Evidence-Based Medicine Is Affordable: The Cost-Effectiveness of Current Compared with Optimal Treatment in Rheumatoid and Osteoarthritis

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ABSTRACT. ***Objective***. To determine the cost-effectiveness of averting the burden of disease. We used secondary population data and metaanalyses of various government-funded services and interventions to investigate the costs and benefits of various levels of treatment for rheumatoid arthritis (RA) and osteoarthritis (OA) in adults using a burden of disease framework.

Method. Population burden was calculated for both diseases in the absence of any treatment as years lived with disability (YLD), ignoring the years of life lost. We then estimated the proportion of burden averted with current interventions, the proportion that could be averted with optimally implemented current evidence-based guidelines, and the direct treatment cost-effectiveness ratio in dollars per YLD averted for both treatment levels.

Results. The majority of people with arthritis sought medical treatment. Current treatment for RA averted 26% of the burden, with a cost-effectiveness ratio of $19,000 per YLD averted. Optimal, evidence-based treatment would avert 48% of the burden, with a cost-effectiveness ratio of $12,000 per YLD averted. Current treatment of OA in Australia averted 27% of the burden, with a cost-effectiveness ratio of $25,000 per YLD averted. Optimal, evidence-based treatment would avert 39% of the burden, with an unchanged cost-effectiveness ratio of $25,000 per YLD averted.

Conclusion. While the precise dollar costs in each country will differ, the relativities at this level of coverage should remain the same. There is no evidence that closing the gap between evidence and practice would result in a drop in efficiency. (First Release Mar 15, 2006; J Rheumatol 2006;33:671–80)

Key Indexing Terms:
OSTEOARTHRITIS RHEUMATOID ARTHRITIS COST EFFECTIVENESS EFFICIENCY

In most countries, it is presumed that good care is directly proportional to the funds available. Investing in evidence-based programs goes beyond effectiveness. Among other things, the decision also requires the consideration of affordability and the magnitude of the additional health gains. We used a method developed for modeling the cost-effectiveness of current and optimal treatment for 10 mental disorders[1,2] to conduct a comparison of the cost and effectiveness of current and evidence-based interventions for rheumatoid arthritis (RA) and osteoarthritis (OA) over a one-year period.

Our method attempts to determine the reduction in burden associated with treatment. In measuring the cumulative disability weight change, policymakers can determine the gaps in care between current and optimal treatment programs (Figure 1), and quantify the need to invest in services or research[3]. No other publications in arthritis have utilized this method. Most studies tend to focus on either the cost-effectiveness of specific interventions or expenditure and disability related to disease[4-8].

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MATERIALS AND METHODS

This was a population-level cost-effectiveness analysis (reference year 2000–2001) based on Australian data. Costs were defined from a government or health service perspective and were calculated as the direct cost of services and treatments. Effectiveness was defined as the benefit experienced by individuals who received the interventions. The measure of health gain was years lived with disability (YLD) averted, the disability component of the disability-adjusted life-years (DALY), and a measure of population disease burden. The DALY was chosen because it is consistent with the epidemiological perspective of the study, and because it allows comparison of efficacy between previous studies in other physical and mental disorders. Consistent with methods used by the World Health Organization[9] the scenario of no treatment was used as the comparator. The scenario of no treatment, the burden evident in a population plus the burden averted by current interventions[2], is the baseline used to measure the reduction in disability (YLD averted) due to current and optimal treatment. The assumptions of the analysis are listed in Figure 2.

The YLD for a disorder is calculated as the product of the prevalence and the associated disability weight. The disability weight, a health state preference value, parallels other measures of severity, but includes societal

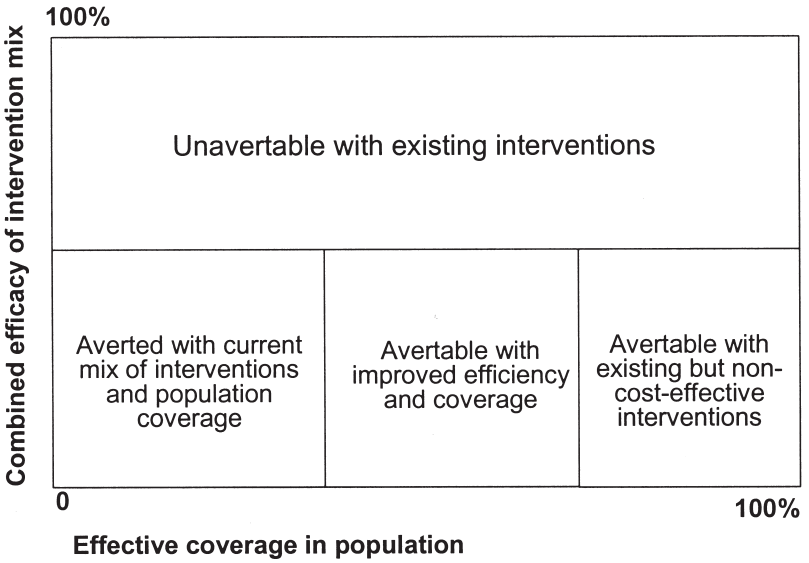

Figure 1. Relative shares of the burden of disease of a given disorder that can and cannot be averted with existing tools; adapted from the WHO model for analyzing the burden of a health problem to identify research needs[3].

perceptions as to the seriousness of the disease[10]. The disability weight is measured on a continuous scale where a score of 0 is "a state akin to perfect health," while a score of 1 is "a state akin to death." Disability weights were obtained from the Australian Burden of Disease and Injury study[11], which in turn were modifications of the EuroQoL 5D[10]. The disability weights were 0.23 for RA and 0.12 for OA and both reflect the estimated distribution of mild to severe cases in each population. The disability weight will lessen with effective treatment, and this change, multiplied by the number of people receiving the treatment, results in the total of the YLD averted in the population under study.

For models of current and optimal treatment, the cost per YLD averted was calculated as the total cost of treatment divided by the total YLD averted. Comparing the cost-effectiveness ratios for each treatment scenario reveals the relative efficiency in cost per years lived with disability averted ($/YLD averted). Discounting was not applied because of the one-year time horizon.

