DRG costs do not include medical or imaging costs. Other costs such as rehabilitation and drug treatment are not included, so the estimated cost of these morbidities will underestimate their 'true' cost.

The total cost of hospitalisations for PUBs in Australia for the 2000-2001 calendar year was estimated at $44.8 million for 18,543 separations – a mean cost of $2,417 per separation. The total cost for hospitalisation for CHF for the same period was estimated at $107.2 million for 26,085 separations, a mean cost per separation of $4,110. These mean costs have been applied to the estimated differential excess admission rates associated with NSAID use.

8.7 Cost-utility Model

Initially it was proposed that two forms of modelling be conducted.

i) *Comparison of side effect profile against nsNSAID* - Given evidence of similar efficacy between the various pharmacotherapies in addressing the symptoms of OA, but reports of a differential side effect profile, an assessment of comparative performance based on drug cost and drug induced morbidity and mortality seemed appropriate – especially to focus on the relative performance of COX-2 and non-specific NSAIDs. However, on further analysis of the key trial data comparing COX-2 (celecoxib) and nsNSAIDs (diclofenac and ibuprofen) in the CLASS study, a lack of conclusive evidence of a differential side effect profile at least between celecoxib and diclofenac suggested that such an analysis was inappropriate.

ii) *Cost-utility analysis* **–** To derive and compare cost/QALY estimates for the subject pharmacotherapies (relative to placebo). Benefit is defined in terms of net utility gain – gain in quality of life through management of OA symptoms, less estimated excess mortality associated with side effects from medication (PUBS and CHF). Cost includes drug cost per patient year, plus estimated mean hospital costs for managing excess admissions for PUBS and CHF.

It was decided to adopt a cost-utility analysis, as the evidence does not support the existence of a differential side-effect profile, but more importantly to enable comparisons with the assessment of performance of the other modalities

Overview of the model

Outcomes from seminal studies notably baseline and follow-up scores, as summarised in Table 8.1 have been translated into utility estimates using the 'Transfer to Utility' technique, developed for this study, (as described in Chapter 3). An estimate of the net utility gain in symptom management for each pharmacotherapy has been calculated as the comparison between difference between base-line and endpoint scores (that is utility gain) for the intervention and control cohorts.

In selecting clinical trials from which to derive benefits, only placebo-controlled studies were included. This was necessary given the size of the placebo effect typically reported in studies of OA. It had been planned to undertake a cost-utility study of rofecoxib as well as celecoxib. However the only long-term morbidity data identified for rofecoxib is based on two studies, neither of which were considered suitable for use in modelling rofecoxib morbidity. The VIGOR study was based in patients with rheumatoid arthritis and listed prophylactic aspirin as an exclusion criterion (Bombardier *et al.*, 2000). Aspirin use may affect both symptom management and the rate of side effects. The study by Langman *et al* (1999) pooled data from 8 different rofecoxib studies of differing durations in patients with OA. Additionally, Langman *et al* (1999) did not identify if aspirin had been an exclusion criteria in the 8 studies included in the analysis. Because of these problems, and as morbidity and subsequent mortality has a large impact on QALYs, it was not considered possible at this stage to undertake a cost-utility analysis for rofecoxib. As a corollary to this, the major reported trial that we identified of rofecoxib for patients with OA, involving a comparison between rofecoxib and diclofenac with no placebo arm, (Cannon *et al.,* 2000), found no significant difference in efficacy or side effect profile between the two drugs.

The utility gain associated with symptom management is adjusted for mortality loss associated with serious side effects. For all NSAIDs (ns and COX-2) the same excess mortality rates are applied. These relate to GI and cardiac events, as discussed in Section 8.3. GI side effect profile is derived from the CLASS study. Given the lack of a finding of a significant difference in GI side effect profile between diclofenac and celexcoib, on any definition of adverse events, identical morbidity and mortality rates have been applied for gastric events for nsNSAIDs and for COX-2 NSAIDs (specifically celecoxib) use. The excess mortality rate for GI complications is estimated to be 0.00213/patient year. An additional mortality rate of 0.00025 per patient year for excess cardiac deaths is also presumed, (as explained in Section 8.3). Presuming a life expectancy in these patients of 18.5 years (the mean life expectancy at 65 years of age), this is equivalent to an estimated loss of **0.044** life years per patient year use of NSAID use. In relation to non-fatal case of GI or heart failure, the loss in quality of life that would occur has not been included in the analysis. This reflects a lack of study resources, and means that the impact of side effects on utility and thus total QALYs will be understated.

The estimated change in utility – derived as the sum of the utility gain from symptom control and utility loss from excess mortality - is brought together with cost (drug cost plus any costs of hospitalisations) to derive estimated cost/QALY for each pharmacotherapy. As noted because of the failure to include any quality of life loss from non-fatal case of GI or heart disease, the estimated cost/QALY estimates for ns and COX-2 NSAIDs will be somewhat too favourable. A summary table of results has been prepared, Table 8.5, in which the cost-utility estimates are recorded, incorporating key assumptions as described in Tables 8.6, and limited sensitivity analysis. This shows the effect of varying the presumed discount rate on future life years, and of taking clinical an upper and lower estimate of clinical trial results (+/- 1 SD). Intermediate calculations are shown in the Appendix Table A8.3, (but with upper and lower bounds shown as +/- 2SD).

8.8 Results of cost-utility analysis

The analysis is based on 12 months use of pharmacotherapies and assumes that the use of drugs and benefits accrued are contiguous. For the nsNSAIDs the modelling is based on diclofenac and naproxen and for the COX-2 NSAIDs it is based on celecoxib, and in effect just covers those drugs.

Calculation

Estimated Cost/QALY gain is a combination of:

Cost Mean cost per patient year, plus estimated cost of admissions associated with gastric or cardiac side effects (based on the literature assumed to apply to NSAIDs only). (See Section 8.6.) Where relevant, costs are discounted at 5% pa.

Divided by:

QALYs *Utility gain through symptom control* – Estimated by translating trial outcome scores into a utility value for the intervention and control cohort and calculating the difference. The Transfer To Utility equations as described in Chapter 3 have been used for this purpose. The results are these calculations shown in Table 8.A3;

Less:

Estimated mortality - associated with the cardiac and gastric complications from drug use (as described in Section 8.3, but also reported in Table 8.6 and A8.3);

Less:

Loss in quality of life - associated with the cardiac and gastric complications from drug use (not calculated).

Benefit is defined compared with placebo, and is thus influenced by the change in the placebo group. Given the nature of the symptoms of OA the placebo effect can be quite marked, but also quite variable and potentially influenced by other aspects of the study protocol. In Table E.8.3 utility gain is shown both relative to baseline and relative to placebo, where this is reported, but cost/QALY has only been estimated relative to placebo.

Sensitivity Analysis

i) *Clinical Trial results* - Upper and lower values around the mean scores have been calculated as both 1 and 2 standard deviations around the mean. The former has been used in the summary results table (see Table 8.5), while the latter is used in the calculations in Table A8.3.

ii) *Discounting of future life years* - Two alternative assumptions are incorporated concerning future life years lost associated with current deaths:

- Either that each life year is of equal weighting, with a zero discount rate so that if life is cut short by 18.5 years, this is counted as a full 18.5 years; or
- Future life years lost are discounted at the same rate as costs; that is at 5% pa, in effect saying that a loss of 18.5 years is ‘equivalent’ in some way to a current loss of only 12 life years.

Results

In relation to NSAIDS (non-specific and COX-2), because the net QALY score is the difference of two components, it is highly sensitive to small changes in the calculated utility net gain for symptom control and to the estimated mortality rate from GI and cardiac side effects. This is a problem as both of these measures are highly uncertain. The number of trials on which the estimates of utility gain was based is small, (there are few placebo-controlled trials), but some difference in trial results is apparent. The results for the NSAIDs are also highly sensitive to discounting, which in effect has a dramatic influence on the mortality loss.

As summarised in Table 8.5, the best estimate of cost/QALY (identified as the 'medium estimate') for nsNSAIDs (based on diclofenac and naproxen) is $15,000 if future life years are discounted at 5% pa and losses in excess of gains without discounting. The equivalent results for COX-2 NSAIDS are $32,930/QALY with discounting and, once again, losses in excess of gains without discounting of future life years. The complementary medicines all appear highly cost-effective, at between $2,900 and $4,500/QALY medium estimate, as there is no evidence that the QALY gain from symptom control is offset by mortality loss. For ASU the result is less robust as one trial did not support efficacy relative to placebo in symptom control.

Table 8.5 Cost-utility analysis pharmacotherapies: key results

Key Assumptions	ns NSAIDs[1]	COX-2 NSAIDs[2]	Glucosamine Sulphate	ASU	Topical Capsaicin
0% discount on future life years					
Low estimate (mean -1 SD 2 seminal trials)	∞ negative net benefit	∞ negative net benefit	$5,100	∞ negative net benefit	$5,500
Medium estimate (Mean 2 seminal trial means)	∞ negative net benefit	∞ negative net benefit	$2,900	$4,100	$4,500
High estimate (mean + 1 SD 2 seminal trials)	$23,300	$70,900	$2,400		$3,900
5% discount on future life years					
Low estimate (as above)	$70,000	$83,800			
Medium estimate (as above)	$15,000	$32,900			
High estimate (as above)	$ 8,800	$21,400			

Notes: [1] Represented by diclofenac and naproxen;
[2] Represented by celecoxib; for other assumptions common to all calculations see text and Table 8.6

The cost/QALY for NSAIDs is highly sensitive to quality of life gain in terms of symptom control and the approach to discounting of life years lost through current deaths attributable to side effects. For nsNSAIDs, specifically diclofenac and naproxen, cost/QALY is estimated to fall within the range of a low $8,800 per QALY gain, using a 5% discount rate on future life years and a high estimate for quality of life gain associated with symptom control (+ 1 SD above the mean value); to a negative benefit, that is the gain in symptom control is more than offset by the excess mortality. The latter result applies under the median and low estimate of QALY gain if future life years lost are not discounted. For COX-2 NSAIDs (celecoxib), cost/QALY is found to vary from $21,400 under the most optimistic assumptions, upwards to a net QALY loss under several scenarios, as shown in Table 8.5.

Table 8.6 Key Values adopted for modelling – costs, morbidity and mortality rates

Attribute		Non-selective NSAIDs		COX-2 selective NSAIDs	Complementary & Topical		
		diclofenac	naproxen	celecoxib	Glucos-amine	ASU	Capsaicin
A	Drug cost $/patient year	$175	$104	$391	$180	$333	$236
Morbidity-side effects							
B	Excess PUB rate	0.0195	0.0195	0.0195	0	0	0
C	Excess CHF rate	0.005	0.005	0.005	0	0	0
Morbidity/hospitalisation cost							
D = Bx$2,417	PUB	$ 49	$ 49	$ 49	0	0	$ 0
E = Cx$4,110	CHF	$ 21	$ 21	$ 21	0	0	$ 0
F = D+E	Mean cost hospitalisation	$ 70	$ 70	$ 70	0	0	$ 0
G = A+F	Total annual cost	$245	$174	$461	$180	$333	$236
Mortality –side effects							
H = B*10%	Excess PUB rate	0.00213	0.00213	0.00213	0	0	0
I = C*5%	Excess CHF rate	0.00025	0.00025	0.00025	0	0	0
J = H+I	Total excess mortality	0.00238	0.00238	0.00238	0	0	0

Sources/Notes:

A Annual drug cost based on defined daily dose or estimated equivalent (see text)

B Gastrointestinal morbidity from NSAIDs defined as perforations, ulcerations and bleeds (PUBs). Rates established from CLASS study based on mean CSUGIE/GDU 12 month rate for celecoxib and diclofenac. The one rate is used as there was no significant difference between them. (see Table 8.3).

C CHF = Congestive Heart Failure, based on Page and Henry (2000) excess risk of hospitalisation for CHF in those taking NSAIDs 5/1000 per year compared to non-NSAID users.

D Average cost of hospital admission for PUBs estimated at $2,417, based on AR DRGs (see text)

E Average cost of hospital admission for CHF estimated at $4,110, based on AR DRGs (see text).

H Mortality rate for hospitalisations for PUBs estimated at 10% (Day *et al.*, 1999)

I Mortality rate for hospitalisation for CHF = 5% (estimated from *Heart, Stroke and Vascular Diseases*, National Centre for Monitoring Cardiovascular Disease, April 2001)

J It is assumed that PUBs and CHF are independent of each other

8.9 Conclusions

The development of conclusions about the relative cost-effectiveness of drug therapies for the management of OA is confounded by several factors. These include, the relatively small number of studies that compare drug therapies for managing OA with each other and with placebo, and differences in study design which make comparisons potentially problematic. Furthermore, given the context of the analysis – a wide-ranging study to assess performance of a large number of interventions to reduce disease burden from OA - the depth of analysis is necessarily compromised. A more thorough analysis of pharmacotherapies was not possible - for instance of the differential impact on various patient sub-groups, the performance of formulations other than those studied (especially other nsNSAIDs), and incorporation of the quality of life impact of non-fatal side effects of drug therapies.

Still, a number of provisional conclusions can be drawn about the performance of pharmacotherapies in the management of the symptoms of OA. The failure to demonstrate in clinical trials the superiority of the more expensive COX -2 NSAIDs in terms of symptom control or side effect profile against certain non-specific NSAIDs restriction of COX 2s to selected patient

subgroups with greater capacity to benefit is indicated. Comparing NSAIDs with complementary medications of glucosamine sulphate and topical capsaicin, evidence suggests an approximate equivalence in terms of symptom control, but a lower side effect profile with the latter. Given a similar cost of these medications, improved access to the latter may be warranted. Review of new evidence as it becomes available is important, as this conclusion is based on relatively few studies.

If deaths from the side effects of medication are counted in full, that is future life years lost are not discounted, then both nsNSAIDs and COX- 2 NSAIDs (celecoxib) perform poorly, with any gains in symptom control almost certainly offset by excess mortality. If future life years lost are discounted at 5% pa both ns and COX-2 NSAIDs perform well (relative to placebo), particularly taking middle or upper values for gain in symptom control. Although as noted, given the assumptions of the model COX 2 NSAIDs are dominated by nsNSAIDs (the former being more expensive but of equivalent efficacy and side-effect profile). In relation to both nsNSAIDs and COX-2 NSAIDs, if a sub-population can be identified for whom the morbidity and mortality risk is reduced, performance would be considerably more favourable.

ANNEXURE TO CHAPTER 8

Additional results: CLASS study

Table A8.1 Summary of CSUGIE incidence - first Six Months (intention-to-treat)

	Celecoxib 400 mg BID	Diclofenac 75 mg BID	Ibuprofen 800 mg TID	Log-Rank P Values for Celecoxib vs Diclofenac	Ibuprofen	Both
All Patients	*n = 3987*	*n = 1996*	*n = 1985*			
No. of CSUGIEs	11	9	11			
Week 26 crude rate	0.28%	0.45%	0.55%	**0.264**	**0.073**	**0.092**
No. per 100 patient-yrs	0.76	1.27	1.63			
Patients Not Taking Aspirin	*n = 3154*	*n = 1567*	*n = 1602*			
No. of CSUGIEs	5	4	10			
Week 26 crude rate	0.16%	0.26%	0.62%	**0.476**	**0.005**	**0.037**
No. per 100 patient-yrs	0.44	0.72	1.85			

Source: www.fda.gov/ohrms/dockets/ac/01/ briefing/3677b1_03_med.pdf (page 34)

[Results for celecoxib vs. combined NSAIDs reported in Silverstein et al, 2000, page 1251. Comparisons with individual NSAIDs not reported.]

Table 8A.2 Summary of CSGUIE/GDU incidence – first six months (intention-to-treat)

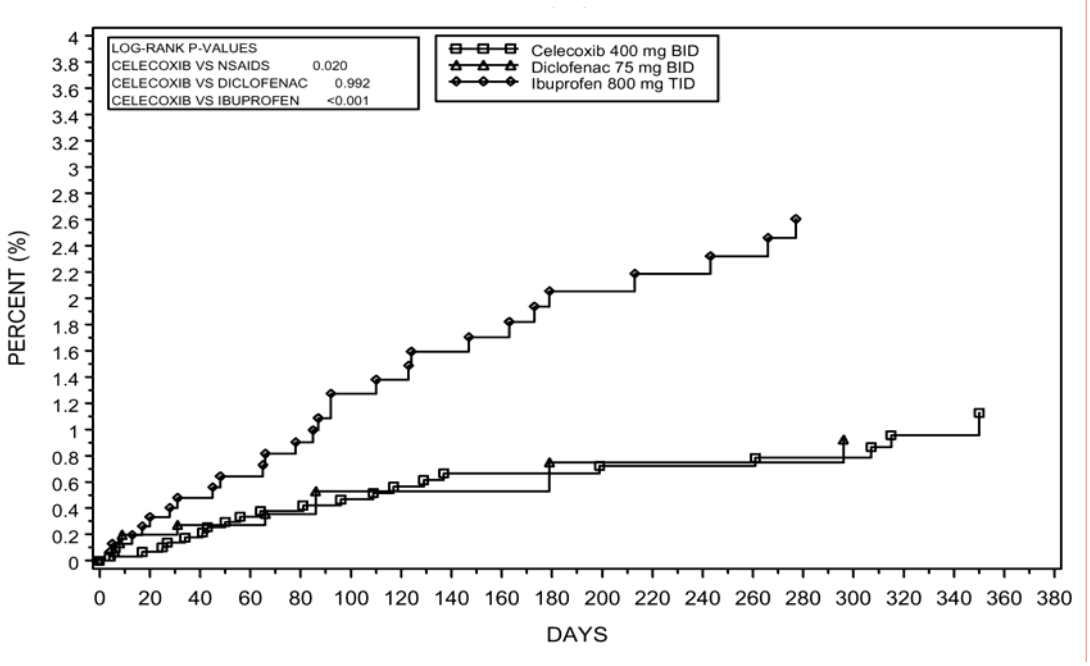
	Celecoxib 400 mg BID	Diclofenac 75 mg BID	Ibuprofen 800 mg TID	Log-Rank P Values for Celecoxib vs. Diclofenac	Ibuprofen	Both
All Patients	n = 3987	n = 1996	n = 1985			
No. of CSUGIE/GDUs	30	20	29			
Week 26 crude rate	0.75%	1.00%	1.46%	**0.308**	**0.005**	**0.023**
No. per 100 patient-yrs	2.08	2.82	4.31			
Patients not Taking Aspirin	n = 3154	n = 1567	n = 1602			
No. of CSUGIE/GDUs	16	9	23			
Week 26 crude rate	0.51%	0.57%	1.44%	**0.760**	**<0.001**	**0.017**
No. per 100 patient-yrs	1.40	1.61	4.25			

Source: www.fda.gov/ohrms/dockets/ac/01/ briefing/3677b1_03_med.pdf (page 43)
[Results for celecoxib vs. combined NSAIDs reported in Silverstein et al, 2000, page 1251. Comparisons with individual NSAIDs not reported.]

CSUGIEs/GDU in patients taking aspirin

Consumption of more than one type of NSAIDs has been shown to greatly increase the risk of GI toxicity compared to consumption of these NSAIDs singularly [Alberto & Rodriguez, 1997]. The CLASS study included a number of patients who were taking aspirin as prophylaxis against cardiovascular disease (~10% of the cohort). The incidence of CSUGIE/GDU among aspirin users for the full study period is shown in Figure 8.2 below. The incidence rate among celecoxib + aspirin users is similar as that for diclofenac + aspirin, indicating no safety benefit in aspirin users from taking celecoxib over diclofenac. The ibuprofen + aspirin group event rate was higher than that observed for celecoxib + aspirin or diclofenac + aspirin. However, as noted in the FDA Medical Officer's Gastroenterology Advisory Committee Briefing Document (p. 46), "One may suggest that the small number of events over time yield statistically meaningless results." The report added that "it appears that tolerability as well as clinically serious UGI events is not better in patients taking celecoxib compared to both traditional NSAIDs in aspirin users."

FIGURE 8.2 Time to Gastroduodenal Ulcer, Bleeding, Perforation or Obstruction Entire Study Period – Patients not Taking Aspirin Log-Rank Test with Censoring Rules Applied



Source: http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b1_05_gi.pdf (page 45)

Table A8.3 (i) Modelling cost-utility analysis - pharmacotherapies in OA : Range = mean +/- 2 SDs

		nsNSAIDs						COX-2 NSAIDs					
		Diclofenac (a)			Naproxen (b)			Celecoxib (b)			celecoxib (c)		
		Upper + 2 SD	**Mean**	Lower - 2 SD	Upper + 2 SD	**Mean**	Lower - 2 SD	Upper + 2 SD	**Mean**	Lower - 2 SD	Upper + 2 SD	**Mean**	Lower - 2 SD
Trial Outcomes : WOMAC (mean ± 2 SD)													
	Baseline		42.5			52.9			50.5			51	
	Trial end point	26.3	30.3	34.3	38.4	41	43.6	34.8	37.2	39.6	35	37.6	40.2
Utility – transformed from WOMAC using pertinent TTU equation – see Chapter 3.													
A_1	Baseline		**0.532**			**0.455**			**0.475**			**0.471**	
A_2	Trial end point	0.641	**0.617**	0.591	0.565	**0.548**	0.529	0.588	**0.573**	0.557	0.587	**0.571**	0.553
A $=A_2-A_1$	Utility gain intervention group	0.109	**0.085**	0.059	0.110	**0.093**	0.074	0.113	**0.098**	0.082	0.116	**0.100**	0.082
B = A – gain placebo arm	Net utility gain (Gain intervention group less gain placebo group)	0.059	**0.035**	0.009	0.068	**0.051**	0.032	0.071	**0.056**	0.04	0.046	**0.030**	0.012
Cost													
C	Annual Drug cost		$ 175			$ 104			$391			$391	
D	Annual excess morbidity cost		$ 70			$ 70			$ 70			$ 70	
E = B+C	Total cost		$ 245			$ 174			$461			$461	
Mortality													
F	Annual excess mortality (p.p)		0.00238			0.00238			0.00238			0.00238	
G = F x 18.5	Years of life lost (undiscounted)		0.044			0.044			0.044			0.044	
	Life years lost (5% disc future life yrs)		0.029			0.029			0.029			0.029	
QALY gain													
H=B-G	Net QALY gain (undiscounted)	0.015	**-0.009**	-0.035	0.024	**0.007**	-0.03	0.027	0.012	-0.004	0.002	-0.014	-0.05
	Net QALY gain (5% disc)	0.030	**0.006**	<0.000	0.039	**0.022**	0.003	0.042	0.027	0.011	0.017	0.001	<0.000
K=E/H	Cost/QALY (undiscounted)	$16,300	∞	∞	$ 7,300	**$ 24,900**	∞	$17,100	**$ 38,400**	∞	$230,500	∞	∞
	Cost/QALY (5% disc)	$ 8,200	**$ 40,800**	∞	$ 4,500	**$ 7,900**	$ 58,000	$ 11,000	**$ 17,100**	$ 41,900	$ 27,100	**$461,000**	∞

Source: (a) Pincus *et al*., 2001 – diclofenac vs paracetamol,(b) Bensen *et al*., 1999 – naproxen vs celecoxib vs paracetamol, (c) Williams et al., 2001 – celecoxib vs placebo

Notes: A. Net utility gain = mean utility change follow-up less baseline intervention arm less mean utility change follow-up less baseline placebo/paracetamol arm

G Years of life lost = 18.5 x annual mortality.

∞ Negative net benefit

Table 8.A3 (i) (contd.)

		Oral Glucosamine Sulphate				ASU	Topical Capsaicin		
		(d_1)			(d_2)	(e)	(f)		
		Upper	Mean	Lower	Mean	Mean	Upper	Mean	Lower
Trial Outcomes									
	Baseline	42.93				41.9	54		
	Trial end point	34.21	37.9	41.55	32.5	24.2	22.2	25	27.8
Estimated Utility									
	Baseline	0.543				0.511	0.446		
	Trial end point	0.592	0.569	0.544	0.602	0.617	0.637	0.620	0.603
A	Utility gain = difference from baseline	0.049	0.026	0.001	0.059	0.106	0.191	0.174	0.157
B	Net utility gain = diff from baseline interv. – difference from baseline control	0.075	0.052	0.027	0.085	0.081	0.070	0.053	0.036
Cost									
E	Total cost = annual drug cost, excess morbidity cost assumed zero	$180				$333	$236		
Mortality									
F	Annual excess mortality	0				0	0		
Performance: QALY gain and cost/QALY									
I=B	Net QALY gain. 0 disc and 5% disc as no mortality loss these are equal	0.075	0.052	0.027	0.085	0.081	0.070	0.053	0.036
K = E/I	Cost/QALY (0 and 5% disc)	$2,400	$3,462	$6,667	$2,118	$4,111	$3,371	$4,453	$6,556

Sources:

(d) Reginster *et al*., 2001 – glucosamine sulphate vs placebo (1) = Intention-to-Treat results (2) = completors only [included as trial was run over 3 years, with only small percentage of drop outs]

(e) Appelboom *et al*., 2000 – ASU vs placebo [upper and lower not modelled as skewed distribution around mean]

(f) Altman *et al*., 1994 – Topical capsaicin vs placebo

Table A8.3 (ii) **Modelling cost-utility analysis – NSAIDS:** **Range = mean ± 1SD**

		NsNSAID						COX-2 NSAIDs					
		Diclofenac (a)			**Naproxen (b)**			**Celecoxib** (b)			**Celecoxib** (c)		
		Upper +1 SD	Mean	Lower -1 SD	Upper +1 SD	Mean	Lower -1 SD	Upper +1 SD	Mean	Lower -1 SD	Upper +1 SD	Mean	Lower -1 SD
Trial Outcomes : WOMAC (mean ±1 SD)		(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(11)	(12)	(13)
A	Net utility gain (from Row B Table 8.3)	0.047	0.035	0.022	0.059	0.051	0.042	0.063	0.056	0.048	0.038	0.030	0.021
		Upper +1 SD Av (1) & (4)		Mean Av (2) & (5**)**		Lower -1 SD Av (3) & (6)		Upper +1 SD Av (7) & (11)		Mean Av (8) & (12)		Lower -1 SD Av (9) & (13)	
B	Mean utility gain	0.053		0.043		0.032		0.0505		0.043		0.0345	
Mortality													
C_1	Life years lost (5% discounted)	0.029						0.029					
C_2	Life years lost (0 discount)	0.044						0.044					
QALY gain													
$D_1 = B\text{-}D_1$	Net utility gain (5% discounted)	0.024		0.014		0.003		0.0215		0.014		0.0055	
$D_2 = B\text{-}D_2$	Net utility gain (0 discount)	0.009		<0		<0		0.0065		<0		<0	
Cost													
E	Total cost (from Row E Table 8.3)	$ 245			$ 174			$461			$461		
F	Mean cost	$210						$461					
$G_1 = F/D_1$	Cost/QALY (5% discounted)	$ 8,750		$15,000		$70,000		$21,440		$32,930		$83,800	
$G_2 = F/D_2$	Cost/QALY (0 discount)	$23,300		∞		∞		$70,920		∞		∞	

Notes see Table 8 A.3

∞ negative net benefit

9. HIP AND KNEE REPLACEMENT SURGERY

9.1 Introduction

Hip or knee replacement surgery is generally undertaken only after failure of other treatments for OA and where the onset of serious disability has occurred. Over 80% of total hip replacement and over 90% of all knee replacement surgery is associated with a primary diagnosis of osteoarthritis. Data from the Australian Orthopaedic Association National Joint Replacement Registry (2001) shows that in 1999-2000 there were 12,263 hip replacements and 14,837 knee replacements for OA (Table 9.1). In Australia the average age for hip replacement surgery is 66 for males and 70 for females, for knee replacement surgery it is 71 for males and 70 for females.

Table 9.2 Estimated numbers of joint replacement operations for OA by age, (1999-2000)

Age group[1]	<39	40-49	50-59	60-69	70-79	80-89	90-99	Total
Total THRs for OA	147	552	1,815	3,679	4,231	1,705	123	12,263
Total UKRs for OA	4	84	483	698	641	196	4	2,109
Total TKRs for OA	15	208	1,456	4,159	6,594	2,302	104	14,837

Source: Australian Orthopaedic Association National Joint Replacement Registry.

Notes:

[1] Age group breakdown per procedure has been based on South Australian estimates

Abbreviations: THR = Total Hip Replacement, UKR = Unicompartmental Knee Replacement, TKR = Total Knee Replacement

9.2 Evidence of efficacy

Overview

No randomised, placebo-controlled trials of total hip or knee replacement (THR or TKR) surgery were identified in the literature search. It is probable that none have been undertaken due to the ethical problems of such a study, given the clear clinical benefits received by those having surgery. The highest quality evidence identified in the literature on outcomes for THR and TKR is from before-and-after cohort studies, where patients' quality of life is measured pre-operatively, then at several time points post-operatively. A number of such studies have followed patients for up to 12 months post-operatively (Bachmeier *et al.*, 2001; Jones *et al.*, 2000; Kirwan, Currey, Freeman *et al*., 1994). Little data is available on longer term outcomes, with only one study identified which reports patient outcomes at greater than 12 months post-operatively (Kirwan *et al.*, 1994). In general, the results from these studies provide a uniform picture of considerable quality of life (QoL) gain for patients following hip or knee replacement surgery, with hip replacement consistently producing greater QoL improvements than that achieved from knee replacement. Although there are no cohort studies of those who might be eligible to receive surgery but do not, the clinical pathway is accepted to be continued and perhaps increasing morbidity.

The study by Kirwan *et a.l* (1994) was a prospective 5 year follow-up study of 293 patients on an orthopaedic waiting list for THR or TKR and with a diagnosis of OA or RA. A total of 164 OA hip operations and 76 OA knee operations were followed-up. Overall, 293 patients (OA+RA) were followed-up for 1 year, 276 for 2 years, 252 for 3 years, 223 for 4 years and 140 for 5 years. A range of outcome measures were recorded, including the Stanford Health Assessment Questionnaire, and VAS pain. The results for VAS pain over 4 years for both hip and knee surgery among OA patients alone are summarised in Table 9.2 and Figure 9.1. These show both a substantial improvement between baseline (prior to surgery) and at 1 year, and that the gain is maintained over a four year follow-up period. However, the authors do note that 14 people who had poor results of surgery have

been excluded from the analysis. That is, these study results only apply to the majority for whom surgery was successful. The important conclusion is that results at 1 year can be taken to indicate longer term outcomes.

