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ECONOMIC EVALUATION OF THE TREATMENT OF RHEUMATOID ARTHRITIS★

Julie A. Ives,† and C. M. Lambert,‡ Western General Hospital, Edinburgh

Because the resources available for health care are limited, those delivering it have a responsibility to ensure that the expenditure represents 'value for money'. Treatment must not only be effective, producing the desired health outcome, but it must also be efficient, that is, producing the desired outcome at least cost. The discipline of health economics enables the systematic appraisal of the costs and benefits of treatment and allows the relative economic efficiency of different medical interventions to be quantified, thus permitting more rational decisions to be made about health care expenditure,

There are two forms of economic efficiency. Allocative efficiency is concerned with the overall apportionment of funding, the issue of whether it is worth achieving a given objective or whether an alternative course of action would yield greater benefit. Quite disparate programmes can be compared, such as whether overall benefit is greater from building a new sewage plant or a new hospital. Operational efficiency, however, starts with the assumption that, in the context of health care, a condition is worth treating and is concerned with the most efficient way of meeting the objective. For example, how can we achieve remission of active rheumatoid arthritis at least cost?

Clearly in this respect a treatment which results in a significantly poorer route to a given outcome than an alternative, for example the conventional treatment, would normally be discounted (Fig 1, line A). However, the situation is not always so clear cut and an economic evaluation can be helpful in making the choice between interventions where the route to the given outcome is only a little better or a little worse than conventional treatment (Fig 1, lines B and C). A cost effectiveness study would make the cost difference explicit and raise the question of whether the increased benefit is worth the increased expenditure.

TYPES OF ECONOMIC ANALYSIS

Once resources have been allocated to health care the technical efficiency with which they are deployed becomes of paramount importance. Value for money can be assessed by four types of economic study, cost-minimisation analysis (CMA), cost–effectiveness analysis (CEA), cost–benefit analysis (CBA) and cost–utility analysis (CUA) (Table 1). If undertaken correctly each identifies costs in the same way but they measure the benefit, or effectiveness of an intervention, in different ways.

In any method of economic analysis it is important to identify, measure and value all the relevant costs and benefits. For example, in a pharmacoeconomic

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†Clinical Research Scientist.
‡Medical Director, Economic and Health Outcomes Research Unit.

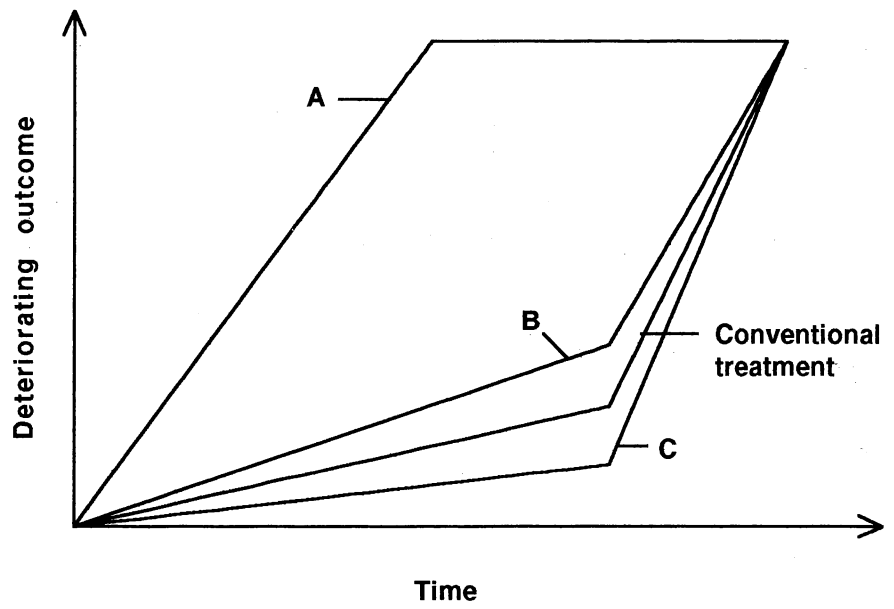

FIGURE 1
Different routes to a given outcome showing the conventional treatment, a significantly poorer route (line A) and two routes which are little better and a little worse than the conventional treatment (lines B and C).