Study populations. The study populations were Australians with RA or OA in contact with healthcare services in the last 12 months. No single population survey provided all the data we needed so we used population data from a variety of sources. Prevalence was taken from Mathers, *et al*[11]. The population rate of any health service contact for each disorder over the year was taken from Andrews, *et al*[12]. Specific services and treatments received were modeled from the ongoing BEACH (Bettering the Evaluation of and Care of Health) survey of general practitioner consultations[13], a hospital outpatient survey[4], and the Australian Institute of Health and Welfare (AIHW) National Hospital Morbidity database[14]. Compared with the other sources, the BEACH study of 100,000 general practitioner (GP) consultations provided detailed data on diagnosis and medications prescribed, and allowed estimates of the annual encounters with health services for people with RA and OA.

Definitions of current and optimal treatment. Current treatment was defined as the services utilized and interventions prescribed in 2000–2001. The services component of current treatment included GP and specialist contacts, imaging, pathology, and hospital care. Interventions consisted of pharmaceuticals, surgery, and exercise. Services and interventions under the domain of allied and alternative health (physiotherapy and occupational therapy, glucosamine, and chondroitin) were not included as they were not subsidized by government at the time. Optimal treatment was based on the same coverage as current treatment, but presumed intervention and number of contacts in accord with evidence-based practice guidelines[15-18].

Modeling treatment outcome as YLD averted. A method was used to transfer changes in symptoms reported in randomized controlled trials (RCT) into changes in health state preference values[19] and consequently into the YLD averted. Changes in symptoms can be expressed as an effect size. The measure incorporates the change made by all those in treatment and thus includes those who improve, remain stable, or worsen. This is calculated as the mean difference in clinician-rated and/or self-reported symptoms after treatment between intervention and placebo groups, divided by the pooled standard deviation (SD). The result, an effect size, can be negative or positive, and in most studies effect sizes range between –1 and +3. Disability weights can only vary between 0 and 1, and changes due to treatment vary within a much smaller range.

Effect sizes therefore had to be adjusted by a conversion factor to represent the change in disability weights. For RA and OA we located 7 studies that had measured symptoms, functionality, and health utility changes on the same group of patients given various interventions[20-26]. The sample-weighted mean utility change score (health state preference value measure) divided by a sample-weighted effect size gave a transfer factor of 0.169. This means that a 1 SD drop in symptoms and functionality is associated with a 0.169 drop on the 0–1 disability weight scale. Thus the effect size of an intervention, multiplied by the transfer factor, gives the disability weight change likely to be associated with that treatment.

The literature was searched for metaanalyses and RCT of interventions used in these 2 disorders, and effect sizes were calculated. Literature reviews and survey data were used to estimate the likely adherence with medication in routine practice[27], and the effect sizes from these efficacy trials were downgraded to account for poor adherence. These adjusted effect sizes were transformed into disability weight changes using the transfer factor. As noted above, the number of people treated with an intervention, multiplied by the disability weight change due to that treatment, gives the number of YLD averted by that intervention in the population.

Intervention types and associated benefit. Pharmaceutical treatments in RA are priority interventions for reducing disability[16,18]. Effect sizes associated with each drug class were weighted by the frequency with which GP prescribed that class. Effect sizes were either adopted from metaanalyses, expressed as standardized mean differences (effect sizes, ES), or were cal-

ASSUMPTION	EVIDENCE
1. A one-year time horizon was used to estimate burden lost, burden averted with interventions, and costs	This project was examining alternative uses of the total one-year expenditure on mental health-related treatment so a one-year timeframe was appropriate. Also, efficacy was estimated from RCT, which rarely measure outcome beyond one year, and it is recommended to model short and longer time horizons separately when the analysis must go beyond the timeframe of the primary data[58]
2. Burden, in disability-adjusted life years (DALY) lost, can be attributed to the people who identified a principal complaint in the previous 12 months, adjusted for time spent symptomatic	Principal complaint choice allows the examination of the relationship between disability and disorder in the presence of comorbidity[12]
3. The true burden of a disease is the burden evident in the population plus the burden averted with current treatment	Measured burden will be ameliorated by the efficacy of existing services, so burden in the absence of services can be estimated by adding measured burden to burden currently averted with existing services
4. Service use can be attributed to the principal complaint during the previous year	This is essential to allow bottom-up costing, as each unit of service is only counted once, attributed to a single disorder
5. It is reasonable to operationalize detailed treatment regimes from metaanalyses and expert reviews	Metaanalyses and expert reviews summarize research and clinical expertise on optimal care for a disorder, and provide the best source for defining optimal care
6. Effectiveness reflects efficacy	Efficacy from RCT includes dropouts and noncompliance if an intent-to-treat analysis is used. In addition, treatment resistance is modeled for a proportion of cases, and thus the actual magnitude of effect applied at a group level lies somewhere between efficacy and effectiveness
7. Individual health benefits can be reflected in population estimates of DALY averted, adjusted for time spent symptomatic	Population health as measured by DALY is an aggregation of individual health, as DALY is loss of healthy years due to premature mortality plus prevalence weighted by severity of disability in individuals
8. The effect size captures both changes in severity and duration of illness used in years lived with disability (YLD) calculations	The effect size (ES) is a standardized mean difference, and summarizes the overall benefit of those who improved and remitted, and who improved but not enough to remit. An overall ES thus implicitly includes the benefit of remitted cases, which is equivalent to a reduced duration
9. The degree of change resulting from treatment in effect size units in clinical trials indicates the degree of change in disability weights used in YLD calculations	The relationship between preferences and ES change was defined for symptoms and disability, whereas ES from metaanalyses predominately summarize change in symptoms

Figure 2. Assumptions of the analysis and corresponding evidence.

culated from individual RCT using Cohen's effect size[28]. Measured effect sizes for pharmaceutical interventions included: disease modifying antirheumatic drugs (DMARD; ES = 0.78)[30-34], nonsteroidal antiinflammatory drugs (NSAID; ES = 0.36)[34-36], and corticosteroids (systemic)[37] (ES = 0.45; Table 1). The benefit of exercise for improving quality of life remains unclear and was therefore not modeled. The benefits are found in muscle strength and aerobic capacity, but remain ambiguous in pain and functional capacity[38]. Most people with RA are likely to utilize more than one type of medication[4]. Treatment outcomes for combined therapies can vary[39], and for this study the disability weight change used for combined therapy was that associated with the treatment with the highest effect size.