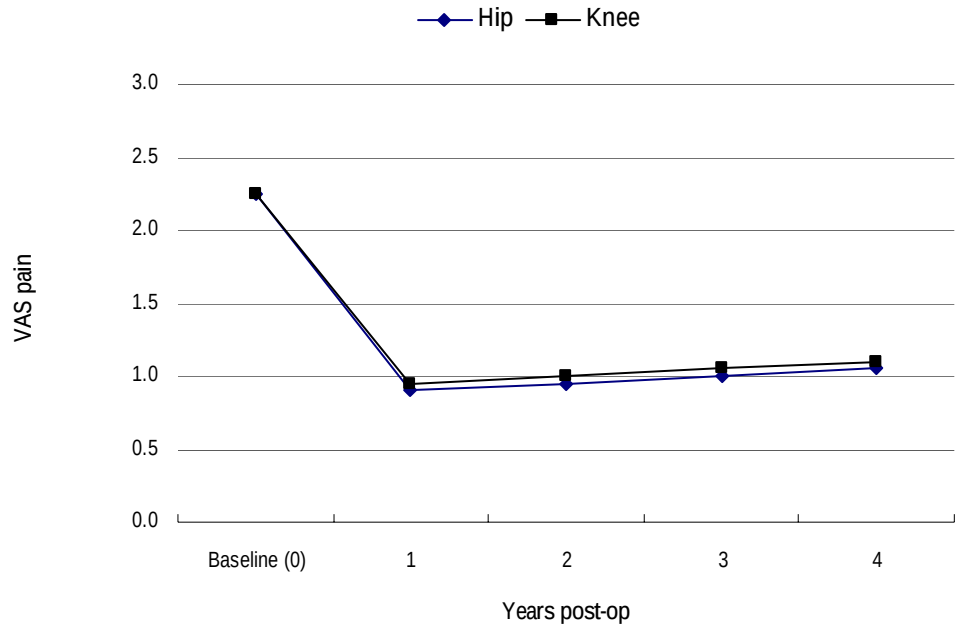
Table 9.3 Longitudinal changes in VAS Pain scores[1] following hip and knee arthroplasty

		Hip	Knee
Baseline – pre surgery	n=293	2.25	2.25
1 year follow-up	n=293	0.90	0.95
2 year follow-up	n=276	0.95	1.00
3 year follow-up	n=252	1.00	1.05
4 year follow-up	n=223	1.05	1.01

Source: Kirwan *et al*., 1994

Notes: [1] VAS scale range (0 to 3), higher score indicates higher pain

Figure 9.2 VAS pain after THR and TKR 4 year follow-up (Kirwan, 1994)



Morbidities

Revision surgery

For both THR and TKR, there is a small but significant rate of prosthesis failure in the years following surgery. This is largely due to either gradual loosening or wearing of the prosthesis, or occasionally infection. In these instances, revision surgery may be required. The rate of revision surgery is widely used as an endpoint in studies to demonstrate the safety of new prostheses or to show general improvements over time in THR or TKR at the level of a health service, hospital, etc. These rates are often provided over 10-year periods. In countries that have established knee or hip prosthesis registries (eg Sweden, Norway), it has been demonstrated that changes in surgical technique have been associated with reductions in the cumulative revision rate (CRR). The Swedish registry, which has been running since 1975, has demonstrated large improvements in the CRR for both THR and TKR over this period (Robertsson, Knutson, Lewold and Lidgren, 2001). Revision rates of 12% and

20% over a 15-year period have been included in the modelling as the major morbidity component of arthroplasty.

Deep Vein Thrombosis/Mortality

DVT is a common occurrence following hip or knee replacement surgery, however in the majority of cases it will not present symptomatically – silent DVT (Eikelboom, Quinlan and Douketis, 2001). In some cases DVT can cause pulmonary emboli, which have the potential to be fatal. Drugs to prevent the development of DVT (thromboprophylaxis) are typically provided for periods following these types of surgery, however the appropriate duration of treatment post-surgery has been debated. Additionally, the rate of post-surgical pulmonary emboli in the absence of such treatment is also uncertain.

Thromboprophylaxis in hospital may include subcutaneous injections of unfractionated or low molecular weight heparin. For practical reasons this is usually stopped upon discharge, however some studies have found that the risk of DVT and pulmonary embolism may continue for weeks or months post-operatively (Scurr, Coleridge-Smith and Hasty, 1988; Huber, Bounameaux and Borst, 1992).

A multi-national study in 13,356 patients undergoing surgery for hip fracture found that a low daily dose of aspirin (160 mg), taken for 35 days, reduced the incidence of pulmonary embolism by 43%, and led to a reduction in fatal pulmonary embolism of 4 per 1000 compared to placebo (Pulmonary Embolism Prevention (PEP) Trial Collaborative Group, 2000). However, in a cohort of patients having hip or knee replacement surgery in the same study (4,088 patients from New Zealand), no significant difference in the rates of pulmonary embolism was found between those assigned aspirin and those assigned placebo, although a trend in favour of prophylaxis was noted (treatment 1.1% vs placebo 1.4%).

In addition to this prospective study, another prospective study also could not find a significant reduction in symptomatic venous thromboembolism following extended duration thromboprophylaxis (Heit, Elliott, Trowbridge *et al*., 2000).

Two recent prospective studies of extended duration thromboprophylaxis following hospital discharge demonstrated that the frequency of new symptomatic DVT or pulmonary embolism in the absence of extended duration thromboprophylaxis was only about 2% after 3 months (Robinson, Anderson, Gross *et al.,* 1998; Leclerc, Gent, Hirsh *et al.,* 1998). Existing international guidelines for prevention of venous thromboprophylaxis recommend 7-10 days of therapy with warfarin or LMW heparin after TKR/THR (Geerts, Heit, Clagett *et al.,* 2001; Nicolaides, 2001).

A recent meta-analysis (Eikelboom *et al.,* 2001) of extended duration prophylaxis with low molecular weight heparin or unfractionated heparin following THR or TKR, found a significant reduction in the frequency of symptomatic venous thromboembolism in those receiving treatment (equivalent to a reduction in 20 symptomatic events per 1,000 patients treated), and on the basis of a 5% case-fatality rate (Douketis, Kearon, Bates *et al.,* 1998), translate this to the prevention of approximately one additional death per 1,000 patients treated. An earlier meta-analysis examining rates of fatal pulmonary embolism with and without prophylaxis in patients undergoing hip replacement (Murray, Britton and Bulstrode, 1996) found a rate of fatal pulmonary embolism of between 1-2 per 1,000 in patients receiving no thromboprophylaxis. Based on these studies, it seems reasonable to assume a mortality rate from pulmonary thrombosis of approximately 1 per 1,000 in patients undergoing knee or hip replacement surgery, assuming post-surgical in-hospital prophylaxis. Further confirmation for this rate comes from a recent prospective observational study undertaken in the UK (Hajat, Fitzpatrick, Morris *et al.,* 2002), in which the rate of fatal pulmonary embolism was estimated at 0.11% in a cohort of 7,151 patients who had undergone total hip replacement. No significant difference was noted between those patients who received thromboprophylaxis and those who did not, however the study was limited in its ability to show a difference for this measure due to the much larger proportion of the study cohort who received thromboprophylaxis.

Eikelboom *et al.* (2001) notes that the rate of pulmonary embolism may be higher after TKR than THR, due to the more severe tissue disruption associated with this procedure. As there no clear data could be identified to support this, rates of fatal pulmonary embolism following both hip and knee replacement surgery have been assumed to be the same (1/1000) for both primary and revision surgery. This is translated into life years lost by adjusting for life expectancy at the time of surgery, which is taken to be 15 years.

9.3 Knee replacement surgery

Knee replacement surgery can be undertaken as either unicompartmental (UKR) or total (TKR). UKR surgery leaves some of the joint intact, and may provide patients with improved flexion (Newman, Shah and Nilen, 1998). It is more likely to be undertaken in younger patients who are more active, but data from the Swedish National Knee Registry indicates a higher rate of revision for UKR compared to TKR (Robertsson *et al.*, 2001). This may be as a result of the younger age and increased activity levels of patients, progression of OA into other compartments of the knee, or problems with surgical technique or prostheses design. Patello/trochlear surgery, a third form of knee replacement surgery generally undertaken on younger individuals, is uncommon.

The Australian Orthopaedic Association National Joint Replacement Registry 2001 Annual report (NJJR 2001) provides data on four categories of knee replacement surgery – patello/trochlear, unicompartmental, primary total knee and revision. In 1999-2000, there were 19,852 operations for knee replacement surgery, 17,717 of which were for primary TKR or UKR. The NJJR indicates that over 95% of all UKR/TKR operations performed in South Australia during 1999-2000 were for OA. This ratio has been used to estimate the total number of UKR and TKR operations performed in Australia for OA.

Costs

Costs for surgery were based on the published cost weights for the relevant AR-DRG codes shown in Table 9.2. AR-DRG costs shown in Table 9.3 were assumed to cover the entire costs of the procedure: $12,312 for total knee replacement without complications and $16,649 with complications, average $12,774 in 1999-2000. An average cost of $14,000 has been used in the modelling to reflect current costs of TKR and to include consultations with surgeons and physician visits prior to surgery. No costs have been included for treatment for deep vein thrombosis or pulmonary embolism, but the cost estimates for knee replacement surgery do however include costs for in-hospital thromboprophylaxis.

There is no AR-DRG code specific for revision knee surgery. However, The cost of this surgery is presumed to be higher, as occurs with revision surgery for the hip, and for which a separate cost is reported. A total of $24,000 was estimated for the cost of revision surgery, based on the cost for hips (see Table 9.6). A present value cost of surgery was calculated over a 15 year period to incorporate the cost and probability of revision, this yielded an expected present value cost for TKR of $15,886 at a 12% revision rate and $17,143 at a 20% revision rate (see Table A9.1 in the annexure to this chapter).

Outcomes

Outcomes for knee replacement surgery have been based on a study by Bachmeir *et al*., (2001) which employed a before and after study design involving 108 patients on waiting lists for TKE on waiting four Sydney hospitals. Both before and follow-up data were collected, and the key results are summarized in Table 9.4. On average, the baseline questionnaires were completed approximately 15 days before surgery. SF-36 scores were translated into utility values using the equivalence regression model developed for this study.
The calculations are shown in full in the annexure to this chapter (see Table A9.4) and the results are reported in Table 9.4 below. Substantial improvements in utility scores were found after knee replacement surgery with an average gain at 12 months of 0.191 over baseline.

Table 9.4 AR-DRGs for knee replacement surgery in 1999-2000

AR-DRG		Separations	Cost by volume ($'000)	Average Cost 1999-2000
I04A	Knee Replacement and Reattachment W Catastrophic CC Private	1,142	19,250	$16,856
I04A	Knee Replacement and Reattachment W Catastrophic CC - Public	892	14,615	$16,384
Sub Total - W Catastrophic CC		**2,034**	**33,864**	**$16,649**
I04B	Knee Replacement and Reattachment W/O Catastrophic CC - Private	10,482	128,163	$12,227
I04B	Knee Replacement and Reattachment W/O Catastrophic CC - Public	6,567	81,746	$12,448
Sub Total - W/O Catastrophic CC		**17,049**	**209,909**	**$12,312**
TOTAL – PRIMARY KNEE REPLACEMENT		**19,083**	**243,774**	**$12,774**

Sources: http://www.aihw.gov.au/publications/hse/ahs99-00/ahs99-00-xd1002/xls and http://www.aihw.gov.au/publications/hse/ahs99-00/ahs99-00-xd1001/xls accessed 25/11/02

Table 9.5 SF-36 scores: total knee replacement surgery study group

SF-36 subscales	Baseline (n=100)	3 months (n=89)	6 months (n=77)	12 months (n=51)
General health	71.3	69.2	69.2	70.2
Bodily pain	33	48.5	54.1	57.8
Physical function	25.2	38.6	47.9	49.7
Physical role function	18	20.2	36.4	49.5
Social function	59.2	70.8	70.8	77.7
Mental health	70.4	72.8	75.6	77.6
Emotional role function	54.2	54	63.2	64.7
Vitality	47	51.2	52.7	58.8
Estimated Utility Scores	0.43776	0.55019	0.59907	0.6284
Gain in utility				0.191

Source: Bachmeier, March and Cross, 2001

Performance

The modelling was undertaken for a cohort of 1,000 persons 56% of whom were female and whose average age was 70 years for the females and 71 years for the males. The gain in QALYs was calculated to be 0.1631[16] per person during the first year (and revision years), and 0.1906 per person for the remaining years. Benefits have been calculated over a 15-year period.

It was assumed that:

i) the 12 month utility gain was maintained over the entire period (except for the revision year);

ii) the mortality rate due to primary and revision surgery was 1/1000;

iii) revision rates were 12% or 20%;

iv) mortality rates were based on the proportion of people dying between exact age x and exact age (x+1) as published by the Australian Bureau of Statistics Catalogue No. 3302.0 (see Table A9.2 in the annexure to this chapter);

v) costs were discounted at 5% per annum; and

vi) benefits were discounted at 0% and 5% per annum.

The results for of the modelling are shown in Table 9.5. When both the costs and benefits are discounted at 5%, the cost/QALY is $10,804 at a 12% revision rate and $11,671 at a revision rate of 20%.

[16] 0.0141 for the first 3 months + 0.0464 for the next 3 months + 0.1027 for the final 6 months = 0.1631

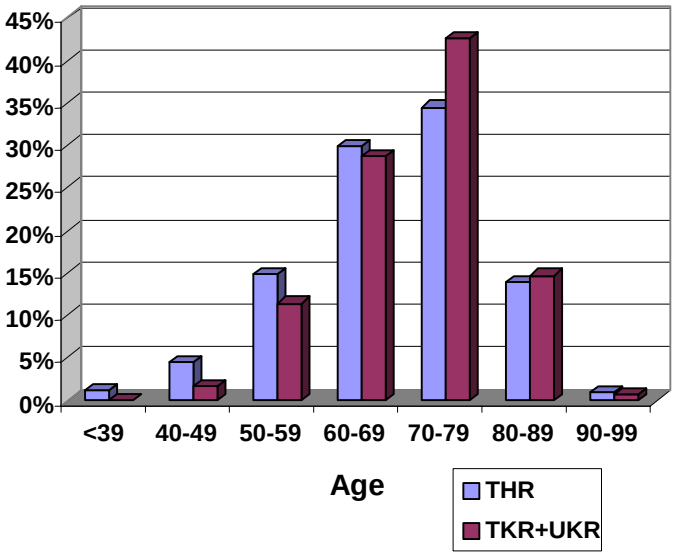
Table 9.6 Cost-utility analysis for total knee replacement (TKR) with total revision rates of 12% and 20% over 15 years

ASSUMED COHORT		1000 persons			
% Female		56.1%			
Average Age		Females=70 years; Males=71 years			
Modelling Period		15 years			
		12% Revision Rate		20% Revision Rate	
OUTCOMES		Disc @ 0%	Disc @ 5%	Disc @ 0%	Disc @ 5%
A	Gain in QALYs due to surgery	2086	1485	2084	1484
B	Life years lost due to surgery	15.3	14.7	15.8	15.1
C=A-B	Net gain in QALYs for cohort	2071	1470	2069	1469
D	Net gain in QALYs per person	2.071	1.470	2.069	1.469
COSTS					
E	Primary Surgery Per Person	$ 14,000	$ 14,000	$ 14,000	$ 14,000
F	Present Value of Revision Per Person	$ 1,886	$ 1,886	$ 3,143	$ 3,143
G=E+F	Present Value Total Cost Per Person	$ 15,886	$ 15,886	$ 17,143	$ 17,143
PERFORMANCE					
H=G/D	**Cost per QALY**	**$7,671**	**$10,804**	**$8,287**	**$11,671**

9.4 Hip replacement surgery

Hip replacement surgery can be undertaken as either primary or partial. In most cases, partial hip replacement is undertaken for a fractured neck of femur, with only a small percentage being for osteoarthritis (NJJR, 2001). Consequently all data used in the THR modelling relate to primary total hip replacement. The NJRR 2001 Annual Report records 22,717 operations for hip replacement surgery in 1999-2000 of which 14,193 were for primary total hip replacement. The age profile of persons who have THR and TKR for OA is similar, as illustrated in Figure 9.2, and predominantly amongst persons aged between 60 and 80 years of age. The evidence suggests revision rates of only 5-10% within 10 years and 15 to 20% after 20 years (Crawford and Murray, 1997).

Figure 9.2 THR and TKR for OA – age breakdown



Costs

Cost of THR surgery has been based on the published DRG weights for the relevant AR-DRGs shown in Table 9.6. Cost ranges from $11,662 to $24,562 depending on the existence or otherwise of complications, and whether it represents revision or primary surgery. The average cost for primary surgery is estimated to be $14,000 and for revision surgery, $24,000 to include addition costs for

surgeon/physician visits prior to surgery and to represent 2002 prices. A present value of cost of hip replacement surgery was calculated over a 15-year period to incorporate the cost and probability of revision. This yielded an expected present value cost of THR of $15,886 at 1 12% revision rate and $17,143 at a 20% revision rate (see Table A9.1 in the annexure to this chapter).

Table 9.7 AR-DRGs for hip replacement surgery in 1999-2000

AR-DRG		Separations	Cost by volume ($'000)	Average Cost 1999-2000
I03A	Hip Revision W Catastrophic or Severe CC - Private	520	12,056	$23,185
I03A	Hip Revision W Catastrophic or Severe CC - Public	484	11,895	$24,577
Total – Revision Surgery W Catastrophic or Severe CC		**1,004**	**23,951**	**$23,856**
I03B	Hip Replacement W Cat or Severe CC or Hip Revision W/O Cat or Severe CC - Private	3,495	46,242	$13,231
I03B	Hip Replacement W Cat or Severe CC or Hip Revision W/O Cat or Severe CC - Public	4,919	71,635	$14,563
Total – Primary W Cat or Severe CC + Revision W/O Cat or Severe CC		**8,414**	**117,878**	**$14,010**
I03C	Hip Replacement W/O Catastrophic or Severe CC - Private	6,750	78327	$11,604
I03C	Hip Replacement W/O Catastrophic or Severe CC - Public	5,518	64,748	$11,734
Total – Primary W/O Catastrophic or Severe CC		**12,268**	**143,075**	**$11,662**

Sources: http://www.aihw.gov.au/publications/hse/ahs99-00/ahs99-00-xd1002/xls and http://www.aihw.gov.au/publications/hse/ahs99-00/ahs99-00-xd1001/xls accessed 25/11/02

Outcomes

Outcomes for surgery have been based on the study by Bachmeier *et al.* (2001) involving 86 patients on waiting lists for THR at four Sydney hospitals. SF-36 scores were recorded at base line (pre-operatively), and 3,6, 9 and 12 months. When the SF-36 values were compared with Australian norms (Australian Bureau of Statistics, 1995 National Health Survey), it is clear that health status of persons who proceed to hip replacement surgery for OA, is far poorer than that of the general population or of a general group with arthritis. This is especially obvious in relation to bodily pain, physical role function, social function, and vitality. Interestingly general health is little affected (See Table 9.7).

Post surgery quality of life/health status is vastly improved, as demonstrated by dramatic gains on the affected subscales, notably bodily pain, physical function and physical role function, social function and vitality. Improvements are pronounced by 3 months, but additional gains are still occurring at 12 months. While improvements are apparent in relation to both hip and knee surgery, the improvements for hip surgery are far greater across all SF-36 sub-scales.

SF-36 scores reported from the Bachmeier *et al*. study were translated into utility values using the SF-36 AQoL equivalence regression model developed for this study and the results are reported in Table 9.7 below. (The calculations are shown in full in Table A9.4 in the annexure to this chapter.) Large improvements in utility are estimated, which was expected given the large gains in most dimensions of the SF-36 sub-scales. Also baseline utility scores are found to be low at 0.463 and 0.438 for the hip and knee surgery groups respectively. Substantial improvements in utility scores were found after hip and knee replacement surgery where the gains were 0.304 and 0.191, respectively. The increase in utility appears to occur quite soon after surgery, with much of the gain already apparent by 3 months.

Table 9.8 SF-36 scores: a) population norms - general population group, b) persons with arthritis and c) study group having hip replacement surgery

SF-36 subscale	SF-36 population norms[1]		Hip replacement surgery group[2]			
	(a) persons 55-74	(b) persons with OA	Baseline (n=73)	3 months (n=71)	6 months (n=57)	12 months (n=53)
Physical Function			26.9	51.8	57.2	66.6
Role Physical	68.1	63.2	14.6	33.2	48.7	58.7
Bodily Pain	70.0	60.2	32.9	60.2	65.5	72.8
General Health	64.8	61.7	66.3	69.6	71.2	73.8
Vitality	62.2	57.3	47.1	60	61.7	67.5
Social Function	83.0	77.3	52.5	69.9	77.8	88.6
Role Emotion	78.7	74.8	60.0	64.3	71.4	71.8
Mental Health	76.3	71.4	71.4	77.4	80.5	81.7
Estimated Utility Score			0.4635	0.67198	0.71359	0.7672
Change in Utility						0.304

Source:

[1] ABS National Health Survey SF-36 Population Norms Cat no 4399.0

[2] Bachmeier, March and Cross (2001)

Performance

The modelling was undertaken for a cohort of 1,000 persons 52.6% of whom were female and whose average age was 70 years for the females and 66 years for the males. The gain in QALYs was calculated to be 0.2590[17] per person during the first year and revision years and 0.3037 per person for the remaining years. Benefits have been calculated over a 15-year period.

It was assumed that:

i) the 12 month utility gain was maintained over the entire period (except for the revision year);

ii) the mortality rate due to primary and revision surgery was 1/1000;

iii) revision rates were 12% or 20%;

iv) mortality rates were based on the proportion of people dying between exact age x and exact age (x+1) as published by the Australian Bureau of Statistics Catalogue No. 3302.0 (see Table A9.2 in the annexure to this chapter);

v) costs were discounted at 5% per annum; and

vi) benefits were discounted at 0% and 5% per annum.

The results of the modelling are shown in Table 9.7. When both the costs and benefits are discounted at 5%, the cost/QALY is $6,437 at a 12% revision rate and $6,953 at a revision rate of 20%.

[17] 0.0261 for the first 3 months, + 0.0677 for the next 3 months + 0.1653 for the final 6 months = 0.2590

Table 9.9 Cost-utility analysis for total hip replacement (THR) with total revision rates of 12% and 20% over 15 years

ASSUMED COHORT		1000 persons			
% Female		52.6%			
Average Age		Females=70 years; Males=66 years			
Modelling Period		15 years			
		12% Revision Rate		20% Revision Rate	
OUTCOMES		Disc @ 0%	Disc @ 5%	Disc @ 0%	Disc @ 5%
A	Gain in QALYs due to surgery	3517.9	2482.5	3514.9	2480.8
B	Life years lost due to surgery	15.3	14.7	15.8	15.1
C=A-B	Net gain in QALYs	3502.6	2467.8	3499.1	2465.7
D	Net gain in QALYs per person	3.5026	2.4678	3.4991	2.4657
COSTS					
E	Primary Surgery Per Person	$ 14,000	$ 14,000	$ 14,000	$ 14,000
F	Present Value of Revision Per Person	$ 1,886	$ 1,886	$ 3,143	$ 3,143
G=E-F	Present Value Total Cost Per Person	$ 15,886	$ 15,886	$ 17,143	$ 17,143
PERFORMANCE					
H=G/D	**Cost per QALY**	**$ 4,535**	**$ 6,437**	**$ 4,899**	**$ 6,953**

9.5 Conclusions

Based on the assumptions noted above, both hip and knee replacement surgery are highly cost-effective procedures. Even though the cost of hip and knee replacement surgery is high at over $14,000 per operation, the expected benefits are very substantial. Cost per QALY is estimated to be between $6,437 and $6,953 for hip replacement surgery, and $10,804 and $11,671 for knee arthroplasty (see Table 9.7). Even if cost of surgery is somewhat underestimated, performance will still be favourable. It should also be noted that a recent study has indicated that there is substantially lower use of health-care resources by people who are post THR and TKR surgery compared with prior to surgery (March *et al.*, 2002). This cost saving has not been included in these estimates, but will only increase the benefits from THR/TKR surgery.

Our modelling supports hip and knee replacement in people with OA refractory to other forms of treatment as providing increased quality of life at modest cost/QALY. This outcome is robust to changes in the estimated 15 year revision rates.

ANNEXURE TO CHAPTER 9

Table A9.1 Modelled costs for TKR and THR over 15 years

Years post-op	Cost of Surgery		15-Year Revision Rate = 20%			15-Year Revision Rate = 12%		
	Primary	Revision	Annual Rate	Annual Cost	Discounted @ 5% pa	Annual Rate	Annual Cost	Discounted @ 5% pa
0	$14,000	$24,000						
0.5			1.0%	$ 240	$ 234	0.60%	$ 144	$ 140
1			1.0%	$ 240	$ 217	0.60%	$ 144	$ 130
2			1.0%	$ 240	$ 206	0.60%	$ 144	$ 123
3			1.0%	$ 240	$ 195	0.60%	$ 144	$ 117
4			1.0%	$ 240	$ 186	0.60%	$ 144	$ 111
5			1.4%	$ 336	$ 247	0.84%	$ 202	$ 148
6			1.4%	$ 336	$ 235	0.84%	$ 202	$ 141
7			1.4%	$ 336	$ 223	0.84%	$ 202	$ 134
8			1.4%	$ 336	$ 212	0.84%	$ 202	$ 127
9			1.4%	$ 336	$ 201	0.84%	$ 202	$ 121
10			1.6%	$ 384	$ 218	0.96%	$ 230	$ 131
11			1.6%	$ 384	$ 207	0.96%	$ 230	$ 124
12			1.6%	$ 384	$ 197	0.96%	$ 230	$ 118
13			1.6%	$ 384	$ 187	0.96%	$ 230	$ 112
14			1.6%	$ 384	$ 178	0.96%	$ 230	$ 107
Present Value Cost of Revision Surgery			**20.0%**	**$ 4,800**	**$ 3,143**	**12.00%**	**$ 2,880**	**$ 1,886**
Present Value Cost of Surgery				**$18,800**	**$17,143**		**$16,880**	**$15,886**

Table A9.2 Female and male death rates used in modelling (proportion dying between exact age x and exact age x + 1)

Age	Females	Males	Age	Females	Males
66	0.00979	0.02095	77	0.03323	0.06197
67	0.01087	0.02311	78	0.03749	0.06831
68	0.01211	0.02548	79	0.04253	0.07525
69	0.01353	0.02809	80	0.04840	0.08285
70	0.01519	0.03098	81	0.05512	0.09113
71	0.01707	0.03419	82	0.06279	0.10022
72	0.01916	0.03776	83	0.07141	0.10999
73	0.02142	0.04171	84	0.08107	0.12041
74	0.02387	0.04608	85	0.09181	0.13134
75	0.02657	0.05090	86	0.10250	0.14335
76	0.02964	0.05618	87	0.11443	0.15646

Source: ABS Catalogue No. 3302.0, pp. 40-41

Table A9.3 Translation of SF-36 scores to utility values: Knee Replacement Surgery (Bachmeier, March and Cross, 2001)

SF-36 Subscale	Utility function translation		Pre-surgery	Post-surgery		
	Weights	Quadratic Adj	Baseline	3 months	6 months	12 months
Constant	-0.199829					
Physical function	0.488052	0.43403	25.2	38.6	47.9	49.7
Physical role function	0.000047		18	20.2	36.4	49.5
Bodily pain	0.002406		33	48.5	54.1	57.8
General health	0.000669		71.3	69.2	69.2	70.2
Vitality	-0.000212		47	51.2	52.7	58.8
Social function	0.001425		59.2	70.8	70.8	77.7
Emotional role function	-0.000041		54.2	54.0	63.2	64.7
Mental health	0.003314		70.4	72.8	75.6	77.6
Utility score + constant			**0.43776**	**0.55019**	**0.59907**	**0.6284**

Table A9.4 Translation of SF-36 scores to utility values: Hip Replacement surgery (Bachmeier, March and Cross, 2001)

SF-36 Subscale	Utility function translation		Pre-surgery	Post-surgery		
	Weights	Quadratic Adj	Baseline	3 months	6 months	12 months
Constant	-0.197601					
Physical function	0.480275	0.46611	0.224	0.322	0.336	0.353
Physical role function	-0.000112		-0.002	-0.004	-0.005	-0.007
Bodily pain	0.243760	0.45615	0.111	0.165	0.173	0.182
General health	0.000340		0.023	0.024	0.024	0.025
Vitality	0.000947		0.045	0.057	0.058	0.064
Social function	0.001750		0.092	0.122	0.136	0.155
Emotional role function	-0.000300		-0.018	-0.019	-0.021	-0.022
Mental health	0.002614		0.187	0.202	0.210	0.214
Utility score + constant			**0.4635**	**0.67198**	**0.71359**	**0.7672**

10. Arthroscopic Surgery and Joint Irrigation

10.1 Introduction

Arthroscopic surgery for OA is a minimally invasive surgical intervention which is often performed with the aim of avoiding or delaying more extensive surgery, such as arthroplasty (Edelson, Burks and Bloebaum, 1995). It has low associated morbidity and can be repeated (Baumgaertner, Dilworth-Cannon, Vittori *et al*, 1990). Arthroscopy may be undertaken diagnostically to determine underlying joint pathologies, but is also commonly used as a treatment itself.

In treatment of OA, it is most commonly undertaken on the knee, but can also be performed on other joints such as the ankle, elbow or shoulder. It is not generally performed on the hip. Two broad types of arthroscopic surgery, debridement and irrigation, are performed to treat OA. Debridement involves the removal or repair of soft tissue within the effected joint. Irrigation (or lavage) aims to remove debris and inflammatory products from the joint which could be associated with the underlying condition. Irrigation is a standard part of arthroscopic procedures, however when applied as a dedicated procedure, greater amounts of saline are passed through the joint than when debridement is the aim. Joint irrigation may be undertaken arthroscopically, or through needle irrigation.

10.2 Evidence

As noted in the *Selecting the Interventions* report (Segal, Day, Chapman and Osborne, 2002), evidence around surgical interventions for OA is weak, due to the lack of randomised controlled trials published. Only 6 randomised studies of arthroscopy/irrigation could be identified in the literature (Kalunian, Moreland, Klashman *et al*, 2000; Bradley, Heilman, Katz, Gsell, 2002; Chang, Falconer, Stulburg *et al.*, 1993; Mosely, Wray, Kuykendall *et al.*; 1996; Ike, Arnold, Rothschild *et al.,* 1992; Ravaud, Moulinier, Giraudeau, Ayral *et al.*, 1999), and only 2 of these have a sufficient number of participants to be considered adequately powered. Kalunian *et al.* (2000) randomized 90 patients to receive large (3000ml) or minimal (250ml) volumes of arthroscopic saline irrigation. The trend over 12 months favoured the higher volume irrigation group for all outcomes, but statistically significant differences between the groups were only noted for pain. No data was provided on the number of patients who dropped out of the study, adding a degree of uncertainty to these results. In a more recent study, Bradley *et al.,* (2002) randomised 180 patients to tidal needle irrigation (1000ml) or sham irrigation in which the knee capsule was not punctured by the needle. This study with more power to detect differences between study arms than that of Kalunian *et al.* (2000) found at 12 months follow up, a large improvement over baseline for WOMAC scores in both the sham and intervention arms, (17% and 18% respectively). There was no statistical difference between arms for any of the outcome measures. The authors of this study suggest that most, if not all of the effect of irrigation, is attributable to a placebo response.

Although there are important differences between needle irrigation and arthroscopic irrigation which may suggest that these two procedures are not comparable in terms of outcome, other studies have been undertaken which support a placebo effect hypothesis. Chang *et al.* (1993) compared arthroscopic surgery (debridement) with closed needle joint lavage, and showed no difference at one year between the study arms for medication costs, utilisation of medical services or indirect costs related to employment or household help.

Additionally, a trend (non-significant) towards better outcomes was noted for the needle lavage group compared to the arthroscopic group (a subgroup of patients with meniscal tears had a higher probability of improvement following arthroscopic surgery). A pilot study by Mosely *et al.* (1996) found that 6 months post-operatively, 4 of the 5 patients who received placebo arthroscopic surgery indicated that they were happy with the results and would recommend it to their family and friends Taken together, these studies indicate no benefit from arthroscopic surgery compared to needle

irrigation, and that a placebo effect may be sufficient to explain any observed benefits from either of these techniques.