TABLE 1
Categories of economic evaluation

Category	*Costs*	*Unit of Benefit*
Cost-minimisation	Monetary	None
Cost-effectiveness	Monetary	Single measures of 'natural' units
Cost-utility	Monetary	Single index of value, incorporating length and quality of life
Cost-benefit	Monetary	Monetary

study it is necessary to include not only the actual cost of providing the medication but also the wider economic implications of its use, for instance the cost of laboratory monitoring or treatment of side effects. The costs must include both the 'direct costs' specifically attributable to drug treatment, for instance co-prescription of a gastroprotective agent with a non-steroidal anti-inflammatory drug (NSAID) and the 'indirect costs' attributable to time off work as a result of drug related side effects. 'Intangible' costs, for instance the inability of a patient to participate in a pastime as a result of side effects, should also be quantified. The benefits of treatment must be considered, measured and valued from an equally wide perspective (Fig 2).

When assessing the cost of health care it is necessary to distinguish between the average and marginal cost. The average cost can be defined as the total cost (i.e. fixed costs, such as overheads together with the variable costs, such as

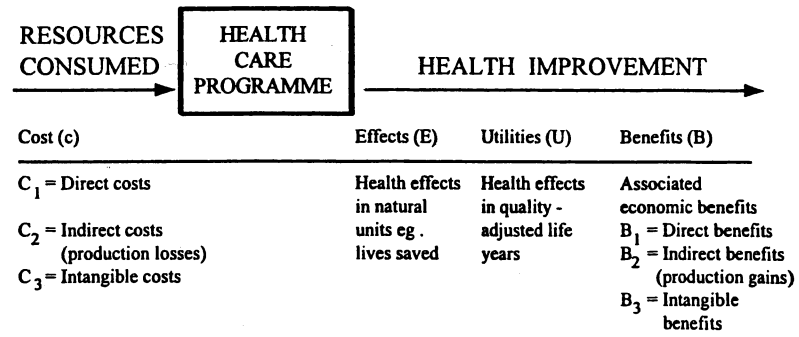

FIGURE 2
Components of an economic evaluation.

catering and medication) divided by the total number of patients treated. In health care, where the issue is normally whether to provide a little more or a little less of a service, the marginal cost is often more appropriate and can be defined as the additional cost of treating one extra patient within an existing programme.

CMA is the technique of choice when previous data has convincingly shown two interventions to be equally effective. The focus, therefore is solely on the differential cost of the treatments and the least expensive is the treatment of preference.

CEA can be used where the effectiveness of two interventions is not equivalent and therefore both the cost and effectiveness need to be compared. CEA assesses the cost per unit gain in health outcome with the latter expressed in natural units. For example we might wish to compare two methods of achieving remission of active rheumatoid arthritis. In this situation CEA could involve measuring the improvement in functional capacity or the relative decrease in erythrocyte sedimentation rate and calculating the cost of achieving this outcome by different treatment regimes.

A weakness of both CMA and CEA is that they allow comparison only of treatments in a particular therapeutic area. For instance they could be used to compare renal dialysis with renal transplantation, but could not compare either of these with treatment for active RA. However, the other two methods, CBA, CUA, value effectiveness in units of benefit which, in theory, do allow cross comparison between different specialties. Use of these methods may facilitate the optimal allocation of resources between different areas of the health service.

CBA values both the costs and benefits in monetary terms which means that it should be possible to compare the benefits arising from quite disparate programmes. However, there is great practical difficulty in valuing the benefit of medical treatment in monetary terms and the methodology to do this is in its infancy. Two approaches have been suggested. The first is based on an individual's hypothetical 'willingness to pay' for the benefit conveyed by a given treatment and the second is based on what risk of immediate death an individual is prepared to accept in return for a cure for their disease, the so called 'standard gamble'. Although some studies have been published which evaluate therapies in

rheumatoid arthritis[1] and anti-hypertensive therapy[2] using these techniques, this type of cost–benefit analysis has not found widespread acceptance.

