MEETING REPORT

Progress towards an OMERACT-ILAR guideline for economic evaluations in rheumatology

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A working report from the OMERACT Health Economics Group. The group is working towards creating common standards for economic evaluation in rheumatology and also towards improving the scientific underpinning of economic evaluation, particularly pertaining to the rheumatic diseases. Preliminary recommendations for "reference cases" in osteoporosis, rheumatoid arthritis, and osteoarthritis are proposed.

The past decade has witnessed remarkable advances in the field of rheumatology with the introduction of several new treatments for rheumatoid arthritis (RA) and other rheumatic diseases. The fundamental biological advances that underlie these discoveries have opened up a new field of research which promises to lead to the introduction of other effective and, hopefully safe, therapeutic agents for these diseases. Although many of these agents are quite costly, they may have major long term benefits, especially slowing disease progression and preventing disability. In our current healthcare fiscal environment, proof of benefit alone is no longer sufficient; it is also necessary to demonstrate that the expected benefits of a new agent are worth the costs associated with its use.

"Economic analyses vary widely in their choice of measures of clinical efficacy"

This can only be shown by formal economic evaluation, a group of analytical methods that allow us to quantify and compare the benefits (such as prevented disability, improved quality of life, etc) and the costs of medical interventions. Unfortunately, the science of economic evaluation and especially its application in rheumatology is not adequately developed to demonstrate convincingly the cost effectiveness of such treatments. A comprehensive review of all published economic evaluations in rheumatology identified only two rheumatological studies that have been conducted according to internationally agreed criteria for economic evaluation.¹ In addition, literature reviews conducted by members of the OMERACT Health Economics Working Group have shown wide variation in the selection of measures of clinical efficacy and whether and how the costs of adverse events are incorporated in economic analyses.^{2–4} This lack of agreement on methods is a threat to the validity, usability, and comparability of such research and has major implications on regulatory decisions because

policy makers allocate resources on the basis of economic efficiency. Rational policy decisions should be based on critical appraisal of economic analyses that consistently employ a valid methodology. Otherwise, apparent differences in the relative cost effectiveness of treatments may be attributable to differences in study methodology rather than to true differences in the cost effectiveness of the interventions.

Thus because the field of economic evaluation is still in development, a discussion of standardisation of methods becomes an essential first step towards identifying research priorities that will aid in moving the discipline forward. Also, several jurisdictions now require economic evaluation as part of the decision making process for reimbursement of health treatments and technologies. The development of such standards will greatly facilitate these processes. Indeed, methodological guidelines for performing such studies have been developed in several countries.^{5–9} Finally, as indicated above, the recent emergence of innovative highly effective, but costly, new treatments for RA has created a need to understand more fully the economic implications of RA treatments.

The goal of this paper is to invite comments on a proposed methodology and set of minimum criteria for standardisation of methods for economic evaluation in rheumatology, in development by the OMERACT Economics Working Group.

The OMERACT (Outcome Measures in Rheumatology) Economics Working Group was assembled in 1997. The overall goals of the group are to promote the development of rigorous scientific methods for economic evaluation in rheumatology and to work towards broad acceptance of these methods by payers, regulatory agencies, pharmaceutical companies, and providers. This working group consists of a team with well established expertise and leadership in clinical rheumatology, epidemiology, health services research, and health economics. The acronym OMERACT was coined at the first conference held in Maastricht, the Netherlands, in 1992. OMERACT is an international informal network of working groups interested in measurement of outcome across the spectrum of rheumatology interventional studies. It strives to improve outcome measures through a data driven iterative consensus process. OMERACT has a five member organising committee with members from three continents, as well as a 15 member scientific advisory

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Abbreviations: NSAID, non-steroidal anti-inflammatory drug; OA, osteoarthritis; RA, rheumatoid arthritis