Effect sizes in OA were adopted from metaanalyses and RCT. Measured pharmaceutical benefits were: NSAID (ES = 0.49)[17], analgesics and antipyretics (ES = 0.11)[40], and corticosteroid injection 3 times a year (ES = 0.32)[17]. There were insufficient data to show the benefit of opioids. Nonpharmaceutical interventions were: exercise (ES = 0.78)[17], hip or knee replacement (ES = 1.07)[41], and arthroscopy (ES = 0.09)[42] (Table 1). As in RA, when there was more than one intervention, the measure of benefit used was that of the treatment with the highest effect size.

Optimal evidence-based treatment

Rheumatoid arthritis. The American College of Rheumatology recommends a therapeutic combination of DMARD to suppress disease activity, NSAID or low-dose corticosteroids for symptom relief, continued patient education, and allied health interventions such as physiotherapy and occupational therapy[16]. With the exception of severe cases, all rheumatic cases were modeled to receive standard DMARD therapy. Severe cases were modeled to a combination DMARD with greatest benefit[39], i.e., methotrexate and leflunomide[43]. Pain relief was modeled for mild to moderate cases using NSAID on a continual basis for 9 months, and low-dose corticosteroids for 3 months. Severe cases were modeled to receive NSAID and low-dose corticosteroids throughout the year. Nonpharmacological interventions such as light exercise are recommended to minimize muscle wastage associated with physical incapacity[44].

Healthcare service contacts were modeled to monitor treatment effects and potential toxicity associated with medication[16]. Rheumatologist visits were recommended for initial treatment and monitoring of intervention efficacy and joint erosion (radiographs taken biannually)[45]. Cases in remission were modeled as requiring 3 to 4 GP consultations, and one specialist visit as requiring a pathology test. For annual doctor consultations, mild to severe cases were modeled on a range of 6 to 8 GP consultations and 3 to 4 specialist visits. Complete blood count, liver function test, and a creatinine test were recommended at each GP encounter to monitor toxicity associated with treatment.

Osteoarthritis. In accord with the international guidelines[15,17], mild to moderate cases would receive daily paracetamol, or paracetamol plus codeine, and exercise at least 3 times a week for discomfort or pain[46]. All hip and knee cases with severe OA (an estimated 80% of severe cases) had joint replacement due to the greater benefit[41] and cost-effectiveness[4] associated with its use. The remaining cases were assigned to management with NSAID and corticosteroid medication. Health service contacts were modeled in the range of 2 to 4 GP visits a year according to severity, for review and prescription renewal, with an additional one to 2 specialist consultations for moderate to severe cases.

Measurement of costs. The cost to government was modeled on services and interventions utilized in a one-year timeframe. Costs were divided into services (GP, specialist, imaging, pathology, hospital including surgery) and interventions (DMARD, NSAID, corticosteroids, analgesics, and opioids). Unit costs for services were obtained from the Australian Medical Benefits Schedule of prices, which the government pays for ambulatory services undertaken by GP and specialists, and for imaging and pathology. Inpatient costs, expressed as Australian National Diagnostic Related Group costs, were obtained from the *National Hospital Cost Data Reference Manual*[48]. Medication unit costs were obtained from the Pharmaceutical Benefits Schedule[49], and adjusted to 2000-2001 prices using the inflator/deflator health consumer price index. One-year medication usage costs was based mainly on BEACH estimates using prescribed daily doses. Total cost for each type of medication was calculated by multiplying a pooled weighted annual unit cost for each medication class by the number of people prescribed the medication.

Optimal treatment was modeled in the absence of any other treatment and with the same health service contact as current treatment. Guidelines were our main source in modeling optimal service at each level of severity[15-18]. In cases of uncertainty, expert opinion was consulted. Unit costs were the same as those for current treatment.

Sensitivity analysis. A sensitivity analysis was conducted for each disorder under study using @Risk software, version 4 (Palisade Corp., Newfield, NY, USA), which employs a Monte Carlo simulation approach to provide 95% confidence intervals around parameters of interest (see Table 5). Every point estimate in the analysis for both current and optimal care was treated as a range of values. With each iteration of the simulation analysis, a value from this range for each estimate was sampled and the parameters of interest recalculated, which provided a range of possible values to allow confidence intervals to be calculated. A multivariate stepwise linear regression was also conducted for each disorder to determine the strongest predictors in variance around the cost-effectiveness estimate. Finally, univariate sensitivity analyses were conducted on variables that were estimated from the treatment guidelines and expert reviews, to determine their effect on the above estimates.

RESULTS

Cost-effectiveness of current treatment. In a national survey[12], 93% of people who identified arthritis as their principal complaint indicated at least one consultation with a medical practitioner in the last 12 months. Services and medications utilized over the year are displayed in Tables 2 and 3.

The prevalence of RA in 2000–2001 was estimated as 0.3% (or 57,762 adults in Australia)[11], with an average disability weight of 0.23. Severity distribution and associated disability weights (DW) were: no disability 38%, DW = 0; mild cases 37%, DW = 0.21; moderate cases 17%, DW = 0.37; and severe cases 10%, DW = 0.94. The current burden in RA, calculated as the product of the prevalence and disability weight, was 13,343 YLD. The baseline burden (defined as current burden plus burden averted with current treatment) was calculated to be 17,791 YLD.

Under current care, DMARD treatment for RA was estimated to reach 70% of people in treatment. This equated to an average disability weight change of 0.106 per case, or a population change of 3,502 YLD averted. The remaining 30% of cases acquired benefit from prescribed NSAID or corticosteroids. This equated to a lower average disability weight change of 0.059 per case, or 947 YLD averted at the population level. Overall, the average disability weight change for RA under current treatment was 0.083. The burden averted with current treatment was 4,448 YLD, or 26% of baseline burden. The average direct government cost of treating a patient with RA was AU $1,597 (Table 2). Total direct cost was $86 million dollars, with a cost-effectiveness ratio of $19,227 per YLD averted. The greatest cost was pharmaceuticals (36%), followed by hospital admission (31%), medical consultations (27%), pathology (3%), and imaging (3%).

Table 1. Model inputs for epidemiology and treatment.