In the context of health care the 'utility' of CUA refers to the subjective level of wellbeing or 'quality of life' experienced by people in different states of health. This may be measured using generic questionnaires which examine the overall state of health of an individual irrespective of the underlying disease. These generic instruments can be grouped in two categories, health indices and health profiles. Health indices such as the Quality of Wellbeing Scale,[3] (QWB), the Euroquol[4] and the Rosser Index[5] generate a single 'utility unit'. Health profiles, on the other hand, provide separate scores for different areas of health such as physical function, mental health and social or work role functioning. Examples include the Nottingham Health Profile[6] and Medical Outcome Studies Short Form 36.[7] Instruments which allow the generation of a single index of health can be used to derive a 'quality of life year' (QALY) to indicate the net benefit of treatment.

Theoretically league tables of cost per QALY can then be used to rank treatments in terms of marginal cost per additional QALY gained. However, the results are based on a number of assumptions; for example the calculation of a QALY assumes that improvement in health is constant over time, an assumption which is often untrue. Therefore the results of such analyses should be interpreted with care.[8,9]

It is difficult, and often inaccurate, to try to assess the costs and benefits of any intervention retrospectively, all the relevant information may not be available and assumptions may be required which are misleading. Another problem inherent in economic studies is that clinical efficacy is usually measured over relatively short periods which may be inadequate to fully assess the total economic consequences.

HEALTH ECONOMICS OF RA

Accepting that there are inherent problems which must be given due consideration when an economic analysis is planned, how then, can health economics be used in assessing the treatment of RA? Whilst it may not be possible to modify the long-term outcome of RA[10] it is, nevertheless, important to provide cost effective treatment which improves quality of life and optimises physical function. Studies of RA which have incorporated some form of economic analysis have so far evaluated different hospital regimes for managing active RA and pharmacological and surgical intervention. Most studies have focussed on technical efficiency using CEA or CBA, whilst a few have adopted the wider perspective of CUA.

Hospital management strategies

A high proportion of the expenditure on patients with active RA is attributable to the direct medical cost of in-patient care.[11,12] Most of these are fixed costs, such as heating, maintenance and capital charges, over which the clinician has little control.[11,13] Several recent studies have addressed the issue of whether in-patient or out-patient care of active RA is more cost effective. A comprehensive Canadian study[14] evaluated the clinical and financial implications of nineteen weeks of treatment which was similar both for in-patients and those treated as out-patients. The benefit of in-patient therapy was shown to be a three fold improvement in efficacy compared with a 2·5 fold increase in cost and suggested

TABLE 2

Summary of economic data from Lambert *et al.*, 1994

Costs	*Day patient* ($n = 10$)	*In-patient* ($n = 10$)
Hospital cost		
Cost per day (£)	59.64	61.99
No. treatment days	94	182
Total hospital cost (£)	*5606*	*11 282*
Transport cost		
Mean distance home/hospital (miles)	9.15	7.10
No. visits to/from hospital	184	39
Total transport cost (£)	*1808*	*306*
Community cost (£)		
Travel	751	790
Medication	713	713
GP visits	472	455
Outpatient rheumatology visits	250	855
Paramedical services	672	127
Total community cost (£)	*2858*	*2940*
Total cost (£)	*10 272*	*14 528*

that in-patient treatment is more cost-effective than out-patient therapy. Other studies, which have not been so well controlled, have suggested that there is short term clinical benefit from in-patient care for active RA compared with out-patient treatment but have not included an economic analysis.[15,16,17,18]

Whilst these studies suggest benefit from hospital admission and care from a multidisciplinary team they do not provide a means of assessing the optimum length of admission or which specific components of hospital therapy contribute to efficacy. Day-patient care, where the fixed costs may be less, could provide an equally efficacious but cheaper alternative. A pilot study comparing in-patient and day-patient care has been carried out in Edinburgh.[19] The study demonstrated that day care is feasible for managing active RA and is acceptable to patients. The preliminary economic data suggested that day care may be substantially less expensive (Table 2) than conventional in-patient therapy and that short term clinical outcome is not compromised by day care. Data from the main study will provide a more definitive answer regarding the cost effectiveness of these treatment regimes.

