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THE COST EFFECTIVENESS OF CANCER CHEMOTHERAPY: A CLINICIAN'S VIEW★

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The purchaser/provider scenario is now integral to current United Kingdom National Health Service practice. Therapeutic advances have improved the treatment options available, but these together with demographic changes and the rise of expectations of a more health conscious public, are placing increasing demands on limited resources. In Oncology, as indeed in many other specialities, in drawing up contracts purchasers are still uncertain as to what they should demand to achieve the best quality and most cost-effective care for their patients. The onus is on expert providers to advise purchasers on up-to-date practice in sensible terms.

VALUE ANALYSIS (ECONOMIC EVALUATION)

Methods of evaluating treatment options include. (1) Cost minimisation, which examines and compares the total costs of using different treatments giving identical outcomes, (2) Cost effectiveness, which relates the cost of therapies to their outcomes, where outcome is assessed in terms of a single health effect, (3) Cost benefit analysis, which compares total benefits of using a given treatment with all the associated costs, with the measurement in financial terms, and (4) Cost utility, which relates the cost of different therapies to the amount of 'well being' produced. One variation of cost-utility assessment is the Quality Adjusted Life Year (QALY), but this has not found universal favour amongst clinicians and managers.

There is an acknowledged lack of outcome measures in Oncology, particularly in terms of palliative therapies where survival data are not particularly relevant. 'Concrete' markers of quality are required with quality of life (QOL) measurement the ideal. Unfortunately, as the considerable array of tests available for the assessment of QOL may indicate, this is not an easy task and such measures are not easily comprehended by health care managers, although some tests do seem to be of value as true reflectors of patients' experience. However, it is generally agreed that objective tumour response (complete, partial or none) as defined by the standard Union Internationale Contre Cancer (UICC) criteria does correlate with quality as far as the patient's perception of benefit is concerned.

CHEMOTHERAPY

The total cost of drug management in cancer therapy must include factors other than the agents used. These costs will also include time and other materials (including nursing/medical resources), and must take into account supporting

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investigations, out-patient and particularly in-patient care, as well as 'hidden' costs such as hospital overheads, including an allowance for capital depreciation.

When assessing the case for new agents, it is important to consider the benefits and costs in both clinical and monetary aspects. Decisions based solely on purchase cost may ignore advantages which in the long-term may outweigh the initial price disadvantage. It is highly desirable to achieve accurate specific patient costing. However, to do so is in itself costly and time consuming. The costs of an average patient in each disease group is easier to identify yet inevitably less precise.

In response to the need for purchasers to know what they are purchasing and at what cost, we have been trying to simplify our data for contracting purposes. A finance-based model has produced a detailed costing for each chemotherapy regimen used at Weston Park Hospital, Sheffield. It will also help the hospital administrators to calculate changes in costs should the numbers of patients treated by a particular regimen vary (i.e. a change in case mix), and therefore the income which the hospital will receive. This costing exercise followed guidance issued by the National Health Service Management Executive known as 'Costing for Contracting' which encourages detailed and more accurate costing.[1] The aim was to produce a cost per regimen for both one day case attendance and one in-patient episode (i.e. one complete visit to the hospital). Day case treatment takes place in a dedicated chemotherapy suite, whilst chemotherapy in-patients are treated together with radiotherapy and other patients on shared care wards.

Weston Park Hospital is a specialist cancer treatment centre, but existing information systems do not cater for costing chemotherapy as a sub-speciality. Therefore, several of the costing stages were completed by allocating costs and applying some form of proxy for the use of chemotherapy resources. However, some data on chemotherapy patients was available from a database managed by pharmacy staff, which detailed all the drugs prescribed to each patient. Total patient activity data was available from the Patient Administration System.

The costing assessment followed several stages:

1. A 'top down' approach classified the whole hospital's costs into fixed, semi-fixed and variable costs. Fixed costs do not vary with patient activity (e.g. a ward must be heated regardless of the number of beds occupied), whereas if patient activity increases significantly, semi-fixed costs increase (as when an extra nurse is required or when more beds are brought into use). Variable costs vary directly with patient activity and this is particularly important for chemotherapy; each extra patient treated incurs the cost of extra cytotoxic drugs and appropriate investigations.
2. The hospital support services (e.g. energy) and overhead (e.g. medical records) costs were allocated to patient treatment services (e.g. dietetics) in proportion to approximate usage. The costs of patient treatment services were then allocated to chemotherapy in proportion to the use made of that service by chemotherapy patients (for example the cost of dietetics was apportioned on the number of consultations for chemotherapy compared to the number for patients in other circumstances).
3. The resulting total costs of chemotherapy, still separated as fixed or semi-fixed and variable costs were divided into in-patient and day case costs, again in proportion to numbers having chemotherapy. From this a cost per in-patient day and day case attendance was derived by dividing the total separated costs by the number in each category. Thus fixed and variable costs rates were calculated per treatment episode. The variable rate *excluded* the cost of cytotoxic drugs, based on the regimens, but included other, variable, costs, for example investigations. The resulting rates were lower than those of the hospital in general, because chemotherapy does not require the use of expensive equipment. The cost of maintenance, capital charges and support services are lower therefore than those incurred by, for instance, radiotherapy.

This 'top down' costing was followed by a 'bottom up' costing for the cytotoxic drugs prescribed and by measurement of the actual average length of stay, from a three month sample of patients. Each regimen was identified from the hospital chemotherapy handbook. It was found that most in-patient advanced breast cancer patients having 'palliative' CMFP (cyclophosphamide, methotrexate, fluorouracil, prednisolone) and non-Hodgkin's lymphoma patients having 'curative' CHOP (cyclophosphamide, hydroxydaurorubicin, Oncovin, prednisolone) stayed only one night and received the same amount of drugs as day case attenders for these regimens. Most testicular cancer patients having 'curative' BEP (bleomycin, etopside, cisplatin) stayed for four nights and received five, daily, chemotherapy doses.

Typical costs for the day cases having oral chemotherapy are £75 per visit and for in-patients having simple parenteral treatment £235 per admission. The cost of more complex treatment ranges from £430 for multi drug regimens to £1,340 for extended toxic treatment per admission. At Weston Park Hospital, the expansion of day case chemotherapy has reduced costs and proved popular with patients.

Such analyses show how the prevailing case mix can present a range of costs to the hospital and how an increase in the number of patients having 'costly' chemotherapy (for example that for cancer of the testis), would increase costs significantly, since purchaser contracts will have been set for whatever case mix was operating at the time of agreement.

Theoretically these fixed, semi-fixed and variable costs can then be added up to give the cost of treating a patient (who may attend on occasions as a day-case, on others as an in-patient) over a period of time, with the potential for deriving an explicit cost per patient value. Realistically, most contracting is still based on 'block' or 'cost and volume'—however the above described costing exercise could go some of the way to providing 'average' costs per patient for each chemotherapy regimen group.

An alternative, clinician based, model has also been derived, breaking down the overall costs of treating particular cancers into individual treatment categories with recognised outcomes. It is then relatively easy to obtain real data on consumption of cytotoxic and supportive drugs by an individual disease group as well as investigations undertaken and to combine these with an agreed estimate of the costs of in-patient stay and out-patient visits. These can be added together to gain an overall assessment of average costs of care. As already indicated the objective response of tumours to chemotherapy (for example in breast cancer), correlates well with 'utility' as judged by patient benefits.[2] There is no reason why this should not apply across a spectrum of cancer treatments. The value of

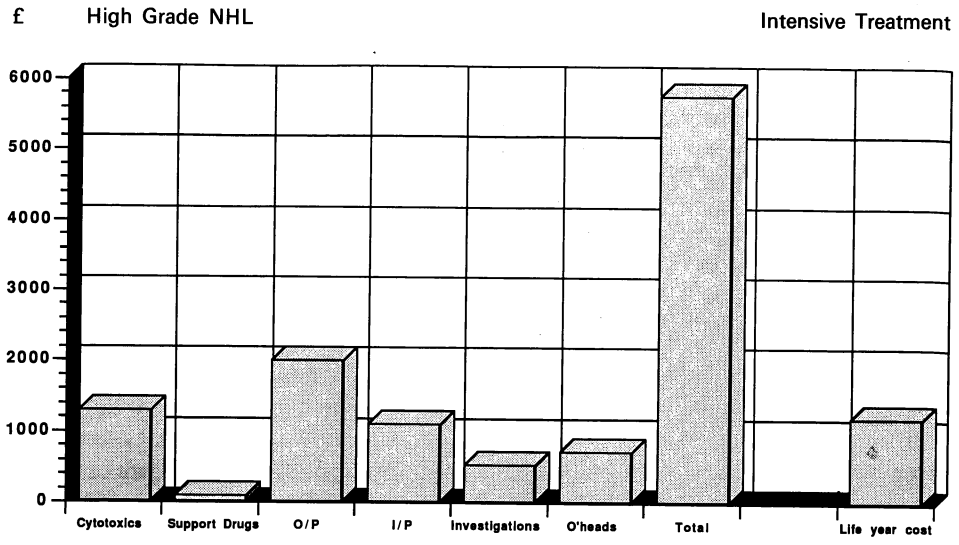

FIGURE 1

Approximate costs of 'curative' combination chemotherapy (CHOP—cyclophosphamide, hydroxydaunorubicin (doxorubicin), Oncovin (vincristine), prednisolone) for high-grade non-Hodgkin's lymphoma.

