How much does it cost to include an economic evaluation in a clinical trial?

What is CREST?

The Centre for Health Economics Research and Evaluation (CHERE) at UTS has been contracted by Cancer Australia to establish a dedicated **Cancer Research Economics Support Team (CREST)** to provide high quality, expert advice and support to Multi-site Collaborative Cancer Clinical Trials Groups.

Factsheets

CREST will produce a series of factsheets as resources for cancer collaborative group researchers wishing to include economic evaluation in their clinical trials.

Authors: R De Abreu Lourenco, M Haas, R Viney

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SUMMARY

There is no single answer to the question "what does it cost to include an economic evaluation in a trial"? The resources required will vary between trials, and depend on whether the evaluation is conducted prospectively or retrospectively, and the extent of modeling and additional data analysis required to translate the trial outcomes to a meaningful incremental cost per unit of health gain. In general the resources required for the data collection and analysis of economic outcomes can be estimated by considering the following issues when planning a clinical trial:

1. Trial design: consider whether the trial design aligns with the economic question. Is a specific economic sub-study required, for example to collect local resource use data or to facilitate the estimation of quality adjusted life years (QALYs)?

2. Data collection: Are there additional data required for the economic evaluation not planned for collection within the trial? Are new data collection methods/tools required? Is access to administrative or secondary datasets required to provide additional data?

3. Data analysis: Is there additional analysis required to estimate and cost the resource use for each trial arm? Is there additional analysis required to translate trial outcomes to outcomes that are meaningful for decision makers. Is there additional modeling required?

Within each step, specific health economics expertise might be required, although others on the clinical trial (such as the trial statistician or CRAs for data collection) might perform some activities. This has implications for the trial budget. Similarly, access to secondary databases or specialised software will also impact on the trial budget. Estimates of these requirements, and those for health economics input (on an annual full time equivalent basis), are provided in this Factsheet.

For more information about CREST, or for other factsheets in this series, please visit our website: www.chere.uts.edu.au/crest

How much does an economic evaluation of a clinical trial cost?

One of the questions most often asked of the team at CREST is "*what is the budget I'll need to allocate to the economic evaluation*?" There is no simple answer to this question. It depends on the approach to be taken in the analysis, the questions to be answered, who will undertake the research, and the timeframes involved.

This Factsheet provides a series of points to consider when planning the resource requirements for undertaking an economic evaluation as part of a clinical trial. By considering these points, researchers and trialists should be well on the way to being able to answer the question of how much it will cost to undertake an economic evaluation alongside a clinical trial.

An overview of the steps involved in undertaking an economic evaluation, and the suggestions for the resources required, is provided in Figure 1. Within this figure, consideration of an economic evaluation is presented alongside the usual elements of the trial process, namely trial design, data collection and data analysis. For each of those elements, corresponding points relevant to the economic evaluation and health economics consideration are presented.

Importantly, this schematic is not intended to present a breakdown of why or how to do prepare an economic evaluation (this is discussed in other Factsheets in this series), but rather the specific points to consider from a health economics perspective. A suggestion as to the resources required to conduct an economic evaluation alongside a clinical trial is provided in the last set of boxes corresponding to each of the relevant trial elements.

Understand the Proposed Evaluation

The questions to be answered: Study Design

Generally speaking, there are two approaches to economic evaluations associated with clinical trials: those which are prospectively designed and undertaken from the outset alongside the clinical trial; and those which are retrospectively designed and undertaken once the trial has been completed. In both cases, modeling beyond the trial outcomes and some manipulation of the resource use estimated in the trial may be required.

In a prospective defined analysis, the question to be answered will determine the data to be collected, and the time required for the analysis. This in turn will impact on the budget required for the analysis.

In a retrospective analysis, the data available will typically restrict the questions that can be addressed. While this might mean fewer resources are needed than if a prospective analysis was conducted, it is also likely that

the results will be less robust and more open to interpretation and uncertainty.

In either case, it is important to consider whether the clinical question fits the economic question and vice versa. For example, there will be some differences in the data required depending on whether the question of interest is investigating the cost-effectiveness of a new tyrosine kinase inhibitor for patients with chronic myeloid leukaemia (CML) in terms of achieving a complete cytogenetic response, or in terms of the QALYs gained, or both.