Pharmacoeconomics

It is estimated that in the UK, in 1989, medications for arthritis accounted for 8 per cent of the total costs of National Health Service pharmaceutical spending.[20] It is therefore appropriate that such significant spending is shown to provide 'value for money'. A number of countries have identified medicines as a major item of expenditure and decided that there is a need to formalise the economic evaluation of drugs prior to licensing.[21,22,23] Whilst numerous trials have demonstrated the short and medium term efficacy of drug therapy, much less attention has been paid to the economic costs and benefits and the global health benefit.

When assessing the 'value for money' provided by a drug therapy it is important to consider all the associated costs of prescribing. The cost of treating

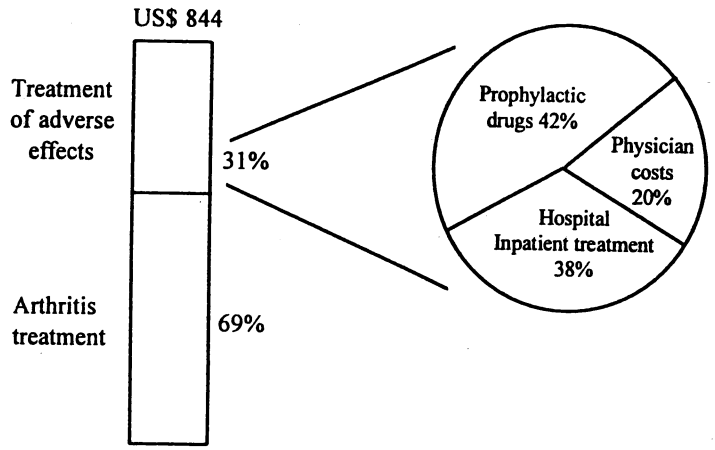

FIGURE 3
Annual costs of arthritis treatment, per patient, in the US (1987).[25]

the adverse effects of a therapy may impact significantly on the overall cost of treatment, a fact which should not be overlooked. If the price of a drug is low it does not necessarily follow that it is cost-effective. Increased risk of gastrointestinal adverse effects is the most important problem associated with the use of NSAIDs in the treatment of arthritis. It has been suggested that the cost of treatment of gastrointestinal adverse effects which include hospitalisation and surgery may be greater in some circumstances than the lifetime cost of treatment of the disease for which the NSAID was originally prescribed.[24] In 1987 the annual cost of arthritis treatment in the US was estimated at $844 per patient, 69 per cent ($580) of which was spent on the direct cost of treatment and 31 per cent ($264) on the treatment of gastrointestinal side effects.[25] The latter sum related to the cost of prophylactic drugs, physician costs and the cost of hospital in-patient treatment (Fig 3).

More recently the 'shadow cost' for various NSAIDs in the UK has been calculated[26] and serves to illustrate further the added expense of treating the complications arising from NSAID therapy. The 'shadow cost' was defined as an estimation of the cost of treating NSAID-induced gastroduodenal damage based on average treatment costs and the rate of ulceration associated with the particular drug. The study involved the use of decision analysis, a technique which has been extensively evaluated.[27] The available choices of treatment and all the potential outcomes of each are identified and the costs relating to these are calculated. The choices and the probability of outcomes can then be modelled to form a decision tree, a simple example of which is shown in Fig 4.

The use of such an economic model may be quicker and cheaper than a prospective study but has a number of disadvantages. Of particular concern is the possibility that the results may be heavily dependent upon the selection of the primary data and that even a sensitivity analysis may not be able to compensate for any bias.[28] Given these limitations studies involving economic models must