Subject	Point Estimate	Variance	Comment [References]
Effect size			
Rheumatoid arthritis			
DMARD	0.78	0.06	An average effect size was calculated for leflunomide [30], methotrexate [31], auranofin [32], sulfasalazine [33], and antimalarials [34]. Effect sizes were then weighted to the frequency of GP prescribing behavior [13]
NSAID	0.36	0.06	Effect sizes were calculated for prescribed NSAID [35-37] and weighted according to the proportion they contributed to GP prescribing behavior [13]
Systemic corticosteroids	0.45	0.02	[38]
Combined methotrexate and leflunomide	1.51	0.08	Benefit limited to cases with persistent RA, despite 6 months on methotrexate treatment [44]
Osteoarthritis			
NSAID	0.49	0.04	[17]
Systemic corticosteroids	0.11	0.04	Ibid
Analgesics	0.11	0.04	[40]
Exercise	0.35	0.02	Calculated as the benefit of regular exercise and medication vs medication alone [17]
Exercise and medication	0.78	0.02	Combined benefit of medication and regular exercise
Joint replacement	1.07	0.01	[41]
Arthroscopy	0.09	0.02	[42]
Epidemiology			
Prevalence, per 1000			
Rheumatoid arthritis	3.1	0.008	Male prevalence 1.9 per 1000; female prevalence 4.1 per 1000 [11]
Osteoarthritis	35.8	0.009	Male prevalence 26.5 per 1000; female prevalence 41.7 per 1000 (Ibid)
Disability weights			
Rheumatoid arthritis	0.23		Ibid
No disability	0.00	—	Ibid
Mild	0.21	—	Ibid
Moderate	0.37	—	Ibid
Severe	0.94	—	
Osteoarthritis	0.12	—	Ibid
Mild	0.01	—	Ibid
Moderate	0.14	—	Ibid
Severe	0.42	—	Ibid
Severity distribution, %			Australian Burden of Disease Report Work Sheets
Rheumatoid arthritis			Point estimates varied in univariate analysis
No disability	38	Univariate	Varied between 10-50%
Mild	35	Univariate	Varied between 10-50%
Moderate	17	Univariate	Varied between 10-50%
Severe	10	Univariate	Varied between 1-20%
Osteoarthritis			
Mild	46	0.02	Ibid
Moderate	41	0.02	Ibid
Severe	13	0.02	Ibid

Table 2. Current treatment for RA in 2000-2001 (no. with RA = 57,762)[1].

Interventions	No. of People Treated, N (%)	Mean No. of Services per Treated Case	Total No. of Services	Mean Service Cost, $	Total Cost, $	Cost Per Case Treated, $
General practitioner consults	53,545 (93)[2]	8[3]	423,600[4]	26[5]	10,955,953	
Specialist consults	53,545 (93)[6]	4[3]	211,800[6]	55[5]	11,712,637	
Imaging Investigations	26,701 (46)[4]	1*	26,701[4]	77[5]	2,051,875	
Pathology Investigations	53,545 (93)[4]	5[3]	252,600[4]	9[5]	2,176,520	
Hospital Separations	4,480 (8)[7]	1*	4,480[7]	5,602[7]	25,097,992	
DMARD	37,627 (65)[8]	NA	—	481[9]	18,085,533	
NSAID	31,056 (54)[4]	NS	—	323[9]	10,022,038	
Corticosteroids	30,521 (53)[4]	NA	—	65[9]	1,976,581	
Analgesics	21,945 (38)[4]	NA	—	157[9]	3,448,181	
Total	53,545 (93)				85,527,309	1,597

* Presumes mean service of 1. 1. Prevalence from Mathers, *et al*[11]. 2. National Survey of Mental Health and Wellbeing[12]. Arthritic cases that contacted a GP at least once in the last 12 months. 3. Total Number of Services divided by Number of People Treated. 4. From the BEACH survey[13]. 5. BEACH[13] and Medical Benefits Schedule[54]. 6. Dunlop, et al[55]. Estimated that the "total number of services" for specialist consults would be half the total number of GP services[56]. 7. Australian Institute of Health and Welfare[14] and National hospital Cost Data Collection hospital Reference manual[48]. 8. BEACH[13], Lapsley, *et al*[4], Ruof, *et al*[7]. Estimates of DMARD use vary between 60% and 90%, respectively. 9. BEACH[13] and Pharmaceutical Benefits Scheme[49].

Table 3. Current treatment for OA in 2000-2001 (no. with OA = 677,842)[1].

Interventions	No. of People Treated, N (%)	Mean No. of Services per Treated Case	Total No. of Services	Mean Service Cost, $	Total Cost, $	Cost Per Case Treated, $
General practitioner consult	628,360 (93)[2]	4[6]	2,673,000[4]	24[7]	64,563,344	
Specialist consult	628,360 (93)[3]	3[6]	1,581,341[3]	57[7]	90,659,258	
Imaging investigation	371,341 (55)[4]	1*[4]	371,341	36[7]	13,426,411	
Pathology investigation	137,700 (20)[4]	1*[4]	137,700	7[7]	933,619	
Hospital separation	57,558 (10)[5]	1*[5]	57,558	8,910[8]	512,861,539	
NSAID	301,487 (44)[4]	NA	—	216[9]	65,160,887	
Analgesics	137,988 (20)[4]	NA	—	199[9]	27,446,117	
Opioids	25,323 (4)[4]	NA	—	472[9]	11,958,021	
Corticosteroids	15,081 (2)[4]	NA	—	51[9]	768,076	
Total	628,360 (93)				787,777,271	1,254

* Presumes mean service of 1. 1. Prevalence from Mathers, et al[11]. 2. NSMHWB[12]. Arthritis cases reported contact with a GP at least once in the last 12 months. 3. NSMHWB[12] and Mathers, et al[55]. Based on ratio of GP to specialist consults estimated to have occurred in 1993–94. 4. BEACH[13]. 5. AIHW[14]. 6. " Total number of services" divided by " number of people treated." 7. BEACH[13] and MBS[54]. 8. AIHW[13] and National Hospital Cost Data Collection Hospital Reference Manual[48]. 9. BEACH[13] and PBS[49].

The prevalence of OA in 2000–2001 was estimated at 3.6% (or 677,842 adults in Australia)[11] with an average disability weight of 0.12. The severity distribution was: 46% mild (asymptomatic grade 2, DW = 0.01), 41% moderate (asymptomatic grade 3 and symptomatic grade 2, DW = 0.14), and 13% severe (symptomatic grade 3, DW = 0.42).