Table 10.1 Placebo effect from arthroscopy (based on tidal irrigation outcomes – Bradley et al., 2002)

Study Arm	WOMAC Scale	WOMAC scores[1]				12 month % change from baseline[1]
		Baseline	3 months	6 months	12 months	
Sham	Pain	14.5	11.2	11.8	11.9	17.9%
	Function	51.5	40.7	42.8	41.9	18.6%
	Stiffness	6.6	5.4	5.7	5.7	13.6%
	Composite	72.6	57.3	60.3	59.5	18.0%
Irrigation	Pain	13.2	10.4	11.1	10.4	21.2%
	Function	45.4	37.9	38.9	37.9	16.5%
	Stiffness	5.8	5.1	5.2	5.1	12.1%
	Composite	64.4	53.4	55.2	53.4	17.1%

Notes:
[1] No significant difference between sham and irrigation arms for any of the outcomes

10.3 Costs and volumes

The cost of arthroscopic surgery for OA varies depending on the actual procedures undertaken. There is no simple way to estimate the mean cost of arthroscopic procedures for OA, or the total costs of such surgery in Australia. Data from the AIHW 1999-2000 Australian Hospitals Data Set indicate that 55,835 arthroscopic procedures were performed in Australia (Table 10.2). However, the proportion of these for knee OA is not reported. This could be established through detailed interrogation of the data set, but this was not possible for this study.

Table 10.2 Arthroscopic procedure 1999-2000

Procedure	Private	Public	Total
Arthroscopic excision of knee	17,122	9,751	26,873
Arthroscopic menisectomy of knee with repair	23,491	5,471	28,962
Total	**40,613**	**15,222**	**55,835**

Source: AIHW Australian Hospitals Data Set

In order to establish the mean cost of arthroscopic surgery for OA, it would be necessary to link the procedures to ICD-10 AM codes, then identify the costs per relevant AR-DRG, focussed only on procedures under-taken primarily for OA. This was not possible to do for this study. Instead, approximate costs for OA arthroscopic procedures have been provided by members of the Advisory Panel, who suggest the cost of the procedure is in the vicinity of $3,500.

We also note that even if just 10% of the procedures identified in Table 10.1 above are for knee OA, the total cost for arthroscopic surgery for OA in Australia would be some $20 million (or at 25% it would be close to $50 million).

10.4 Conclusions

Given the lack of high-quality, randomised studies in the area of arthroscopic surgery for OA, and the range of techniques included in this broad category, the evidence is somewhat equivocal in

relation to beneficial effects. It is possible that most of the gains from these procedures may be attributable to a placebo response. Further research into this area is needed to:

i) clarify the longer term outcomes for individuals following arthroscopic surgery for knee OA, and the relative advantages of the various techniques (lavage, needle irrigation, debridement) – and performance in relation to repeat procedures;
ii) determine rates of progression to knee arthroplasty following arthroscopic surgery;
iii) estimate more precisely the costs & volumes for arthroscopic surgery undertaken for OA;
iv) determine more exactly the nature of the placebo response in arthroscopic surgery and how else that benefit might be obtained;
v) identify the patient groups that might benefit from arthroscopic surgery and irrigation as a treatment for OA; and
vi) determine volume and cost of such surgery performed in Australia on people with OA.

In the meantime, it is not really possible to conduct a cost-utility analysis as the nature of benefits are not sufficiently well demonstrated and defined. Given there is probably a sizeable expenditure on this procedure, establishing its efficacy would seem to be highly desirable.

SECTION III DISCUSSION AND CONCLUSIONS

11. RANKING OF INTERVENTIONS

11.1 Introduction

Through this priority setting research program we have sought to identify desirable resource shifts that might reduce disease burden from osteoarthritis (OA) within current budgets. This has been done by comparing the performance of interventions for the prevention and management of OA. A large number of possible interventions across a range of modalities were identified that might be applied to reduce the incidence of OA and for the management of symptoms. Of all the possible intervention options identified, a total of 19 were selected for the economic evaluation. These covered both prevention and management and several modalities and program types. It was not possible to analyse all feasible interventions, partly due to resource constraints and partly due to gaps in evidence. Economic evaluation of an intervention requires information about efficacy and cost. If this is not available, or the information that is available is of poor quality and/or suggests some confusion about efficacy, then comparison of performance is not possible. In that case additional data collection is indicated. The basis of the choices was discussed in detail in an earlier report (Segal *et al*., 2002). The fact that an intervention has not been analysed should not be taken as any indication of performance. Some interventions were excluded from analysis due to gaps in evidence; for instance, while previous knee injury may be a modifiable risk factor for OA, it could not be included in the modelling given the absence of intervention trials on which to base outcomes. Other possible interventions were excluded simply due to resource constraints on the research team.

The evaluation of several interventions within the one research program is a large task. The evaluation of 19 interventions, within an eighteen-month research program and with a small research team, meant that depth of analysis was inevitably compromised. Of necessity many simplifying assumptions have been adopted, as specified in the descriptions in Chapters 4 to 10. We have also conducted sensitivity analyses to explore the implication of particular assumptions

In order to compare performance of different interventions a common outcome measure was required. As discussed earlier, the QALY has been adopted as the primary outcome measure, with performance defined by cost/QALY. While it is acknowledged that other objectives may be important, such as access to health care, greater equality in health outcomes, greater respect for the consumer in the health system, and community empowerment, health gain was viewed by the Advisory Panel as the dominant concern, and is thus the focus of the performance assessment.

An important advance in this study has been the development of an original method the ‘Transfer to Utility’ (TTU) technique to translate commonly used disease specific or generic health status and quality of life instruments into a utility measure. The technique involved a statistical transformation against the AQoL and is described in detail in Chapters 1 and 3. A commentary on the success of the technique is provided in Chapter 12, where the performance of the Health Sector Wide (HsW) priority-setting model is reviewed. The technique represents an effective mechanism for translating reported outcomes into a single metric, a utility score, which can be combined with time in health state to generate QALY gain or loss for each intervention. The analysis could not have proceeded without such a tool. Not only does it allow comparison between instruments used in OA and interventions applied to OA, it potentially allows comparisons across the entire health sector.

In assessing the performance of the studied interventions, we have sought to classify them on the basis of cost/QALY as either: i) highly cost-effective, for which an expansion of services to support

access, where clinically indicated, should make a net contribution to wellbeing; ii) highly cost-**in**effective, where tighter targeting of services on those most able to benefit appears warranted; and iii) interventions of uncertain value, where the evidence is inadequate to develop sound conclusions and for which additional data gathering is the priority. The quality of the evidence on which the cost-utility estimates are based is variable, with limited trial evidence from RCTs that could be drawn on for this study.

The interventions that have been analysed in this priority setting exercise are listed below in Table 11.1. The key assumptions of the model that underpin the estimates are summarised in Table 11.2. Two attributes commonly varied for the sensitivity analysis: firstly the discounting of future life years lost associated with current deaths, or of quality of life gains associated with THR or TKR surgery, either counted at full ie 0 discount rate, or discounted at 5% pa; and secondly clinical trail results based on either 95% confidence limits (+/- 2 SDs) or +/- 1 SD. Other assumptions have been introduced that are pertinent to specific interventions.

Table 11.1 Interventions for the prevention and management of OA selected for economic evaluation

PRIMARY PREVENTION

Programs to achieve weight loss

- Comprehensive media campaign
- Intensive primary care (GP/nurse) diet and behavioural intervention for overweight/obese patients
- Intensive primary care diet/behavioural program for overweight/obese persons with previous knee injury
- Surgery for obese persons.

PATIENT MANAGEMENT for persons with OA

Patient education

- Lay led program
- GP/clinical nurse educator led (not completed)*

Physical therapies

- Knee brace for person with OA

Exercise/strength training

- Home based basic program
- Home based intensive program
- Primary care clinic intensive program
- Outpatient clinic manual physical therapy and exercise program

Pharmacotherapies – prescription and over-the-counter medications

- Non specific NSAIDs – diclofenac and naproxen
- COX-2 specific NSAIDs - celecoxib

Pharmacotherapies – complementary medicines

- Oral glucosamine sulphate
- ASU (Avocado soybean unsaponifables)
- Topical capsaicin

Surgery

- Total knee replacement
- Total hip replacement
- Knee arthroscope with lavage (Not completed)*

Notes * Cost-utility analysis not completed due insufficient evidence of efficacy.

Table 11.2 Key assumptions underlying the modelling

Attribute and Modality	Key Assumptions
Duration of Benefits	
Primary prevention	20 years
Education/Self Management	2 years
Exercise	1 year
Knee Brace	18 months to 3 years
Total hip and knee replacement	15 years – adjusted for all-cause mortality (ABS mean death rates for a cohort commencing 69 years of age)
NSAIDs[1]	12 months (with treatment assumed to be contiguous with benefit)
Complementary pharmaco-therapies	12 months (with treatment assumed to be contiguous with benefit)
Discount Rates: all modalities	
Costs – incurred or cost savings	Beyond 12 months discounted at 5% per annum
QALY – gains or losses	0% (undiscounted) and 5% per annum
Morbidity	
NSAIDs	Rate of hospital admissions assumed the same across all NSAIDs[1] GI[2] admissions = 2.13/100 patient years CHF[3] admissions = 0.5 /100 patient years
Mortality	
NSAIDs	Death rate assumed the same across all NSAIDs[1] GI = 10% GI hospitalisation rate = 0.00231/ person year NSAID use CHF = 5% CHF hospitalisation rate = 0.00025 Deaths associated with a mean loss of 18.5 years (life expectancy at 65 years of age)
Total hip and knee replacement	Assumed death rate from surgery = 1/1000
Sensitivity analyses	
Common	Discount rate of QALYs 0% and 5% Clinical trial results: where available +/- 2 SD (95% confidence intervals) or +/- 1 SD for NSAIDs
Various	See Chapters 4 to 10

Notes:

4 NSAIDs – diclofenac, naproxen, celecxoib

5 Gastro-intestinal admissions – perforations, ulcers and bleeds

6 CHF chronic heart failure.

11.2 Performance

Appropriateness of care

In considering the relative performance of the various interventions, it must be remembered that they do not all constitute substitutes. In fact modalities will sometimes be complementary to each other, achieving the best results when applied together. Some interventions will be clinically indicated for particular sub-populations of arthritis sufferers. Thus a simple hierarchical interpretation of the results is not appropriate. Rather the results should be interpreted in the context of clinician/expert

advice. The primary filter or decision criteria should be the appropriateness of care, with cost-effectiveness a secondary criteria. The priority-setting task is designed to answer the question of when society should support resource allocation to services that are clinically appropriate, given resource scarcity, which means that not all clinically appropriate services can be funded. It is taken as given that services which are not effective or not clinically appropriate for a particular patient population should not be funded.

Comparative Performance

The performance of the selected interventions is summarised in Table 11.3 and also illustrated in Figure 11.1. Interventions vary in both effectiveness and cost-effectiveness.

The most effective intervention by far is ***hip replacement surgery***. Firstly the estimated utility gain against baseline of 0.304 is higher than any other intervention, and secondly the benefits from surgery accrue over several years, without further investment (except in a small proportion who will require revision surgery – which has been factored into the analysis, as has all-cause mortality, and expected operative mortality of 1/1000). Estimated total QALY gain is 3.52 per hip replacement. ***Knee replacement surgery*** is also highly effective and also confers benefits over many years. Estimated QALY gain per knee replacement is 2.086 While these interventions are high cost at $16,000 to $17,000 on average, because of the high level of benefit cost/QALY is still low at $4,500 to $7,000 for hip replacement and $7,700 to $11,700 for knee replacement surgery.

These results are extremely favourable relative to society expectations regarding 'payment for a life year'. The clearest indication is the decisions by the PBAC in relation to the listing of pharmaceuticals on the Pharmaceutical Benefits Schedule. An analysis of these decisions for 1991-96 by George, Harris and Mitchell (2000) suggests a community norm of at least $40,000/QALY ($1996) as an acceptable threshold for funding. They found that the vast majority of drugs with a cost/QALY of less than $40,000 were recommended for listing 'at current price', while those in the $40,000 to $70,000 range were sometimes recommended for listing, while listing was rare at >$70,000/QALY or life year. Segal and McNeil (1999) have also explored this question, and found that a figure of $40,000/life year is also consistent with the value of life incorporated into decisions concerning road traffic initiatives.

In terms of management of symptoms, many interventions yield a similar level of quality of life utility gain compared to baseline of between 0.08 to 0.12. This includes non-specifics and COX-2 NSAIDS, intensive exercise and strength training, use of knee brace and complementary medicines. However, compared with placebo, the utility gain from all pharmacotherapies is around 0.04 to 0.05. While intensive exercise performs somewhat better at between 0.08 and 0.10

In terms of net QALY gain, ***nsNSAIDs and COX-2 NSAIDs*** perform least well, primarily because of the serious negative side effect profile resulting in an increased risk of hospitalisation and death. This loss in QALYs may, depending on the assumptions, be equivalent to the gains in symptom control, resulting in zero net QALY gain, or at best a net QALY gain of around 0.02.

In relation to the COX-2 NSAIDs (represented by celecoxib), the 'best estimate' based on mean values from seminal clinical trails is a cost/QALY gain of $33,000 discounting future life years lost associated with elevated mortality, or a net QALY loss if future life years lost are counted in full. COX-2 NSAIDs, represented by celecoxib are absolutely dominated by the non-specific NSAIDs, represented by naproxen and diclofenac. This reflects clinical trial results that report equivalent efficacy in symptom control and FDA analysis of side effect profile data, which concludes a failure to establish any differential in mortality or morbidity in the face of a considerably higher price for the COX 2 NSAIDS compared with the nsNSAIDs. This does not preclude the possibility of identifying sub-populations for whom COX 2 NSAIDs are superior.

Primary prevention - appears to be potentially cost-effective, with estimated cost/QALY ranging from $2,000 to $48,000/QALY. However, this estimate is based on observational studies and

modelling, rather than any direct evidence of the effect of weight loss programs on the incidence of OA. It is difficult to gain direct evidence, given the lengthy follow-up period that would be required. The modelling supports the allocation of resources to address obesity through the program types studied: a comprehensive community based media campaign, an intensive primary care intervention for overweight or obese persons, or surgery for persons who are seriously obese. Support for such interventions is also the conclusion of studies of other obesity related disease such as type 2 diabetes[18]. The role for primary prevention strategies targeted at other potentially modifiable risk factors for OA, such as recreational or work related injury, could not be established from the available literature. Research into this possibility would be desirable.

Education – In general the evidence concerning patient education is slight and of uneven quality with contradictory results emerging. Additional RCTs are urgently needed, especially of the lay-lead programs, which appear most promising. A direct comparison with an exercise program might be especially useful. The Lorig group program, run by professionally trained lay-teachers, appears to yield important changes in behaviour and possibly some modest gain in quality of life, which if confirmed suggests a program that is highly cost-effective. However, as the VAS pain result used to estimate QoL gain did not show a statistically significant improvement, definite efficacy could not be presumed. There is no consistent evidence that the professionally lead education programs in OA work, thus a cost-effectiveness estimate could not be calculated.
Knee bracing - using a specially fitted and made product is identified as highly cost-effective, at between $3,700 and $12,200/QALY. The main uncertainty concerns the time for which the brace will be worn.
Exercise/strength training is estimated to be highly cost-effective when delivered via an intensive clinic based program – whether in primary care or an outpatient setting at between $3,000 and $15,000/QALY, (best estimate $5,300 and $8,000/QALY respectively), These results are based on two good quality studies. Home based exercise is less cost-effective, with the more intensive program performing far better than a basic program in terms of effectiveness (0.1 utility gain compared with 0.022 utility gain), and also better in terms of cost-effectiveness - $14,500/QALY (range $10,000 to $34,000), compared with $18,400/QALY (range $9,000 to no benefit).

The natural pharmacotherapies, ***topical capsaicin*** (for knee, hand, elbow and ankle OA) and ***glucosamine sulphate*** are identified as highly cost-effective at less than $5,000/QALY. These drugs demonstrate equivalent efficacy to NSAIDs with an apparently benign side effect profile. The performance of ***ASU*** is less clear with contradictory results from the available studies. The result for topical capsaicin is based on only one study.

[18] Segal et al (1998). Cost-effectiveness of the primary prevention of non-insulin dependent diabetes mellitus. Health Promotion International, vol 13(3):197-209.

Table 11.3 Summary of cost-utility analyses of interventions for Osteoarthritis – prevention and management OA [1]

Program	Est. mean QALY gain per person (0% disc rate)	Est. mean program cost $/person	Estimated mean net $ cost/QALY [2]	Comment
PRIMARY PREVENTION – modelled over 20 years				
1. Comprehensive mass media program for weight loss		4	r 0%: 2,000 - 30,600 r 5%: 3,100 - 48,200	Key assumption - % that engage with program - varied from 0.1% to 1% of target
2. Intensive primary care GP/dietitian intervention for weight loss for overweight/obese persons	0.09	720	r 0%: 7,000 r 5%: 11,400	No long-term data. Impact based on observed relationship between obesity and incidence of OA.
3. As above for overweight/obese persons with previous knee injury	0.08	720	r 0%: 8,400 r 5%: 13,400	
4. Surgery (eg stomach stapling) for obese persons	1.05	15,000	r 0%: 13,100 r 5%: 19,900	Good quality evidence re weight loss. Effect on incidence presumed from epidemiology.
MANAGEMENT				
Education - modelled over 2 years				
5. Lay led group education	0.072	162	R: 2,400 to ∞	Lay led possibly cost-effective. Low cost program, but doubt about efficacy. Further trial evidence required.
6. Primary care – GP/ clinical nurse educator phone support	Equivocal	200-400	∞	Professional led, no evidence of benefit.
Exercise/strength training - modelled over 1 year (discount rate not relevant)				
7. Home based exercise - basic	0.022	400	Best Est 18,400 R: 9,000 to ∞	
8. Home based exercise - intensive	0.100	1,420	Best Est 14,500 R: 10,000 to 34,000	
9. Intensive clinic based exercise - primary care	0.091	480	Best Est 5,300	R_1 based on cost interv ($590) less control ($290), R_2 = based on full interv cost,
10. - outpatient	0.078	590	Best Est 8,000 R_1: 3,000 to 7,600 R_2: 6,100 to 15,000	
Knee brace - modelled over 18 months to 3 years				
11. Specially fitted knee brace	0.12 to 0.355	1,300	Best est 6,000 R: 3,700 to 12,200	Efficacy highly significant and substantial. Range reflects brace used for 18 months to 3 years, and 95% confidence limits on clinical trial results.

Table 11.3 (contd.)

Program	Est. mean QALY gain/ person 0% disc rate	Estimated program cost $/person	Estimated net mean cost/QALY	Comment
Pharmacotherapies				
Prescription / OTC medications – contiguous with treatment				
12. Non specific NSAIDs - naproxen, diclofenac	QoL gain +0.043 mortality loss -0.029 to -0.044	drug 140/yr morbidity 70/yr	r 0%: best est. ∞ R 47,000 to ∞ r 5%: best est. 15,000 R 8,800 to 70,000	Result very sensitive to mortality, discounting of future QALY loss. Cost/QALY range based on +/- 1 SD clinical trial results. Under many assumptions net QALY loss.
13. COX-2 NSAIDs - celecoxib	QoL gain +0.043 mortality loss -0.029 to - 0.044	drug 391/y morbidity 70/yr	r 0%: best est ∞ R 70,900 to ∞ r 5%: best est 32,930 R 21,400 to 83,800	
Complementary medicines – contiguous with treatment				
14. Glucosamine Sulphate	Mean 0.052	180	best estimate 2,900 R 2,400 to 5,100	Based on one study of glucosamine relative to placebo. But other studies report equiv. efficacy to nsNSAIDs. No evidence of serious side effect profile.
15. ASU (Avocado, soy, unsaponifables)	Mean 0.081	333	best estimate 5,000 R 4,000 to ∞	Two studies show large improvement in ASU group, but 1 no sign. diff. (due to massive improvement in placebo group). Ideally requires further evidence.
16. Topical capsaicin	Mean 0.053	236	best estimate 4,500	Efficacy based on 1 RCT in knee, ankle, elbow, wrist, shoulder. Requires additional trial evidence.
Surgery – modelled over 15 years				
17. Total Knee replacement	QoL gain + 2.086 Mortality – 0.015	16,500	r 0%: R 7,700 - 8,300 r 5%: R 10,800 -11,700	QoL gain substantial. Range reflects alt. rate of revision surgery (12% or 20% over 15 yrs). Age/ gender specific mortality applied to cohort as it ages
18. Total Hip replacement	QoL gain + 3.52 Mortality - 0.015	15,900 to 17,100	r 0%: R 4,500 to 4,900 r 5%: R 6,400 to 7,000	
19. Knee arthroscopy with lavage	Equivocal	3,500	∞	Wide range of techniques, results contradictory, some important trials suggest no difference from placebo

Notes: r = discount rate

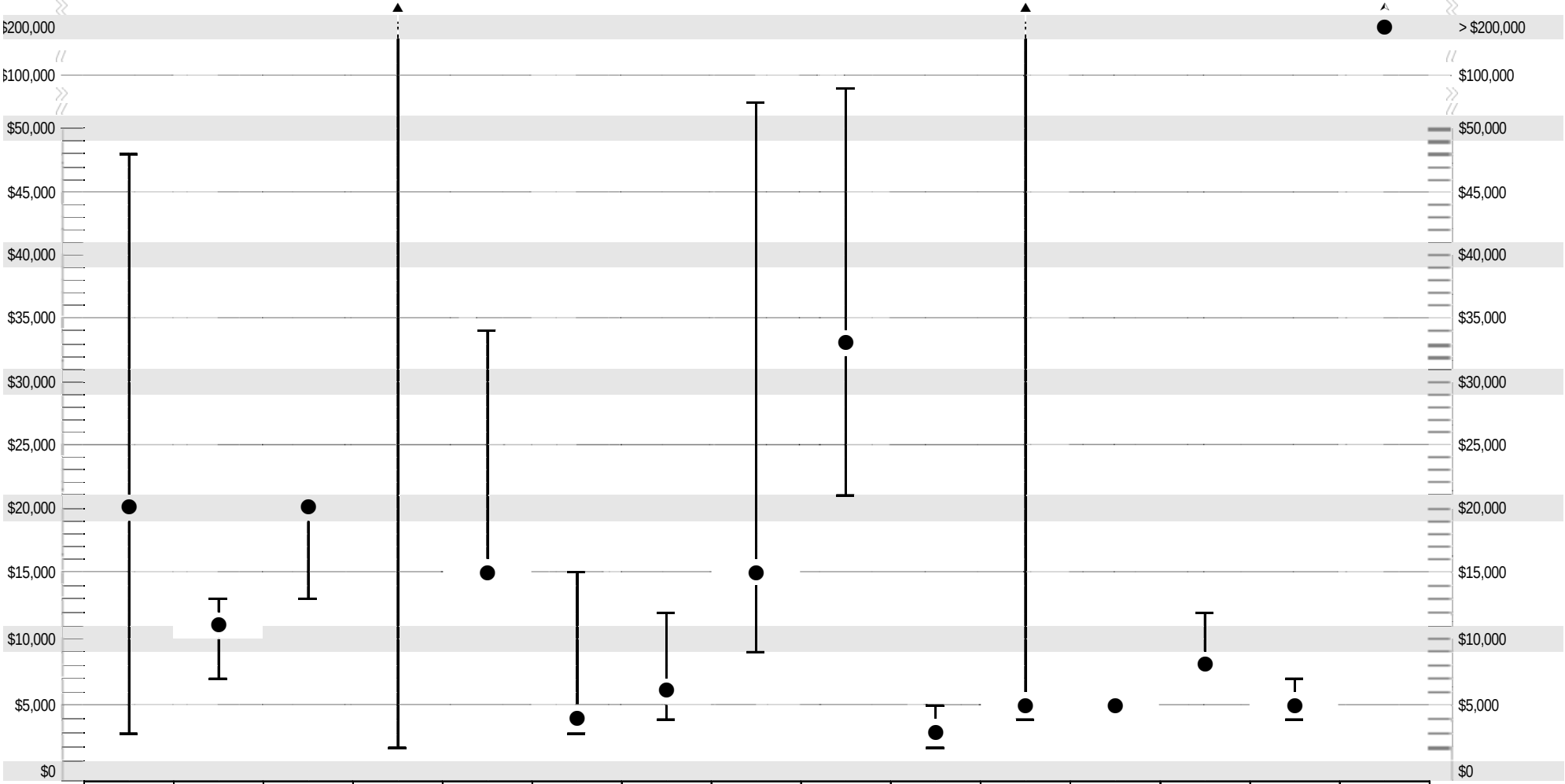
R = range

∞ = no evidence of benefit

[1] Relative to placebo, sub-therapeutic intervention or no intervention for THR and TKR surgery

[2] Rounded to nearest $100.

Figure 11.1 Sensitivity analysis and ranking of interventions (QALYs discounted at 5%)



	Media	GP/Dietitian	Surgery	Lay Led	Home	Clinic	Knee	Non-Specific	COX-2	Glucosamine	ASU	Top Capsaicin	TKR	THR	Arthroscopy	
	Primary Prevention Via Weight Loss			*Education*	*Intensive Exercise*		*Bracing*	*NSAIDs* [1]		*Complementary Medicines*			*Surgery*			
Best Estimate	$20,000	$11,000	$20,000		$15,000	$ 4,000	$ 6,000	$15,000	$33,000	$ 3,000	$ 5,000	$ 5,000	$ 8,000	$ 5,000	>$200,000	Best Estimate
Upper Range	$48,000	$13,000	$20,000	>$200,000	$34,000	$15,000	$12,000	$70,000	$84,000	$ 5,000	>$200,000		$12,000	$ 7,000		Upper Range
Lower Range	$ 3,000	$ 7,000	$13,000	$ 2,000	$15,000	$ 3,000	$ 4,000	$ 9,000	$21,000	$ 2,000	$ 4,000		$ 8,000	$ 4,000		Lower Range

Notes: [1] Non-specific NSAIDs represented by diclofenac and naproxen, COX-2s represented by celebrex

11.3 Other objectives

Improving access to services on the basis of need, and especially to disadvantaged groups, is a stated objective of health policy, and brief consideration is given here to this matter. More detailed consideration of the implication for equity and access and other health system objectives could form a component of future priority setting exercises. Although it can be noted that the Advisory Panel concluded that health gain was the primary objective of the health system and the legitimate concern of a priority setting exercise.

The intervention options vary markedly in their funding base and level of subsidy and out-of-pocket costs to consumers. This has a major influence on access to services. NSAIDs, through their listing on the PBS, are probably the most accessible of all the interventions modelled. They are subsidised and the volume of services provided is open-ended and thus highly responsive to demand, which is determined by the prescribing behaviour of clinicians. All other interventions modelled are less accessible; either they receive no government subsidy – eg complementary medicines (on which the GST is payable), or where subsidised are subject to tight supply restrictions so that supply cannot respond to demand. This results in queues and unmet and unexpressed demand. For instance, typical waiting periods for THR and TKR surgery is over 18 months in the public system. Access to specialised exercise/strength-training programs and to specially fitted knee brace are also restricted by capped funding. Government funding of primary prevention, through programs to control obesity is also limited, with the vast majority of weight loss programs delivered through private providers, at full cost to the user. This has both equity and efficiency consequences.

Whilst a formal study of the distributional impacts has not been completed, it is almost certain that recommendations based on efficiency considerations, if support with public funding, will be consistent with equity objectives.

11.4 Conclusions – desirable resource shifts and research agenda

Because all interventions are not potential substitutes, drawing conclusions about desirable resource shifts from evidence of comparative performance is not entirely straightforward. What can be said is that on efficiency grounds, where an intervention is recommended as clinically appropriate and it is also cost-effective, then health funding and delivery arrangements should ensure that this demand can be met. In this way, burden of harm, will be minimised. If other objectives are considered pertinent, it may be necessary to modify these conclusions.

- Provisions of intensive ***exercise/strength training*** programs for persons with OA should be considered for expansion to allow access to all those for whom it is clinically appropriate.
- Long delays in access to ***THR and TKR surgery*** for persons with OA for whom surgery is clinically indicated is reducing net community wellbeing, given the highly effective and cost-effective nature of these procedures.
- Further evidence for ***lay lead group education*** is needed before definite conclusions can be developed about this modality, given the inconclusive nature of the published evidence.
- The literature on both ***non-specific and COX-2 NSAIDs*** is large and complex. Both drug classes appear effective in managing the symptoms of OA. However the benefits are to some extent offset by the serious side effect profile. It has not yet been established that the higher cost of the COX-2 NSAIDs (represented by celecoxib) compared with the nsNSAIDs - naproxen and diclofenac - is associated with additional benefits, a situation of dominance. But even the nsNSAIDs are less cost-effective than some other modalities. This suggests their use should be targeted at patient sub-groups with greatest capacity for benefit and lower side effect profile (or for whom current quality of life is more important than an elevated risk of death).

- Additional research into NSAIDs is desirable to identify patient groups for whom NSAIDs offer symptom control without excess mortality risk. The analysis of other nsNSAIDs, most of which have a worse side effect profile than the drugs studied, is also important to support conclusions about their resourcing.
- ***Glucosamine and topical capsaicin*** appear to be effective and cost-effective, based on a small number of good quality trials. Additional evidence from further RCTs (some of which are under-way) would be helpful. Access to these therapies is now restricted by funding arrangements, which provide no government subsidy, but rather impose a GST tax.
- There are a number of ***other promising pharmacotherapies*** were not included in this study due to lack of capacity of the study team (such as opioids, chondroitin). This is no comment on their likely cost-effectiveness, which would ideally be evaluated in a follow-up study.
- ***Hip and knee replacement surgery*** is identified as highly effective, with hip surgery identified as the most effective intervention. Both provide substantial relief to persons who otherwise experience a very poor quality of life. There is also evidence of deterioration in health status, while awaiting surgery and poorer outcomes associated with longer waiting time.
- Evidence in relation to the benefits of ***arthroscope with lavage or debridement*** is equivocal, with some important studies showing no difference from placebo and others showing some benefit – albeit against baseline. (This analysis does not concern the role of arthroscopy in investigation but rather in relation to symptom management.) Further investigation of the benefits of this procedure as a component of management seems to be required, but in the interim its use questioned.

These conclusions are summarised in Table 11.5. Specifically interventions that appear highly cost-effective and potentially warrant greater access where clinically indicated include:

- exercise and strength training - the more intensive clinic based programs;
- hip and knee replacement surgery;
- knee brace for persons with knee OA;
- complementary pharmacotherapies - topical capsaicin and glucosamine sulphate.

Therapies that seem to be less cost-effective are generally those that have not been proven to be efficacious compared with placebo, notably arthroscopy and professionally-run patient education.

In relation to both ns and COX-2 NSAIDs a modest immediate quality of life gain is in part countered by an excess mortality risk. The relative balance between the quality of life gain and mortality risk is somewhat difficult to establish from the available evidence, but it would seem that the use of these therapies might be excessive relative to the net benefits obtained and their cost.

There are a number of modalities for which evidence is particularly incomplete. These include primary prevention through weight loss or other strategies, and ASU (a complementary medicine). In relation to primary prevention, under some assumptions this approach is highly cost-effective, and given that obesity is a risk factor for a wide range of chronic conditions, its involvement in the incidence of OA is a further reason to support obesity control.

Further research is required to consider how best to action these findings, to determine the policy response that will best achieve the desired changes in behaviour and resourcing.

Table 11.5 Identified resource shifts that should contribute to a reduction in disease burden from osteoarthritis.

