UNIVERSITY
OF YORK

CENTRE FOR HEALTH ECONOMICS
HEALTH ECONOMICS CONSORTIUM

Measuring Cost and Quality of Life in Radiotherapy Treatments

by

Jenny Morris
Maria Goddard
Douglas Coyle and
Michael Drummond

DISCUSSION PAPER 112

MEASURING COST AND QUALITY OF LIFE

IN RADIOTHERAPY TREATMENTS

by

Jenny Morris

Maria Goddard

Douglas Coyle

Michael Drummond

October 1993

The Authors

Jenny Morris is a Research Fellow in the York Health Economics Consortium. Maria Goddard is an Economic Advisor at the NHS Management Executive. Douglas Coyle and Michael Drummond are respectively Research Fellow and Professor of Economics at the Centre for Health Economics.

Acknowledgements

We would like to thank the Medical Research Council and the Department of Health for funding this programme of work. We would also like to thank Professor Ann Barrett and Professor Stanley Dische for their helpful comments on an earlier draft of this paper and Vanessa Windass for secretarial assistance. A shortened version of the paper was published in the European Journal of Cancer 1993; 29A (5): 766–770. We are grateful to the editors for allowing us to publish the full version here.

Further Copies

Further copies of this document are available (at price £4.50 to cover the cost of publication, postage and packing) from:

The Publications Office,

Centre for Health Economics,

University of York,

YORK,

YO1 5DD.

Please make cheques payable to University of York. Details of other papers can be obtained from the same address or telephone York (0904) 433648 or 433666.

ABSTRACT

Arguments are being made more frequently to incorporate economic evaluations and quality of life assessments into clinical trials. Using two randomised, multicentre, trials of radiotherapy for cancer as an example, this paper outlines: (1) the importance of including such assessments; (2) the practical considerations associated with the design of such trials; (3) the methods for collecting resource use and quality of life data; and (4) how such data can be used. Finally, it is emphasised that the anticipated benefits of collecting data relating to resource use and quality of life should outweigh the associated costs to research funding organisations.

1. INTRODUCTION

1.1 Economic Evaluations

In recent years there has been considerable growth in the number of economic evaluations being integrated into clinical trials. Perhaps one of the most important reasons for such development is the recognition that the diffusion of many medical interventions takes place rapidly, prior to the assessment of associated costs and benefits.[1] The incorporation of economic analysis at an early stage can provide useful information to assist in the rational diffusion of new technologies in the health care system[2]. Resources for health care can be used more efficiently, providing maximum patient benefit at minimum cost to the health service only if systematic evidence relating to the costs and benefits of interventions is available. Cancer therapies are often resource intensive and the potential patient population likely to receive the therapy may be large. Thus economic evaluations, integrated into cancer clinical trials may indicate, in advance, the resource consequences of widespread adoption of new interventions.

1.2 Quality of Life Assessments

In general, clinical assessments in cancer trials focus on the physical domain, relying upon data obtained from the WHO performance status scale (which, for example, ranges from 0 = able to carry out all normal activity without restriction to 4 = completely disabled; cannot carry out any self-care, totally confined to bed or chair) or the Karnofsky Performance Status Scale, and from assessments of the side effects of treatment vis-a-vis levels of toxicity. Such

a focus excludes psychological and social functioning and, perhaps more importantly, the patients' perception of the effects of treatment; that is an assessment of the impact of treatment upon quality of life.

Most health-related quality of life instruments are designed to cover four core domains: physical functioning, psychological functioning, social interaction, and disease and treatment related symptoms. Given the toxicity and morbidity associated with the three main modes of treatment for cancer (surgery, radiotherapy and chemotherapy), and the relatively limited survival associated with many cancers, consideration should be given to the inclusion of quality of life assessments into some cancer clinical trials.

Assessments of patients' quality of life can, and should:

(i) clarify the views of patients, clinicians and purchasers when making decisions about treatment, especially when there are major differences between two treatments in the quality of patients' lives without any significant improvement in survival or local tumour control;

(ii) provide information to which patients can relate about the likely consequences of treatment;

(iii) quantify the extent to which levels of psychosocial morbidity vary according to treatment regimes, and thus provide a focus for investigating ways in which such morbidity could be reduced; and

(iv) together with cost information, help determine the relative cost–effectiveness of different methods of treatment.