Table 1 Methodological issues for economic evaluation in rheumatology

Issue	Definition/question
1. Model horizon	How long should costs and benefits be forecast?
2. Duration of treatment	What duration of treatment should be included in economic evaluations?
3. Extrapolation beyond trial duration	Can extrapolation beyond the duration of clinical trials be performed in a valid and reliable manner?
4. Modelling beyond trial duration	Can extrapolation beyond treatment duration be performed in a valid and reliable manner?
5. Synthesis of comparisons where clinical trials do not exist	Can comparisons be synthesised in a valid manner where experimental data are not available?
6. Outcome measures	What are the most meaningful clinical outcomes for economic evaluation?
7. Mortality	How should mortality be considered in economic analysis?
8. Valuation of health (e.g. QALYs)	What are the optimal sources of health state values?
9. Resource use	What are the optimal approaches to estimating resource use?
10. Classification and reporting of adverse events	What are the optimal approaches to measuring, classifying, and reporting toxicity?
11. Discontinuation of treatment	What are the optimal approaches to determining drug discontinuation and adherence rates?
12. Therapeutic strategies	Should data on therapeutic strategies (as opposed to individual treatments) be incorporated into economic evaluations?
13. Population risk stratification	What are the optimal approaches to incorporating data on the risk status of the population under study in economic evaluations?

committee, composed of international opinion leaders from nine countries. The OMERACT Economics Working Group held its first meeting in 1997 and has worked together actively and regularly since that time. The group has published several articles, including a series of editorials, dealing with controversies in economic evaluation,^{10–15} as well as reports of the two major conferences (1997 and 1999).^{16–18} In addition to holding scientific meetings and consensus conferences, members of the group play an active part in the conduct of original methodological research in economic analysis in the rheumatic diseases.^{2 11–14 19–34}

“The increasing cost of new RA treatments requires a grasp of their economic implications”

The latest scientific meeting of the OMERACT Economics Working Group was held in New York City, 22–23 February 2001. In attendance were Sherine E Gabriel (Chair), Peter Tugwell (Co-Chair), Drs Maarten Boers, Douglas Coyle, Ann Cranney, Michael Drummond (Co-Chair), Francis Guillemain, David Henry, Dick Jonsson, Andreas Maetzel, Bernie O’Brien, Brian Ruff, Joerg Ruof, Maria Suarez-Almazor, Rod Taylor, George Torrance, and Anna Tosteson. The objective of that meeting was to build on the work of the health economics module from OMERACT V (held in Toulouse, France, 4–7 May 2000) to develop a reference case for rheumatology. The term “reference case” was first coined by Marthe Gold and colleagues during the development of the US Public Health Service appointed Panel on Cost-Effectiveness in Health and Medicine, where the panel was unable to agree on optimal methodological approaches for economic evaluation.⁷ Dr Gold suggested the term “reference case” to indicate a proposed set of minimum criteria that all economic analyses should include in order to allow comparability across studies. Importantly, Dr Gold emphasised that a reference case does not imply consensus. Rather, it is a tool to facilitate comparisons. Indeed, investigators are encouraged to go beyond these minimum criteria in their individual studies. Using this construct, which is very

similar to the “core set” construct used in OMERACT efficacy discussions, the economics working group began developing a reference case for rheumatology. The rheumatology reference case is an applied version of the generic reference case, in that it sets out proposed minimum criteria for clinical data sources and assumptions in economic evaluation in rheumatology. Excellent progress was made towards this goal during OMERACT V; however, several issues remained unresolved at the conclusion of that conference. This follow up meeting in New York City was held to focus specifically on the 13 most controversial methodological issues for economic evaluation in rheumatology and to propose reference case recommendations for each of these issues across the three most prevalent musculoskeletal disorders.

Table 1 defines the 13 methodological issues and table 2 contains a preliminary outline of the proposed recommendations for the reference cases across three musculoskeletal disorders. These issues are common across different types of interventions, including pharmacological, surgical, and rehabilitation interventions, but the outcomes (such as mortality) may be specific to different interventions.