Interventions that appear highly cost-effective	Interventions that appear less cost-effective	Additional evidence required
Supported by strong evidence 1. Hip replacement and knee replacement surgery *Reduce waiting times for those that meet criteria for surgery*	1. COX-2 NSAIDs appear less cost-effective and dominated by nsNSAIDs. *Reduce use. Consider if a target group with greater net benefits can be identified*	Identify possible programs to reduce rate of occupational and recreational knee injury and impact on incidence of OA
2. Exercise/strength training- especially intensive clinic based *Increase public funding and access to such services*	2. Arthroscopy with lavage *Reduce use. Consider withdrawing public subsidy*	Additional trial evidence required concerning complementary medicines ASU
3. Knee brace		Patient education
Supported by weaker evidence		
1. Complementary medicines – topical capcaisin, glucosamine sulphate *Improve access but also seek additional evidence*		
2. Primary prevention – through weight loss – eg intensive primary case based, *Implement pilot, monitor results to establish effect on incidence of OA and overall impact on QoL*		

12. PERFORMANCE OF THE HEALTH SECTOR WIDE (HSW) PRIORITY SETTING MODEL

12.1 Introduction – key issues

There were two primary purposes in conducting a priority setting exercise for osteoarthritis. Firstly to establish the desirable resource shifts for the prevention and management of OA that would reduce disease burden associated with OA; and secondly to further test and refine the selected model – the HsW disease-based priority setting model. The conclusions regarding desirable resource shifts have been discussed in Chapter 11 above, while the performance of the model is considered here.

There were four key issues to be explored in the application of the model to OA:

i. *Feasibility of identifying and classifying a comprehensive set of interventions* and selecting a sub-set for analysis in a way that meet the defined criteria – such as comprehensiveness, access to data/suitability of outcome measure etc.?

ii. *Capacity to develop and apply a single outcome measure*: given OA is a disease that largely influences quality of life, was it possible to compare interventions designed primarily for symptom control and where a wide range of outcome measures would be used that would normally be considered non-comparable?

iii. *Capacity to develop sound conclusions* - given the quality of evidence and techniques available to allow comparison between modalities.

iv. *The value of extending the original model to incorporate a formal Advisory Panel* to assist in access to seminal studies, to provide comment on draft material, and more generally to support the study team as required and to provide an interface between the research team and the clinical community, government officers and consumers.

The first and third research question had already been explored in the context of application of the HsW model to non-insulin dependent diabetes. The model was found to perform successfully in relation to identification of a comprehensive set of interventions for study and in providing a suitable framework for the conduct of comparative economic analysis from which to draw robust conclusions about desirable resource shifts. However, successful application of the Model to another health problem/disease area would enhance confidence in the generalizability of the model and/or suggest modifications as appropriate. As will be discussed, the current application to OA has involved several important refinements, notably the establishment of an expert Advisory Panel, the choice of the QALY as the primary outcome measure, and the development of a specific technique to translate diverse outcomes into a utility score.
Performance of the HsW model in this application to OA relation to these aspects is now considered.

12.2 Identification and selection of interventions

It was possible for the research team to gain an adequate understanding of OA, its disease etiology and factors affecting outcomes and quality of life, to categorise possible intervention options in a useful way. Specifically we established a structure that supported the identification of existing options, plus other plausible options not currently offered to reduce disease burden from OA.

The classification system developed – with only two disease stages, prevention and management – was further subdivided into modality and program type. This proved an effective means to describe options and to draw together the relevant literature. With a capacity to investigate some 18 different interventions, it proved possible to achieve a reasonable spread across modalities and to include all commonly applied therapies, as required by the model.

The criteria for selection of interventions for study proposed in the model proved to be sensible and workable. The model required that the Advisory Panel not be relied upon for this task – which proved appropriate and ensured a wider range of therapies were explored than those with which the Advisory Panel were familiar.

12.3 Adoption/development of single outcome measure

Perhaps the most important and profound contribution of this study was the development of a robust approach to the task of comparing across interventions, where outcomes are expressed in different units.
This represents a major challenge for any large-scale priority setting task. Other studies have traditionally compared only a narrow range of interventions that are expressed in the same units, or attempted to estimate QALYs (as in the Oregon League Table exercise) or DALYs, not directly from the trial literature but from a process involving expert opinion. Recent work with mental health has attempted to use effect size in combination with DALYs as the approach to outcome measurement, but with indifferent success.

All of the alternative methods are seriously flawed. They do not provide a standard measure that has any meaning outside the particular study, and/or they are unable to combine quality of life with mortality, and/or they rely heavily on expert opinion - exposed by the evidenced-based movement in health care as a flawed approach to performance measurement.

The approach developed for this study allows the use of trial outcome data as reported - in terms of a variety of instrument based scores – to be translated into a utility equivalent. The net utility gain, relative to baseline or placebo, can then be calculated and combined with length of time in the health state and estimated mortality impacts to yield an outcome expressed in the same unit - the QALY. This is extremely powerful in enabling comparisons between interventions across various modalities where several instruments are used to measure outcomes.

The technique, which we have called the Transformation to Utility Technique or TTU, is described in full in Chapter 3. In brief it involves the statistical transformation between the instruments commonly used to measure outcomes (in OA) and a utility value. The regression equations for the transformation were based on a survey of persons (with OA) using a specially constructed questionnaire of the common outcome instruments (in this case four) plus a utility instrument – in this case the AQoL. Basic information covering disease site, management approaches adopted, and demographic variables were also collected and tested for significance in the modelling. The sample chosen for this study was a strategic sample. The main requirement was that the sample included people with a range of severity, in terms of health-state, which as reported in Chapter 3 was achieved. The Advisory Panel members were invaluable in assisting us to access, at short notice, a suitable sample of persons with OA.

The robustness of the technique is best assessed by the correlation between the instruments and the AQoL, which was good in the context of individual data at 0.42 (for VAS pain), 0.52 (for the WOMAC) and 0.67 (for the SF-36), and certainly adequate for our purposes. In short, as part of this study we have developed and demonstrated a new technique, the TTU, for comparing outcomes across interventions, which allows existing trial data to be used. This results in a single outcome measure that incorporates both quality of life and mortality, and it is simple to implement and seems robust.

12.4 Capacity to develop conclusions

Gathering of evidence

With any priority setting exercise the gathering of pertinent trial evidence is important. Invariably, regardless of the subject disease, only limited evidence is available of sufficient quality for use in assessing and comparing performance of the various intervention options. One of the outputs of a priority setting exercise is the identification of data gaps, where additional trial evidence is urgently needed. As with the prior priority setting exercise with NIDDM, despite some gaps in the trial evidence, sufficient data of acceptable quality was identified to enable a large number of disparate interventions to be analysed. Similarly, important interventions/modalities for which the evidence is weak, and/or incomplete and for which additional trials are required, were also identified. This additional evidence is needed to ensure appropriate clinical practice as well as for priority setting.

In relation to the management of OA, we identified several hundred potentially pertinent studies – of which over 100 were analysed in detail. Reviews were found to be of limited usefulness, as they tend not to describe interventions or outcomes precisely enough for developing estimates of costs or benefits. Reports of individual trials were accessed to yield the required level of detailed information. As required by the model, evidence of effectiveness and descriptions for costings were based entirely on published studies. Expert opinion was not used for this purpose. The approach of relying entirely on the published literature was found to be feasible as well as preferable.

Capacity to compare performance

Given the evidence we were able to gather and the technique developed to translate trial results into a utility equivalent, it was possible to compare performance across all 18 therapies studied in terms of cost/QALY. This provided for a clear and unequivocal comparison between interventions and a potentially useful contribution to decision making. Although as noted in Chapter 11, this does not mean a simple hierarchy of interventions is appropriate – given the need to ensure choice to meet the needs of different sub-populations and complementarity of some interventions - but rather that advice can be provided concerning which modalities to be expanded and those to be contracted, always in the context of clinical relevance.

A limitation of this study is the failure to take into account any other objectives of health policy – such as equity or community empowerment, or industry support. A means to adequately incorporate other possible objectives has not been established in this study and is a suitable matter for further study.

Policy implications

As noted, it has proved possible to develop conclusions about desirable resource shifts and also research priorities. Ideally this priority setting would be followed by a research program to explore the policy levers, or means available to achieve the desirable resource shifts to establish the most efficient means to modify provider and consumer behaviour so that the potential gains in health and wellbeing can be realised.

12.5 Role of Advisory Panel

The use of an Advisory Panel was a modification to the HsW priority setting model introduced for this application. It is a feature of other approaches to priority setting, such as PBMA.
The role of the Advisory Panel in this application was somewhat different to their use elsewhere. Specifically, the Panel was established to support the research team in accessing the relevant literature, to provide feedback on draft material and broadly to provide an interface between the researchers, clinicians, health department officers and consumers/patients. This proved to be a successful component of the model.

Interestingly, support in relation to access to the literature or in relation to evidence concerning efficacy was least necessary – whereby standard literature searches proved to be most productive. However their strength was in responding to particular technical questions as needed, and that interface between the clinical community, government and consumers and the research team. Of immense value was their support in the development of the ‘Transfer to Utility’ technique, in

providing access to a suitably diverse population of persons with OA to complete the questionnaire. Further, their critical feedback on draft material was most welcome. The possibility of communicating study results to the clinical community, health agencies and consumers is also of potential value. Should the research proceed to exploration of options for implementation, this could benefit from a continued role of an expanded Advisory Panel.

In terms of the process for working with Advisory Panel members, we found drawing together members for a face-to-face meeting a difficult task given the pressing commitments of members, but that the occasional face-to-face meeting supported by email contact as required proved an effective means of communication.

We would now adopt the Advisory panel as a basic feature of the HsW Priority setting model.

12.6 Overview: success of the HsW priority setting model

Overall the model worked extremely well and provided a valid and workable approach to the establishment of priorities for reducing disease burden from OA. It has also enabled a research agenda to be identified to address critical data gaps. The TTU technique developed to translate the outcome results from various disease specific and health status instruments into utility values proved extremely valuable and is likely to have wide application.

The HsW model has now been applied to two distinct diseases with clear success and within quite modest research budgets (of less than $300,000) we have no reason to believe its application to other diseases or health problems would not meet with similar success.

REFERENCES

Alberto, L. and Rodriguez, G. (1997) "NSAID,ulcers and risk : a collaborative meta-analysis", *Seminars in Arthritis and Rheumatism,* **26,** pp. 16-20.

Altman, R., Aven, A., Holmburg, C., Pfeifer, L., Sack, M. and Young, G. (1994) "Capsaicin cream 0.025% as monotherapy for osteoarthritis : a double-blind study", *Seminars in Arthritis & Rheumatism,* **23**, pp. 25-33.

American College of Rheumatology (2000) "Recommendations for the medical management of OA of the hip and knee", *Arthritis and Rheumatism,* **43**, pp. 1905-1915.

Angst, F., Aeschlimann, A., Steiner, W. and Stucki, G. (2001) "Responsiveness of the WOMAC osteoarthritis index as compared with the SF-36 in patients with osteoarthritis of the legs undergoing a comprehensive rehabilitation intervention", *Ann Rheum Dis,* **60,** pp. 834-40.

Appelboom, T., Schuermans, J., Verbruggen, G., Henrotin, Y. and Reginster, J. Y. (2001) "Symptoms modifying effect of avocado/soybean unsaponifiables (ASU) in knee osteoarthritis. A double blind, prospective, placebo-controlled study", *Scand J Rheumatol,* **30**, pp. 242-7.

Ashley, J. M., St Jeor, S. T., Schrage, J. P., Perumean-Chaney, S. E., Gilbertson, M. C., McCall, N. L. and Bovee, V. (2001) "Weight control in the physician's office", *Arch Intern Med,* **161,** pp. 1599-604.

Association, A. O. (2001) "National Joint Replacement Registry Annual Report 2001".

Australian Bureau of Statistics (1995) *National Health Survey: Cat 4399.0*.

Australian Bureau of Statistics (1995) *National Health Survey: Cat 4399.0*.

Bachmeier, C., March, L. and Cross, M. (2001) "A comparison of outcomes in OA patients undergoing total hip and knee replacement", *Osteoarthritis and Cartilage,* **9,** pp. 137-146.

Bachmeier, C., March, L. and Cross, M. (2001) "A comparison of outcomes in OA patients undergoing total hip and knee replacement", *Osteoarthritis and Cartilage,* **9,** pp. 137-146.

Baker, K. R., Nelson, M. E., Felson, D. T., Layne, J. E., Sarno, R. and Roubenoff, R. (2001) "The efficacy of home based progressive strength training in older adults with knee osteoarthritis: a randomized controlled trial", *J Rheumatol,* **28,** pp. 1655-65.

Baumgaertner, M., Dilworth-Cannon, W., Vittori, J. *et al.* (1990) "Arthroscopic debridement of the Arthritis Knee", *Clinical Orthopaedics and Related Research,* **253,** pp. 197-202.

Bellamy, N., Kaloni, S., Pope, J., Coulter, K. and Campbell, J. (1998) "Quantitative rheumatology: a survey of outcome measurement procedures in routine rheumatology outpatient practice in Canada", *J Rheumatol,* **25,** pp. 852-8.

Bensen, W. Fiechtner, J., McMillen, J., *et al*. (1999) "Treatment of OA with celecoxib, a cyclooxygenase-2 inhibitor: a rondamised, controlled trial", *Mayo Clinical Proceedings*, **74**, pp. 109-1105.

Blotman, F., Maheu, E., Wulwik, A., Caspard, H. and Lopez, A. (1997) "Efficacy and safety of avocado/soybean unsaponifiables in the treatment of symptomatic osteoarthritis of the knee and hip. A prospective, multicenter, three-month, randomized, double-blind, placebo-controlled trial", *Rev Rhum Engl Ed,* **64**, pp. 825-34.

Bombardier, C., Laine, L., Reicin, A., *et al*. (2000) "Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis", *NEJM*, **343**, pp. 1520-1528.

Bowerman, S., Bellman, M., Saltsman, P., Garvey, D., Pimstone, K., Skootsky, S., Wang, H. J., Elashoff, R. and Heber, D. (2001) "Implementation of a primary care physician network obesity management program", *Obes Res,* **9 Suppl 4,** pp. 321S-325S.

Bradley, J. D., Brandt, K. D., Katz, B. P., Kalasinski, L. A. and Ryan, S. I. (1991) "Comparison of an antiinflammatory dose of ibuprofen, an analgesic dose of ibuprofen, and acetaminophen in the treatment of patients with osteoarthritis of the knee", *N Engl J Med,* **325**, pp. 87-91.

Bradley, J. D., Heilman, D. K., Katz, B. P., Gsell, P., Wallick, J. E. and Brandt, K. D. (2002) "Tidal irrigation as treatment for knee osteoarthritis: a sham- controlled, randomized, double-blinded evaluation", *Arthritis Rheum,* **46,** pp. 100-8.

Brazier, J., Usherwood, T., Harper, R. and Thomas, K. (1998) "Deriving a preference-based single index from the UK SF-36 Health Survey", *Journal of Clinical Epidemiology,* **51,** pp. 1115-28.

Buchbinder, R., Jolley, D. and Wyatt, M. (2001a) "Breaking the back of back pain", *Medical Journal of Australia,* **175,** pp. 456-457.

Buchbinder, R., Jolley, D. and Wyatt, M. (2001b) "Population based intervention to change back pain beliefs and disability: three part evaluation", *BMJ,* **322,** pp. 1516-20.

Cannon, G., Caldwell, J., Holt, P., *et al*. (2000) "Rofecoxib, a specific inhibitor of cyclooxygenase 2, with clinical efficacy comparable with that of diclofenac sodium: results of a one year randomised, clinical trial with patients with OA of the knee and hip", *Arthritis and Rheumatism*, **43**, pp. 978-987.

Carter, R., Stone, C., Vos, T., Hocking, J., Mihalopoulos, C., Peacock, S. Stephen, C. (2001) *Trial of Program Budgeting and Marginal Analysis (PBMA) to Assist Cancer Control Planning in Australia,* Centre for Health Program Evaluation, Melbourne.

Chang, R., Falconer, J., Stulburg, S. *et al.* (1993) "A randomised, controlled trial of arthroscopic surgery versus joint lavage for patients with OA of the knee", *Arthritis and Rheumatism,* **36,** pp. 289-296.

Coggon, D., Croft, P., Kellingray, S., Barrett, D., McLaren, M. and Cooper, C. (2000) "Occupational physical activities and osteoarthritis of the knee", *Arthritis Rheum,* **43,** pp. 1443-9.

Coggon, D., Reading, I., Croft, P., McLaren, M., Barrett, D. and Cooper, C. (2001) "Knee osteoarthritis and obesity", *Int J Obes Relat Metab Disord,* **25,** pp. 622-7.

Cohen, J. (1988) *Statistical power analysis for the behavioral sciences*, Hillside, NJ, L. Erlbaum Associates.

Cushnaghan, J., McCarthy, C. and Dieppe, P. (1994) "Taping the Patella Medially - a New Treatment for Osteoarthritis of the Knee Joint", *Bmj,* **308,** pp. 753-755.

Deal, C. L., Schnitzer, T. J., Lipstein, E., Seibold, J. R., Stevens, R. M., Levy, M. D., Albert, D. and Renold, F. (1991) "Treatment of arthritis with topical capsaicin: a double-blind trial", *Clin Ther,* **13**, pp. 383-95.

Deyle, G. D., Henderson, N. E., Matekel, R. L., Ryder, M. G., Garber, M. B. and Allison, S. C. (2000) "Effectiveness of manual physical therapy and exercise in osteoarthritis of the knee. A randomized, controlled trial", *Ann Intern Med,* **132,** pp. 173-81.

Douketis,J.D, Kearon, C., Bates, S., *et al*. (1998) "Risk of fatal pulmonary embolism in patients with treated venous thromboembolism", *JAMA,* **279**, pp. 458-62.

Draper, E. R., Cable, J. M., Sanchez-Ballester, J., Hunt, N., Robinson, J. R. and Strachan, R. K. (2000) "Improvement in function after valgus bracing of the knee. An analysis of gait symmetry", *J Bone Joint Surg Br,* **82,** pp. 1001-5.

Eccles, M., Freemantle, N. and Mason, J. (1998) "North of England evidence based guideline development project: guideline on the use of aspirin as secondary prophylaxis for vascular disease in primary care. North of England Aspirin Guideline Development Group", *Bmj,* **316**, pp. 1303-9.

Edelson, R., Burks, R. and Bloebaum, R. (1995) "Short term effects of knee washout for OA", *American journal of Sports Medicine,* **23,** pp. 345-349.

Ehrich, E.W., Davies, G.M., Watson, D.J., Bolognese, J.A., Seidenberg, B.C. and Bellamy, N. (2000) "Minimal perceptible clinical improvement with the Western Ontario and McMaster Universities osteoarthritis index questionnaire and global assessments in patients with osteoarthritis", *J Rheumatol*, **27**, pp. 2635-41.

Eikelboom, J. W., Quinlan, D. J. and Douketis, J. D. (2001) "Extended-duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of the randomised trials", *Lancet,* **358,** pp. 9-15.

Ettinger, W. H., Burns, R., Messier, S. P., Applegate, W., Rejeski, W. J., Morgan, T., Shumaker, S., Berry, M. J., O'Toole, M., Monu, J. and Craven, T. (1997) "A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. The Fitness Arthritis and Seniors Trial (FAST)", *Jama,* **277,** pp. 25-31.

Felson, D. T. and Zhang, Y. (1998) "An update on the epidemiology of knee and hip osteoarthritis with a view to prevention", *Arthritis Rheum,* **41,** pp. 1343-55.

Felson, D. T., Anderson, J. J., Naimark, A., Walker, A. M. and Meenan, R. F. (1988) "Obesity and knee osteoarthritis. The Framingham Study", *Ann Intern Med,* **109,** pp. 18-24.

Geba, G. P., Weaver, A. L., Polis, A. B., Dixon, M. E. and Schnitzer, T. J. (2002) "Efficacy of rofecoxib, celecoxib, and acetaminophen in osteoarthritis of the knee: a randomized trial", *Jama,* **287**, pp. 64-71.

Geerts, W.H., Heit, J.A., Clagett, G.P., *et al*. (2001) "Prevention of venous thromboembolism", *Chest*, **119**, pp. 132S-75

George, B., Harris, A. and Mitchell, A. (2001) "Cost-effectiveness analysis and the consistency of decision making: evidence from pharmaceutical reimbursement in Australia (1991 to 1996)", *Pharmacoeconomics,* **19,** pp. 1103-9.

George, B., Harris, A. and Mitchell, A. (2001) “Cost-effectiveness analysis and the consistency of decision making: evidence from pharmaceutical reimbursement in Australia (1991-1996)”, *Pharmacoeconomics*, **19**, pp. 1103-9.

Guccione, A. A., Felson, D. T., Anderson, J. J., Anthony, J. M., Zhang, Y., Wilson, P. W., Kelly-Hayes, M., Wolf, P. A., Kreger, B. E. and Kannel, W. B. (1994) "The effects of specific medical conditions on the functional limitations of elders in the Framingham Study", *Am J Public Health,* **84,** pp. 351-8.

Hajat, S., Fitzpatrick, R., Morris, R. *et al*. (2002) "Does waiting for total hip replacement matter? Prospective cohort study'. *J Health Serv Res Policy*, **7(1)**, pp.19-25

Hawker, G., Melfi, C., Paul, J., Green, R. and Bombardier, C. (1995) "Comparison of a generic (SF-36) and a disease specific (WOMAC) (Western Ontario and McMaster Universities Osteoarthritis Index) instrument in the measurement of outcomes after knee replacement surgery", *J Rheumatol,* **22,** pp. 1193-6.

Hawthorne, G., Richardson, J. and Day, N. (2001) "A comparison of the Assessment of Quality of Life (AQoL) with four other generic utility instruments", *Ann Med,* **33,** pp. 358-370.

Hawthorne, G., Richardson, J. and Osborne, R. (1999) "The Assessment of Quality of Life (AQoL) Instrument: a psychometric measure of health related quality of life", *Quality of Life Research,* **8,** pp. 209-224.

Heit, J.A., Elliott, C.G., Trowbridge, A.A., *et al*. for the Ardeparin Arthroplasty Study Group. (2000) "Ardeparin sodium for extended out of hospital prophylaxis against venous thromboembolism after total hip or knee replacement. A randomised, double-blind, placebo-controlled trial", *Ann Intern Med*, **132**, pp. 853-861.

Henry, D. and Robertson J. (1993) "Nonsteroidal anti-inflammatory drugs and peptic ulcer hospitalization rates in New South Wales", *Gasteroenterology*, **104**, pp. 1083-91.

Henry, D., Lim, L., Rodriguex, L., *et al.* (1996) "Variability in risk of GI complications with individual NSAIDs: results of a collaborative meta-analysis", *BMJ*, **312**, pp. 1563-1566.

Hernandez-Diaz, S. and Rodriguez, L. A. (2002) "Incidence of serious upper gastrointestinal bleeding/perforation in the general population: review of epidemiologic studies", *J Clin Epidemiol,* **55**, pp. 157-63.

Hewett, T. E., Noyes, F. R., Barber-Westin, S. D. and Heckmann, T. P. (1998) "Decrease in knee joint pain and increase in function in patients with medial compartment arthrosis: a prospective analysis of valgus bracing", *Orthopedics,* **21,** pp. 131-8.

Hogan, D. B., Campbell, N. R., Crutcher, R., Jennett, P. and MacLeod, N. (1994) "Prescription of nonsteroidal anti-inflammatory drugs for elderly people in Alberta", *Cmaj,* **151**, pp. 315-22.

Huber, O., Bounameaux, H. and Borst, F. (1992) "Postoperative pulmonary embolism after hospital discharge: an underestimated risk", *Arch Surg*, **127**, pp. 310-313.

Ike, R., Arnold, W., Rothschild, E. *et al.* (1992) "Tidal irrigation versus conservative medical management in patients with OA of the knee : a prospective randomised study", *Journal of Rheumatology,* **19,** pp. 772-779.

Juni, P., Rutjes, A.W. and Dieppe, P.A. (2002) "Are selective COX 2 inhibitors superior to traditional non steriodal anti-inflammatory drugs?", *BMJ*, **324**, pp. 2387-8.

Kalunian, K., Moreland, L., Klashman, D. *et al.* (2000) "Visually-guided irrigation in patients with early knee OA : a multicentre randomised, controlled trial", *Osteoarthritis and Cartilage,* **8,** pp. 412-418.

Karlsson, J., Sjostrom, L. and Sullivan, M. (1998) "Swedish obese subjects (SOS)--an intervention study of obesity. Two-year follow-up of health-related quality of life (HRQL) and eating behavior after gastric surgery for severe obesity", *International Journal of Obesity & Related Metabolic Disorders,* **22,** pp. 113-26.

Karvetti, R. L. and Hakala, P. (1992) "A seven-year follow-up of a weight reduction programme in Finnish primary health care", *Eur J Clin Nutr,* **46,** pp. 743-52.

Kirkley, A., Webster-Bogaert, S., Litchfield, R., Amendola, A., MacDonald, S., McCalden, R. and Fowler, P. (1999) "The effect of bracing on varus gonarthrosis", *J Bone Joint Surg Am,* **81,** pp. 539-48.

Kirwan, J., Currey, H., Freeman, M. *et al.* (1994) "Overall long-term impact of total hip and knee joint replacement surgery on patients with OA and RA", *British Journal of Rheumatology,* **33,** pp. 357-360.

Langman, M.J., Jensen, D.M., Watson, D.J., Harper, S.E, Zhao, P.L., Quan, H., Bolognese, J.A. and Simon, T.J. (1999) "Adverse upper gastrointestinal effects of rofecoxib compared with NSAIDs", *JAMA*, **282**, PP. 1929-33.

Leclerc, J.R., Gent, M., Hirsh, J., *et al*. (1998) "The incidence of venographic venous thromboembolism during and after prophylaxis with enoxaparin: a multi-institutional cohort study in patients who underwent hip or knee arthroplasty", *Arch Intern Med,* **158**, pp. 873-78.

Lequesne, M., Maheu, E., Cadet, C. and Dreiser, R. L. (2002) "Structural effect of avocado/soybean unsaponifiables on joint space loss in osteoarthritis of the hip", *Arthritis Rheum,* **47**, pp. 50-8.

Lindenfeld, T. N., Hewett, T. E. and Andriacchi, T. P. (1997) "Joint loading with valgus bracing in patients with varus gonarthrosis", *Clin Orthop,***,** pp. 290-7.

Lord, J., Victor, C., Littlejohns, P., Ross, F. M. and Axford, J. S. (1999) "Economic evaluation of a primary care-based education programme for patients with osteoarthritis of the knee", *Health Technol Assess,* **3,** pp. 1-55.

Lorig, K. and Holman, H. R. (1989) "Long-term outcomes of an arthritis self-management study: effects of reinforcement efforts", *Social Science & Medicine,* **29,** pp. 221-4.

Lorig, K., Lubeck, D., Kraines, R. G., Seleznick, M. and Holman, H. R. (1985) "Outcomes of self-help education for patients with arthritis", *Arthritis Rheum,* **28,** pp. 680-5.

Lorig, K., Seleznick, M. Lubeck, D. Ung, E. Chastain, R.L., Holman, H>R> (1989) "The benefitical outcomes of the arthritis self-management course are not adequately explained by behavior change", *Arthritis and Rheumatism,* **32,** pp. 91-95.

Maheu, E., Mazieres, B., Valat, J. *et al*. (1998) "Symptomatic efficacy of avocado/soybean unsaponifiables in the treatment of OA of the knee and hip.", *Arthritis and Rheumatism,* **41**, pp. 81-91.

Manek, N. J. (2001) "Medical management of osteoarthritis", *Mayo Clin Proc,* **76**, pp. 533-9.

March, L., Cross, M., Tribe, K., Lapsley, H., Courtenay, B. and Brooks, P. (2002) "Cost of joint replacement surgery for osteoarthritis: the patients' perspective", *J Rheumatol,* **29,** pp. 1006-14.

March, L., Irwig, L., Schwarz, J., Simpson, J., Chock, C. and Brooks, P. (1994) "n of 1 trials comparing a non-steroidal anti-inflammatory drug with paracetamol in osteoarthritis", *BMJ,* **309**, pp. 1041-5; discussion 1045-6.

Mathers, C., Penm, R. (1999a) *Health system costs of injury, poisoning and musculoskeletal disorders in Australia 1993-94,* AIHW: Cat No HWE 12, Canberra.

Mathers, C., Vos, T., Stevenson, C. (1999b) *The Burden of Disease and Injury in Australia,*AIHW, Canberra.

Matsuno, H., Kadowaki, K. M. and Tsuji, H. (1997) "Generation II knee bracing for severe medial compartment osteoarthritis of the knee", *Arch Phys Med Rehabil,* **78,** pp. 745-9.

Mazzuca, S. A., Brandt, K. D., Katz, B. P., Chambers, M., Byrd, D. and Hanna, M. (1997) "Effects of self-care education on the health status of inner-city patients with osteoarthritis of the knee", *Arthritis Rheum,* **40,** pp. 1466-74.

Mazzuca, S. A., Brandt, K. D., Katz, B. P., Hanna, M. P. and Melfi, C. A. (1999) "Reduced utilization and cost of primary care clinic visits resulting from self-care education for patients with osteoarthritis of the knee", *Arthritis & Rheumatism,* **42,** pp. 1267-73.

McAlindon, T. E., Cooper, C., Kirwan, J. R. and Dieppe, P. A. (1993) "Determinants of disability in osteoarthritis of the knee", *Ann Rheum Dis,* **52,** pp. 258-62.

Miles, A. (2001) "Using the mass-media to target obesity: an analysis of the characteristics and reported behaviour change of participants in the BBC's 'Fighting Fat, Fighting Fit' campaign", *Health Education Research,* **16,** pp. 357-72.

Moseley, J., Wray, N., Kuykendall, D. *et al.* (1996) "Arthroscopic treatment of OA of the knee : a prospective randomised placebo-controlled trial : results of a pilot study", *Am J Sports Med,* **24,** pp. 28-34.

Muller-Fassbender, H. (1987) "Double-blind clinical trial of S-adenosylmethionine versus ibuprofen in the treatment of osteoarthritis", *Am J Med,* **83**, pp. 81-3.

Murray, D. W., Britton, A. R. and Bulstrode, C. J. (1996) "Thromboprophylaxis and death after total hip replacement", *J Bone Joint Surg Br,* **78,** pp. 863-70.

National Prescribing Service (2000) *COX-2-selective NSAIDs : New wonder drugs ?,* National Prescribing Service, Sydney.

Newman, J., Shah, C. and Nilen, A. (1998) "Unicompartmental or total knee replacement ? Five-year results of a prospective randomised trial of 102 OA knees with unicompartmental arthritis.", *Journal of Bone and Joint Surgery,* **80,** pp. 862-865.

Nicolaides,A.N..(2001) "Prevention of venous thromboembolism: International Consensus Statement – guidelines compiled in accordance with the scientific evidence", *Int Angiol*, **20**, pp. 1-37

O'Reilly, S. C., Muir, K. R. and Doherty, M. (1999) "Effectiveness of home exercise on pain and disability from osteoarthritis of the knee: a randomised controlled trial", *Annals of the Rheumatic Diseases,* **58,** pp. 15-9.

Osborne, R. H., Segal, L. and Day, S. (2001) *Priority Setting in Musculoskeletal Disorders: A Focus on Osteoarthritis,* Working Paper 128, Health Economics Unit, Monash University, Melbourne.

Osborne, R. H., Segal, L. and Day, S. (2001) *Priority Setting in Musculoskeletal Disorders: A Focus on Osteoarthritis,* Working paper 128, ISBN 1 876662 48 4, Health Economics Unit, Monash University, Melbourne.

Page, J. and Henry, D. (2000) "Consumption of NSAIDs and the development of congestive heart failure in elderly patients ; an underrecognised public health problem", *Archives of Internal Medicine,* **160**, pp. 777-784.

Peloso, P. M. (2001) "Opioid therapy for osteoarthritis of the hip and knee: use it or lose it?", *J Rheumatol,* 28, pp. 6-11.