Current burden in OA, calculated as the product of the prevalence and disability weight, was 80,522 YLD. The baseline burden (again defined as current burden plus burden averted with current treatment) was estimated at 111,701 YLD.

Current treatment for OA involved a variety of interventions. From BEACH, 76% received effective medication. The national health survey suggests that roughly 35% of self-reported OA cases reported doing effective exercise (defined as walking or moderate exercise daily or second daily). The national hospital morbidity database indicates that 57,558 people, or 10% of cases with OA, were admitted for surgery. Drawing these data together presents the following current healthcare scenario: one-third of the cases prescribed medication also exercised regularly and had an average disability weight change of 0.11. This equated to a change in population burden of 14,384 YLD averted. In contrast, cases who relied on medication alone had an average disability weight change of 0.04 (or 11,156 YLD averted). Ten percent of cases who underwent treatment as a hospital inpatient had an average disability weight change of 0.13 (5,640 YLD averted). The remaining 24% of people in contact with the health system received no beneficial intervention. The average disability weight change for OA under current treatment was 0.065. The burden averted with current treatment was 31,180 YLD, or 27% of the baseline bur-

Table 4. Optimal treatment cost for RA in a one year period (no. of treated cases = 53,545).

	No Disability	Mild	Moderate	Severe	Total Services	Unit Cost, $	Total Cost, $
Epidemiology							
Proportion of treated cases[1], %	38	35	17	10			
No. of treated cases[2]	20,347	18,741	9,103	5,355			
Intervention per case treated							
No. of GP consults[3]	4	6	7	8	300,388	26[4]	7,769,217
No. of specialist consults[3]	3	3	4	4	175,093	55[4]	9,682,705
Annual DMARD cost[5], $	342[6]	342	514[7]	2,338[8]	NA	571[9]	30,579,175
Annual NSAID cost[5], $	—	242[10]	242[10]	323[11]	NA	158[12]	8,466,894
Annual corticosteroid cost, $	—	16[13]	16[13]	65[14]	NA	16[15]	797,568
Annual hospital separation costs per admitted case[16], $	—	—	—	5,602	4,480[16]	5,602	25,097,992
FBC/ESR investigations[17]	4	8	8	12	368,391	7[4]	2,497,724
LFT/C-REACT/CRTIN investigations[17]	4	8	8	12	368,391	12[4]	4,442,517
Rheumatoid factor investigations[17]	1	2	2	2	86,743	10[4]	853,009
Imaging investigations[5]	0.5[18]	0.5	0.5	0.5	26,773	77[4]	2,057,376
Totals, $	14,963,323	21,187,239	12,588,271	43,505,344			92,244,177

1. Severity distribution from Mathers, et al[11]. 2. NSMHWB[12]; 93% of arthritis cases who contacted a GP in the last 12 months were extrapolated equally to all severity levels. 3. Estimates derived from international guidelines[16,18]. 4. BEACH[13] and MBS[54]. 5. BEACH[13] and American College of Rheumatology guidelines[16]. 6. Cost based on average prescribed daily dose per DMARD. 7. Moderate cases modeled to receive one and a half DMARD per annum. 8. Severe case modeled to receive leflunomide ($2,214) and methotrexate ($123) due to ineffective DMARDs used in the past[49]. 9. Average DMARD cost under optimal treatment. 10. NSAID costed to 9 months of the year. The Scottish Intercollegiate Guidelines Network (SIGN)[18] recommends abstaining from concomitant NSAID and steroid use. 11. NSAID cost to 12 months of the year for severe cases. 12. Average NSAID cost under optimal treatment. 13. Corticosteroid costed to a maximum of 3 months' use within a year[13,18]. 14. Corticosteroid costed all year for severe cases. 15. Average costs of corticosteroid under optimal treatment. 16. Admitted cases under optimal treatment are equal in cost and numbers to cases admitted under "current care." 17. Recommended levels of monitoring adopted from Lee, et al[57]. 18. Biannual radiographs recommended for all cases[16,18].

Table 5. Optimal treatment cost for OA in a one year period (no. of treated cases = 628,360).

	Mild	Moderate	Severe	Total Services	Unit Cost, $	Total Cost, $
Epidemiology						
Proportion of treated cases[1], %	46	41	13			
No. of treated cases[2]	287,327	260,474	80,559			
Intervention per case treated						
No. of GP consults[3]	2	3	4	1,638,313	24[4]	40,537,773
No. of specialist consults[3]	0	1	2	421,592	57[4]	24,170,137
Annual analgesic cost[5], $	199	—	—	NA	199	57,150,034
Annual NSAID cost[5], $	—	216	216	NA	216	59,778,926[6]
Annual corticosteroid cost[5], $	—	—	51	NA	51	820,954[6]
Annual hospital separation costs per admitted case, $	—	—	14,000	64,447[7]	14,000[8]	902,260,810
Imaging investigations[3]	1	1	2	708,919	36[4]	25,632,075
Totals, $	81,418,926	99,522,034	929,409,390			1,110,350,350

1. Severity distribution from Mathers, et al[11]. 2. NSMHWB[12]; 93% of arthritis cases who contacted a GP in the last 12 months were extrapolated equally to all severity levels. 3. Lapsley[4]. 4. BEACH[13] and MBS[53]. 5. BEACH[13] and PBS[48]. 6. Twenty percent of cases with OA associated with other joints and are modeled to "received benefit from medication"[14]. 7. An estimated 80% of hip or knee cases have knee or hip OA[14] who qualify for joint replacement. 8. AIHW[14] and National Hospital Cost Data Collection Hospital Reference Manual[47]. Average weighted cost of joint replacement.

den. The average direct government cost of current treatment was AU $1,254 per case (Table 3). Total direct cost was estimated at $787 million dollars, with a cost-effectiveness ratio of $25,226 per YLD averted (Table 6). The greatest proportion of cost of OA was hospital separations (predominately for joint replacement surgery: 80%), followed by pharmaceutical expenditure (10%), medical consultations (7%), and imaging investigations (3%).