O/P out-patient attendances
I/P in-patient stays
O'heads—hospital overheads (15%)

the course of chemotherapy to a patient with cancer may be displayed best by calculating the number of months or years of benefit that the treatment will provide. Treatment cost can then be justified either in terms of extended life (survival costs) or improved quality of life (quality costs). Thus having derived the total costs of treatment for a particular disease group, the subsequent duration of remission (survival time free of symptomatic illness) and overall survival can be used as denominators to obtain two different assessments of cost effectiveness for the chosen outcome considered, i.e. quality, by cost per unit disease free time, and quantity, by cost per unit of survival time. This approach can perhaps be illustrated by details of our study costing lymphoma treatment. For example, high grade non-Hodgkin's lymphoma, which is highly chemosensitive, shows long term remission rates of about 40 per cent with aggressive chemotherapy. We first looked at the cost for an average patient, by calculating the mean cost of all those who were treated. Whilst not being an accurate representation of the cost of any individual patient's treatment, this allows easy comparisons to be made between different treatment regimens and different disease types. We calculated that the total cost of treatment of such a patient was in the region of £6,000 with an acknowledged 'average' survival benefit to the group as a whole of at least five years thus giving a patient benefit year cost (i.e. the cost of extending a patient's life for an extra year) of less than £1,200 (Fig 1).

Costing was also assessed by treatment category. Approximately 35 per cent of patients were managed successfully on first-line chemotherapy alone, 25 per cent received further chemotherapy after relapsing, 10 per cent received chemo-

TABLE 1

Cost of treating lymphoma according to therapy required

Therapy type	*Percentage of patients so treated*	*Cost per patient (£)*
Radiotherapy	10	2,000
First-line chemotherapy	35	4,500
Chemotherapy and radiotherapy	10	7,000
Salvage chemotherapy	25	10,000
Nothing	10	500
High dose chemotherapy	10	25,000

therapy and radiotherapy, and a further 10 per cent receiving radiotherapy alone. Some patients, particularly the elderly and those diagnosed at a late stage of the disease, died without receiving active treatment (10 per cent) whilst a significant minority (about 10 per cent) went on to have high dose chemotherapy and other procedures including autologous bone marrow transplantation; clearly this group of patients proved very expensive. The cost of treating high grade non-Hodgkin's lymphoma is shown in Table 1.

It is not therefore difficult to establish the cost utility of treatment used in curing cancer. Health economists in the United States demonstrated that successful treatment of teratoma in one year produced sufficient economic benefit to support all the drug development costs of the preceding 17 years of the National Cancer Institute's programme.[3] Likewise, we have estimated that the average cost of treating a patient with persistent gestational trophoblastic disease is no greater than £6,000; as this treatment leads to a good quality life expectency in excess of 95 per cent for a patient of child bearing age, the cost per life year saved of such patients is less than £500, which makes it one of the most cost efficient of all specialist medical treatments.[4]

Palliative treatments however, are more problematic. Consider for example the treatment of advanced breast cancer. CMFP is an effective drug treatment that is inexpensive; however since this treatment only increases average life expectancy by a couple of months and gains about six months of quality benefit, the treatment is therefore relatively expensive (Fig. 2). It has recently been esitmated by the Guy's Hospital team that the average cost of treating such patients for a survival of 17 months was almost £8,000.[5] However, by employing cost utility measures such as the QALY, the treatment of incurable common cancers may appear relatively favourable when compared with other, seemingly inexpensive non-controversial treatments, (such as beta-blockers for hypertension).[6]

It has long been a popular misconception that chemotherapy is expensive. The majority of the chemotherapy regimens used at Weston Park Hospital cost less than £1,500 for the drugs and many only a fraction of this figure.