Peloso, P. M., Bellamy, N., Bensen, W., Thomson, G. T., Harsanyi, Z., Babul, N. and Darke, A. C. (2000) "Double blind randomized placebo control trial of controlled release codeine in the treatment of osteoarthritis of the hip or knee", *Journal of Rheumatology,* **27**, pp. 764-71.

Pencharz, J. N., Grigoriadis, E, Jansz, G.F., Bombardier, C. (2001) "A Critical Appraisal of Clinical Practice Guidelines for the Treatment of Lower Limb Osteoarthritis", *Arthritis Research,* **4**, pp. c36-44.

Pincus, T., Koch, G. G., Sokka, T., Lefkowith, J., Wolfe, F., Jordan, J. M., Luta, G., Callahan, L. F., Wang, X., Schwartz, T., Abramson, S. B., Caldwell, J. R., Harrell, R. A., Kremer, J. M., Lautzenheiser, R. L., Markenson, J. A., Schnitzer, T. J., Weaver, A., Cummins, P., Wilson, A., Morant, S. and Fort, J. (2001) "A randomized, double-blind, crossover clinical trial of diclofenac plus misoprostol versus acetaminophen in patients with osteoarthritis of the hip or knee", *Arthritis Rheum,* **44**, pp. 1587-98.

Pulmonary Embolism Prevention (PEP) Trial Collaborative Group (2000) "Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial", *Lancet*, **355**(9212), pp.1295-1302.

Quiding, H., Grimstad, J., Rusten, K., Stubhaug, A., Bremnes, J. and Breivik, H. (1992) "Ibuprofen plus codeine, ibuprofen, and placebo in a single- and multidose cross-over comparison for coxarthrosis pain", *Pain,* **50**, pp. 303-7.

Ravaud, P., Moulinier, L., Giraudeau, B., Ayral, X., Guerin, C., Noel, E., Thomas, P., Fautrel, B., Mazieres, B. and Dougados, M. (1999) "Effects of joint lavage and steroid injection in patients with osteoarthritis of the knee: results of a multicenter, randomized, controlled trial", *Arthritis & Rheumatism,* **42,** pp. 475-82.

Reginster, J. Y., Deroisy, R., Rovati, L. C., Lee, R. L., Lejeune, E., Bruyere, O., Giacovelli, G., Henrotin, Y., Dacre, J. E. and Gossett, C. (2001) "Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial", *Lancet,* **357**, pp. 251-6.

Robertsson, O., Knutson, K., Lewold, S. and Lidgren, L. (2001) "The Swedish Knee Arthroplasty Register 1975-1997: an update with special emphasis on 41,223 knees operated on in 1988-1997", *Acta Orthop Scand,* **72,** pp. 503-13.

Robinson, K.S., Anderson, D.R., Gross, M. *et al*. “Ultrasonic screening before hospital discharge for deep vein thrombosis after arthroplasty: the post-arthroplasty screening study – a randomised controlled trial” *Ann Intern Med* (10907); **127**, pp. 439-45

Saag, K., van der Heijde, D., Fisher, C. *et al*. (2000) "Rofexocib, a new COX-2 inhibitor, shows sustained efficacy, comparable with other NSAIDs: a 6-week and 1 year trial inpatients with OA:, *Archives of Family Medicine*, **9**, pp. 1124-1134.

Scott, D. L., Berry, H., Capell, H., Coppock, J., Daymond, T., Doyle, D. V., Fernandes, L., Hazleman, B., Hunter, J., Huskisson, E. C., Jawad, A., Jubb, R., Kennedy, T., McGill, P., Nichol, F., Palit, J., Webley, M., Woolf, A. and Wotjulewski, J. (2000) "The long-term effects of non-steroidal anti-inflammatory drugs in osteoarthritis of the knee: a randomized placebo-controlled trial", *Rheumatology (Oxford),* **39**, pp. 1095-101.

Scurr, J.H., Coleridge-Smith, P.D., Hasty, J.H. (1988) “Deep venous thrombosis: a continuing problem”, *BMJ* 1988; 297:28.

Segal, L. (2000) *Allocative Efficiency in Health: Development of a Priority Setting Model and Application to Non-insulin Dependent Diabetes Mellitus,* Monash University, Melbourne.

Segal, L. (2000) *Allocative Efficiency in Health: Development of a Priority Setting Model and Application to Non-insulin Dependent Diabetes Mellitus,* Monash University, Melbourne.

Segal, L. and Chen, Y. (2000) *Priority Setting For Health: Options Paper,* Report to the Population Health Division, Department of Health and Aged Care, Monash University, Melbourne.

Segal, L. and Chen, Y. (2001) *Priority Setting Models for Health,* Working Paper 119, Health Economics Unit, Monash University, Melbourne.

Segal, L. and Chen, Y. (2001a) *Priority Setting Models for Health,* Working Paper 119, Health Economics Unit, Monash University, Melbourne.

Segal, L. and Chen, Y. (2001b) *Priority setting models for health. The role of priority setting and a critique of alternative models - full report,* Research Report 22, Health Economics Unit, Monash University, Melbourne.

Segal, L. and McNeill, H. (2000) *Quality of life and obesity*, Research Report No. 17, Health Economics Unit, Centre for Health Program Evaluation, Monash University, Melbourne.

Segal, L., Day, S., Chapman, A. and Osborne, R. (2002) *Priority setting in osteoarthritis: selecting the interventions,* Report to the Population Health Division, Department of Health and Ageing, Health Economics Unit, Monash University, Melbourne

Segal, L., Day, S., Chapman, A. and Osborne, R. (2002) *Priority setting in osteoarthritis: selecting the interventions,* Report to the Population Health Division, Department of Health and Ageing, Health Economics Unit, Monash University, Melbourne.

Segal, L., Day, S., Chapman, A. and Osborne, R. (2002) *Priority setting in osteoarthritis: selecting the interventions,* Report to the Population Health Division, Department of Health and Ageing, Health Economics Unit, Monash University, Melbourne.

Segal, L., Day, S., Chapman, A. and Osborne, R. (2002) *Priority setting in osteoarthritis: selecting the interventions,* Report to the Population Health Division, Department of Health and Ageing, Health Economics Unit, Monash University, Melbourne.

Segal, L., Day, S., Chapman, A. and Osborne, R. (2002) *Priority setting in osteoarthritis: selecting the interventions,* Report to the Population Health Division, Department of Health and Ageing, Health Economics Unit, Monash University, Melbourne.

Sharma, L., Song, J., Felson, D. T., Cahue, S., Shamiyeh, E. and Dunlop, D. D. (2001) "The role of knee alignment in disease progression and functional decline in knee osteoarthritis", *JAMA,* **286,** pp. 188-95.

Silverstein, F., Faich, G., Goldstein, J. *et al*. (2000) "GI toxicity with celecoxib vs NSAIDs for OA and RA: the CLASS Study : a randomised controlled trial.", *JAMA,* **284**, pp. 1247-1255.

Stevens, J., Cai, J., Pamuk, E. R., Williamson, D. F., Thun, M. J. and Wood, J. L. (1998) "The effect of age on the association between body-mass index and mortality", *N Engl J Med,* **338,** pp. 1-7.

Stevens, J., Cai, J., Pamuk, E. R., Williamson, D. F., Thun, M. J. and Wood, J. L. (1998) "The effect of age on the association between body-mass index and mortality", *N Engl J Med,* **338,** pp. 1-7.

Straus, W. L. and Ofman, J. J. (2001) "Gastrointestinal toxicity associated with nonsteroidal anti-inflammatory drugs. Epidemiologic and economic issues", *Gastroenterol Clin North Am,* **30**, pp. 895-920.

Sun, Y., Sturmer, T., Gunther, K. P. and Brenner, H. (1997) "Reliability and validity of clinical outcome measurements of osteoarthritis of the hip and knee--a review of the literature", *Clin Rheumatol,* **16,** pp. 185-98.

Taylor, C. B., Fortmann, S. P., Flora, J., Kayman, S., Barrett, D. C., Jatulis, D. and Farquhar, J. W. (1991) "Effect of long-term community health education on body mass index. The Stanford Five-City Project", *American Journal of Epidemiology,* **134,** pp. 235-49.

Tengs, T. O., Adams, M.E., Pliskin, J.S., Safran, D.G. Seigel, J.E., Weinstein, M.C., Graham, J.D. (1995) "Five-hundred life-saving interventions and their cost-effectiveness. [see comments.]", *Risk Analysis,* **15,** pp. 369-390.

Towheed, T. E., Anastassiades, T. P., Shea, B., Houpt, J., Welch, V. and Hochberg, M. C. (2001) "Glucosamine therapy for treating osteoarthritis (Cochrane Review)", *Cochrane Database Syst Rev,* 1, pp.

van Baar, M. E., Assendelft, W. J., Dekker, J., Oostendorp, R. A. and Bijlsma, J. W. (1999) "Effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a systematic review of randomized clinical trials", *Arthritis Rheum,* **42,** pp. 1361-9.

van Baar, M. E., Dekker, J., Oostendorp, R. A., Bijl, D., Voorn, T. B., Lemmens, J. A. and Bijlsma, J. W. (1998) "The effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a randomized clinical trial", *J Rheumatol,* **25,** pp. 2432-9.

Wardle, J., Rapoport, L., Miles, A., Afuape, T. and Duman, M. (2001) "Mass education for obesity prevention: the penetration of the BBC's 'Fighting Fat, Fighting Fit' campaign", *Health Educ Res,* **16,** pp. 343-55.

Ware, J. E., Jr. (2000) "Using generic measures of functional health and well-being to increase understanding of disease burden", *Spine,* **25,** pp. 1467.

WHO (1998) *Obesity: Preventing and Managing the Global Epidemic,* World Health Organisation, Geneva.

Williams, G. W., Hubbard, R. C. Yu, S. S., Zhao, W., *et al*. (2001) "Comparison of once-daily and twice daily administration of celecoxib for the treatment of OA of the knee", *Clin Ther,***23**, pp. 213-227.

Wolfe, F. (1999) “Determinants of WOMAC function, pain and stiffness scores: evidence for the role of low back pain, symptom counts, fatigue and depression in osteoarthritis, rheumatoid arthritis abd fibromyalgia:, *Rheumatology (Oxford)*, **38**, pp. 366-61.

APPENDIX 1 - QUESTIONNAIRE

OSTEOARTHRITIS

AND

QUALITY OF LIFE

A study is being undertaken to find out how osteoarthritis affects people's quality of life. You can take part in this study by answering the following questions. There are no right or wrong answers. We realise some questions are repeated. But it is important to the study that you answer every question as best you can. Your answers will be entirely confidential.

When you have finished could you please return the questionnaire in the envelope provided. If you have any questions please speak to the person who gave you the questionnaire or phone Susan Day at Monash University on (03) 9496-4408.

We thank you for taking the time to participate in the study.

1. Background Question

1. In which joints do you have osteoarthritis? Please tick ☑ all that apply.

☐ Back ☐ Hand ☐ Hip ☐ Knee

☐ Other (Please list) .....

.....

2. Osteoarthritis Index

Think about the pain you felt due to your arthritis **in the last 48 hours**.

Please TICK ☑ ONE BOX for each question.

QUESTION: How much pain do you have?

	None	Mild	Moderate	Severe	Extreme
1. Walking on a flat surface	☐	☐	☐	☐	☐
2. Going up or down stairs	☐	☐	☐	☐	☐
3. At night while in bed (i.e. pain that disturbs your sleep)	☐	☐	☐	☐	☐
4. Sitting or lying	☐	☐	☐	☐	☐
5. Standing upright	☐	☐	☐	☐	☐

Think about the stiffness (not pain) you felt due to your arthritis **during the last 48 hours.** Stiffness is a sensation of decreased ease in moving your joint. Please TICK ☑ ONE BOX for each question.

	None	Mild	Moderate	Severe	Extreme
6. How severe is your stiffness after first wakening in the morning	☐	☐	☐	☐	☐
7. How severe is your stiffness after sitting, lying or resting later in the day	☐	☐	☐	☐	☐

Think about the difficulty you had in doing the following daily physical activities due to your arthritis **during the last 48 hours**. By this we mean you ability to move around and look after yourself.

Please TICK ☑ ONE BOX for each question.

QUESTION: What degree of difficulty do you have?

	None	Mild	Moderate	Severe	Extreme
8. Descending (going down) stairs	☐	☐	☐	☐	☐
9. Ascending (going up) stairs	☐	☐	☐	☐	☐
10. Rising from sitting	☐	☐	☐	☐	☐
11. Standing	☐	☐	☐	☐	☐
12. Bending to the floor	☐	☐	☐	☐	☐
13. Walking on a flat surface	☐	☐	☐	☐	☐
14. Getting in or out of a car, or getting on or off a bus	☐	☐	☐	☐	☐
15. Going shopping	☐	☐	☐	☐	☐
16. Putting on your socks or stockings	☐	☐	☐	☐	☐
17. Rising from bed	☐	☐	☐	☐	☐
18. Taking off your socks or stockings	☐	☐	☐	☐	☐
19. Lying in bed	☐	☐	☐	☐	☐
20. Getting in or out of the bath	☐	☐	☐	☐	☐
21. Sitting	☐	☐	☐	☐	☐
22. Getting on or off the toilet	☐	☐	☐	☐	☐
23. Performing heavy domestic duties	☐	☐	☐	☐	☐
24. Performing light domestic duties	☐	☐	☐	☐	☐

3. Quality of life

For each of the following questions, please TICK ☑ ONE alternative that best describes your situation **during the last week.**

1. Concerning my use of prescribed medicines:
   - ☐ I do not, or rarely, use any medicines at all.
   - ☐ I use one or two medicines regularly.
   - ☐ I need to use three or four medicines regularly.
   - ☐ I use five or more medicines regularly

2. Do I need any help looking after myself?
   - ☐ I need no help at all.
   - ☐ Occasionally I need some help with personal care tasks.
   - ☐ I need help with the more difficult personal care tasks.
   - ☐ I need daily help with most or all personal care tasks.

3. When doing household tasks? (For example, preparing food, gardening, using the video recorder, radio, telephone or washing the car)
   - ☐ I need no help at all.
   - ☐ Occasionally I need some help with household tasks.
   - ☐ I need help with the more difficult household tasks.
   - ☐ I need daily help with most or all household tasks.

4. Thinking about how easily I can get around my home and community:
   - ☐ I get around my home and community by myself without any difficulty.
   - ☐ I find it difficult to get around my home and community by myself.
   - ☐ I cannot get around the community by myself, but I can get around my home with some difficulty.
   - ☐ I cannot get around either the community or my home by myself.

5. Because of my health, my relationships (for example: with my friends, partner or parents) generally:
   - ☐ Are very close and warm.
   - ☐ Are sometimes close and warm.
   - ☐ Are seldom close and warm.
   - ☐ I have no close and warm relationships.

6. Thinking about my relationships with other people:
   - ☐ I have plenty of friends, and am never lonely.
   - ☐ Although I have friends, I am occasionally lonely.
   - ☐ I have some friends, but am often lonely for company.
   - ☐ I am socially isolated and feel lonely.

7. Thinking about my health and my relationships with my family:
   - ☐ My role in the family is unaffected by my health.
   - ☐ There are some parts of my family role I cannot carry out.
   - ☐ There are many parts of my family role I cannot carry out.
   - ☐ I cannot carry out any part of my family role.

8. Thinking about m vision, including when using my glasses or contact lenses if needed:
   - ☐ I see normally.
   - ☐ I have some difficulty focusing on things, or I do not see them sharply. For example: small print, a newspaper or seeing objects in the distance.
   - ☐ I have a lot of difficulty seeing things. My vision is blurred. For example: I can see just enough to get by with.
   - ☐ I only see general shapes, or am blind. For example: I need a guide to move around.

9. Thinking about my hearing, including using my hearing aid if needed:
   - ☐ I hear normally.
   - ☐ I have some difficulty hearing or I do not hear clearly. For example: I ask people to speak up, or turn up the TV or radio volume.
   - ☐ I have difficulty hearing things clearly. For example: Often I do not understand what is said. I usually do not take part in conversations because I cannot hear what is said.
   - ☐ I hear very little indeed. For example: I cannot fully understand loud voices speaking directly to me.

10. When I communicate with others (for example: by talking, listening, writing or signing):
   - ☐ I have no trouble speaking to them or understanding what they are saying.
   - ☐ I have some difficulty being understood by people who do not know me. I have not rouble understanding what others are saying to me.
   - ☐ I am only understood by people who know me well. I have great trouble understanding what others are saying to me.
   - ☐ I cannot adequately communicate with others.

11. If I think about how I sleep:
   - ☐ I am able to sleep without difficulty most of the time.
   - ☐ My sleep is interrupted some of the time, but I am usually able to go back to sleep without difficulty.
   - ☐ My sleep is interrupted most nights, but I am usually able to go back to sleep without difficulty.
   - ☐ I sleep in short bursts only. I am awake most of the night.

12. Thinking about how I generally feel:
    - ☐ I do not feel anxious, worried or depressed.
    - ☐ I am slightly anxious, worried or depressed.
    - ☐ I feel moderately anxious, worried or depressed.
    - ☐ I am extremely anxious, worried or depressed.

13. How much pain or discomfort do I experience?
    - ☐ None at all.
    - ☐ I have moderate pain.
    - ☐ I suffer from severe pain.
    - ☐ I suffer unbearable pain.

4. Osteoarthritis Severity

Please TICK ☑ ONE BOX for each question.

1. Do you have pain or discomfort at night when in bed?
    - ☐ None or insignificant
    - ☐ Only on movement or in certain positions
    - ☐ With no movement

2. Do you have morning stiffness or pain after rising?
    - ☐ 1 minute or less
    - ☐ More than 1 minute but less than 15
    - ☐ 15 minutes or more

3 Do you have pain after standing for 30 minutes?
    - ☐ No
    - ☐ Yes

4 Do you have pain while walking?
    - ☐ No, none
    - ☐ Yes, after walking some distance
    - ☐ Yes, after initial walking and increasingly with continued walking

5. Do you have pain or discomfort from prolonged sitting (eg for 2 hours)?
    - ☐ No
    - ☐ Yes

6. How far can you walk (even with pain)?
   - ☐ Unlimited
   - ☐ More than 1 km (more than ½ mile) but limited
   - ☐ About 1 km (about ½ mile) in about 15 minutes
   - ☐ From ½ to 1 km (about 500 yards to ½ mile) in about 8 to 15 minutes
   - ☐ From 300 metres to ½ km (about 300 to 500 yards)
   - ☐ From 100 to 300 metres (about 100 to 300 yards)
   - ☐ Less than 100 metres (less than 100 yards)

7. Do you use a walking stick or crutch?
   - ☐ No
   - ☐ Yes, one walking stick or crutch
   - ☐ Yes, two walking sticks or crutches

8. Can you climb up a standard flight of stairs?
   - ☐ Without difficulty
   - ☐ With some difficulty
   - ☐ No

9. Can you climb down a standard flight of stairs?
   - ☐ Without difficulty
   - ☐ With some difficulty
   - ☐ No

10. Can you squat or bend at the knees?
    - ☐ Without difficulty
    - ☐ With some difficulty
    - ☐ No

11. Can you walk on uneven ground?
    - ☐ Without difficulty
    - ☐ With some difficulty
    - ☐ No

12. Can you put on your socks by bending forward?
    - ☐ Without difficulty
    - ☐ With some difficulty
    - ☐ No

13. Can you pick up an object from the floor?
    - ☐ Without difficulty
    - ☐ With some difficulty
    - ☐ No

14. Can you get into and out of a car?

- ☐ Without difficulty
- ☐ With some difficulty
- ☐ No

5. Pain and Restriction

The following questions ask you to rate the pain and restriction to your activities of daily living due to your osteoarthritis on a scale from 0 (none) to 100 (worst possible). This is done by placing a cross (X) on the line that best describes your situation. The closer you place the cross to **0 the less** pain or restriction you have and the closer you place it to **100 the more** pain or restriction you have due to your osteoarthritis.

Place a cross (X) on the line to show:

1. The average amount of pain you felt **over the past week**.

No pain — Worst possible pain

2. The average amount of pain felt **over the past week** when resting.

No pain — Worst possible pain

3. The average amount of restriction to your daily activities **over the past week**

No restriction — Worst possible restriction

6. General Health

Please TICK ☑ ONE BOX for each question.

1. In general, would you say your health is:

   ☐ excellent
   ☐ very good
   ☐ good
   ☐ fair
   ☐ poor

2. Compared to one year ago, how would you rate your health in general now?

   ☐ much better now than one year ago
   ☐ somewhat better now than one year ago
   ☐ about the same as one year ago
   ☐ somewhat worse now than one year ago
   ☐ much worse now than one year ago.

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

   Please TICK ☑ ONE BOX on each line.

	Yes, limited a lot	Yes, limited a little	No, not limited at all
Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	☐	☐	☐
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf	☐	☐	☐
Lifting or carrying groceries	☐	☐	☐
Climbing several flights of stairs	☐	☐	☐
Climbing one flight of stairs	☐	☐	☐
Bending, kneeling or stooping	☐	☐	☐
Walking more than a kilometre	☐	☐	☐
Walking half a kilometre	☐	☐	☐
Walking 100 metres	☐	☐	☐
Bathing and dressing yourself.	☐	☐	☐

Please TICK ☑ ONE BOX on each line.

4. During the **past four weeks**, have you had any of the following problems with your work or regular daily activities **as a result of your physical health?**

	Yes	No
Cut down on the amount of time you spent on work or other activities	☐	☐
Accomplished less than you would like	☐	☐
Were limited in the kind of work or other activities	☐	☐
Had difficulty performing the work or other activities (for example, it took extra effort).	☐	☐

5. During the **past four weeks**, have you had any of the following problems with your work or other regular daily activities **as result of any emotional problems** (such as feeling depressed or anxious)?

	Yes	No
Cut down on the amount of time you spent on work or other activities	☐	☐
Accomplished less than you would like	☐	☐
Didn't do work or other activities as carefully as usual.	☐	☐

Please TICK ☑ ONE BOX for each of the following questions.

6. During **the past four weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups?

   ☐ not at all
   ☐ slightly
   ☐ moderately
   ☐ quite a bit
   ☐ extremely.

7. How much bodily pain have you had during the **past four weeks**?

   ☐ no bodily pain
   ☐ very mild
   ☐ mild
   ☐ moderate
   ☐ severe
   ☐ very severe.

8. During the **past four weeks**, how much did pain interfere with your normal work (including work both outside the home and housework)?

   ☐ not at all
   ☐ a little bit
   ☐ moderately
   ☐ quite a bit
   ☐ extremely.

9. These questions are about how you feel and how things have been with you during the **past four weeks.** For each question, please indicate the one answer that comes closest to the way you have been feeling. Please TICK ☑ ONE BOX on each line.

   How much of the time during the **past four weeks:**

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
did you feel full of life?	☐	☐	☐	☐	☐	☐
have you been a very nervous person?	☐	☐	☐	☐	☐	☐
have you felt so down in the dumps that nothing could cheer you up?	☐	☐	☐	☐	☐	☐
have you felt calm and peaceful?	☐	☐	☐	☐	☐	☐
did you have a lot of energy?	☐	☐	☐	☐	☐	☐
have you felt down?	☐	☐	☐	☐	☐	☐
did you feel worn out?	☐	☐	☐	☐	☐	☐
have you been a happy person?	☐	☐	☐	☐	☐	☐
did you feel tired?	☐	☐	☐	☐	☐	☐

10. During **the past four weeks**, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

    ☐ all of the time
    ☐ most of the time
    ☐ some of the time
    ☐ a little of the time
    ☐ none of the time.

11. How true or false is each of the following statements for you?

Please TICK ☑ ONE BOX on each line

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
I seem to get sick more easily than other people	☐	☐	☐	☐	☐
I am as healthy as anybody I know	☐	☐	☐	☐	☐
I expect my health to get worse	☐	☐	☐	☐	☐
My health is excellent.	☐	☐	☐	☐	☐

12. During the past four weeks, has anything happened to you which has had a major impact on your physical health or emotional well-being?

☐ yes

☐ no

6. Treatments

We would like to know whether or not you have tried each of the following treatments to help deal with your osteoarthritis symptoms and, if you have tried them, how helpful they have been. Please TICK ☑ ONE BOX for each type of treatment.

		Have Not Tried	Not Helpful	Slightly Helpful	Moderately Helpful	Extremely Helpful
1.	Oral Medications (such as Panadol, Aspirin, Celebrex, Panadeine, and so on)	☐	☐	☐	☐	☐
2.	Education / self help programs	☐	☐	☐	☐	☐
3.	Exercise	☐	☐	☐	☐	☐
4.	Physiotherapy	☐	☐	☐	☐	☐
5.	Aids (such as braces and taping)	☐	☐	☐	☐	☐
6.	Injections into the joint	☐	☐	☐	☐	☐
7.	Removal of fluid/debris from the joint (arthroscopy)	☐	☐	☐	☐	☐
8.	Joint replacement surgery	☐	☐	☐	☐	☐

9. If you have tried any complementary and alternative therapies and medicines (for example: acupuncture, TENS, glucosamine, capsaicin, SAMe) would you please list those you have tried and TICK ☑ ONE BOX to show how helpful you found it. If you have not tried any please go to question 10.

	Not Helpful	Slightly Helpful	Moderately Helpful	Extremely Helpful
……	☐	☐	☐	☐
……	☐	☐	☐	☐
……	☐	☐	☐	☐
……	☐	☐	☐	☐

10. Thinking about the treatments that are available for osteoarthritis, are there any that you have not tried but would like to, or that you use less than you would like? (Please TICK ☑ ONE BOX.)

☐ No → Go to question 12 ☐ Yes

11. If you answered Yes to question 11, please list the treatments that you would like to try, or use more of, and what is discouraging you from doing so (for example: costs too much, long waiting time, not available in Australia, did not know about it).

……

……

7. Personal details

12. Are you ☐ Female or ☐ Male

13. In what year were you born? ……..

14. What is your weight? …….(kilograms) Or …….(stone/pounds)

15. What is your height? …….(metres) Or …….(feet/inches)

Please add any other comments you would like to make.

……

……

……

Thank you very much for completing this questionnaire

Please return it in the postage paid, addressed envelope as soon as possible to Dr L Segal, CHPE, Monash University, P.O. Box 477, Heidelberg. Vic. 3081

APPENDIX 2 – LITERATURE REVIEW

A1 Primary Prevention

A1.1 Overview

The aim of primary prevention strategies is to reduce the risk of developing OA through the reduction in modifiable risk factors. The potentially modifiable risk factors are obesity, physical inactivity, quadriceps weakness, diet and occupational and recreational injury and avoidable problems associated with knee malalignment. The latter has been estimated to increase the risk of developing knee OA by 4-5 times (Osborne, Segal and Day, 2001).

The evidence in relation to overweight in the development of OA is based on epidemiological data, supported by evidence that long-term weight reduction can modify disease progression, reducing the likelihood of surgical intervention for knee OA (Coggon, Reading, Croft, McLaren *et al.*, 2001). Coggon and colleagues estimated that, compared with a BMI of 20-25 (acceptable weight range) the risk of knee OA increases progressively from 0.1 for a BMI of <20, to 6.8 for a BMI of >30 (and higher for those with a BMI>35). They conclude that 'if all overweight and obese people reduced their weight by 5 kg or until their BMI was within the acceptable range, 24% of surgical cases of knee OA might be avoided'. The relative risk associated with obesity is even greater when combined with previous history of knee injury (RR=78). They conclude that OA requiring surgery could be substantially reduced by reducing obesity, suggesting in the first instance programs targeted at persons with previous knee injury.

Felson and Zhang (1998) estimated that eliminating obesity had the potential to reduce the incidence of symptomatic knee OA by 27%-52% for men and 28%-53% for women and the incidence of symptomatic hip OA by 26% for men and 27% for women. Our analysis of the ABS Health survey shows a marked difference in prevalence and incidence of OA by BMI category (age and sex adjusted).

We estimated the mean incidence of OA is 54.5/1000 for persons with a reported BMI of 20-25, 90/1000 for those with a BMI of >25 to 30 and 185/1000 for persons who are obese (BMI > 30)[19] These relative risks are somewhat lower than reported in other studies, which will reflect, in part the use of self report data in the ABS survey. This means that any analysis undertaken using ABS health survey data will tend to underestimate the potential benefits from primary prevention.

Thus, even though there do not appear to be any primary prevention programs currently in place for OA, it does not mean that such interventions are not desirable. It is possible to conceive of interventions targeted at OA risk factors of weight, quadriceps strength, and occupational or recreational injury. But, given the lack of OA specific primary prevention programs, the description of intervention options and evidence on costs and effectiveness must rely on interventions designed for other purposes. This limits the types of interventions that can be considered. For instance while there is a substantial literature on interventions for weight loss, there is no literature from which to describe or model possible interventions to prevent OA related workplace or recreational injury. Given the evidence of a relationship between weight or BMI and incidence of OA, then information concerning the effectiveness of weight loss programs can be used to estimate the effectiveness and cost-effectiveness of weight loss programs to prevent OA. Some of the evidence concerning weight-loss programs is introduced below.

A1.2 Population-based primary prevention programs

The role of population based strategies is to alter risk behaviours of the community as a whole. Population based approaches will be most relevant to conditions which potentially affect a large proportion of the population, and where the modifiable risk factors are widely distributed. In Australia, researchers point to program such as *Slip! Slop! Slap*! (for better sun protection) and *Quit* (anti-smoking) to indicate the effectiveness of population-based strategies in altering health-related, lifestyle behaviours. However, literature on population-based primary prevention strategies designed to reduce weight, increase physical activity, increase quadriceps strength is slight.

Weight Reduction

Douketis, Feightner, Attia and Feldman (1999) undertook a systematic review of the evidence base for the prevention and treatment of obesity in adults aged between 18 to 65. They located three studies of multi-faceted community-based obesity prevention programs that appeared to have sufficient methodological quality to be included in their review (Fortmann, Williams, Hulley, Haskell *et al.*, 1981; Taylor, Fortmann, Flora, Kayman *et al.*, 1991; Jeffery, 1993). Subsequent analysis suggested definitive conclusions were not possible because of the methodological limitations of the studies. The important Stanford five cities study (Farquhar, 1990), a combined media community based lifestyle campaign, reported changes in some behaviours such as smoking, but the impact on weight was equivocal – with the cohort study suggesting some impact but the random sample no change.

Exercise

Marcus, Owen, Forsyth, Cavill *et al.* (1998) undertook a review of the literature on physical activity campaigns and noted that early campaigns, which were activity based, generally reported positive outcomes – but in terms of awareness of the campaigns and interest in exercise, not actual behaviour change. The conclusion from this review was that the *'ability of these campaigns to influence physical activity behaviour remains debatable'*. Despite this equivocal conclusion, Bennett and Magnus (1994) report that walking for recreation or exercise and other forms of less vigorous exercise became significantly more popular during the 1980s in Australia and this trend appears to have continued during the early 1990s. As shown in Table 2.2 between 1989-90 and 1994-95 there were increases in the proportion of women and men 'walking for exercise'. While there are difficulties in establishing a definitive role of media campaigns, such as *Life – Be In It*, they may be an important component 'providing an overall framework or umbrella under which a broader range of health promotion initiatives can take place' (Cavill, 1998).

Conclusion

Theoretically, it appears that population-based media campaigns have the potential to change behaviour and thereby reduce the risk factors of overweight and physical inactivity for the development of OA. However, there is difficulty in linking the interventions with behaviour change.