Cost-effectiveness of optimal treatment. Under optimal treatment, all people with RA received DMARD therapy generating a disability weight change of 0.145. The burden averted increased from 26% to 48% of the baseline burden, or 7,758 YLD. Total cost was AU $92 million dollars (Table 4), 7% more expensive than current treatment, but offset by an 85% improvement in health gain. The cost per case was $1,723, and the average cost per case by severity was: no

Table 6. Comparative efficiency, in cost per year lived with disability (YLD) averted, of current and optimal treatment for RA and OA.

	YLD Averted	Efficacy 95% CI	% Burden Averted	Cost per Treated Case ($) Point Estimate	Total Cost of Treatment $ (millions)	95% CI	Efficiency $ per YLD Averted	95% CI
Rheumatoid Arthritis								
Current treatment, N = 53,545	4,448	2,380–12,629	26	1,597	85.5	77.1–190.5	19,227	11,251–44,116
Optimal treatment, N = 53,545	7,758	3,561–19,680	48	1,723	92.1	62.5–248.9	11,890	9,082–25,930
Osteoarthritis								
Current treatment, N = 597,957	31,180	14,724–48,257	27	1,245	787.7	479.7–1,667.6	25,226	14,450–67,151
Optimal treatment, N = 597,957	43,690	18,648–67,341	39	1,767	1,110.3	545.2–2449.2	25,414	19,650–51,338

disability $697, mild $1,131, moderate $1,383, and severe disability $8,163. The high cost among severe cases was driven by hospital separations and pharmaceutical expenditure. Increasing the coverage of DMARD use to all cases in contact with healthcare services improves the cost-effectiveness ratio of optimal treatment ($11,890) compared with that of current treatment ($19,227) per YLD averted (Table 6).

Optimal treatment for OA generally entails 3 aspects: (1) increasing the level of exercise activity among mild to moderate cases; (2) shifting from antiinflammatories to analgesics for mild cases; (3) increasing the number of joint replacements for severe cases of OA. The combination of exercise and medication resulted in an average disability weight change of 0.05 per case, or 30,342 YLD averted at the population level. For joint surgery, the change in disability weight was 0.181 per case (11,642 YLD averted). The averted burden under optimal treatment was about 39% of the baseline burden, or 43,690 YLD averted. Under optimal treatment (Table 5), OA cost AU $1,110 million dollars compared with $787 million for current treatment, a 40% increase in budget for a 40% increase in health gain. The average cost per case rose to $1,767 due to increasing joint replacements. The average cost per case for each severity level was $283 for mild cases, $382 for moderate cases, and $11,537 for severe cases. The cost-effectiveness ratio of optimal treatment ($25,414) was similar to that for current treatment ($25,226; Table 6).

Sensitivity analysis. Many of the variables for both arthritic disorders had substantial uncertainty, reflected in the width of the confidence intervals (Table 6). In the regression model, the variance in the efficiency (cost per YLD averted) for each disorder was predicted by hospital costs, prevalence estimates, and the conversion factor. For optimal treatment, significant predictors for each disorder were the conversion factor, hospital costs, prevalence, and severity levels. Univariate analysis was used to determine the effect of changing point estimates if distribution estimates were not available. For OA, it was exercise. Our point estimate was modeled at 35% and was varied between 5% and 60%. The variation around this estimate did not produce costs per YLD averted outside the 95% confidence intervals reported in Table 6. For RA, all variables had appropriate distribution estimates.

DISCUSSION

Our aim was to determine the level of burden currently being averted in RA and OA, and to estimate whether this would improve with optimal treatment. Survey and registry data were used to estimate the level of input used under "current care," while output was measured using a change in disability weight due to treatment. Optimal treatment was modeled from treatment guidelines and expert opinion, and output was measured similarly. Costs associated with treatment were limited to government expenditures.

The perspective of the study explored the allocative efficiency of resources invested into the treatment of RA and OA. Traditional cost-effectiveness analyses explore comparative benefits of single interventions. Our study departed from the traditional model, investigating the potential benefit of all interventions and combining them to determine the most efficient combination[9].

In RA, optimal treatment required 7% more funds but resulted in an 85% increase in health gains. The incremental gain in optimal treatment equated to AU $2000 per YLD averted, which suggests a very attractive situation even though half the burden seemed to be unavertable in the light of current knowledge. In OA, optimal treatment required a 40% increase in funds to produce a corresponding 40% increase in health gain. Yet the incremental gain of optimal treatment equated to AU $26,000 per YLD averted. This raises the issue that healthcare for this disorder might well be advised to focus on prevention, by stressing weight loss, regular exercise, and the use of dietary supplements like glucosamine and chondroitin, especially as 60% of the burden seems to be unavertable in light of current knowledge.

Limitations. The main limitation was the lack of primary data on prevalence and one-year service and medication usage. Nevertheless the convergence of the multiple sources of data, especially from the Australian Burden of Disease Study on prevalence[11] and the BEACH data on GP activities[13], produced estimates that were acceptable. The assumption that efficacy data can be used as a proxy for effectiveness can lead to an overestimate of the benefit in both current and optimal treatment.

Both RA and OA can have associated comorbid diseases. The disability weights employed here consider only the burden associated with each disease[10]. There were no data to model the proportion of cases in which the use of DMARD in RA or surgery in OA would be contraindicated. Thus all patients were presumed to be eligible for these treatments. The benefits of optimal treatment could therefore be overestimated.

A further threat to reliability was the need to model one-year medication consumption for OA from cross-sectional data, whereas the availability of longitudinal outpatient data for RA informed the combination of medications used over a year.

The width of the confidence intervals in the sensitivity analysis reflects the limitation of the data available. Of primary concern was the need to ascertain better estimates of disease prevalence and severity for both arthritic disorders. Self-reporting chronic disease from national health surveys overestimates disease prevalence[49]; consequently, alternative estimates from Mathers, *et al*[11] were utilized.

