Workshop Report

Economic Analysis Alongside Clinical Trials: Practical Considerations

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Practical issues surrounding the incorporation of economic analysis in clinical trials were examined by considering potential studies in the 6 major clinical areas. In each case a scenario was presented whereby a clinical trial was planned and 5 key issues were examined. These are discussed in turn.

Relevance of Economic Considerations

It was considered relevant to include economic analysis in trials where a new therapy was likely to be much more costly than current treatment, such as a new intravenous biologic agent in treatment of early arthritis.

Economic analysis may also be relevant where therapies are frequently applied, such as physiotherapy in ankylosing spondylitis (AS), or where the alternatives impose costs on different parties, such as in a comparison of physiotherapy with a self-exercise program in the treatment of low back pain.

Form of Economic Evaluation

In most of the scenarios examined, cost minimization was unlikely to suffice because it was rare for the 2 alternative therapies to be identical in their clinical effects.

In most cases the choice lay between cost effectiveness and cost-utility analysis. In some situations, such as in an evaluation of alternative drugs for osteoarthritis (OA), it might be possible to present results in terms of the cost per fracture averted, but in most situations the most relevant measures were in terms of improvements in quality of life. Therefore, the key question was whether changes in a number of quality of life domains should be presented as a profile and merely related to costs, or whether they should be unified as a single preference weighted index in a cost-utility analysis.

We recognized that failure to use a single preference weighted index would lead to problems of interpretation if one therapy failed to dominate another on all domains (e.g., on the SF-36 scale). However, it was also recognized that utility measures, while enabling calculation of the cost per quality adjusted life-year for communication to public policymakers, also had problems of interpretation. In addition, many utility measures were in various stages of development.

Therefore, the preferred approach might be to use more than one form of analysis, including both cost effectiveness and cost-utility analysis. This is consistent with the guidelines for economic analysis currently proposed by the Canadian Coordinating Office for Health Technology Assessment (CCOHTA)[1], which suggest that a number of quality of life scales be used (generic, general health profile, and health index), and that the quality of life data be presented as an array before combination into a single index.

Measurement of Resource Items Alongside the Clinical Trial

The major items relate to the direct costs, mainly borne by the health care sector. The paper by Thompson, *et al*[2] on oral gold therapy for rheumatoid arthritis (RA) included a wide range of resource items. These comprised outpatient visits, medications, radiographs, laboratory tests, aids and devices, surgery, hospitalizations, nursing home care, and paid and unpaid help.

There was debate about the relevance of tracking indirect costs and their importance in an economic evaluation. One suggestion was that loss of work time is a useful indicator of the patient's functional status, quite apart from any effect on national production.

The other problem with indirect costs was their measurement. Whereas in most health care systems data exist on the quantities of direct costs used, and their prices (unit costs), indirect costs need to be estimated by questionnaires to patients. There are also alternative approaches to the valuation of losses in productivity[3].

Inclusion of Quality of Life Measures

The arguments for and against the inclusion of various quality of life measures are discussed elsewhere[4]. In the context of economic evaluation, the additional issue is whether particular scales will be helpful in establishing value for money.

Overall, the conclusion was that in trials in rheumatology and related fields, a range of quality of life measures needs to be included. Although in the short term this may have

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additional resource implications, much could be gained from including a number of measures alongside each other in the same study.

Modifications to the Clinical Trial Design

Most of the requirements for economic analysis result in additional data collection needs. However, it may also be that the ideal design for economic analysis differs from that for an efficacy study.

Examples of this potential conflict were identified. First, economic analysis may require increased frequency of data collection, perhaps necessitating additional followup visits. For example, if resource use data were being obtained from patients, it would be unwise to set data collection points more than one month apart, for example, owing to problems with memory recall.

Second, economic data collection may suggest a longer period of followup than is typical for an efficacy study. This leads to a dilemma. Should followup be increased at additional cost, or should modelling approaches be used to link final outcomes with the intermediate outcomes assessed in trials? For example, in trials of therapies for osteoporosis, can changes in bone mineral density reliably be linked to the incidence of fractures, or do the fractures themselves have to be observed?

Third, the assessment of economic data may suggest larger sample sizes, owing to the greater variability in some of the economic variables. However, none of the working groups suggested that the size of the proposed trial should be increased in order to increase the statistical power of the economic analysis.

Finally, some examples were identified where the need to do an economic analysis may compromise some of the objectives of an efficacy study. For example, in a trial comparing hormone replacement therapy (HRT) with calcitriol for osteoporosis, a naturalistic protocol, which would be favored for economic analysis, would not mandate renal ultrasound in the HRT group, since to do this would be to induce care that otherwise may not have been given. This would mean that it would not be possible to assess the induced rate of kidney stones from calcium supplementation.

Conclusion

The working groups' discussions explored, in a more practical way, some of the issues raised in the plenary session. The general view was that it was worthwhile to include economic evaluation alongside many clinical trials, but that the practical and methodological issues needed careful consideration.

REFERENCES

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