Table A.1 Proportion of adults undertaking walking for exercise

Age Group	Females		Males	
	1989-90	1994-95	1989-90	1994-95
18-34 years	50%	61%	36%	47%
35-54 years	48%	62%	40%	53%
55 years and over	49%	53%	50%	59%
All	49%	59%	41%	53%

Source: AIHW (1996) Australia's Health: Improving the Health of Australians
http://www.aihw.gov.au/inet/publications/heath/ah96/ah96-c03.html

[19] The data is based on self-reported height and weight and will tend to understate the actual differences between BMI classes .

A1.3 Primary prevention targeted to at-risk populations

Primary prevention programs may be targeted at people who currently exhibit the risk factors for the development of OA. As noted these factors include both potentially modifiable risk factors of obesity, physical inactivity, quadriceps weakness, occupational or recreational injury and factors that do not lend themselves to modification, namely age, gender, genes, socio-economic status. As noted we have not identified any interventions in the literature designed specifically to reduce the incidence of OA. There are, however, interventions designed to modify risk factors for OA, notably for weight reduction, exercise and multi-faceted lifestyle interventions. While occupational and recreational injury are acknowledged risk factors, no interventions were identified designed to modify these risk behaviours. The Workcover 'back campaign' is one of the few health promotion interventions directed at musculoskeletal health (Buchbinder, Jolley and Wyatt, 2001) but it does not seem to be relevant to OA. Thus it is only possible to consider at this stage interventions focused on obesity and possibly exercise.

Weight Reduction

Miller *et al* (1997) in their review report that across 53 studies using *diet alone*, the average reduction in BMI at the end of the program (~15 weeks) was 4 kg/m2 (~11%). While exercise alone was less successful for weight loss (based on 27 studies average reduction in BMI was 0.8 (~3%) at the end of the program (~21 weeks). Diet plus exercise had a similar outcome as *diet alone* with a mean reduction in BMI across 43 studies of 4.2 kg/m2 (~12%), at the end of the program (~13 weeks). Miller and colleagues note the limited evidence for long-term effectiveness. They could find no exercise studies reporting follow-up data for up to 2 years post intervention and 'only a handful' of diet or diet plus exercise studies (Miller, Koceja and Hamilton, 1997).

The difficulties in sustaining weight loss in the long term is highlighted by Glazer, (2001). In this review reporting on six studies with at least two and a half years follow up of dietary and behaviour treatments for obesity, at three and a half years, the proportion of lost weight that had been regained was 60%-86%, and at 5 years the weight gain relative to the initial weight loss was 75%-121%. Studies which demonstrate long term success are more likely to include on-going support. Dietary counselling when supported by behavioural therapy (5 RCTs and 4 prospective cohort studies) through individual or group sessions focusing on lifestyle modifications result in modest weight loss, sustained in the long-term in typically around 30% of patients.

Surgery for weight loss is found to be highly successful with consistent reports of over 90% success rate (at least 50% reduction in excess weight at 2 years post surgery).

In short, while evidence concerning interventions for weight loss is mixed, there is a sufficient literature to consider weight reduction programs as an option for reducing disease burden from OA by preventing its emergence.

Exercise

Marcus *et al* (1998) reviewed the impact of physical activity interventions (four community-based interventions; six workplace-based interventions; eleven health care setting). The studies were mostly small and the findings across the 21 studies indicated some increases in physical activity, at least in the short term; and inclusion of brief telephone contacts plus an initial face-to-face intervention enhanced adherence with home based programs. Eaton *et al* (1998) undertook a systematic review of physical activity promotion in primary care settings and concluded that the 'evidence for the efficacy of such an approach is modest at best'. King *et al* (1998) in a review of community-based interventions to promote physical activity among people aged 50 years of age and over (26 RCTs, 3 quasi-experimental) report mean participation rates of 75% (range 36% to 98%).

One Australian study, which targeted sedentary, older patients (≥60 years of age) at two GP practices in SA, reported physical activity increased at 12 months compared with a control group

(Halbert, Silagy, Finucane, Withers *et al.*, 2000). Reviewers note that few studies report long term follow-up of at least 1 year post intervention.

Multi-Faceted Lifestyle Interventions
A number of multi-faceted lifestyle programs are also reported which target a range of life style behaviours, not just diet and exercise but also smoking, workplace safety etc. Such studies tend to report improvements across a range of behaviours.

Conclusion
Given the prevalence and incidence of obesity and its implication in both the onset and progression of OA, and the capacity to model the effect of weight reduction on the incidence of OA, it is recommended that targeted weight reduction programs be included in the modelling process. Various modalities for weight reduction could be covered. Modelling of a media based program is also recommended, provided suitable studies can be identified for this purpose.

While, physical inactivity and quadriceps strength are risk factors in their own right for the onset and progression of OA, and modest changes in behaviour and muscle strength can result from exercise interventions, the precise nature of the relationship between physical activity/quadriceps strength and OA has not been established. The difficulty in deriving a clear description of activity levels is part of the problem. At this stage interventions addressed at physical activity/exercise are not recommended for including in the modelling process. Similarly there is considered to be too little evidence to include interventions directed at occupational and recreational injury and knee malalignment to model. A research program directed at these risk factors may however be valuable.

A2 Management of those with OA

A2.1 Self-Management, Education and Telephone Support

Overview
Holman and Lorig, (1997) argue that there is 'substantial evidence' of the benefits of patient education in the management of OA. In 1998 a review by Superio-Cabuslay, Ward and Lorig (1996) comparing patient education interventions to NSAID treatment, appears to have been influential and is often cited in the literature. The authors conclude that patient education interventions provide significant benefits, although not equivalent to NSAIDs. A review of the Superio-Cabuslay study by The Centre for Reviews and Dissemination (2001) query whether any beneficial effect of education has been demonstrated. March and Stenmark (2001) refer to the article by Superio-Cabuslay in support of their conclusion that: 'Patient education and self-help courses have been shown in randomised trials to be cost-effective and associated with reduced pain, increased well-being, increased knowledge, reduced use of health care services and increased compliance with exercises, and these effects have been shown to be sustainable for up to 12 months. This has been shown for both patients with osteoarthritis and rheumatoid arthritis.' (March and Stenmark, 2001)
Lord, Victor, Littlejohns, Ross *et al.* (1999) conclude that the results of meta-analyses show: 'there were no significant benefits from education for the OA patients either for pain or for functional disability'. However they suggest the 'evidence for the efficacy of patient education for OA is still inconclusive', due to the lack of good quality published evidence, the varied diagnoses of participants and the heterogeneity of the interventions.

Despite this uncertainty, patient education and self-management courses are recommended in all the guidelines for management of OA reviewed by (Pencharz *et al*., 2001).

According to Hawley (1995) psycho-educational interventions can be grouped as follows; i) self-management programs – focused on using information, problem solving and coping skills to manage OA symptoms, ii) cognitive-behavioural therapy – usually emphasising control of pain by understanding the interaction of emotions and cognition with physical and behavioural aspects of

pain, iii) traditional classroom-type programs including pamphlets, books and computerized instruction, iv) individual instruction, v) psychotherapy, vi) support groups, and vi) telephone support.

This taxonomy is not widely used with the various psycho-educational programs variously referred at as 'education', 'self-management' or 'support', with no particular consistency. For the purposes of this project, patient education programs delivered in a face-to-face setting with the aim of increasing patients' self-management have been classified as 'self-management/education' and those delivered by telephone (but which may include an initial interview or training session) have been classified as telephone support.

Self-Management/Education

Self-management programs aim to assist persons with OA in the use information and with problem-solving and coping skills to better manage their symptoms. Programs can be run by lay leaders or by health professionals. Harvey, Eagar, Perkins, Owen *et al.* (2000) also classified the literature on self-management into narrow focussed and wide focussed studies, the former patient focused and the latter including also training for health-care providers.

Cohen, Sauter, deVellis and deVellis (1986) conducted an RCT to compare the relative effectiveness of a self-management course run by lay people, one run by health professionals and a non-instructional control group. The course led by lay-people was modelled on the self-management course developed by Lorig at the Stanford Arthritis Centre in the US. The course led by the health professionals was designed to represent the type of community education program usually offered in the US. The results of the research indicated that there were no differences between the lay led and professional led groups in terms of various outcome measures. Relative to a control group both interventions were associated with an increase in patient knowledge and use of exercise, but there was no improvement in pain or functioning.

Narrow focused studies: the most well known work in this area is the Arthritis Self-Management Program (ASMP) run by the Stanford Arthritis Centre in the US. The program was based on needs assessment of patients and input from practicing rheumatologists, which identified pain as the main concern of patients, followed by disability, fear, depression and deformity. In the original trial (commenced in 1984), courses were run by trained lay leaders (who receive 20 hours instruction and a teaching manual) and held in community settings. Each course consisted of 6 two-hour sessions over four months with 15-20 participants with arthritis. Participants were recruited through the mass media, and community clinics. Based on published results, the impact of the ASMP is an increase in knowledge and adoption of taught behaviours (eg exercise and relaxation), improved self-efficacy, modest decreases in pain, but with no change in physical function (Lorig, Lubeck, Kraines, Seleznick *et al.*, 1985; Lorig, 1989; Lorig, Mazonson and Holman, 1993; Lorig, Sobel, Stewart, Brown *et al.*, 1999).

Wide focussed studies: The Sharing Health Care Initiative in Australia is a broader initiative consisting of a number of demonstration projects that are seeking to find ways to improve the management of people with chronic diseases. The initiative consists of patient-focussed self-management and education initiatives at the community level as well as a provider-focussed intervention aimed at increasing the skills and knowledge of practitioners in the management of patients with chronic diseases. Some of the projects are modelled upon the ASMP, notably a project in Queensland and one in the ACT (DHAC, 2001). The OAK study in the UK is primarily a patient education/self-management intervention, which also covers professional development training on knee OA at each of the primary care practices participating in the study (Lord *et al.*, 1999).

Telephone support

The telephone can be used to support health care in a number of ways: consultation, 'helplines', and triage and professional medical advice. Helplines such as the one run by Arthritis Victoria provide information and support and are staffed by lay persons. The Tasmanian project in the Sharing Health Care Initiative planned to include a 1300 telephone contact number to provide information support to the persons with Arthritis. (This program has only recently commenced). The first round of

the After Hours Primary Medical Care Trial (AHPMCT) also included a telephone triage service. In all but the Perth trial, the telephone triage services offered advice on self-management as well as referring the caller to the most appropriate source of medical care for the presenting problem.

The AHPMCT triaging was undertaken by health professionals (nurses and GPs). Balas, Jaffrey, Kuperman, Boren *et al.* (1997) note that the telephone can be used for follow-up care to extend and/or substitute for traditional clinic or inpatient care and that it is a way to develop patient support within the community.

Conclusion
Despite the difficulties of interpreting the results of the self-management programs in relation to OA, its inclusion in guidelines for the management of OA and the importation of the design principles of ASMP into the Australian context, it was considered important to include self-management in the modelling process. It is suggested that both a lay led and professional led program be reviewed. Telephone support is an emerging area and it is recommended that it be included in the modelling provided there are the time and research resources available.

A2.2 Physiotherapy and physical therapies

The types of interventions included in this modality are exercise (for strengthening, flexibility and weight reduction), therapeutic ultrasound (low level laser therapy), knee bracing, including patella taping and ambulatory aids such as heel wedges. These are briefly considered in turn.

Exercise/Weight reduction
There is evidence that increasing muscle strength, and aerobic capacity through exercise has the potential to reduce the disability related to the symptoms of OA, particularly OA of the knee [10]. However a systematic review undertaken by van Baar, Assendelft, Dekker, Oostendorp *et al.* (1999) of exercise programs in OA concluded that only two trials had sufficient validity and power to draw any firm conclusions. The effect sizes of both these trials indicate small to moderate beneficial effects of exercise therapy on pain, a small beneficial effect on disability and moderate to great beneficial effects based on patient global assessment. The studies included in the review include home-based, clinic-based and a combination of both programs led by health professionals.

Three additional studies published since this review have demonstrated improvement through exercise programs in patients with OA compared to placebo/no-treatment groups, with the greatest benefit coming from those studies involving more intensive contact with exercise-therapists (O'Reilly, Muir and Doherty, 1999; Baker, Nelson, Felson, Layne *et al.*, 2001; Deyle, Henderson, Matekel, Ryder *et al.*, 2000).

Obesity has been implicated in the radiographic progression of knee OA (Dougados, Gueguen, Nguyen, Thiesce *et al.*, 1992; Schouten, van den Ouweland and Valkenburg, 1992) justifying interventions for weight reduction in persons with OA who are overweight. The review of the guidelines for the treatment of lower limb OA undertaken by Pencharz *et al* (2001). Pencharz *et al.*(2001) note that weight loss is a recommended intervention strategy in all four guidelines (ADMMC OA Guidelines, ICSI Guidelines, ACR Guidelines and the EULAR Guidelines.)

The EULAR guidelines state that while ‘weight reduction is recommended to virtually all patients with knee OA’ the evidence on which the recommendation is made is weak (Pendleton, Arden, Dougados, Doherty *et al.*, 2000). The only study cited was for patients with general OA, an RCT of a weight loss drug undertaken in 1981 in the USA. Two further studies were located relating specifically to weight reduction and OA. Shafshak *et al* (1995) investigated the use of acupuncture and exercise to reduce weight for people with knee OA. The results suggested substantial weight loss (5-10 kg) in most (89%) of participants. Although follow-up was only 8 weeks and the sample size was small. Huang, Chen, Chen, Weng *et al* (2000) investigated the effect of three weight loss interventions (diet and exercise only, diet, exercise and electrotherapy (TENS) and TENS only).

Compared with the TENS only group, weight reduction, pain, walking speed and changes in the Lesquesne's Functional Index were greater for patients who received either diet/exercise intervention. They also report that improvement in VAS pain scores and Lequesne's Index were highly correlated with the percentage of body weight lost (r_{VAS}=0.81 and r_{LI}=0.78).

A role for weight loss in obese patients who need joint replacement surgery (arthroplasty) for severe hip or knee OA has also been studied, is also noted to reduce complications of surgery and improve patient outcomes (Bowditch and Villar, 1999; Parvizi, Trousdale and Sarr, 2000).

Therapeutic ultrasound (low level laser therapy)
A review by Marks and de Palma (1999) of low power laser therapy concluded that although the six studies included in the review report that laser therapy led to a reduction in pain and tenderness post-laser treatment, the quality of the studies was such that no definitive statements could not be made regarding the clinical efficacy in OA. A more recent review by Brosseau, Welch, Wells, deBie *et al.*, (2001) based on 5 studies (all that could be identified), one OA of the thumb, three OA of the knee and one that did not specify the site, report conflicting results for pain: two of the three knee OA trials found no improvement and the trials with thumb and unspecified OA found a significant improvement. There was no statistical improvements in localized swelling, muscle strength, functional status, joint tenderness or global assessment. The reviewers note difficulties drawing conclusions due to heterogeneity of the interventions - different dosages, wavelengths and type of low level laser therapy. Brosseau *et al* (2001) conclude that, theoretically, laser should have a beneficial effect in terms of pain relief, but that there is insufficient evidence to draw any firm conclusions requiring further high quality studies.

Knee bracing

Knee malalignment has been implicated in the progression of knee OA. In a study by Sharma, Song, Felson, Cahue *et al.* (2001) varus[20] alignment at baseline was associated with a four-fold increase in the odds of medial progression, and valgus[21] alignment associated with a nearly 5-fold increase in the odds of lateral progression. In each case the severity of the alignment correlated with joint space loss over the following 18 months. They report that an alignment of more than five degrees in either direction in both knees at baseline is associated with significantly greater functional deterioration over the next 18 months, after adjusting for age, sex, BMI and pain.

A number of recent studies provide evidence that bracing of knees affected by OA, for instance through patella taping, using tape to strap the patella (kneecap) in position, can reduce the symptoms and disability associated with advanced or severe knee OA and may alter disease progression. In Japan, a study by Matsuno, Kadowaki and Tsuji (1997) 20 patients with severe OA (aged 55+) of the medial (middle) compartment of the knee were recruited for a 12-month trial of a knee brace. Each patient wore the brace on the knee with the most severe symptoms for the 12 months and removed it only at night. Use of new oral drugs or other treatment was not allowed from 1 month before the trial and throughout the trial. At 12 months none of the patients reported an exacerbation of pain and 19 of the 20 experienced pain relief. Quadriceps muscle strength increased for 17 patients, decreased in 2 and was unchanged in one. The authors concluded that 'bracing of late stage medial OA of the knee resulted in decreased pain, improved functioning in the activities of daily life, increased quadriceps muscle strength and stabilization of the knee'. In the UK Draper, Cable, Sanchez-Ballester, Hunt *et al.* (2000) recruited 30 patients aged 35 to 70 years who had radiologically demonstrable OA of the medial compartment of the knee, to wear a brace continually for 3 months. They report that wearing the brace provided 'immediate symptomatic improvement with less pain on walking' and the brace gave a 'significant and immediate improvement in function as measured by an analysis of gait symmetry'.

Hewett *et al* (1998) recruited 18 patients with symptomatic medial compartment arthrosis, and potential candidates for knee surgery. The brace was worn for 7 hours a day, 5 days a week for 1 year. At 9 weeks statistically significant improvements were found for all pain parameters and these improvements continued.

> 'Before brace wear, 78% had pain with activities of daily living, but after the first evaluation, only 39% continued to have such pain, and at the second evaluation, only 31% were so affected. Before brace wear, patients had a walking tolerance of 51 minutes prior to the onset of pain symptoms. At the first evaluation, patients could walk 138 minutes without pain, and after 1 year, they could walk 107 minutes without pain.' (Hewett, Noyes, Barber-Westin and Heckmann, 1998)

Lindenfeld, Hewett and Andriacchi (1997)also report that the use of a brace may provide sufficient relief to obviate the need for more invasive procedures. Potential candidates for a high tibial osteotomy were offered the use of a brace prior to the osteotomy, with some patients electing not to undergo the surgical procedures, given the pain relief and increased activities achieved with the brace.

Of those studies reporting patient-derived outcomes, many were found to be underpowered to detect differences between study arms, and only one randomised study could be identified which had sufficient numbers of participants per arm to provide statistically robust results (Kirkley, Webster-Bogaert, Litchfield, Amendola *et al.*, 1999). Kirkley et al randomised 119 patients to receive either a fitted unloader-knee brace, an over-the-counter neoprene knee sleeve or to a control group. Evaluations at 6 months showed considerable improvement in the knee-brace group compared to the sleeve and control groups.

[20] Bent inward – a deformity in which the angulation of the knee is toward the midline of the body.

[21] Bent outward – a deformity in which the angulation of the knee is away from the midline of the body.

In 1994 Cushnaghan, McCarthy and Dieppe reported the results from a study of patella taping in patients with established, symptomatic OA of the knee with both clinical and radiographic evidence. They found that medial taping resulted in a 25% reduction in knee pain (VAS). They concluded that 'patella taping is a simple, safe, cheap way of providing short term pain relief' for people with OA of the patella-femoral joint.

Ambulatory aids (heel and sole wedges)
Balint and Szebenyi (1997)report that walking aids, crutches and shoe insoles are useful for some forms of OA. Two studies on the use of heel wedges for alleviation of the pain associated with knee OA indicate that the use of lateral heel wedges are associated with pain relief, especially for those patients with early or milder medial OA of the knee (Keating, Faris, Ritter and Kane, 1993; Tohyama, Yasuda and Kaneda, 1991).

Occupational therapy
Occupational therapy is designed to reduce the disability that accompanies OA. However, the literature indicates that it not a well researched modality. Walker-Bone, Javaid, Arden and Cooper (2000) in reviewing the literature on the non-surgical management of OA could identify no formal RCTs of OT, but note that on the basis of anecdotal evidence there may be a role of OT in OA. Given the lack of studies published in peer reviewed journals is not recommended that this modality be included in the modelling at this stage.

Conclusion
There is evidence of modest benefits from exercise programs in reducing pain and increasing function – depending on compliance. Self management/education programs often emphasise the importance of exercise. Exercise can be home or clinic based, and led by professionals from different disciplines. It is recommended that exercise interventions be included in the cost-effectiveness modelling.

The evidence of the effectiveness of low level laser therapy is mixed. A major problem with published studies is the range of OA sites and differences in applying the intervention. At this stage it is not recommend it for inclusion in the modelling.

Knee bracing and patella taping is of interest given the apparent role of knee malalignment in the progression of knee OA and studies which suggest a potential benefit from knee bracing for people with advanced OA of the knee and possibility of delaying surgery.

Patella taping is a simple intervention, but suffers from few reported studies. If resources and time allow it is recommended that this modality be included in the modelling, and also the use of heel wedges as a low cost modest intervention for people who have mild knee OA.

A2.3 Pharmacological management – oral agents

Paracetamol (acetaminophen)
The most common pharmacological treatments for OA are simple analgesics, particularly paracetamol (acetaminophen). Paracetamol is usually administered early in the disease process and continues to provide some relief even in the later stages of the disease. It is listed as the first choice drug for treatment of OA in a number of international guidelines (American College of Rheumatology, 2000; Eccles, Freemantle and Mason, 1998). Paracetamol is considered effective in reducing pain from OA and has a superior safety profile to non-steroidal anti-inflammatory drugs (NSAIDs).

Few (if any) studies compare paracetamol with placebo in the management of OA. The focus has been comparison between paracetamol and NSAIDs, but studies show conflicting results. Two commonly cited clinical trials comparing paracetamol with commonly prescribed NSAIDs in patients with OA report no differences in efficacy between ibuprofen and paracetamol over a short (4 week)

treatment period (Bradley, Brandt, Katz, Kalasinski *et al.*, 1991) or between naproxen and paracetamol over a long treatment (2 year) period (Williams, Ward, egger and al, 1993). The later trial noted greater benefits from ibuprofen compared with paracetamol at 6 weeks. A 2 year study, comparing two different NSAIDs (indomethacin and tiaprofenic acid) with paracetamol in patients with knee OA, reported significant improvements in pain for both NSAIDs compared with paracetamol at 4 weeks, but no significant difference thereafter (Scott, Berry, Capell, Coppock *et al.*, 2000).

In contrast to these findings, a recent 12 week cross-over study found significant improvements in WOMAC and SF-36 scales in patients receiving an NSAID (diclofenac) together with a gastro-protective agent (misoprostol) compared with paracetamol (Pincus, Koch, Sokka, Lefkowith *et al.*, 2001). They also report significantly more adverse events, in the diclofenac arm compared with the paracetamol arm. The authors further note that the differential benefit of diclofenac + misoprostol over paracetamol was most pronounced in patients with more severe OA. This is consistent with findings by Williams *et al.* (1993) that patients with more severe OA were less likely to discontinue naproxen due to lack of efficacy. Additionally, a mail survey of 1,031 patients with OA found that while 32% found NSAIDs and paracetamol about the same in terms of overall satisfaction, 52% found NSAIDs better, with 15% finding paracetamol better (Wolfe, Zhao and Lane, 2000).

While the risks of adverse events from paracetamol are significantly lower than those from NSAIDs, the long-term regular consumption of paracetamol has been implicated in the development of end stage renal disease (Perneger, Whelton and Klag, 1994). The relative risk of renal disease due to paracetamol compared with NSAIDs remains poorly defined. Paracetamol can also be hepato-toxic in high doses, with the risk increasing with doses over 4g/day, and in patients with established liver disease or alcoholics (McColl, 2001).

Non-specific non-steroidal anti-inflammatory dugs – (NSAIDs)

NSAIDs (apart from aspirin) are widely administered to reduce pain and inflammation in OA, through prescription and over the counter sales. A large number of different NSAIDs are available, however the evidence suggests that there is little difference between them with respect to treatment of pain and general symptom control in patients with OA. A systematic review of randomised controlled trials of NSAIDs in treating hip OA report that 24 of 29 trials (83%) which compared two (or more) different NSAIDs, found no statistically significant difference in efficacy between them (Towheed, Shea, G and Hochberg, 2001).

A two year trial comparing placebo with diclofenac (an NSAID) in treatment of patients with knee OA, found that almost 50% of patients taking placebo were the same or better at the end of the study (Dieppe, Cushnaghan, Jasani, McCrae et al., 1993). Further research is needed to establish which patients are most likely to respond to NSAIDs and which are not (Walker, Sheather-Reid, Carmody, Vial et al., 1997). Scholes, Stergachis, Penna, Normand *et al*. (1995) comparing time to discontinuation of 4 different NSAIDs in patients with OA found that NSAID discontinuation was highest in the first two months of follow-up, with only 15-20% of those started on a study NSAID still using the same drug at the end of one year.

NSAIDs have well known side-effects. Not only do NSAIDs inhibit prostaglandins in areas of the body with inflammation, they also inhibit prostaglandins which serve important functions in other parts of the body, accounting for some of the toxicity of these agents (National Prescribing Service, 2000). NSAIDs are known to cause significant gastro-intestinal (GI) problems, and have also been associated with renal and cardiac toxicity, particularly in the elderly (Heerdink, Leufkens, Herings *et al*., 1998; Henry, Page, Whyte *et al*., 1997; Page and Henry, 2000;Whelton, 1999). Studies have indicated that the gastro-toxic effects of NSAIDs are related to their dose and half-life. NSAIDs vary substantially and significantly in terms of side effect profile, with some agents having several time the risk of others in terms of GI toxicity (Henry, Lim, Rodriguez *et al*., 1996). The evidence concerning NSAID side-effect profile is summarised in our previous report, (Segal, Day, Chapman and Osborne, 2002).

COX-2 specific non-steroidal anti-inflammatory drugs (COX-2s)
Unlike traditional NSAIDs, which are non-selective and inhibit both forms of the COX enzyme, COX-2 inhibitors selectively inhibit only the COX-2 enzyme, the isoform primarily expressed in response to inflammation (National Prescribing Service, 2000). Two COX-2 specific inhibitors became available in Australia in 2000/2001 – celecoxib and rofecoxib. Celecoxib is indicated specifically for treatment of symptomatic osteo- and rheumatoid arthritis and rofecoxib only for OA.

A large number of trials demonstrate that neither have greater efficacy compared with traditional NSAIDs in treating OA (Bensen, Fiechtner, McMillen *et al.,* 1999). One recent study comparing both celecoxib and rofecoxib with paracetamol in patients with OA found COX-2s were more effective than paracetamol in reducing pain from OA over 6 weeks (Geba, Weaver, Polis, Dixon *et al*., 2002).

COX-2s are been promoted as having an improved GI side-effect profile over non-specific NSAIDs. Based on 6 month data, COX-2s show reduced relative risk for serious GI complications compared with standard NSAIDs with reported absolute risk reduction of 7 cases per 1000 treatment years, (National Prescribing Service, 2000). Subsequent analysis of 12 month data from the major celecoxib trial (CLASS) (Silverstein, Faich, Goldstein and al, 2000), show a halving of the benefit at 12 months. According to the FDA (2000), the difference was not significant at either 6 or 12 months based on the primary safety end-points. Using an expanded safety end-points the difference was still not significant relative to diclofenac but it was in comparison with ibuprofen. FDA analysis of trial data comparing rofecoxib to naproxen found no overall safety benefit of rofecoxib, noting in particular a doubling of the relative risk for cardiovascular thrombotic events in those receiving rofecoxib compared with naproxen (FDA, 2001). While this was not found in the CLASS (celecoxib) study, prophylactic aspirin was not an exclusion criterion in this trial, but was the major exclusion criterion in the rofecoxib study (VIGOR). It is unclear whether the observed increase is specific to rofecoxib, or if naproxen (the comparator NSAID in the VIGOR study) has a cardioprotective effect (National Prescribing Service, 2000). More information on COX-2 side-effects is also summarised in our previous report (Segal, Day, Chapman and Osborne, 2002)

Both rofecoxib and celecoxib are listed on the Pharmaceutical Benefits Scheme at a dispensed price equivalent to approximately 2 to 3 times that of non-specific NSAIDs.

Opioids
For late stage disease, where other forms of pain control have failed, or even for primary therapy, opioids such as codein/codein are used in the management of OA. The extent of use is not known. Physicians may be reluctant to prescribe opioids due to regulatory sanctions, a perceived risk of psychological dependency and a lack of knowledge about opioid efficacy in OA (Peloso, 2001; Peloso, Bellamy, Bensen, Thomson *et al.*, 2000). Opioids are supported for use in chronic pain conditions by the American Geriatric Society who state that “for many patients chronic opioid therapy may have fewer life threatening risks than the long term daily use of NSAIDs.” (anonymous, 1998) A summary of 15 trials of narcotics in OA noted superiority of a range of opioids over placebo, paracetamol and NSAIDs. Studies which have examined addictive behaviour to opioids have noted very low rates of abnormal use in individuals with OA. Additionally, there is no evidence that long term opioid use creates any irreversible physical changes in any organ system (Peloso, 2001).

Conclusion
Oral pharmaceuticals are routinely used in treatment of osteoarthritis. Paracetamol is available over-the-counter or on prescription, as are a number of non-specific NSAIDs. COX-2 specific NSAIDs are currently available only on prescription. These drugs provide clear and measurable short-term pain relief from osteoarthritis. Clinical trials in general show better efficacy for NSAIDs than paracetamol in treating pain from OA, but with a poorer side-effect profile related to dose of drug and age of the patient. However these trials have had difficulty in showing clear benefit from NSAIDs over paracetamol beyond 8-12 weeks. Little research has been undertaken on opioids in treating OA, but opioids appear to offer greater pain relief than NSAIDs or paracetamol with possibly a better side-effect profiles. Ideally all these agents would be covered in the modelling.

A2.4 Topical pharmaceuticals

NSAIDs

Topical NSAID treatments are used primarily to treat knee or hand OA. In hip OA, they are not considered effective due to the depth of the diseased joint. A potential benefit of topical application of NSAIDs is the reduction in side effects associated with oral consumption (Hosie and Bird, 1994). A systematic review of 37 controlled clinical trials of topical NSAIDs across a range of conditions noted five trials in which topical NSAIDs were compared with placebo in OA. Three of the five demonstrated significant benefit of the topical NSAID compared with placebo, but two showed no difference. Two trials compared a topical NSAID with an active oral NSAID comparator in OA and showed approximate equivalence between the two treatment arms. Across all 37 trials, adverse effects with topical NSAIDs were no more common than with placebo (Moore, Tramer, Carroll and al, 1998). A record linkage case-control study of admissions to hospital found that topical NSAIDs did not increase the risk of admission for upper GI bleeding and perforation, after adjustment for the confounding effects of concomitant use of oral anti-inflammatory drugs and ulcer healing drugs (Evans, McMahon, McGilchrist, White et al., 1995).

Capsaicin

Capsaicin is an alkaloid derived from seeds and membranes of the Nightshade family. Topically applied, capsaicin has been shown to be effective in providing pain relief from OA in a number of studies (see Rains and Bryson, 1995). Capsaicin is thought to act by depleting the endogenous neuropeptide substance P, locally in tissues, thereby reducing chemical stimulation of the nociceptor pain fibres (March and Stenmark, 2001). Raised levels of substance P have been found in the synovium of patients with OA, suggesting a possible role in the pathogenesis of pain associated with the disease.

A trial of topical capsaicin applied to the knee in patients with OA, found it to be significantly superior to placebo after 2 weeks of treatment (Deal, Schnitzer, Lipstein, Seibold et al., 1991). Altman et al 1994 compared topical capsaicin with placebo in patients with OA of the knee, ankle, elbow, wrist or shoulder in a 12 week double-blind trial and found significant reductions in pain and tenderness in the capsaicin treated group compared with placebo (Altman, Aven, Holmburg, Pfeifer et al., 1994). Topical capsaicin is not associated with any severe systemic adverse effects, however stinging and burning, particularly during the first week of therapy, is reported by many patients (Rains and Bryson, 1995). In summary, topical capsaicin appears to be a useful and safe treatment for OA.