Comparative cost-effectiveness. Segal, *et al*[5] calculated the cost-effectiveness of individual treatments for OA. They found that joint replacement and exercise programs were the most cost-effective interventions. They were less optimistic about the cost-effectiveness of medication or arthroscopy. They did not study RA. Andrews, *et al*[1] studied the cost-effectiveness of current and optimal treatment for 10 mental disorders using the same method as in our study. They calculated that about 13%, or one-eighth, of the burden of mental disorders was being averted by current treatment, in part due to low levels of coverage for people with substance use or anxiety disorders. The proportion of burden being averted by current treatment was similar across these 4 diseases, but the cost-effectiveness of current treatment was not. Depression and anxiety disorders cost some $20,000/YLD averted, whereas the treatment of alcohol use disorders and schizophrenia cost $100,000/YLD and $200,000/YLD averted, respectively. These latter figures are well beyond the threshold for an affordable treatment. The cost-effectiveness of both current and optimal treatment of arthritis is affordable and is similar to that of depression and anxiety disorders. The burden averted in arthritis was greater, in part because the majority of people with arthritis seek treatment.

REFERENCES

1. Andrews G, Issakidis C, Sanderson K, Corry J, Lapsley HM. Comparison of the cost and effectiveness of treatment of ten mental disorders: utilising survey data for public policy. Br J Psychiatry 2004;184:526-33.
2. Andrews G, Sanderson K, Corry J, Issakidis C, Lapsley H. Cost effectiveness of current and optimal treatment for schizophrenia. Br J Psychiatry 2003;183:427-35.
3. Ad Hoc Committee on Health Research Relating to Future Intervention Options. Investing in health research and development. Document TDR/Gen/96.1. Geneva: World Health Organization; 1996.
4. Lapsley HM, March LM, Tribe KL, Cross MJ, Courteny BG, Brooks PM. Living with rheumatoid arthritis: expenditures, health status, and social impact on patients. Ann Rheum Dis 2002;61:818-21.
5. Segal L, Day SE, Chapman AB, Osborne RH. Can we reduce disease burden from osteoarthritis? Med J Aust 2001;180 Suppl:S11-S17.
6. Ruof J, Hulsemann JL, Stucki G. Evaluation of costs in rheumatic disease: a literature review. Curr Opin Rheumatol 1999;11:104-13.
7. Ruof J, Hulsemann JL, Mittendorf T, et al. Costs of rheumatoid arthritis in Germany: a micro-costing approach based on healthcare payer's data sources. Ann Rheum Dis 2003;62:544-9.
8. Maetzel A, Li LC, Pencharz J, Tomlinson G, Bombardier C; Community Hypertension and Arthritis Project Study Team. The economic burden associated with osteoarthritis, rheumatoid arthritis, and hypertension: a comparative study. Ann Rheum Dis 2004;63:395-401.
9. Murry CJL, Evans DB, Acharya A, Baltuseen RM. Development of WHO guidelines on generalized cost-effectiveness analysis. Health Econ 2000;9:235-51.
10. Stouthard M, Essink-Bot M, Bonsel G, Barendregt J, Krammers P. Disability weights for diseases in the Netherlands. Rotterdam: Department of Public Health, Erasmus University; 1997.
11. Mathers C, Vos T, Stevenson C. The burden of disease and injury in Australia. AIHW cat. no. PHE 17. 2004. Canberra: Australian Institute of Health and Welfare; 2004.
12. Andrews G, Henderson S, Hall W. Prevalence, comorbidity, disability and service utilisation. Overview of the Australian National Mental Health Survey. Br J Psychiatry 2001;178:145-53.
13. Britt H, Miller GC, Knox S, et al. General practice activity in Australia 2000-2001. AIHW cat. no. GEP 8. Canberra: Australian Institute of Health and Welfare; 2002.
14. Australian Institute of Health and Welfare (AIHW). Australian hospital statistics 2000-2001. AIHW cat. no. HSE 20. Canberra: Australian Institute of Health and Welfare; 2002.
15. Altman RD, Hochberg MC, Moskowitz RW, Schnitzer TJ. Recommendations for the medical management of osteoarthritis of hip and knee. Arthritis Rheum 2000;43:1905-15.
16. American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis. Arthritis Rheum 2002;46:328-46.
17. Pendleton A, Arden N, Dougados M, et al. 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 2000;59:936-44.
18. Royal College of Physicians Edinburgh. Scottish Intercollegiate Guidelines Network. Management of early rheumatoid arthritis. Edinburgh: Royal College of Physicians; 2000. Available at: http://www.sign.ac.uk/guidelines/fulltext/48/index.html. Accessed December 20, 2005.
19. Altman RD, Hochberg MC, Moskowitz RW, Schnitzer TJ. Recommendations for the medical management of osteoarthritis of the hip and knee. Arthritis Rheum 2000;43:1905-15.
20. Sanderson K, Andrews G, Corry J, Lapsley HM. Using the effect