In the case of the former, the analysis relies on clinical data readily collected as part of the clinical management of patients with CML. In the case of the latter, the trial will need to include additional instruments to allow QALYs to be estimated, and additional time will be required for the collection and analysis of those data.

This might result in sub-studies being established within the context of the overall study to address questions specific to the economic evaluation. These sub-studies might address a specific question within a subgroup of study participants, apply a specific method within a group of participants (such as a discrete choice experiment to measure participant preferences for treatments or health states), or assess health care use in a detailed manner.

The approach to the analysis: Data Collection

In general, for a trial of a given size, it will be more costly to collect data prospectively than to conduct a retrospective analysis (Note however that retrospective data collection such as chart audits and medical record reviews is resource intensive, and hence may be more expensive than prospectively designed data collection, and less accurate). However, what the latter gains in terms of reduced costs to the researcher, it is likely to lose in terms of precision and accuracy in measuring the resource use associated with the treatments (and their sequelae) under investigation.[1] This diminishes the capacity of such analyses to address adequately the questions of interest for the economic evaluation. Where possible it is preferable that data collection for the purposes of economic evaluations be specified prospectively.[2,3]

Thereafter, the cost of carrying out the evaluation will depend to a large extent on the manner in which resource use is to be assessed:

1. A bottom up approach. In this case, the intention is to measure as completely as possible all health care use by patients from the outset of the study. This might be through the use of patient diaries, specific resource utilisation case report forms (CRFs), prospectively available secondary data sources (such as Medicare Australia or hospital databases) or a combination thereof.

2. A protocol driven analysis in which the resource use for each patient is not tracked separately, but rather patients with a given clinical event are assigned health care use as derived from a clinical protocol. This approach assumes that it is possible to define a "typical" patient, that all patients behave in the same manner as that patient, and that there will be an high rate of compliance (by patients and practitioners) with the treatment protocol.

3. A combination of the above approaches.

The implications of choosing one of these approaches for the required budget for the economic evaluation are essentially that the more detailed the data collection, the more resources that are required for the evaluation in terms of designing the requisite forms, data monitoring/cleaning, analysis and reporting.

Use of administrative datasets, such as the Medicare Australia data, may reduce data collection costs while still accurately reflecting clinically relevant practice (see the Factsheet *Medicare Australia data for research: an introduction* accessible at http://www.chere.uts.edu.au/crest/pdfs/Factsheet-Medicare_Australia-FINAL.pdf).

Who will undertake the research?: HE Requirements

It is not the case that health economists are required for all aspects of an economic evaluation. There are some activities within an economic evaluation that can be undertaken by others within the trial group, such as statisticians (in terms of analysing outcomes such as survival, estimating resource use based on observed trial data etc) and clinical trialists (developing resource use CRFs).

Similarly, the depth of health economics input will impact on the costs involved. Typically, the type of person involved will be an individual with post-graduate experience in conducting or supervising the conduct of economic evaluations. Whether you need one or more such individuals will depend on the approach being adopted, the length of the trial, and the complexity of the question being addressed. A reasonable starting point for budgeting purposes is to assume that the type of human resources needed are at the level of a post-graduate qualified individual.

In a prospective trial, the duration will also impact on the cost of conducting the economic evaluation, and importantly how those costs will be incurred over time. For a prospective evaluation, there will be a reasonable level of activity in the first stages of the trial (say the first year), minimal activity while the trial is ongoing, and then significant activity during the data collection, analysis, interpretation and reporting phases.

Specify the Activities Involved

Once the above questions have been answered, it is a matter of building a budget

as would normally be done for any funding application.

As much as possible, this should break the economic evaluation component of the trial into its discrete tasks. The precise tasks will depend on the nature of the evaluation as described previously. An example of a list of tasks is provided below.

Cost the Resources Needed

For each task, an estimate of the number of days and the type of person required for that task should be made. These might be reasonably expressed as FTEs for each type of person required for the conduct of the evaluation. An appropriate salary can then be allocated to each type of person anticipated to be required for the conduct of the economic evaluation.