Conclusion

Topical pharmaceuticals may provide similar benefits to oral pharmaceuticals in treating pain from OA (except n the hip), without the systemic side-effects. Inclusion in the modelling is recommended if time and resources allow.

A2.5 Intra-articular injection of pharmaceutical agents

Corticosteroids

In situations where OA is severe, painful or inflamed, corticosteroids may be injected into the joint to reduce discomfort and increase function (McColl, 2001). Intra-articular injections of corticosteroids have been used in the treatment of OA of the knee for more than 30 years, but few studies have been undertaken to measure their effect (Gosal, Jackson and Bickerstaff, 1999). Triamcinolone hexacatamide has been recommended in one study as the most efficacious preparation for intra-articular injection (Creamer, 1997), however there is little comparative data published, and other agents (eg depot-medrol) may be equally efficacious [personal correspondence, P. Brooks]. Painful short term OA ‘flares’ may benefit most from this type of treatment, as pain relief is usually short term, lasting from 1-4 weeks. Joints should not generally be injected more than 3-4 times per year because of the possibility of cartilage damage from repeated injections. Patients who require more than this number to control symptoms may be good candidates for surgical intervention (Manek and Lane, 2000).

Hyaluronans
In joints affected by osteoarthritis, the synovial fluid's capacity to lubricate and to absorb shock is reduced. These changes may be partly due to a reduction in the size and concentration of hyaluronic acid (hyaluronan) molecules naturally present in synovial fluid (Anonymous, 1999). Injection of material designed to increase the viscosity and elasticity of the synovial fluid has been shown to be beneficial (Huskisson and Donnelly, 1999) and one recent study has indicated that hyaluronan may act to modify the structural organization of the knee synovium in OA (Pasquali Ronchetti, Guerra, Taparelli, Boraldi et al., 2001). A number of different products are marketed for visco-supplementation in knees with OA (Adams, Lussier and Peyron, 2000). In Australia, Hylan G-F 20 (Synvisc) is the available preparation indicated for knee OA. It is provided as a course of 3 times weekly injections, with a maximum recommended dose of 6 injections within a 6 month period. Injections can be performed by any medical practitioner experienced in knee joint aspiration and injection techniques using strict no-touch aseptic technique (March and Stenmark, 2001).

While, clinical trials to determine the efficacy of hyaluronan have shown conflicting results, the balance of evidence suggests a benefit compared with placebo. A recent review of 14 clinical trials of intra-articular hyalurons report that they were, in general, more efficacious in reducing knee pain and improving function compared with placebo, and were comparable with non-specific NSAIDs (Hochberg, 2000). Studies of the two common products Hylan G-F 20 and Hyalgan report significant benefits over placebo in treating OA (Wobig, Dickhut, Maier and Vetter, 1998), (Dougados, Nguyen, Listrat and Amor, 1993). However other studies have found no difference between these products and placebo (Henderson, Smith, Pegley and Blake, 1994).

Adverse events due to intra-articular hyalurons are noted in a number of trials. A review by Lussier et al 1996 of clinical practice in Canada suggests that the incidence of adverse events is strongly influenced by the injection technique used. (Lussier, Cividino, McFarlane, Olszynski et al., 1996).

Conclusion
Corticosteroids provide strong short-term pain relief (up to approximately 4 weeks) in OA affected joints and are widely used by GPs and specialists in relieving pain from OA. Clinical trial evidence to support their efficacy in treating OA is limited, however they have been used in this way for over 50 years. Hyaluronans are injected exclusively into the knee joint, and appear to provide longer-term pain relief from knee OA. Differences in the size and weight of the injected hyaluronans may be important in determining their benefits, with clinical trials showing mixed results. Side-effect rates vary, and appear to be related to the position of the knee joint during the procedure. Intra-articular Hyaluronans are recommended for inclusion in the modelling if tiem and resources allow.

A2.6 Complementary and alternative therapies

Overview
A broad range of complementary, alternative and natural therapies are used by persons with OA. These therapies span the oral, topical, and physical modalities. In 1989 Cronan, Kaplan, Posner, Blumberg et al. found that 84% of people reporting musculoskeletal symptoms used alternative therapies for relief. The Arthritis Foundation in the USA report that in excess of $3 billion per annum is spent for ‘unproven arthritis treatments’ (Ramsey, Spencer, Topolski, Belza et al., 2001). A recent survey of participants taking part in a trial of warm water exercise therapy for OA found that nearly half the participants (47%) reported using at least one type of ‘alternative care’ during the 20-week period of the intervention, most commonly massage therapy, chiropractic services and non-prescribed alternative medicines [111].

Glucosamine
Glucosamine sulphate is a basic building block for the glycosaminoglycans and proteoglycans that are important constituents of articular cartilage. Glucosamine is widely used by people with OA. It has been shown to favourably effect cartilage metabolism in vitro, and has demonstrated anti-

arthritis effects in animal models. In controlled clinical trials in patients with OA (Towheed and Anastassiades, 2000), glucosamine has been shown to be more effective than placebo and as effective as NSAIDs in reducing pain. Glucosamine may also be capable of slowing progression of OA through increasing proteoglycan synthesis in articular cartilage (Reginster, Deroisy, Rovati, Lee et al., 2001). Side effects associated with glucosamine have been found to be comparable to placebo (Towheed and Anastassiades, 2000). Although glucosamine sulphate is a prescription drug in over 40 countries (including Italy, France and Germany), it is available as an over-the-counter preparation in pharmacies in Australia, and is regarded as a food supplement in the USA and the UK.

Avocado/Soybean unsaponifiables (ASU)
ASU is made of unsaponifiable extracts of one-third avocado oil and two-thirds soybean oil. In vitro studies have shown that ASU stimulates collagen synthesis in articular chondrocyte cultures and may promote transforming growth factor B-induced matrix repair mechanisms in articular cartilage (Long, Soeken and Ernst, 2001). Three randomised, placebo-controlled, double-blind clinical trials have been performed in patients with OA to determine the efficacy and safety of ASU in the treatment of OA (Appelboom, Schuermans, Verbruggen, Henrotin et al., 2001; Blotman, Maheu, Wulwik, Caspard et al., 1997; Maheu, Mazieres, Valat and al, 1998).

A recent review pooling two of these trials found beneficial effects from ASU on pain control, function and global arthritis assessment, compared with placebo, as well as a reduction in NSAID intake, without any serious adverse effects (March and Stenmark, 2001). Both the Blotman et al (1997) and Maheu et al., (1989 studies report that patients with OA of the hip have greater improvement than patients with OA of the knee, (Little and Parsons, 2001).

Chondroitin
Chondroitin, like glucosamine, is a component of the proteoglycan matrix structure of cartilage (March and Stenmark, 2001). The compound is also derived from animal cartilage and is believed to work through similar mechanisms to glucosamine. A meta-analysis of 9 studies of chondroitin in 799 patients with OA found a large pooled effect size (0.78; 95%CI 0.60-0.95), but noted that the true magnitude of the effect is unclear because of inconsistencies in study methods (Reginster, 2000).

Other herbal medicines
A recent meta-analysis of clinical trials of herbal medicines for treatment of OA identified high quality trials of: Articulin-F (a mixed herbo-mineral formulation), ASU (see above), capsaicin (see above), devil's claw (a medicinal plant native to Africa), eazmov (a mixed herbal preparation), ginger extract, gitadyl (a mixed herbal preparation), phytodolor (a mixed herbal preparation), stinging nettle (applied topically) and willow bark extract (the original source of salicylates). The treatments which showed the best evidence for effectiveness were ASU, capsaicin, devil's claw and phytodolor. Glucosamine and chondtroitin were not considered in this review (Long, Soeken and Ernst, 2001).

Vitamin and Mineral treatments
A number of studies indicate that deficiencies in certain vitamins or trace elements may be associated with osteoarthritic conditions, suggesting the use of supplements in management of OA.

Ascorbic Acid (Vitamin C) – Ascorbic acid is required for the synthesis of collagen, an important structural protein of joint cartilage. In participants in the Framingham Osteoarthritis Cohort Study, a higher intake of vitamin C was associated with a reduced risk of cartilage loss and disease progression in individuals with knee OA (McAlindon, Jacques, Zhang, Hannan et al., 1996).

Vitamin D – Vitamin D plays a role in normal turnover of articular cartilage. A prospective study of 556 participants from the Framingham study found that low dietary intake of Vitamin D and low serum levels were associated with an increase in radiographic progression of knee OA, but not the incidence of newly diagnosed OA (McAlindon, Felson, Zhang, Hannan et al., 1996). In an 8 year study of 237 female participants with hip OA, the odds of progressive joint space narrowing were

found to be 3-times higher for subjects in the lower and middle tertiles for serum 25-Vitamin D, compared to subjects in the highest tertile (Lane, Gore, Cummings, Hochberg et al., 1999).

Vitamin E – D-alpha-tocopherol has been found to have anti-inflammatory activity and may also inhibit prostaglandin synthesis. Although its mechanism of action in OA is uncertain, clinical trials have shown significant beneficial effects.
A placebo-controlled, randomised, 10-day cross-over trial in 29 patients with OA found that 52% reported a reduction in pain while taking Vitamin E compared to 4% on placebo ($p<0.01$) (Machtey and Ouaknine, 1978). A 3-week double-blind, randomised, active comparator trial of Vitamin E (d-alpha- tocopherol acetate) and diclofenac (an NSAID) in patients with hip or knee OA, found there to be no significant difference in the efficacy of the two drugs, however Vitamin E had a much better side-effect profile (Scherak, Kolarz, Schodl and Blankenhorn, 1990). In contrast, a recent a 6 month, double-blind, randomised, placebo controlled study of 77 patients with symptomatic knee OA, showed no benefit over placebo at 1, 3 or 6 months (Brand, Snaddon, Bailey and Cicuttini, 2001).

Niacinamide – a member of the water soluble B vitamin group, is used in the production of fatty acids, steroids and cholesterol. The treatment of arthritis using niacinamide was described by Kaufman in the 1950s. Improvements in symptoms were generally noted at 3-4 weeks after initiating treatment (Gaby, 1999). A recent study by Jonas et al 1996 of niacinamide in 72 patients with OA in a 12 week, double-blind, placebo-controlled study report reduction in anti-inflammatory medications and increase in joint mobility compared with placebo. Side-effects were slightly higher in the niacinamide group compared with the placebo group (Jonas, Rapoza and Blair, 1996).

Boron – Boron is a mineral found in trace amounts in fruits and vegetables. It appears to participate in hydroxylation reactions, which play a role in the synthesis of steroid hormones and vitamin D (Gaby, 1999). Evidence recently reviewed by Gaby 1999 in the journal Alternative Medicine Reviews that suggests boron may be useful in the management of OA. The evidence cited includes epidemiological studies relating low boran intake with high rates of OA, and experimental evidence, (Newnham, 1994). A double-blind placebo-controlled study of boron supplementation in 20 subjects with OA reported improvement in 50% of subjects receiving the supplement compared to 10% in the placebo group. (The results were better for those who complied with treatment 71% compared with 12.5% respectively). This result suggests that boron supplementation may be useful for individuals whose diets are low in this mineral (this may be likely in Australia, where much of the food is grown on soil deficient in boron) (Gaby, 1999).

S-adenosylmethionine (SAMe) – A large number of clinical trials (total enrolment ~22,000 patients) suggest that SAMe is as effective as NSAIDs in treatment of OA, but with fewer side-effects (Gaby, 1999). A 30-day, double-blind study comparing SAMe to placebo or naproxen (NSAD) in 734 patients with OA of the hip, knee, spine or hand found that both drugs were significantly more effective than placebo. SAMe was significantly better tolerated than naproxen, and recorded the same number of side-effects as placebo (Caruso and Pietrogrande, 1987). For most measures, naproxen was significantly better by day 15, whereas statistical significance was not observed with SAMe until study end (at 30 days). Similar results have been shown for smaller clinical trials of SAMe compared with NSAIDs, (indomethacin Vetter (1987), ibuprofen Muller-Fassbender (1987) and piroxicam Maccagno, Di Giorgio, Caston and Sagasta (1987). Moreover, in the piroxicam trial, improvement in pain score was maintained in the SAMe group for at least 8 weeks after discontinuation of treatment, whereas a significant worsening was seen in the piroxicam group 28 days after treatment. Long-term treatment of SAMe was evaluated in a 2-year open-trial of 108 patients with OA of the hip, knee or spine (Konig, 1987). At the end of 2-years, 97 patients were still in the trial, and 18 of these had experienced total remission of symptoms. More than 90% of the physicians and 85% of the patients assessed the effects of the treatment as ‘very good’ or ‘good’. The side effects profile is considered acceptable. SAMe has been used in Europe for many years, and has recently become available in the USA (Gaby, 1999).

Acupuncture

A systematic review by Ezzo, Hadhazy, Birch, Lao et al., (2001) included seven trials of acupuncture for patients with knee OA. Four of the trials were rated as low quality. The three high-quality studies compared real acupuncture with sham acupuncture. Two of the trials reported 'positive results for pain', indicating that acupuncture was more effective in reducing pain than sham acupuncture. All three assessed function but the outcomes were inconclusive. In relation to the other lower quality trials, there was limited evidence that acupuncture is more effective than being on a waiting list or usual care.

Transcutaneous electrical nerve stimulation (TENS)

Carroll, Moore, McQuay, Fairman et al., (2001) undertook a systematic literature review of the use of TENS for chronic pain (≥ 3 months) which included nineteen RCTs. They conclude that the results were 'inconclusive' and that the published studies provide insufficient information about the nature of the intervention or their long term effectiveness. Osiri, Welch, Brosseau, Shea et al., (2000) undertook a review of the use of TENS for knee OA. The review concluded that while TENS and acupuncture-like TENS (AL-TENS) appeared to be 'effective in pain control over placebo' large, well-designed studies with standardised protocols were needed before firm conclusions could be drawn about effectiveness in the treatment of OA.

Conclusion

A wide range of oral complementary treatments are available for management of OA. The amount and quality of evidence is mixed. But some treatments demonstrate benefits in high quality clinical trials. Apart from the benefits of reducing pain and stiffness from OA, products like glucosamine may also have joint modifying properties that slow the rate of OA progression. ASU and SAMe are shown to provide clear benefit for patients with OA based on large clinical trials, and a better side effect profile than NSAIDs.

Depending on time and resources it is recommended that oral complementary therapy studies be included in the modelling process, ideally to include Glucosamine, ASU, boron and SAMe. Key studies are summarised in Segal, Day, Chapman and Osborne (2002)notably on Glucosamine, Reginster et al., (2001) and on ASU, Blotman et al., (1997), Maheu et al., (1998) and Appelboom et al., (2001).

It is not recommended that acupuncture or TENS be included in the modelling at this stage due to the limited empirical evidence, short duration of the interventions and limited follow-up (≤ 3 months).

A2.7 Surgical management

There are few criteria for determining the point at which surgery should be used to treat OA, or the type of surgical intervention to perform. The American College of Rheumatology recommends that patients with severe symptomatic OA who have pain that has failed to respond to medical therapy, and who have progressive limitation in activities of daily living, should be referred to an orthopaedic surgeon for evaluation (American College of Rheumatology, 2000).

Although a greater range of surgical options exists for patients with severe knee OA than hip OA, total hip replacement generally provides better outcomes than similar interventions for knee OA. In both cases, total joint replacement is generally considered to be one of the most effective of all surgical interventions, able to restore patients to near-normal function. Treatment is also considered to be highly cost-effective (Chang, Pellisier and Hazen, 1996). Given that the procedures and outcomes are somewhat different for knee and hip OA, they are considered separately.

Arthroscopy for knee OA

A number of surgical options exist for patients with severe, refractory knee OA. These include arthroscopic debridement and lavage, realignment osteotomy, unicompartmental and total knee arthroplasty, and arthrodesis. Evidence to support any of these interventions is weak, as there are very few published randomised controlled trials surgical interventions either with each other or alternative non-surgical interventions.

Arthroscopic surgery for knee OA can be used for either diagnostic purposes or surgical removal of damaged osseous or soft tissues (debridement). Diagnostically, arthroscopy can be used to provide information about the position and extent of damage to the knee joint to assist in decision making for treatment. However less invasive procedures such as radiography usually serve this purpose. Arthroscopic surgery may be performed in the hope of avoiding or delaying more extensive surgery, such as total knee replacement (Edelson, Burks and Bloebaum, 1995). However, although arthroscopy has low morbidity and can be repeated (Baumgaertner, Dilworth-Cannon, Vittori and al, 1990), there is limited published evidence of its effectiveness in treating OA. The rationale for arthroscopic debridement is that soft tissue injuries such as torn menisci, synovitis and loose bodies are remediable causes of morbidity in OA patients (Chang, Falconer, Stulburg and al, 1993). Joint irrigation (or lavage) is an integral part of all arthroscopies, necessary to distend the joint for adequate exploration and to remove blood and debris that cloud the inspections of intra-articular structures (Kalunian, Moreland, Klashman and al, 2000). Six studies were identified which involved randomisation of patients with OA to receive either arthroscopic treatment or other treatment(s), see Table 3. In each of these, arthropscopic joint irrigation was compared with either standard arthroscopic surgery (debridement) (Chang et al., 1993; Mosely, Wray, Kuykendall et al, 1996), conservative medical management (Ike, Arnold, Rothschild et al., 1992), minimal irrigation (Kalunian et al., 2000), intra-articular steroids (Ravaud, Moulinier, Giraudeau, Ayral et al., 1999) or ‘sham’ or placebo surgery (Bradley, Heilman, Katz, Gsell et al., 2002; Mosely et al., 1996).

Mosely et al (1996) report pilot results from 10 patients randomised to 3 groups, so statistical inferences cannot be drawn. Ike et al 1992 found beneficial effects from joint irrigation compared with conservative medical management, but provide only 12 week follow-up. Each of the Chang et al, Bradley et al and Kalunian and Moreland studies had a follow-up of 12 months.

Kalunian and Moreland randomised patients to receive either larger than standard amounts of isotonic solution through the knee joint, or minimal irrigation. Sustained benefit for up to 12 months was shown in both groups, however patients who had received the larger volume of irrigation had significantly reduced pain at 12 months compared with the control group (Kalunian et al., 2000). Ravaud et al (1999) also found functional benefits and reductions in pain up to 6 months post-operatively, in patients receiving 1 litre saline intra-articular lavage. Minor, short-term benefits were observed with the addition of intra-articular steroids post-surgery (Ravaud et al., 1999). Chang et al. (1993) found that removal of soft-tissue abnormalities via arthroscopic surgery did not generally improve pain and knee dysfunction associated with non-end stage OA of the knee compared with lavage - 44% of surgery subjects reported improvement at 12 months compared to 58% of patients receiving needle tidal irrigation. The authors noted that the probability of benefit from surgery increased with the presence of any lateral meniscal tear or a tear of the anterior two-thirds of the medial meniscus (Chang et al., 1993). A recent study by Bradley et al. (2002) of 180 patients found no difference in pain or physical function between patients receiving needle tidal irrigation or sham tidal irrigation at 3, 6 or 12 months post-surgery. Although both groups displayed improvement and little use of oral pharmacological treatments in the subsequent 12 months.

The mechanism of pain relief in arthroscopic lavage of knee OA is thought to be through removal of water soluble mediators of inflammation as well as fragments of articular cartilage (Edelson, Burks and Bloebaum, 1995), however a surgical placebo effect is also postulated (Ike et al., 1992;Mosely et al., 1996) and supported in a recent high quality trial (Bradley et al., 2002). Unfortunately, many of the trials in this area may have been under-powered to detect even large clinical effects.

More extensive randomised, controlled trials are needed to clarify this issue, and to determine the validity of arthroscopic surgery as a treatment for OA.

Arthroplasty - knee replacement

Arthroplasty of the knee involves replacement of all or some of the knee joint with an artificial joint. In late-stage disease one or more joints may be totally replaced. The materials used in replaced joints tend to last between 5 and 15 years, and prostheses are generally replaced after a period of 10 to 15 years (Knutsson and Engberg, 1999). In patients with severe, refractory OA, arthroplasty can

offer a sudden reduction in pain and increased movement for most people. There are two surgical options for arthroplasty. Osteoarthritis may occur in one or more of the three compartments (lateral, patello-femoral and medial compartments) of the knee. Commonly, arthroplasty involves total knee replacement (TKR) with a prosthesis, however where OA primarily or solely effects one compartment, unicompartmental arthroplasty may be undertaken. Studies which have measured outcomes before and after TKR have shown large and sustained changes in pain and function in most recipients (Bachmeier, March and Cross, 2001; Jones, Voaklander, Johnston and Suarez-Almazor, 2001; Kirwan, Currey, Freeman and al, 1994) with little difference in improvement between younger and older recipients (Jones et al., 2001). Compared with TKR, unicompartmental arthroplasty preserves both cruciate ligaments and bone stock in the opposite compartment and patello-femoral joint. A five-year randomised study comparing the two showed lower perioperative morbidity and increased range of motion among those receiving unicompartmental arthroplasty (Newman, Shah and Nilen, 1998). Important factors in determining the success of unicompartmental knee arthroplasty include stringent patient selection, careful surgical technique and a proven prosthetic design. Increased body weight has been associated with an increased failure rate of unicompartmental arthroplasty (Hanssen, MJ, RD and al, 2000).

A systematic review carried out in 1990 noted that >60% of TKR was for patients with OA. TKR is the recommended treatment for severe knee OA in most published consensus guidelines. There are however no randomised trials of TKR in patients with OA which compare arthroplasty with non-surgical treatments. Most published studies are observational, and many use the survival of the prosthesis as the main or only outcome measure. Additionally a wide variety of prostheses and outcome measures may be used, making comparisons between studies difficult. While the basis for specified indication for TKR in knee OA are not based in evidence there is some consistency in views. A postal survey by Mancuso et al 1996 of orthopaedic surgeons showed most agreed that severity of daily pain with attendant X-ray evidence of loss of joint space, were key indications for TKR (Mancuso, Ranawat, Esdaile, Johanson et al., 1996). High patient motivation was also cited as a reason for going ahead with surgery, while co-morbidities and technical difficulties were reasons for not going ahead. Consensus management guidelines in which surgeons have been involved suggest that pain severity, functional impairment and the presence of night pain are key factors in deciding on surgery (Dieppe, Basler, Chard, Croft et al., 1999).

Conclusion re surgery for knee OA

A number of surgical interventions are available for refractory knee OA, the two most common of which are arthroscopy and arthroplasty. Arthroscopy has been used for many years either to visualise damage to the knee joint, or as a treatment to wash the joint or debride loose tissue from joint surfaces. Few clinical trials have examined the impact of arthroscopic surgery but it appears possible from published evidence that observed benefits compared with base line may largely be a placebo effect.

Arthroplasty, in cases of severe OA, produces significant and long lasting benefits for the majority of patients, with relatively few side-effects. It is recommended that both arthoscopy and arthoplasty be included in the C-E modelling.

The timing and need for surgery is still contentious. Some patients who attend surgeons for consideration of TKR decide not to proceed with surgery, which may in part, reflect a settling down of 'flare-ups' of OA. Non-surgical management of patients on waiting lists has been found to reduce the number requiring surgery (Roy and Hunter, 1996). Chang et al (1993) noted that of 200 OA patients selectable for an arthroscope, less than half met the criteria for surgery after 3 months of conservative management. Other studies suggest a worsening of symptoms and poorer outcomes of surgery with delay in treatment. In comparison with SF-36 norms for men and women, patients on surgical waiting lists are severely compromised on a number of the SF-36 subscales, especially role physical, bodily pain and physical function subscales.

Arthroscopy for hip OA

Arthroscopic investigation or treatment is less commonly employed in hip OA than knee OA. This is in part due to the difficulties in accessing the hip joint space with an arthroscope. However recent studies indicate benefit from the technique for providing more accurate diagnosis but not for treatment. A prospective study in which 328 patients with hip pain were given 'standard' diagnoses, followed by arthroscopy of the hip, found that arthroscopy altered the initial diagnosis in 53% of cases, enabling more specific diagnoses (Baber, Robinson and Villar, 1999). Santori and Villar (1999) found that diagnostic arthroscopy for hip pain (<6 months hip symptoms) enabled diagnosis of OA in 60 of 186 patients (32.2%) who were pre-operatively radiographically normal and for whom OA had not been diagnosed.

Total hip replacement

Total hip replacement (THR) is considered a highly effective and relatively safe operation, with lasting benefits to the recipient. Approximately 85% of all patients undergoing THR have a diagnosis of OA.Studies show that outcomes for patients with OA receiving hip replacements are even better than those for TKR (Bachmeier, March and Cross, 2001; Jones et al., 2001; Kirwan et al., 1994). Indications for THR, developed at the National Institutes of Health (NIH) consensus conference, include 'radiographic evidence of joint damage and moderate to severe persistent pain or disability, or both, that is not substantially relieved by an extended course of non-surgical management' (American College of Rheumatology, 2000). However, studies have not shown a close relationship between radiographic evidence and preoperative status or outcome (as measured by SF-36 and WOMAC scales) after THR. Although radiographic changes indicative of OA is often used as criteria for surgeons in determining whether or not to perform THR (Nilsdotter, Aurell, Siosteen and al, 2001).

Following THR, 90 to 95% of patients can expect to have their prosthesis functioning at 10 years, and 85% will still be functioning at 20 years. Implant survivorship after an average of 18 years of follow-up in men less than 50 is 80-85% (Crawford and Murray, 1997). Other factors important in THR outcome include high BMI, which has been found to be associated with lower post-operative functional status and increased post-operative pain (Braeken, Lochhaas-Gerlach, Gollish and al, 1997). There is considerable debate regarding the relative merits of cemented compared with non-cemented implants. The evidence from countries where hip registries are maintained suggests that the higher the percentage of non-cemented implants, the higher the implant failure rate. The type of implant used may also be an important indicator of outcomes. Although new implants are regularly released onto the market, there is often little assessment of their benefits compared with current implants. (Crawford and Murray, (1997)noted that in 1996 there were over 60 different primary total hip prostheses available in the UK, with wide variation in cost. Over half of these had been introduced in the preceding 5 years, most with no published clinical results).

Conclusion re surgery for hip OA

Hip replacement provides extensive and long-lasting benefits in those with severe refractory hip OA. It is a relatively safe and well established procedure with over 30 years of application in most developed countries. Arthroscopy of the hip is not a commonly undertaken procedure, but may lead to a more accurate diagnosis of hip pathology compared with radiography. THR is to be included in the modelling. Key studies are: Bachmeier, March and Cross, 2001; Jones et al., 2001;Kirwan et al., 1994.

LITERATURE REVIEW REFERENCES

Adams, M. E., Lussier, A. J. and Peyron, J. G. (2000) "A risk-benefit assessment of injections of hyaluronan and its derivatives in the treatment of osteoarthritis of the knee", *Drug Saf,* **23,** pp. 115-30.

Altman, R., Aven, A., Holmburg, C., Pfeifer, L., Sack, M. and Young, G. (1994) "Capsaicin cream 0.025% as monotherapy for osteoarthritis : a double-blind study", *Seminars in Arthritis & Rheumatism,* **23,** pp. 25-33.

American College of Rheumatology (2000) "Recommendations for the medical management of OA of the hip and knee", *Arthritis and Rheumatism,* **43,** pp. 1905-1915.

Anonymous (1998) "AGS clinical practice guidelines: the management of chronic pain in older persons", *Geriatrics,* **53 Suppl 3,** pp. S6-7.

Anonymous (1999) "Hyaluronan or hylans for knee osteoarthritis?", *Drug Ther Bull,* **37,** pp. 71-2.

Appelboom, T., Schuermans, J., Verbruggen, G., Henrotin, Y. and Reginster, J. Y. (2001) "Symptoms modifying effect of avocado/soybean unsaponifiables (ASU) in knee osteoarthritis. A double blind, prospective, placebo-controlled study", *Scand J Rheumatol,* **30,** pp. 242-7.

Baber, Y., Robinson, A. and Villar, R. (1999) "Is diagnostic arthroscopy of the hip worthwhile ? A prospective review of 328 adults investigatred for hip pain.", *Journal of Bone and Joint Surgery,* **81B,** pp. 600-603.

Bachmeier, C., March, L. and Cross, M. (2001) "A comparison of outcomes in OA patients undergoing total hip and knee replacement", *Osteoarthritis and Cartilage,* **9,** pp. 137-146.

Baker, K. R., Nelson, M. E., Felson, D. T., Layne, J. E., Sarno, R. and Roubenoff, R. (2001) "The efficacy of home based progressive strength training in older adults with knee osteoarthritis: a randomized controlled trial", *J Rheumatol,* **28,** pp. 1655-65.

Balas, E. A., Jaffrey, F., Kuperman, G. J., Boren, S. A., Brown, G. D., Pinciroli, F. and Mitchell, J. A. (1997) "ELECTRONIC COMMUNICATION WITH PATIENTS - EVALUATION OF DISTANCE MEDICINE TECHNOLOGY [Review]", *Jama: Journal of the American Medical Association,* **278,** pp. 152-159.

Balint, G. and Szebenyi, B. (1997) "Non-pharmacological therapies in osteoarthritis", *Baillieres Clinical Rheumatology,* **11,** pp. 795-815.

Baumgaertner, M., Dilworth-Cannon, W., Vittori, J. and al, e. (1990) "Arthroscopic debridement of the Arthritis Knee", *Clinical Orthopaedics and Related Research,* **253,** pp. 197-202.

Bennett, S. A. and Magnus, P. (1994) "Trends in cardiovascular risk factors in Australia. Results from the National Heart Foundation's Risk Factor Prevalence Study, 1980-1989", *Medical Journal of Australia,* **161,** pp. 519-27.

Bensen, W., Fiechtner, J., McMillen, J. and al, e. (1999) "Treatment of OA with celecoxib, a cyclooxygenase-2 inhibitor : a randomised, controlled trial", *Mayo Clinical Proceedings,* **74,** pp. 109-1105.

Blotman, F., Maheu, E., Wulwik, A., Caspard, H. and Lopez, A. (1997) "Efficacy and safety of avocado/soybean unsaponifiables in the treatment of symptomatic osteoarthritis of the knee and hip. A prospective, multicenter, three-month, randomized, double-blind, placebo-controlled trial", *Rev Rhum Engl Ed,* **64,** pp. 825-34.

Bowditch, M. G. and Villar, R. N. (1999) "Do obese patients bleed more? A prospective study of blood loss at total hip replacement", *Ann R Coll Surg Engl,* **81,** pp. 198-200.

Bradley, J. D., Brandt, K. D., Katz, B. P., Kalasinski, L. A. and Ryan, S. I. (1991) "Comparison of an antiinflammatory dose of ibuprofen, an analgesic dose of ibuprofen, and acetaminophen in the treatment of patients with osteoarthritis of the knee", *N Engl J Med,* **325,** pp. 87-91.

Bradley, J. D., Heilman, D. K., Katz, B. P., Gsell, P., Wallick, J. E. and Brandt, K. D. (2002) "Tidal irrigation as treatment for knee osteoarthritis: a sham- controlled, randomized, double-blinded evaluation", *Arthritis Rheum,* **46,** pp. 100-8.

Braeken, A., Lochhaas-Gerlach, J., Gollish, J. and al, e. (1997) "Determinants of 6-12 month postoperative functional status and pain after elective hip replacement", *International Journal for Quality in Health Care,* **9,** pp. 413-418.

Brand, C., Snaddon, J., Bailey, M. and Cicuttini, F. (2001) "Vitamin E is ineffective for symptomatic relief of knee osteoarthritis: a six month double blind, randomised, placebo controlled study", *Ann Rheum Dis,* **60,** pp. 946-9.