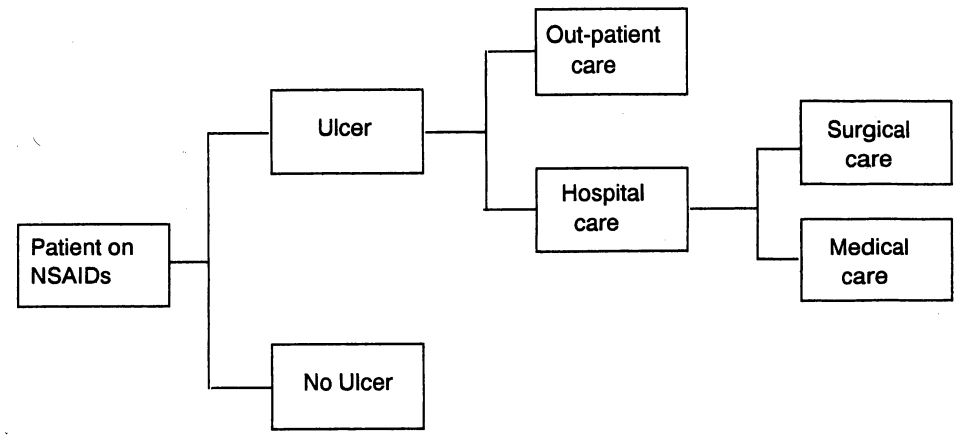

FIGURE 4
A simple decision tree.

be interpreted with caution and should not be considered as a substitute for prospective clinical and economic appraisals.

The only prospective, randomised, controlled trial of disease modifying antirheumatic drugs (DMARDS) which included economic evaluation was a six month study of oral gold versus placebo.[29] Functional outcome was measured using the Health Assessment Questionnaire (HAQ) and the QWB scale was used to derive a utility value to measure net health outcome. The authors described the net benefit of auranofin treatment as an improvement in HAQ score, equivalent to being able to walk outside on level ground with *much* difficulty at baseline to being able to walk outside on level ground with *some* difficulty after treatment. The additional benefit of oral gold on QWB score was equivalent to the improvement from being able to move one's own wheelchair without help to walking with physical limitations. The total additional medical cost of this treatment was US$1160 per annum which included auranofin (US$405), in-patient treatment (US$406), out-patient visits (US$153) and laboratory tests (US$226). Making the economic costs and health benefits explicit allows one to question whether the observed improvement in health is worth $US1160 per annum.

Unfortunately CBA was not possible in this study because the authors had not assessed the monetary value that patients would be prepared to forego to obtain the actual benefit they had obtained.[1] CUA was also impossible because the calculation of cost per QALY assumes that improvement over six months would be sustained over one year and this clearly may not be the case.[30] A longer duration of study or alternatively some attempt to integrate utility values over time would have been necessary to derive a cost per QALY. This study failed to reach a firm economic conclusion but nevertheless serves to highlight the difficulties of combining economic and clinical evaluation and provides a model for further work in this area.

Surgical treatment for RA

Despite the high costs involved, which in one study amounted to 69 per cent of the direct costs of treating RA,[31] there is good evidence that surgical intervention

can be extremely cost effective.[32,33,34] In one study CBA was applied to the indirect costs and benefits of surgical synovectomy using a population of 366 patients, the majority of whom had RA.[32] The study demonstrated that the procedure provided a net economic benefit despite the fact that it was used on only 19 per cent of the patients and only the indirect benefits arising from returning to employment was used in the calculation. This indirect benefit offset the cost of treating all 366 patients.

A Swedish study of 54 patients with RA undergoing hip or knee arthroplasties also demonstrated net economic benefit as well as the expected improvement in locomotor function.[34] Although only four patients returned to work the annual gain to society from them was equal to the cost of 12 hip or 7–8 knee replacements. In addition there was a substantial annual saving from the decrease in social support required by these patients.

CONCLUSION

It seems probable that health economic assessment will play an increasingly central role in the allocation of resources within the health service. In many therapeutic areas guidelines for recording core clinical outcome measures in clinical trials are being developed. An example of this is the recent consensus, by an international group, on the core outcome measures for use in all trials of treatment for RA.[35] These recommendations have been widely endorsed. Perhaps now is the time to establish a similar consensus on economic outcomes to be included in all clinical trials. Not only could this lead to improved operational efficiency in managing individual conditions, but ultimately it may also provide data that would improve allocative efficiency in the wider context of health care provision.

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