1.3 When Should Such Assessments be Included in Clinical Trials?

Ideally, data on quality of life should be included in comparative trials of treatment regimes which are likely to have a significant impact upon patients' physical, psychological or social functioning, and/or if there is likely to be a trade–off between quantity and quality of life. These might include trials of treatment versus no treatment; trials which compare treatment modalities or treatments of varying intensity and/or duration; and trials of treatment in which survival is expected to be equivalent, but the quality of life different[3].

The advantages and disadvantages of incorporating economic analysis into clinical trials have been considered by others[4], and criteria for judging the appropriateness of doing so have been proposed[5]. In addition to consideration of the potential overall impact on resources, economic evaluation can also be used where the resource impact on different agencies such as the hospital sector, community sector and the patients and relatives is expected to differ between the alternatives being assessed. This is important as treatments which are cost–effective for one sector, such as the hospital, may not necessarily be cost–effective when considered from a wider viewpoint such as the community health services or society in general.

1.4 When Should Such Assessments NOT be Included in Clinical Trials?

Where it can be predicted that quality of life differences are likely to be small, where the unit cost difference between alternatives is likely to be small or where the therapy will be relevant only for small numbers of patients, then the costs of collecting the data will probably outweigh the benefits. Also, such assessments should not be included when the treatment of the comparison group is so atypical that generalisations to normal practice cannot easily be made, as economic evaluation conducted alongside the trial may be misleading. In such situations it might be better to base the economic evaluation on a synthesis of data from a number of sources.

2. THE CHART TRIAL (CONTINUOUS, HYPERFRACTIONATED, ACCELERATED RADIOTHERAPY)

Conventional radiotherapy given with curative intent, is commonly delivered over a period of up to seven weeks, often consisting of daily treatment with breaks at weekends. However, scientific evidence suggests that tumour cells can proliferate during the course of treatment, causing problems with tumour control which can ultimately be a major reason for treatment failure; a shorter treatment duration has been shown to be beneficial in terms of tumour control. In addition, research has also shown that giving radiotherapy in many small doses, rather than in fewer larger doses, can reduce the incidence of late radiation damage[6].

The CHART regime offers an alternative mode of delivery aimed at achieving both these objectives. The treatment is continuous (given without interruption over weekends),

hyperfractionated (small doses given three times daily), and accelerated (given over a period of 12 consecutive days). The reason for the 12 day duration is to ensure that the course is completed before acute reactions occur which would necessitate a rest period whilst the side-effects subsided.

Pilot studies of the CHART regime for head and neck and bronchus patients have shown good results in terms of tumour response, and limited late normal tissue damage[7,8]. Two multi-centre randomised controlled trials are testing these results by comparing the CHART regime with conventional radiotherapy for patients with head and neck cancer and non-small cell carcinoma of the bronchus. Ten centres in the UK are participating in the trials, as well as two from Europe where economic and quality of life assessments are not being performed.

The trials of CHART and conventional radiotherapy raise important resource and quality of life issues as well as those related to tumour control, survival and morbidity. The CHART treatment involves a radical departure from the normal practice in radiotherapy departments, involving weekend and out of hours work which may have significant resource implications, especially in terms of overtime payments to radiographers and technicians. Secondly, conventional therapy is usually given on an out-patient basis, except where the patient lives too far away to travel daily, or where old age or sickness necessitates an in-patient stay. However, patients in the CHART arm will normally be in-patients for the duration of their treatment (sometimes accommodated in a hostel ward which is clearly less expensive than a fully staffed ward), except in the unusual circumstances where they live near enough to visit the centre three times daily, and/or do not wish to receive treatment as an

inpatient. These differences will have resource implications for the hospital in terms of the provision of beds and will also affect resources for travel. If the hospital provides ambulances or hospital cars, those receiving conventional therapy will make more demands on these facilities than the CHART patients. Similarly, if patients finance their own transport the costs are likely to vary between the two arms of the trial. Hospitalisation immediately post treatment due to side effects of treatment may also vary. Pilot studies have indicated that CHART might reduce the extent of late radiation changes, and a lower incidence of necrosis may also reduce the need for salvage surgery after treatment[7,8]. Finally, variations between arms in the incidence and severity of side effects may influence the use of community health services such as general practitioners and district nurses. The overall difference in resource use will depend upon the direction and magnitude of all the above factors.