Brosseau, L., Welch, V., Wells, G., deBie, R., Gam, A., Harman, K., Morin, M., Shea, B. and Tugwell, P. (2001) "Low level laser therapy (Classes 1, II and III) for treating osteoarthritis", *The Cochrane Database of Systematic Reviews,***,** pp.

Buchbinder, R., Jolley, D. and Wyatt, M. (2001) "Population based intervention to change back pain beliefs and disability: three part evaluation", *BMJ,* **322,** pp. 1516-20.

Carroll, D., Moore, R. A., McQuay, H. J., Fairman, F., Tramer, M. and Leijon, G. (2001) "Transcutaneous electrical nerve stimulation (TENS) for chronic pain", *The Cochrane database of systematic reviews,***,** pp.

Caruso, I. and Pietrogrande, V. (1987) "Italian double-blind multicenter study comparing S-adenosylmethionine, naproxen, and placebo in the treatment of degenerative joint disease", *Am J Med,* **83,** pp. 66-71.

Cavill, N. (1998) "National campaigns to promote physical activity: can they make a difference?", *International Journal of Obesity & Related Metabolic Disorders,* **22 Suppl 2,** pp. S48-51.

Center for Reviews Dissemination (2001) "Patient education interventions in osteoarthritis and rheumatoid arthritis: a meta-analytic comparison with nonsteroidal antiinflammatory drug treatment",**,** pp.

Chang, R., Falconer, J., Stulburg, S. and al, e. (1993) "A randomised, controlled trial of arthroscopic surgery versus joint lavage for patients with OA of the knee", *Arthritis and Rheumatism,* **36,** pp. 289-296.

Chang, R. W., Pellisier, J. M. and Hazen, G. B. (1996) "A cost-effectiveness analysis of total hip arthroplasty for osteoarthritis of the hip", *JAMA,* **275,** pp. 858-65.

Coggon, D., Reading, I., Croft, P., McLaren, M., Barrett, D. and Cooper, C. (2001) "Knee osteoarthritis and obesity", *Int J Obes Relat Metab Disord,* **25,** pp. 622-7.

Cohen, J. L., Sauter, S. V., deVellis, R. F. and deVellis, B. M. (1986) "Evaluation of arthritis self-management courses led by laypersons and by professionals", *Arthritis Rheum,* **29,** pp. 388-93.

Crawford, R. W. and Murray, D. W. (1997) "Total hip replacement: indications for surgery and risk factors for failure", *Annals of the Rheumatic Diseases,* **56,** pp. 455-7.

Creamer, P. (1997) "Intra-articular corticosteroid injections in osteoarthritis: do they work and if so, how?", *Ann Rheum Dis,* **56,** pp. 634-6.

Cronan, T. A., Kaplan, R. M., Posner, L., Blumberg, E. and Kozin, F. (1989) "Prevalence of the use of unconventional remedies for arthritis in a metropolitan community", *Arthritis Rheum,* **32,** pp. 1604-7.

Cushnaghan, J., McCarthy, C. and Dieppe, P. (1994) "Taping the patella medially: a new treatment for osteoarthritis of the knee joint?", *BMJ,* **308,** pp. 753-5.

Deal, C. L., Schnitzer, T. J., Lipstein, E., Seibold, J. R., Stevens, R. M., Levy, M. D., Albert, D. and Renold, F. (1991) "Treatment of arthritis with topical capsaicin: a double-blind trial", *Clin Ther,* **13,** pp. 383-95.

Deyle, G. D., Henderson, N. E., Matekel, R. L., Ryder, M. G., Garber, M. B. and Allison, S. C. (2000) "Effectiveness of manual physical therapy and exercise in osteoarthritis of the knee. A randomized, controlled trial", *Ann Intern Med,* **132,** pp. 173-81.

DHAC (2001) *National Evaluator for the evluation of the Sharing Health Care Initiative,* Department, of Health and Aged Care, Canberra.

Dieppe, P., Basler, H. D., Chard, J., Croft, P., Dixon, J., Hurley, M., Lohmander, S. and Raspe, H. (1999) "Knee replacement surgery for osteoarthritis: effectiveness, practice variations, indications and possible determinants of utilization", *Rheumatology (Oxford),* **38,** pp. 73-83.

Dieppe, P., Cushnaghan, J., Jasani, M. K., McCrae, F. and Watt, I. (1993) "A two-year, placebo-controlled trail of non-steroidal anti-inflammatory therapy in osteoarthritis of the knee joint", *Br J Rheumatol,* **32,** pp. 595-600.

Dougados, M., Gueguen, A., Nguyen, M., Thiesce, A., Listrat, V., Jacob, L., Nakache, J. P., Gabriel, K. R., Lequesne, M. and Amor, B. (1992) "Longitudinal radiologic evaluation of osteoarthritis of the knee", *J Rheumatol,* **19,** pp. 378-84.

Dougados, M., Nguyen, M., Listrat, V. and Amor, B. (1993) "High molecular weight sodium hyaluronate (hyalectin) in osteoarthritis of the knee: a 1 year placebo-controlled trial", *Osteoarthritis Cartilage,* **1,** pp. 97-103.

Douketis, J. D., Feightner, J. W., Attia, J. and Feldman, W. F. (1999) "Periodic health examination, 1999 update: 1. Detection, prevention and treatment of obesity. Canadian Task Force on Preventive Health Care. [see comments]", *CMAJ,* **160,** pp. 513-25.

Draper, E. R., Cable, J. M., Sanchez-Ballester, J., Hunt, N., Robinson, J. R. and Strachan, R. K. (2000) "Improvement in function after valgus bracing of the knee. An analysis of gait symmetry", *J Bone Joint Surg Br,* **82,** pp. 1001-5.

Eaton, C. B. and Menard, L. M. (1998) "A SYSTEMATIC REVIEW OF PHYSICAL ACTIVITY PROMOTION IN PRIMARY CARE OFFICE SETTINGS [Review]", *British Journal of Sports Medicine,* **32,** pp. 11-16.

Eccles, M., Freemantle, N. and Mason, J. (1998) "North of England evidence based guideline development project: guideline on the use of aspirin as secondary prophylaxis for vascular disease in primary care. North of England Aspirin Guideline Development Group", *Bmj,* **316,** pp. 1303-9.

Edelson, R., Burks, R. and Bloebaum, R. (1995) "Short term effects of knee washout for OA", *American journal of Sports Medicine,* **23,** pp. 345-349.

Evans, J. M., McMahon, A. D., McGilchrist, M. M., White, G., Murray, F. E., McDevitt, D. G. and MacDonald, T. M. (1995) "Topical non-steroidal anti-inflammatory drugs and admission to hospital for upper gastrointestinal bleeding and perforation: a record linkage case-control study", *Bmj,* **311,** pp. 22-6.

Ezzo, J., Hadhazy, V., Birch, S., Lao, L., Kaplan, G., Hochberg, M. and Berman, B. (2001) "Acupuncture for osteoarthritis of the knee: a systematic review", *Arthritis Rheum,* **44,** pp. 819-25.

Farquhar, J. W. (1990) "Effects of communitywide education on cardiovascular disease risk factors. The Stanford Five-City Project", *JAMA,* **264,** pp. 359-65.

FDA (2000) *FDA. Celecoxib Medical Officer Review.,* NDA 20-998/S-009, FDA.

FDA (2001) "VIOXX Gastrointestinal Safety. FDA advisory committee briefing document. NDA 21-042, s007.",**,** pp.

Felson, D. T. and Zhang, Y. (1998) "An update on the epidemiology of knee and hip osteoarthritis with a view to prevention", *Arthritis Rheum,* **41,** pp. 1343-55.

Fortmann, S. P., Williams, P. T., Hulley, S. B., Haskell, W. L. and Farquhar, J. W. (1981) "Effect of health education on dietary behavior: the Stanford Three Community Study", *American Journal of Clinical Nutrition,* **34,** pp. 2030-8.

Gaby, A. R. (1999) "Natural treatments for osteoarthritis", *Altern Med Rev,* **4,** pp. 330-41.

Geba, G. P., Weaver, A. L., Polis, A. B., Dixon, M. E. and Schnitzer, T. J. (2002) "Efficacy of rofecoxib, celecoxib, and acetaminophen in osteoarthritis of the knee: a randomized trial", *Jama,* **287,** pp. 64-71.

Glazer, G. (2001) "Long-term pharmacotherapy of obesity 2000: a review of efficacy and safety", *Archives of Internal Medicine,* **161,** pp. 1814-24.

Gosal, H. S., Jackson, A. M. and Bickerstaff, D. R. (1999) "Intra-articular steroids after arthroscopy for osteoarthritis of the knee. [see comments]", *Journal of Bone & Joint Surgery - British Volume,* **81,** pp. 952-4.

Halbert, J. A., Silagy, C. A., Finucane, P. M., Withers, R. T. and Hamdorf, P. A. (2000) "Physical activity and cardiovascular risk factors: effect of advice from an exercise specialist in Australian general practice. [see comments]", *Medical Journal of Australia,* **173,** pp. 84-7.

Hanssen, A., MJ, S., RD, S. and al, e. (2000) "Surgical options for middle aged patients with OA of the knee joint", *Journal of Bone and Joint Surgery,* **82(A),** pp. 1768-1781.

Harvey, R., Eagar, K., Perkins, D., Owen, A., Sansoni, J. and Adamson, L. (2000) *Draft National Evaluation Framework for the Sharing Health Care,* Centre for Health Service Development, University of Wollongong, Wollongong.

Hawley, D. J. (1995) "Psycho-Educational Interventions in the Treatment of Arthritis", *Baillieres Clinical Rheumatology,* **9,** pp. 803-823.

Heerdink, E., Leufkens, G., Herings, R. and al, e. (1998) "NSAIDs associated with increased risk of congestive heart failure in elderly patients taking diuretics", *Archives of Internal Medicine,* **158,** pp. 1108-1112.

Henderson, E. B., Smith, E. C., Pegley, F. and Blake, D. R. (1994) "Intra-articular injections of 750 kD hyaluronan in the treatment of osteoarthritis: a randomised single centre double-blind placebo- controlled trial of 91 patients demonstrating lack of efficacy", *Ann Rheum Dis,* **53,** pp. 529-34.

Henry, D., Lim, L., Rodriguez, L. and al, E. (1996) "Variability in risk of GI complications with individual NSAIDs : results of a collaborative meta-analysis.", *BMJ,* **312,** pp. 1563-1566.

Henry, D., Page, J., Whyte, I. and al, e. (1997) "Consumption of NSAIDS and the development of functional renal impairment in elderly subjects. Results of a case-control study", *British Journal of Clinical Pharmacology,* **44,** pp. 85-90.

Hewett, T. E., Noyes, F. R., Barber-Westin, S. D. and Heckmann, T. P. (1998) "Decrease in knee joint pain and increase in function in patients with medial compartment arthrosis: a prospective analysis of valgus bracing", *Orthopedics,* **21,** pp. 131-8.

Hochberg, M. C. (2000) "Role of intra-articular hyaluronic acid preparations in medical management of osteoarthritis of the knee", *Semin Arthritis Rheum,* **30,** pp. 2-10.

Holman, H. R. and Lorig, K. R. (1997) "Overcoming barriers to successful aging. Self-management of osteoarthritis", *West J Med,* **167,** pp. 265-8.

Hosie, G. and Bird, H. (1994) "The topical NSAID Felbinac vs oral NSAIDS : a critical review", *European Journal of Rheumatology and Inflammation,* **14,** pp.

Huang, M.-H., Chen, c.-H., Chen, T.-W., Weng, M.-C., Wang, W.-T. and Wang, Y.-L. (2000) "The Effects of Weight Reduction on the Rehabilitation of Patients with Knee Osteoarthritis and Obesity", *Arthritis Care and Research,* **13,** pp. 398-405.

Huskisson, E. C. and Donnelly, S. (1999) "Hyaluronic acid in the treatment of osteoarthritis of the knee", *Rheumatology (Oxford),* **38,** pp. 602-7.

Ike, R., Arnold, W., Rothschild, E. and al, e. (1992) "Tidal irrigation versus conservative medical management in patients with OA of the knee : a prospective randomised study", *Journal of Rheumatology,* **19,** pp. 772-779.

Jeffery, R. W. (1993) "Minnesota studies on community-based approaches to weight loss and control", *Ann Intern Med,* **119,** pp. 719-21.

Jonas, W. B., Rapoza, C. P. and Blair, W. F. (1996) "The effect of niacinamide on osteoarthritis: a pilot study", *Inflamm Res,* **45,** pp. 330-4.

Jones, C., Voaklander, D., Johnston, D. and Suarez-Almazor, M. (2001) "The effect of age, pain, function and quality of life after total hip and knee arthroplasty", *Archives of Internal Medicine,* **161,** pp. 454-460.

Kalunian, K., Moreland, L., Klashman, D. and al, e. (2000) "Visually-guided irrigation in patients with early knee OA : a multicentre randomised, controlled trial", *Osteoarthritis and Cartilage,* **8,** pp. 412-418.

Keating, E. M., Faris, P. M., Ritter, M. A. and Kane, J. (1993) "Use of lateral heel and sole wedges in the treatment of medial osteoarthritis of the knee", *Orthopaedic Review,* **22,** pp. 921-4.

King, A. C., Rejeski, W. J. and Buchner, D. M. (1998) "Physical activity interventions targeting older adults. A critical review and recommendations", *American Journal of Preventive Medicine,* **15,** pp. 316-33.

Kirkley, A., Webster-Bogaert, S., Litchfield, R., Amendola, A., MacDonald, S., McCalden, R. and Fowler, P. (1999) "The effect of bracing on varus gonarthrosis", *J Bone Joint Surg Am,* **81,** pp. 539-48.

Kirwan, J., Currey, H., Freeman, M. and al, e. (1994) "Overall long-term impact of total hip and knee joint replacement surgery on patients with OA and RA", *British Journal of Rheumatology,* **33,** pp. 357-360.

Knutsson, S. and Engberg, I. B. (1999) "An evaluation of patients' quality of life before, 6 weeks and 6 months after total hip replacement surgery", *Journal of Advanced Nursing,* **30,** pp. 1349-59.

Konig, B. (1987) "A long-term (two years) clinical trial with S-adenosylmethionine for the treatment of osteoarthritis", *Am J Med,* **83,** pp. 89-94.

Lane, N. E., Gore, L. R., Cummings, S. R., Hochberg, M. C., Scott, J. C., Williams, E. N. and Nevitt, M. C. (1999) "Serum vitamin D levels and incident changes of radiographic hip osteoarthritis: a longitudinal study. Study of Osteoporotic Fractures Research Group", *Arthritis Rheum,* **42,** pp. 854-60.

Lindenfeld, T. N., Hewett, T. E. and Andriacchi, T. P. (1997) "Joint loading with valgus bracing in patients with varus gonarthrosis", *Clin Orthop,***,** pp. 290-7.

Little, C. V. and Parsons, T. (2001) "Herbal Therapy for treating osteoarthritis (Cochrane Review)", *Cochrane Database Syst Rev,* **1,** pp.

Long, L., Soeken, K. and Ernst, E. (2001) "Herbal medicines for the treatment of osteoarthritis: a systematic review", *Rheumatology (Oxford),* **40,** pp. 779-93.

Lord, J., Victor, C., Littlejohns, P., Ross, F. M. and Axford, J. S. (1999) "Economic evaluation of a primary care-based education programme for patients with osteoarthritis of the knee", *Health Technol Assess,* **3,** pp. 1-55.

Lorig, K., Lubeck, D., Kraines, R. G., Seleznick, M. and Holman, H. R. (1985) "Outcomes of self-help education for patients with arthritis", *Arthritis Rheum,* **28,** pp. 680-5.

Lorig, K. R., Mazonson, P. D. and Holman, H. R. (1993) "Evidence suggesting that health education for self-management in patients with chronic arthritis has sustained health benefits while reducing health care costs", *Arthritis & Rheumatism,* **36,** pp. 439-46.

Lorig, K. R., Sobel, D. S., Stewart, A. L., Brown, B. W., Jr., Bandura, A., Ritter, P., Gonzalez, V. M., Laurent, D. D. and Holman, H. R. (1999) "Evidence suggesting that a chronic disease self-management program can improve health status while reducing hospitalization: a randomized trial", *Medical Care,* **37,** pp. 5-14.

Lussier, A., Cividino, A. A., McFarlane, C. A., Olszynski, W. P., Potashner, W. J. and De Medicis, R. (1996) "Viscosupplementation with hylan for the treatment of osteoarthritis: findings from clinical practice in Canada", *J Rheumatol,* **23,** pp. 1579-85.

Maccagno, A., Di Giorgio, E. E., Caston, O. L. and Sagasta, C. L. (1987) "Double-blind controlled clinical trial of oral S-adenosylmethionine versus piroxicam in knee osteoarthritis", *Am J Med,* **83,** pp. 72-7.

Machtey, I. and Ouaknine, L. (1978) "Tocopherol in Osteoarthritis: a controlled pilot study", *J Am Geriatr Soc,* **26,** pp. 328-30.

Maheu, E., Mazieres, B., Valat, J. and al, e. (1998) "Symptomatic efficacy of avocado/soybean unsaponifiables in the treatment of OA of the knee and hip.", *Arthritis and Rheumatism,* **41,** pp. 81-91.

Mancuso, C. A., Ranawat, C. S., Esdaile, J. M., Johanson, N. A. and Charlson, M. E. (1996) "Indications for total hip and total knee arthroplasties. Results of orthopaedic surveys", *Journal of Arthroplasty,* **11,** pp. 34-46.

Manek, N. J. and Lane, N. E. (2000) "Osteoarthritis: current concepts in diagnosis and management", *Am Fam Physician,* **61,** pp. 1795-804.

March, L. and Stenmark, J. (2001) "Non-pharmacological approaches to managing arthritis", *Medical Journal of Australia,* **175,** pp. S102-S107.

Marcus, B. H., Owen, N., Forsyth, L. H., Cavill, N. A. and Fridinger, F. (1998) "Physical activity interventions using mass media, print media, and information technology", *American Journal of Preventive Medicine,* **15,** pp. 362-78.

Marks, R. and de Palma, F. (1999) "Clinical efficacy of low power laser therapy in osteoarthritis", *Physiotherapy Research International,* **4,** pp. 141-57.

Matsuno, H., Kadowaki, K. M. and Tsuji, H. (1997) "Generation II knee bracing for severe medial compartment osteoarthritis of the knee", *Arch Phys Med Rehabil,* **78,** pp. 745-9.

McAlindon, T. E., Felson, D. T., Zhang, Y., Hannan, M. T., Aliabadi, P., Weissman, B., Rush, D., Wilson, P. W. and Jacques, P. (1996) "Relation of dietary intake and serum levels of vitamin D to progression of osteoarthritis of the knee among participants in the Framingham Study", *Ann Intern Med,* **125,** pp. 353-9.

McAlindon, T. E., Jacques, P., Zhang, Y., Hannan, M. T., Aliabadi, P., Weissman, B., Rush, D., Levy, D. and Felson, D. T. (1996) "Do antioxidant micronutrients protect against the development and progression of knee osteoarthritis?", *Arthritis Rheum,* **39,** pp. 648-56.

McColl, G. (2001) "Pharmacological therapies in the treatment of OA", *Medical Journal of Australia,* **175,** pp. 108-114.

Miller, W. C., Koceja, D. M. and Hamilton, E. J. (1997) "A meta-analysis of the past 25 years of weight loss research using diet, exercise or diet plus exercise intervention. [see comments]", *International Journal of Obesity & Related Metabolic Disorders,* **21,** pp. 941-7.

Moore, R., Tramer, R., Carroll, D. and al, e. (1998) "Quantitiative systematic review of topically aplied NSAIDS", *BMJ,* **316,** pp. 333-338.

Mosely, J., Wray, N., Kuykendall, D. and al, e. (1996) "Arthroscopic treatment of OA of the knee : a prospective randomised placebo-controlled trial : results of a pilot study", *The American Journal of Sports Medicine,* **24,** pp. 28-34.

Muller-Fassbender, H. (1987) "Double-blind clinical trial of S-adenosylmethionine versus ibuprofen in the treatment of osteoarthritis", *Am J Med,* **83,** pp. 81-3.

National Prescribing Service (2000) *COX-2-selective NSAIDs : New wonder drugs ?,* National Prescribing Service, Sydney.

Newman, J., Shah, C. and Nilen, A. (1998) "Unicompartmental or total knee replacement ? Five-year results of a prospective randomised trial of 102 OA knees with unicompartmental arthritis.", *Journal of Bone and Joint Surgery,* **80,** pp. 862-865.

Newnham, R. E. (1994) "Essentiality of boron for healthy bones and joints", *Environ Health Perspect,* **102 Suppl 7,** pp. 83-5.

Nilsdotter, A.-K., Aurell, Y., Siosteen, A.-K. and al, e. (2001) "Radiographic stage of OA or sex of the patient doesn not predict one year outcome after total hip arthroplasty", *Annals of Rheumatic Diseases,* **60,** pp. 228-232.

O'Reilly, S. C., Muir, K. R. and Doherty, M. (1999) "Effectiveness of home exercise on pain and disability from osteoarthritis of the knee: a randomised controlled trial", *Annals of the Rheumatic Diseases,* **58,** pp. 15-9.

Osborne, R. H., Segal, L. and Day, S. (2001) *Priority Setting in Musculoskeletal Disorders: A Focus on Osteoarthritis,* Working paper 128, ISBN 1 876662 48 4, Health Economics Unit, Monash University, Melbourne.

Osiri, M., Welch, V. V., Brosseau, L., Shea, B., McGowan, J., Tugwell, P. and Wells, G. (2000) "Transcutaneous electrical nerve stimulation for knee osteoarthritis (Cochrane Review)", *Cochrane Database Syst Rev,* **4,** pp.

Page, J. and Henry, D. (2000) "Consumption of NSAIDs and the development of congestive heart failure in elderly patients ; an underrecognised public health problem", *Archives of Internal Medicine,* **160,** pp. 777-784.

Parvizi, J., Trousdale, R. T. and Sarr, M. G. (2000) "Total joint arthroplasty in patients surgically treated for morbid obesity", *J Arthroplasty,* **15,** pp. 1003-8.

Pasquali Ronchetti, I., Guerra, D., Taparelli, F., Boraldi, F., Bergamini, G., Mori, G., Zizzi, F. and Frizziero, L. (2001) "Morphological analysis of knee synovial membrane biopsies from a randomized controlled clinical study comparing the effects of sodium hyaluronate (Hyalgan) and methylprednisolone acetate (Depomedrol) in osteoarthritis", *Rheumatology (Oxford),* **40,** pp. 158-69.

Peloso, P. M. (2001) "Opioid therapy for osteoarthritis of the hip and knee: use it or lose it?", *J Rheumatol,* **28,** pp. 6-11.

Peloso, P. M., Bellamy, N., Bensen, W., Thomson, G. T., Harsanyi, Z., Babul, N. and Darke, A. C. (2000) "Double blind randomized placebo control trial of controlled release codeine in the treatment of osteoarthritis of the hip or knee", *Journal of Rheumatology,* **27,** pp. 764-71.

Pencharz, J. N., Grigoriadis, E, Jansz, G.F., Bombardier, C. (2001) "A Critical Appraisal of Clinical Practice Guidelines for the Treatment of Lower Limb Osteoarthritis", *Submitted for publication,***,** pp.

Pendleton, A., Arden, N., Dougados, M., Doherty, M., Bannwarth, B., Bijlsma, J. W., Cluzeau, F., Cooper, C., Dieppe, P. A., Gunther, K. P., Hauselmann, H. J., Herrero-Beaumont, G., Kaklamanis, P. M., Leeb, B., Lequesne, M., Lohmander, S., Mazieres, B., Mola, E. M., Pavelka, K., Serni, U., Swoboda, B., Verbruggen, A. A., Weseloh, G. and Zimmermann-Gorska, I. (2000) "EULAR recommendations for the management of knee osteoarthritis: report of a task force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT)", *Ann Rheum Dis,* **59,** pp. 936-44.

Perneger, T. V., Whelton, P. K. and Klag, M. J. (1994) "Risk of kidney failure associated with the use of acetaminophen, aspirin, and nonsteroidal antiinflammatory drugs. [see comments]", *New England Journal of Medicine,* **331,** pp. 1675-9.

Pincus, T., Koch, G. G., Sokka, T., Lefkowith, J., Wolfe, F., Jordan, J. M., Luta, G., Callahan, L. F., Wang, X., Schwartz, T., Abramson, S. B., Caldwell, J. R., Harrell, R. A., Kremer, J. M., Lautzenheiser, R. L., Markenson, J. A., Schnitzer, T. J., Weaver, A., Cummins, P., Wilson, A., Morant, S. and Fort, J. (2001) "A randomized, double-blind, crossover clinical trial of diclofenac plus misoprostol versus acetaminophen in patients with osteoarthritis of the hip or knee", *Arthritis Rheum,* **44,** pp. 1587-98.

Rains, C. and Bryson, H. M. (1995) "Topical capsaicin. A review of its pharmacological properties and therapeutic potential in post-herpetic neuralgia, diabetic neuropathy and osteoarthritis", *Drugs Aging,* **7,** pp. 317-28.

Ramsey, S. D., Spencer, A. C., Topolski, T. D., Belza, B. and Patrick, D. L. (2001) "Use of alternative therapies by older adults with osteoarthritis", *Arthritis Rheum,* **45,** pp. 222-7.

Ravaud, P., Moulinier, L., Giraudeau, B., Ayral, X., Guerin, C., Noel, E., Thomas, P., Fautrel, B., Mazieres, B. and Dougados, M. (1999) "Effects of joint lavage and steroid injection in patients with osteoarthritis of the knee: results of a multicenter, randomized, controlled trial", *Arthritis & Rheumatism,* **42,** pp. 475-82.

Reginster, J.-Y. (2000) "Review : Glucosamine and chondroitin improve outcomes in OA, but the magnitude of effect is unclear", *Amerrican College of Physicians Journal Club,* **133,** pp. 58.

Reginster, J. Y., Deroisy, R., Rovati, L. C., Lee, R. L., Lejeune, E., Bruyere, O., Giacovelli, G., Henrotin, Y., Dacre, J. E. and Gossett, C. (2001) "Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial", *Lancet,* **357,** pp. 251-6.

Roy, C. W. and Hunter, J. (1996) "What happens to patients awaiting arthritis surgery?", *Disabil Rehabil,* **18,** pp. 101-5.

Santori, N. and Villar, R. (1999) "Arthroscopic findings in the initial stages of hip OA", *Orthopedics,* **22,** pp. 405-.

Scherak, O., Kolarz, G., Schodl, C. and Blankenhorn, G. (1990) "[High dosage vitamin E therapy in patients with activated arthrosis]", *Z Rheumatol,* **49,** pp. 369-73.

Scholes, D., Stergachis, A., Penna, P. M., Normand, E. H. and Hansten, P. D. (1995) "Nonsteroidal antiinflammatory drug discontinuation in patients with osteoarthritis", *J Rheumatol,* **22,** pp. 708-12.

Schouten, J. S., van den Ouweland, F. A. and Valkenburg, H. A. (1992) "A 12 year follow up study in the general population on prognostic factors of cartilage loss in osteoarthritis of the knee", *Ann Rheum Dis,* **51,** pp. 932-7.

Scott, D. L., Berry, H., Capell, H., Coppock, J., Daymond, T., Doyle, D. V., Fernandes, L., Hazleman, B., Hunter, J., Huskisson, E. C., Jawad, A., Jubb, R., Kennedy, T., McGill, P., Nichol, F., Palit, J., Webley, M., Woolf, A. and Wotjulewski, J. (2000) "The long-term effects of non-steroidal anti-inflammatory drugs in osteoarthritis of the knee: a randomized placebo-controlled trial", *Rheumatology (Oxford),* **39,** pp. 1095-101.

Segal, L., Day, S., Chapman, A. and Osborne, R. (2002) *Priority setting in osteoarthritis: selecting the interventions,* Report to the Population Health Division, Department of Health and Ageing, Health Economics Unit, Monash University, Melbourne.

Shafshak, T. S. (1995) "Electroacupuncture and exercise in body weight reduction and their application in rehabilitating patients with knee osteoarthritis", *Am J Chin Med,* **23,** pp. 15-25.

Sharma, L., Song, J., Felson, D. T., Cahue, S., Shamiyeh, E. and Dunlop, D. D. (2001) "The role of knee alignment in disease progression and functional decline in knee osteoarthritis", *JAMA,* **286,** pp. 188-95.

Silverstein, F., Faich, G., Goldstein, J. and al, e. (2000) "GI toxicity with celecoxib vs NSAIDs for OA and RA: the CLASS Study : a randomised controlled trial.", *JAMA,* **284,** pp. 1247-1255.

Superio-Cabuslay, E., Ward, M. M. and Lorig, K. R. (1996) "Patient education interventions in osteoarthritis and rheumatoid arthritis: a meta-analytic comparison with nonsteroidal antiinflammatory drug treatment", *Arthritis Care Res,* **9,** pp. 292-301.

Taylor, C. B., Fortmann, S. P., Flora, J., Kayman, S., Barrett, D. C., Jatulis, D. and Farquhar, J. W. (1991) "Effect of long-term community health education on body mass index. The Stanford Five-City Project", *American Journal of Epidemiology,* **134,** pp. 235-49.

Tohyama, H., Yasuda, K. and Kaneda, K. (1991) "Treatment of osteoarthritis of the knee with heel wedges", *International Orthopaedics,* **15,** pp. 31-3.

Towheed, T., Shea, B., G, W. and Hochberg, M. (2001) "Analgesia and non-aspirin, non-steroidal anti-inflammatory drugs for OA of the hip", *The Cochrane database of systematic reviews,***,** pp.

Towheed, T. E. and Anastassiades, T. P. (2000) "Glucosamine and chondroitin for treating symptoms of osteoarthritis: evidence is widely touted but incomplete", *Jama,* **283,** pp. 1483-4.

van Baar, M. E., Assendelft, W. J., Dekker, J., Oostendorp, R. A. and Bijlsma, J. W. (1999) "Effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a systematic review of randomized clinical trials", *Arthritis Rheum,* **42,** pp. 1361-9.

Vetter, G. (1987) "Double-blind comparative clinical trial with S-adenosylmethionine and indomethacin in the treatment of osteoarthritis", *Am J Med,* **83,** pp. 78-80.

Walker, J. S., Sheather-Reid, R. B., Carmody, J. J., Vial, J. H. and Day, R. O. (1997) "Nonsteroidal antiinflammatory drugs in rheumatoid arthritis and osteoarthritis: support for the concept of "responders" and "nonresponders"", *Arthritis Rheum,* **40,** pp. 1944-54.

Walker-Bone, K., Javaid, K., Arden, N. and Cooper, C. (2000) "Regular review: medical management of osteoarthritis", *BMJ,* **321,** pp. 936-40.

Whelton, A. (1999) "Nephrotoxicity of NSAIDs ; physiologic foundations and clinical implications", *The American Journal of Medicine,* **106,** pp. 13S-24S.

Williams, H., Ward, J., egger, M. and al, e. (1993) "Comparison of naproxen and acetaminophen in a 2-year study of treatment of OA of the knee", *Arthritis and Rheumatism,* **36,** pp. 1196-1206.

Wobig, M., Dickhut, A., Maier, R. and Vetter, G. (1998) "Viscosupplementation with hylan G-F 20: a 26-week controlled trial of efficacy and safety in the osteoarthritic knee", *Clin Ther,* **20,** pp. 410-23.

Wolfe, F., Zhao, S. and Lane, N. (2000) "Preference for nonsteroidal antiinflammatory drugs over acetaminophen by rheumatic disease patients: a survey of 1,799 patients with osteoarthritis, rheumatoid arthritis, and fibromyalgia", *Arthritis Rheum,* **43,** pp. 378-85.