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The Real Costs of Emesis

THE ARTICLE by Cunningham *et al.* (pp. 303–306) provides an interesting example of economic analysis in the area of cancer treatment. Although the importance of taking an economic perspective on cancer has been stressed many times in the past [1–4], there are still relatively few good economic studies in this area, despite the substantial quantity of health care resources devoted to cancer. However, in the face of limited resources for health care and an increasing pressure to audit both the use of resources and the outcomes of procedures and treatments, such analyses should, in future, become more frequent.

This study illustrates how an economic perspective can highlight some important issues and potentially influence policies for purchasing health care. First, they ensured that their cost analysis was not limited to the acquisition costs of drugs alone but included the additional costs associated with the use of each drug—the costs of administering the drug, "rescue" medication and the materials, nursing and medical time costs of dealing with emesis or adverse events. These calculations illustrate that whilst these additional costs accounted for only 6% of mean utilisation costs in the ondansetron group, the corresponding figure in the metoclopramide group was substantially higher at 41% (calculated from Table 4). This was due mainly to the extra costs associated with the administration of the antiemetic and nursing staff time.

As the authors note, taking a wider viewpoint for the assessment of costs reduces the cost ratio between the two drugs and produces useful information for both the purchasers and providers of health care. In particular, it highlights the fact that some of the non-drug costs associated with the two antiemetics will fall on other budgets in varying amounts, for example, the use of ondansetron had no impact on the medical staff budget whereas metaclopramide had a small but positive impact. The advantages of adopting a wider viewpoint and considering such additional costs has been illustrated in other studies, and the non-drug costs of providing chemotherapy (such as in-patient stays, staff time costs of administering the drugs and the numerous tests associated with cytotoxic treatment) have received attention in the past [5–8]. One example of the implications of changing the viewpoint of an economic analysis is the comparison of carboplatin and cisplatin for the treatment of ovarian cancer [9]. Cisplatin is the cheaper drug, but requires in-patient admission due to the need for intensive hydration before and after treatment, whereas carboplatin is a more expensive drug but can be delivered on an out-patient basis. If the focus was on drug costs alone (and assuming outcomes were equal), cisplatin would always appear to be the most cost-effective option. However, despite the fact that the use of carboplatin would impose higher costs on the pharmacy department, it may be the most cost-effective option from the point of view of the hospital as a whole. Decisions made purely on the narrow basis of drug costs alone may therefore encourage the inefficient use of resources.

The other important feature of this study relates to the combination of the cost data with details of the effectiveness of the alternative drugs. Ondansetron appeared to be superior to metoclopramide as patients in the former group had a higher probability of avoiding significant emesis than those in the latter group. In addition, emesis experienced by those taking ondansetron was judged to be less severe (measured in terms of the number of emetic episodes per "failure") than those taking metoclopramide. Taking these differences into account affects the economic results substantially and the cost per *successfully treated* patient becomes almost equal for both drugs. Some of the economic analyses which have been undertaken in the cancer field have focused only on the costs of alternative treatments, using the assumption that outcomes are equivalent. For example, the costs of alternative treatments for prostatic cancer [10] and for breast cancer [11] have been compared on this basis. Whilst this is a valid approach where the clinical evidence of equal effectiveness is well-established, it could be misleading to compare alternatives on the basis of costs alone in situations where there is some uncertainty about the relative effectiveness of each treatment. Clearly, in the comparison of ondansetron vs. metaclopramide, such an approach would have produced rather different results and, as the authors note, might lead to the inefficient use of National Health Service funds.

The authors point out that although their results indicate that the drugs are equally cost-effective, ondansetron may offer significant benefits to patients as a result of avoiding emesis, or reducing the extent of emesis if it occurs. As they note, patients find this aspect of chemotherapy treatment very distressing and avoidance would enhance the quality of life of patients undergoing such treatments. Increasing attention has been given to the impact on patient's quality of life of cancer and treatment for cancer, especially as treatments are often aimed at palliation rather than cure and thus the quality of the remainder of a patient's life becomes paramount. The measurement and valuation of such outcomes is very complex and, like many others, this study does not attempt to quantify these benefits. However, intuitively it can be assumed that patients would prefer *not* to experience emesis and thus as both drugs are equally cost-effective, ondansetron would appear to be the preferred option. In other contexts, economic evaluation is often less straightforward as patients may obtain more benefits from higher cost alternatives and in such cases decision makers must decide whether the extra benefits are worth the extra costs. The advantage of an economic perspective is that it makes such choices explicit and subject to rationale decision-making.

The study involves small numbers of patients and the reliability of the results may therefore be questioned. In addition, it was conducted over a short time period and longer term follow-up of the occurrence of adverse events would provide more compelling evidence of the relative effectiveness of the two drugs. However, the study can be seen as providing data which is suggestive of the advantages of ondansetron and can be used to guide the design of any future studies. It is also clear that, in some circumstances, it is possible to gain useful insights from small, short-term economic studies which are relatively cheap to undertake and do not entail the organisational and financial

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problems associated with large clinical trials. As purchasers and providers become more aware of the need for economic analysis to inform decision-making, they will also need the relevant data quite rapidly if it is to be of immediate use and studies such as this one show that this is indeed possible in some contexts. However, such an approach would not always be appropriate and large scale, longer term clinical and economic evaluations will be needed in many cases if robust results are to be obtained.

In conclusion, this study provides insights for decision makers and can guide the efficient use of resources devoted to health illustrating how a narrow focus on one aspect of costs alone can provide misleading and inappropriate conclusions. It also highlights some of the methodological issues involved in the economic analysis of cancer treatments. It shows how such analyses can sometimes be undertaken on a small scale, and in a simple manner, yet still provide useful information and whilst the small numbers and short time scale remind us to view it perhaps as a pilot study rather than a definitive trial, it will clearly be useful to those involved in the provision of care for patients undergoing chemotherapy for cancer.

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Workshop on Suramin with Emphasis on Prostate Cancer: Re-evaluation of Response Criteria

Ruud E.N. van Rijswijk, Esteban Cvitkovic, John Wagstaff and Charles E. Myers, on behalf of the participants of the meeting*

DURING THE seventh NCI/EORTC symposium† a workshop took place with the aim of discussing the present status of suramin in the treatment of cancer. The meeting was intended to have a broader perspective, however, as suramin analogues are oncoming. A common language regarding the response criteria to be of use in clinical trials with these novel agents was therefore felt to be of special importance. Two main topics were listed on the agenda. Firstly, to critically reconsider response criteria of trials in prostate cancer involving growth factor antagonists. Secondly, to evaluate the anticancer activity of suramin.

The initiative for this meeting arose from the opinion, expressed especially by European investigators, that the toxicity of suramin might offset its use as an anticancer agent. In particular the severe motor neuropathy observed in a number of patients treated with the drug had led to this concern. During the past year it has, however, become evident that the schedules of administration of suramin used in early studies were not optimal. It is now apparent that the peculiar pharmacokinetics (mean $T_{\frac{1}{2}}$-α value of 14 h and mean $T_{\frac{1}{2}}$-β value of 55 days) of suramin require an individualised dosing schedule in order to keep peak and trough concentrations within suramin's narrow therapeutic window. The minimal concentration required to obtain an antitumour effect has not been clearly defined. Based on IC_{50} values of various prostate cancer cell lines exposed to suramin, Myers felt that a trough concentration of at least

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