Depending on whether or not the "salary" cost includes some additional component for non-salary reimbursement (such as on-costs), additional personnel related costs might need to be factored into the costing exercise. Costs associated with other tasks, and which are not specifically related to salaries eg. costs associated with acquiring data (such as the development, publication and retrieval of CRFs), data management and storage, acquisition of secondary data (such as are available from Medicare Australia), or specific computer software as might be required to conduct the analysis, should also be factored into the costing process.

Calculate the Required Budget

Finally, the estimates of the salary costs (over each year of the trial), together with any allowable non-salary costs can be aggregated to calculate a budget for the conduct of the economic evaluation component alongside the clinical trial.

For more information

For more information on any part of this factsheet, please contact:

crest@uts.edu.au

References

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2. Glick H, Doshi J, Sonnad S, Polsky D. Designing economic evaluations in clinical trials. In: Gray A, Briggs A, eds. Economic Evaluation in Clinical Trials Oxford: Oxford University Press; 2007.

3. Ramsey S, Wilke R, Briggs A, et al. Good research practices for cost-effectiveness analysis alongside clinical trials: the ISPOR RCT-CEA Task Force Report. Value in Health 2005;8:521-33.

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CREST
CANCER RESEARCH ECONOMICS SUPPORT TEAM

Abbreviations: CHEREL, Centre for Health Record Linkage; FTE, full time equivalent; HE, health economist; ICER, incremental cost-effectiveness ratio; LPLV, last patient last visit; MBS, Medicare Benefits Schedule; PBS, Pharmaceutical Benefits Scheme; QoL, quality of life; RA, research assistant.

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How much does it cost to include an economic evaluation in a clinical trial?

Specifying the Activities for an Economic Evaluation.

An economic evaluation is being developed alongside a Phase III trial of denosumab for the prevention of skeletal related events in patients with bone metastases secondary to renal cell carcinoma. The trial runs for three years. The trial group has agreed to use a bottom up costing method that will consider not only the costs of the intervention (denosumab or placebo, both in addition to standard care) but also ongoing medical management. The research group has determined that the activities for the HE analysis comprise the following:

Pre-trial phase:

1. *Input to the trial protocol (particularly clinical endpoints, adverse event reporting) and investigators' brochure.*
2. *Development of resource utilisation CRF.*
3. *Choice and acquisition of the license to use a quality of life questionnaire.*
4. *Development of ethics submission to seek access to Medicare Australia data (for subsequent assessment of ongoing care).*

Intra-trial phase:

1. *Participate in ongoing trial monitoring committee.*
2. *Availability to answer queries on resource utilisation CRF.*

Post-trial phase:

1. *Obtain access to Medicare Australia data.*
2. *Liaise with trial statisticians and data monitoring groups regarding data cleaning and availability for analysis.*
3. *Obtain inputs (prices) for resources used as described in resource utilisation analysis.*
4. *Analyse resource utilisation, quality of life and relevant trial endpoints (such as occurrence of skeletal related events).*
5. *Confer with trial clinicians as to whether reported resource utilisation patterns reflect observed use; and if not include "missing" treatments.*
6. *Prepare economic evaluation.*
7. *Prepare stand-alone economic evaluation for publication alongside clinical trial report.*

Other Titles in the CREST FactSheet Series:

- **Factsheet - Sample size calculation in economic evaluation**
- **Factsheet - Economic evaluations in cancer clinical trials - why would I do an economic evaluation as part of my clinical trial?**
- **Factsheet - Medicare Australia data for research: an introduction**
- **Factsheet - Health related quality of life for economic evaluations in cancer - why do clinical trials need economic evaluation-specific quality of life measures?**
- **Factsheet - Step by step guide to economic evaluation in cancer trials**
- **Factsheet - Command Files to Generate EQ-5D Weights for Australia - EQ-5D TTO DCE Weights**
- **Factsheet - Command Files to Generate EQ-5D Weights for Australia - EQ-5D-5L Scores**

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http://www.chere.uts.edu.au/crest/resources/documents.html