Recommendations Concerning Economic Evaluations and Cancer Clinical Trials

Prepared by the Committee on Economic Evaluation (formerly the Working Group on Economic Analysis) of the National Cancer Institute of Cancer Clinical Trials Group

Background

Rising health care costs, expensive new health care technologies and increasing patient expectations are placing huge pressures on the publicly funded health care system in Canada. As a result, policy makers need information on the cost and cost-effectiveness of new therapies in addition to their clinical benefits. In response to this need, the National Cancer Institute of Canada Clinical Trials Group (NCIC CTG) established a Committee on Economic Analysis (CEA) to provide advice on the economic evaluation of new cancer therapies. One role of this group is to make recommendations about which clinical trials would be most appropriate for an economic analysis. This document outlines the procedure by which the Committee makes its recommendations.

Factors limiting the conduct of economic evaluations

Although the inclusion of an economic evaluation alongside a clinical trial adds value, it also adds to the burden and cost of conducting a trial. In addition, the limited availability of research funds to support health services research and the small number of health economists interested in cancer in Canada are factors that limit the conduct of economic analysis alongside clinical trials. Thus, it is neither feasible nor desirable to recommend that all cancer clinical trials have an economic analysis.

Potential Recommendations to be made by the CEA

The CEA could make one of three recommendations

1. That an economic analysis be conducted concurrently with the proposed trial
2. That an economic analysis is warranted but be conducted using a modelling approach once the trial is completed
   (Note: with this recommendation some additional data collection to facilitate future modeling may be required)
3. That an economic analysis not be undertaken

The criteria used to reach a recommendation are detailed below.

Criteria for Determining Clinical Trials Appropriate for Economic Evaluation

Some clinical trial designs are not suitable to answer economic questions. Trials must be at least partly pragmatic and relate to actual clinical practice to be appropriate for an economic analysis. The NCIC's CEA recommends that at least one of the following criteria be met before an economic analysis is undertaken alongside an NCIC CTG clinical trial.

1. The new intervention is anticipated to have only a modest therapeutic benefit in a potentially large population.

An example of such a trial is the randomized trial of anastrozole versus tamoxifen in postmenopausal women with early stage breast cancer. After a median follow-up of 47 months,

anastrozole provided approximately a 2% (p = 0.03) absolute risk reduction in disease-free survival. Given the large number of patients who are potentially eligible to receive this treatment, an economic evaluation would be informative to policy makers. A large incremental cost might not justify the modest benefits.

2. The new therapy is potentially very costly.

If the treatment intervention is known to be very expensive and is expected to be used frequently enough to produce a large aggregate cost, then an economic evaluation alongside a clinical trial may be helpful in determining whether the new treatment is sufficiently cost-effective to warrant adoption. An example would be the use of high dose interleukin-2 (IL-2) in patients with stage IV melanoma. The requirement for hospitalization to manage the substantial treatment-related toxic effects and the high cost of IL-2 are important cost drivers. In addition, the clinical benefit is small, yielding only a low rate of tumour regression. These factors are compelling reasons to undertake an economic analysis in a trial of IL-2 in melanoma, as economic information would help to inform a policy decision about whether to fund the intervention.

It should be noted that an economic analysis is unlikely to be required to evaluate a high-cost but infrequently used therapy. Similarly, a high-cost but highly effective treatment (the treatment cures a high proportion of patients) is unlikely to require an economic analysis.

3. There is a high degree of uncertainty about the economic impact of the treatment of interest.

A new treatment may appear to produce health benefits but be associated with significant side effects or other impacts that make it uncertain whether the net economic impact is positive or negative. In this situation, the economic analysis should ideally take the form of a cost-utility study, as this is the best way to capture the impact of side effects on the economic profile of a new treatment. The evaluation of chemotherapy regimens in advanced non small-cell lung cancer is a good example. There are multiple regimens, which are comparable in terms of tumour response and overall survival but unique in their side effect profile. Patient utilities (information on the health states experienced by the patients) captured during a comparative trial would enable the determination of the cost per QALY gained relative to the current standard.

4. An economic evaluation associated with equivalence trials may yield information to guide the determination of routine practice.

In the case of an equivalence trial, the economic evaluation has the potential to yield important information when considered from different perspectives, including that of the patient, the provider, the government or society as a whole. Side effects, ease of administration and cost are the major parameters that guide policy development in this situation.

A recent example is the use of zoledronic acid as an alternative to pamidronate for the prevention of skeletal related events (SREs) in advanced breast cancer and multiple myeloma. A clinical trial demonstrated that zoledronic acid is equivalent to pamidronate in the prevention of SREs, but zoledronic acid can be infused over 15 to 30 minutes as compared with two to four hours for pamidronate. However, zoledronic acid is approximately twice the cost of pamidronate. From the perspective of the government as payer, an economic evaluation would be of value to determine whether the increased cost of the zoledronic acid is offset by reduced treatment administration costs. An economic evaluation from the patient perspective may show reduced out-of-pocket expenses as a result of reduced parking and care provider costs. Full economic data and data collected prospectively on patient preferences would be of value to policy makers in this situation.

5. Economic data will assist future economic evaluations of new therapies.

For some studies, adding an economic analysis in the form of a cost-of-illness study or estimating the cost of side effects will provide resource utilization data and cost information that can be used in future studies, including modeling studies. Resource utilization data captured in the course of conducting a trial that failed to yield a significant therapeutic benefit may still be useful for future studies.

6. The study must have a suitable number of Canadian patients

Finally to have economic information of value from a Canadian perspective, the clinical trial must have resource utilization data on a sufficient number of Canadian patients. This requirement may become an increasingly important barrier to economic evaluations as more trials are conducted as international cooperative group studies with only a small number of Canadian patients.