As a nation we spend less on cancer chemotherapy than we do on laxatives or analgesics and only a little more than we spend on antibiotic remedies for acne. Future research and development strategies in cancer therapy must incorporate economic evaluation as well as the standard clinical and quality measures. Meanwhile we are getting better at costing our therapies but this can only prove a worthwhile exercise if clinicians as well as accountants are enthusiastically involved.

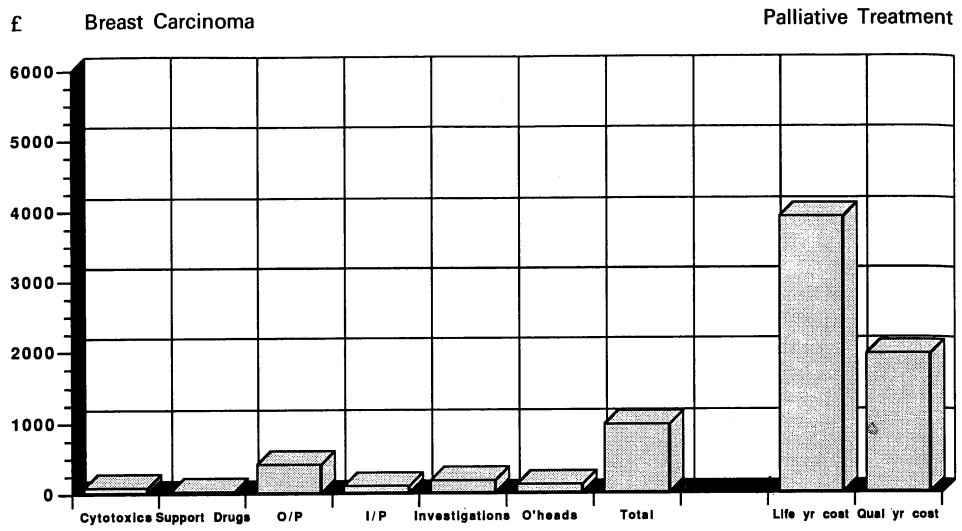

FIGURE 2

Approximate costs of 'palliative' combination chemotherapy (CMFP—cyclophosphamide, methotrexate, fluorouracil, prednisolone) for advanced breast carcinoma.
O/P out-patient attendances
I/P in-patient stays
O'heads—hospital overheads (15%)

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THE COST EFFECTIVENESS OF CANCER THERAPY: THE HEALTH ECONOMIST'S VIEW*

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I am not a physician, although I spend a sizeable part of my academic life collaborating closely with physicians actively engaged in clinical research. Whilst attending to the medical needs of their patients, as their vocation demands, academic clinicians are simultaneously attempting to develop and assess new therapeutic techniques for the benefit of future generations. My role is to evaluate whether or not we, as a society, are likely to be able to afford these new techniques. Having a high regard for the talents of my clinical colleagues, I must confess that my role does occasionally give me cause for concern. After all, the simple act of healing the sick is enough to ask of anyone, without requiring that it be done economically.

My conscience notwithstanding, it is a simple fact that economic considerations have become increasingly important in health care policy in recent years. This importance was crystallised in the 1989 White Paper which pre-figured the 1990 National Health Services and Community Care Act: 'If the NHS is to provide the best service it can for its patients, it must make the best use of the resources available to it. The quest for value for money must be an essential element in its work'[1] (Section 1.15). The reasons for this strong emphasis on economics were not hard to detect. First, as the White Paper pointed out, there existed evidence of widespread variations in average inpatient costs, waiting times, drug costs and general practitioner referral rates throughout the country, evidence suggestive either of the inefficient use of resources or of inadequate provision of treatments in some regions. Second, at a national level, the health service appeared to be locked on an upward spiral, offering more and more courses of treatment each year, absorbing an ever-increasing proportion of national resources, whilst being faced with a growing waiting list for hospital admission. The overt pursuit of economic efficiency, it was felt, offered a solution to both the regional disparity and cost escalation problems.

Not surprisingly, the past few years have seen an increase in demands on the services of health economists. Their advice is sought by health care agencies when planning changes in care management, and it is increasingly difficult for clinical researchers to obtain funding unless economic evaluations are included in their protocols. Of all the techniques available to an economist, *cost-effectiveness analysis* is the one most frequently called upon. In this paper, I examine the cost-effectiveness issues in cancer therapy, which, accounts for around 7 per cent of UK health service spending.[2] We begin, with the obvious question.

WHAT IS COST-EFFECTIVENESS?

Economists consider productive systems as processes, involving the translation of

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