As shown in table 2, some of the proposed minimum criteria are different across musculoskeletal disorders. These differences are due to differences in the natural history and management of the disorders, as well as outcomes of accepted clinical importance and validity. For example, because over 50% of patients receiving disease modifying antirheumatic drug treatment for RA change treatment within one year, the proposed minimum criteria for model horizon is one year, and estimates of benefit should be limited to what is available from efficacy trials.³⁵ In contrast, because patients with osteoarthritis (OA) continue treatment for long periods, but use drugs intermittently as needed to control pain, the base case is lifetime with continuous, intermittent use for model horizon and duration of treatment. Furthermore, clinical adverse events were deemed to be important outcomes of RA and OA treatments (such as perforations, obstructions, and bleeds), but adverse effects resulting from osteoporosis treatments were considered less significant from the perspective of

Table 2 Preliminary proposed recommendations for reference cases in each of three musculoskeletal disorders

Methodological issue	Osteoporosis	Rheumatoid arthritis	Osteoarthritis (NSAIDs)
1. Model horizon	Lifetime	One year	Lifetime
2. Duration of treatment	i. Typical for specific drug ii. Ideal for specific drug iii. 5 Years	Continuous	Continuous or intermittent use
3. Extrapolation beyond trial duration	Continued effect size while receiving treatment adjusted by withdrawal rates from observational studies	Estimates of benefit based on trial data; estimates of withdrawal and long term outcomes based on observational data	Continued effect size whilst receiving treatment adjusted by withdrawal rates from observational studies
4. Modelling beyond trial duration	Linear decline of effect size after treatment is continued	No benefit or harm if treatment is stopped	
5. Synthesis of comparisons where clinical trials do not exist	Not recommended owing to uncertain validity of transitive comparisons		
6. Outcome measures	Clinical fractures	<ul style="list-style-type: none"> • ACR 20 sustained for 6 months • EULAR improvement criteria • Clinical adverse events 	OARSI—20% improvement Clinical adverse events
7. Mortality	Hazard for mortality from observational studies		Incorporate additional hazard attributable to drug based on observational data
8. Valuation of health (e.g. QALY)	Values from general public for policy makers; values from patients for clinicians	Values from general population using direct measurement	Values from general public for policymakers; values from patients for clinicians
9. Resource use	Include all associated direct medical costs in the analysis, but report indirect and non-medical costs separately		
10. Classification and reporting of adverse events	Report adverse events with patients as the unit of analysis using common toxicity criteria (under development by OMERACT Toxicity Working Group, Woodworth)		
11. Discontinuation of treatment	Use discontinuation rates from observational studies		
12. Therapeutic strategies	Include modelling of most commonly used therapeutic strategy with sensitivity analysis to consider other strategies		
13. Population risk stratification	Include clear definition of underlying population including low and high risk groups		

economic analysis. These examples illustrate how the “reference case” needs to be specific to the clinical condition.

This preliminary outline represents only the first step in developing a set of reference case recommendations. The outline is presented here in order to invite comments and suggestions from the broad rheumatology community. The OMERACT Health Economics Working Group will compile these comments, combine them with input from previous and forthcoming meetings, and modify the outline accordingly. The revised proposal will be presented for final review and consensus at the next OMERACT conference.

Another important goal of these discussions is to refine a research agenda for each of these methodological issues. A full report, including details of the research agenda, as well as additional details for the proposed recommendations, is currently under preparation.

The OMERACT Health Economics Working Group is an active, engaged, and hardworking team that has generated a great deal of momentum. Indeed, two additional meetings are planned within the next year to maintain this momentum and further our goals. Through these efforts, we hope to continue to work towards achieving the ultimate goal of not only creating common standards for economic evaluation in rheumatology but also improving the scientific underpinnings of economic evaluation, particularly as it pertains to the rheumatic diseases.

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