size to model change in preference values from descriptive health states. Qual Life Res 2004;13:1255-64.
21. Bombardier C, Ware J, Russell IJ, et al. Auranofin therapy and quality of life in patients with rheumatoid arthritis: results of a multicentre trial. Am J Med 1986;81:565-78.
22. Bennett KJ, Torrance GW, Moran LA, Smith F, Goldsmith CH. Health state utilities in knee replacement surgery: the development and evaluation of McKnee. J Rheumatol 1997;24:1796-805.
23. Calfas KJ, Kaplan RM, Ingram RE. One year evaluation of cognitive-behavioral intervention in osteoarthritis. Arthritis Care Res 1992;5:202-9.
24. Hurst NP, Lambert CM, Forbes J, Lochhead A, Major K, Lock P. Does waiting matter? A randomized controlled trial of new non-urgent rheumatology outpatient referrals. Rheumatology Oxford 2000;39:369-76.
25. Lambert MC, Hurst NP, Forbes JF, et al. Is day care equivalent to inpatient care for active rheumatoid arthritis? A randomized controlled clinical and economic evaluation. BMJ 1998;316:965-9.
26. Laupacis A, Bourne R, Rorabeck C, et al. The effect of elective total hip replacement on health-related quality of life. J Bone Joint Surg Am 1993;75:1619-26.
27. Verhoeven AC, Bibo JC, Boers M, et al. Cost-effectiveness and cost-utility of combination therapy in early rheumatoid arthritis: randomized comparison of combined step-down prednisolone, methotrexate and sulphasalazine with sulphasalazine alone. Br J Rheumatol 1998;37:1102-9.
28. de Klerk E, van der Heijde D, Landewe R, van der Tempel H, Urquhart J, van der Linden S. Patient compliance in rheumatoid arthritis, polymyalgia rheumatica, and gout. J Rheumatol 2003;30:44-54.
29. Glass GV, McGaw B, Smith ML. Measuring study findings. In: Glass GV, McGaw B, Smith ML, editors. Meta-analysis in social research. London: Sage Publications; 1981:93-152.
30. Osiri M, Shea B, Robinson V, et al. Leflunomide for treating rheumatoid arthritis (Cochrane Review). In: The Cochrane Library, Issue 2, 2004. Chichester, UK: John Wiley & Sons, Ltd.
31. Suarez-Almazor ME, Belseck E, Shea B, Wells G, Tugwell P. Methotrexate for treating rheumatoid arthritis (Cochrane Review). In: The Cochrane Library, Issue 2, 2004. Chichester, UK: John Wiley & Sons, Ltd.
32. Suarez-Almazor ME, Spooner CH, Belseck E, Shea B. Auranofin versus placebo in rheumatoid arthritis (Cochrane Review). In: The Cochrane Library, Issue 2, 2004. Chichester, UK: John Wiley & Sons, Ltd.
33. Suarez-Almazor ME, Belseck E, Shea B, Wells G, Tugwell P. Sulfasalazine for treating rheumatoid arthritis (Cochrane Review). In: The Cochrane Library, Issue 2, 2004. Chichester, UK: John Wiley & Sons, Ltd.
34. Suarez-Almazor ME, Shea B, Homik J, Wells G, Tugwell P, Belseck E. Antimalarials for treating rheumatoid arthritis (Cochrane Review). In: The Cochrane Library, Issue 2, 2004. Chichester, UK: John Wiley & Sons, Ltd.
35. Garner S, Fidan D, Frankish R, et al. Celecoxib for rheumatoid arthritis (Cochrane Review). In: The Cochrane Library, Issue 2, 2004. Chichester, UK: John Wiley & Sons, Ltd.
36. Gotzsche P. Sensitivity of effect variable in rheumatoid arthritis: a meta-analysis of 130 placebo controlled NSAID trials. J Clin Epidemiol 1990;43:1313-8.
37. Gotzsche P, Johansen HK. Short term low dose corticosteroid vs placebo and NSAIDS in rheumatoid arthritis (Cochrane Review). In: The Cochrane Library, Issue 2, 2004. Chichester, UK: John Wiley & Sons, Ltd.
38. Criswell LA, Saag KG, Sems KM, et al. Moderate-term, low-dose corticosteroids for rheumatoid arthritis (Cochrane Review). In: The Cochrane Library, Issue 2, 2004. Chichester, UK: John Wiley & Sons, Ltd.
39. Van den Ende CHM, Vliet Vlieland TPM, Munneke M, Hazes JMW. Dynamic exercise therapy in rheumatoid arthritis. Br J Rheumatol 1998;37:677-87.
40. Verhoeven AC, Boers M, Tugwell P. Combination therapy in rheumatoid arthritis: Updated systemic review. Br J Rheumatol 1998;37:612-9.
41. Case JP, Baliunas AJ, Block JA. Lack of efficacy of acetaminophen in treating symptomatic knee osteoarthritis: a randomized, double-blind, placebo-controlled comparison trial with diclofenac sodium. Arch Intern Med 2004;163:169-78.
42. Bachmeier CJ, March LM, Cross MJ, et al. A comparison of outcomes in osteoarthritis patients undergoing total hip and knee replacement surgery. Osteoarthritis Cartilage 2001;9:137-46.
43. Moseley JB, O'Malley K, Petersen NJ. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. N Engl J Med 2002;347:81-8.
44. Kremer JM, Genovese MC, Cannon GW, et al. Concomitant leflunomide therapy in patients with active arthritis despite stable dose methotrexate: A randomized, double blind, placebo-controlled trial. Ann Intern Med 2002;137:726-33.
45. Stenstrom CH, Minor MA. Evidence for the benefit of aerobic and strengthening exercise in rheumatoid arthritis. Arthritis Rheum 2003;49:428-34.
46. Clemens LE. The role of the rheumatologist in managing arthritis. Med J Aust 2001;175 Suppl:S97-S101.
47. March LM, Stenmark J. Non-pharmacological approaches to managing arthritis. Med J Aust 2001;175 Suppl:S102-7.
48. Acute and Coordinated Care Branch, Health Services Division. National Hospital Cost Data Collection Hospital Reference Manual 5. Canberra: Commonwealth Department of Health and Aged Care; 2000.
49. Health Insurance Commission. Schedule of pharmaceutical benefits. Commonwealth Department of Health and Aged Care. 2004. Available at: http://www1.health.gov.au/pbs/scripts/search.cfm. Accessed December 9, 2005.
50. Kriegsman D, Pennix B, van Eijk J, Boek A, Deeg D. Self-reports and general practitioner information on the presence of chronic disease in community dwelling elderly. J Clin Epidemiol 1996;49:1407-17.
51. Blumenauer B, Judd M, Wells G, et al. Infliximab for the treatment of rheumatoid arthritis. In: The Cochrane Library, Issue 2, 2004. Chichester, UK: John Wiley & Sons, Ltd.
52. Kremer JM, Genovese MG, Cannon GW, et al. Concomitant leflunomide therapy in patients with active rheumatoid arthritis despite stable doses of methotrexate. Ann Intern Med 2002;137:726-33.
53. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary definitions of improvement in rheumatoid arthritis. Arthritis Rheum 1995;38:727-35.
54. Department of Health and Aged Care. Medicare benefits schedule book. November ed. 1999. Canberra: Publications Production Unit, Commonwealth Department of Health and Aged Care; 1999.
55. Dunlop DD, Manheim LM, Yelin EH, Song J, Chang RW. The cost of arthritis. Arthritis Rheum 2003;49:101-13.
56. Mathers C, Stevenson C, Carter R, Penm R. Disease costing methodology used in the Disease Costs and Impact Study 1993-94. AIHW cat. no. HWE series 3, 1-84. 1998. Canberra: Australian Institute of Health and Welfare. Health and Welfare Expenditure Series; 1998.
57. Lee ATY, Pile K. Disease modifying drugs in adult rheumatoid arthritis. Aust Prescr 2003;26:36-40.
58. Gold MR, Siegel JE, Russell LB, Weinstein MC. Cost-effectiveness in health and medicine. New York: Oxford University Press; 1996.