The relative effectiveness of the alternative radiotherapy regimes is being assessed in terms of disease free survival, local tumour control and morbidity (indicated by the presence and severity of acute and late side effects). However, this does not encompass the psychological and social effects of treatment on the patient, nor the patients' perception of the severity of treatment side effects such as oesophagitis. For example, in the pilot study of CHART, dysphagia caused by radiation oesophagitis resulted in 24% of a sample of 76 patients treated for non-oat cell carcinoma of the bronchus being restricted to fluids only, and some 16% of patients had not returned to a normal diet by 10 weeks post-treatment[9]. Furthermore, there may be variations in the psychological reactions to the radiotherapy regimes followed. For some, the short regime involving treatment as an inpatient may be preferable to undergoing more protracted therapy necessitating many visits; for others the strain of receiving treatment three times daily may be great.

Salvage surgery may be required for those patients with head and neck cancers where radiotherapy has failed. It is important, therefore, to document the impact that such treatment may have upon the quality of life of these patients about which comparatively little is known[10,11].

3. ISSUES IN COLLECTING ECONOMIC AND QUALITY OF LIFE ASSESSMENTS

3.1 Practical Consideration

Ideally, if economic evaluations and quality of life assessments are to be incorporated into clinical trials, this should be decided at the outset. This would ensure that the design of the trial met the requirements of the different methodologies used. It would also provide the time needed to pilot the instrumentation, and a period during which the data collectors could familiarise themselves with the nature of the data collection forms. This is particularly important in trials where the data collectors do not have research experience, and/or are not familiar with resource and quality of life issues. For various reasons, the clinical trial of CHART had been designed prior to the decision being made to collect resource and quality of life information. As the CHART trial was being undertaken in 10 centres in the UK, the decision had to be made as to whether resource and quality of life data should be collected from patients in all 10 centres, or whether the focus should be upon a subsample of the centres. It was finally decided to collect information from all the participating UK centres as a targeted subsample would not have been representative of the 10 centres for the following reasons:

- the recruitment of patients into both trials at each centre was limited (on average, 50 patients per centre, per annum for both trials);

- the centres varied in terms of whether they stood alone as Oncology Units or whether they were situated within a district general hospital; and

- the size of the radiotherapy departments varied between centres.

The data collectors were either radiographers or nurses, and only a few had research experience. An attempt was made, therefore, to ensure that the same member of staff at each centre was responsible for data collection throughout the study period. Whilst this was difficult to arrange at one centre at the start of the trial, this approach proved satisfactory both to the data collectors and to the study co-ordinators at York.

Visits were made to all centres to ensure that the rationale for collecting such information was clear to the staff, and that they understood how the various forms should be completed. Such visits have continued on an annual basis throughout the study and have resulted in a high level of co-operation between the data collectors and the study co-ordinators at York. It is recommended that this practice is adopted in all trials where resource and quality of life data are collected.

3.2 Measuring and Valuing Resource Use Data

One of the possible drawbacks of adding an economic analysis to clinical trials is the potential to exacerbate the already complicated and time consuming data collection process. In choosing the method of data collection it is, therefore, important to limit the amount of data collected whilst ensuring that the main variations in resource use will be covered. Failure to recognise the burden imposed on the data collectors may result in the collection of large quantities of data only at the expense of quality.

The clinical pilot studies of CHART were used to highlight the areas of potential differences in resource use as indicated in section 2 above. Data collection forms were designed to collect information relating only to activity or the quantity of resources used and cover the following areas: number and timing of treatments; days as inpatient, outpatient and hostel patient both during and after treatment; method of travel and miles of travel; number of GP, District Nurse and other community health and social service visits; surgical and other procedures carried out during and after treatment.

As well as accurately measuring resource use in physical terms, an equally important requirement of an economic evaluation is that the resources measured are credibly valued[12]. Thus, the most time-consuming aspect of the analysis of resource use has been obtaining credible valuations (or prices) for resources used in each centre.

The methods of valuing resource items to arrive at a total cost of treatment per individual patient are illustrated in Table 1 and Figure 1. Table 1 details the method of costing, the data required and the source of data used to value individual items of resource use. Figure 1 details how the total cost per patient will be derived from the cost of the four main elements of resource use:- hospitalisation, radiotherapy, travel and community services.

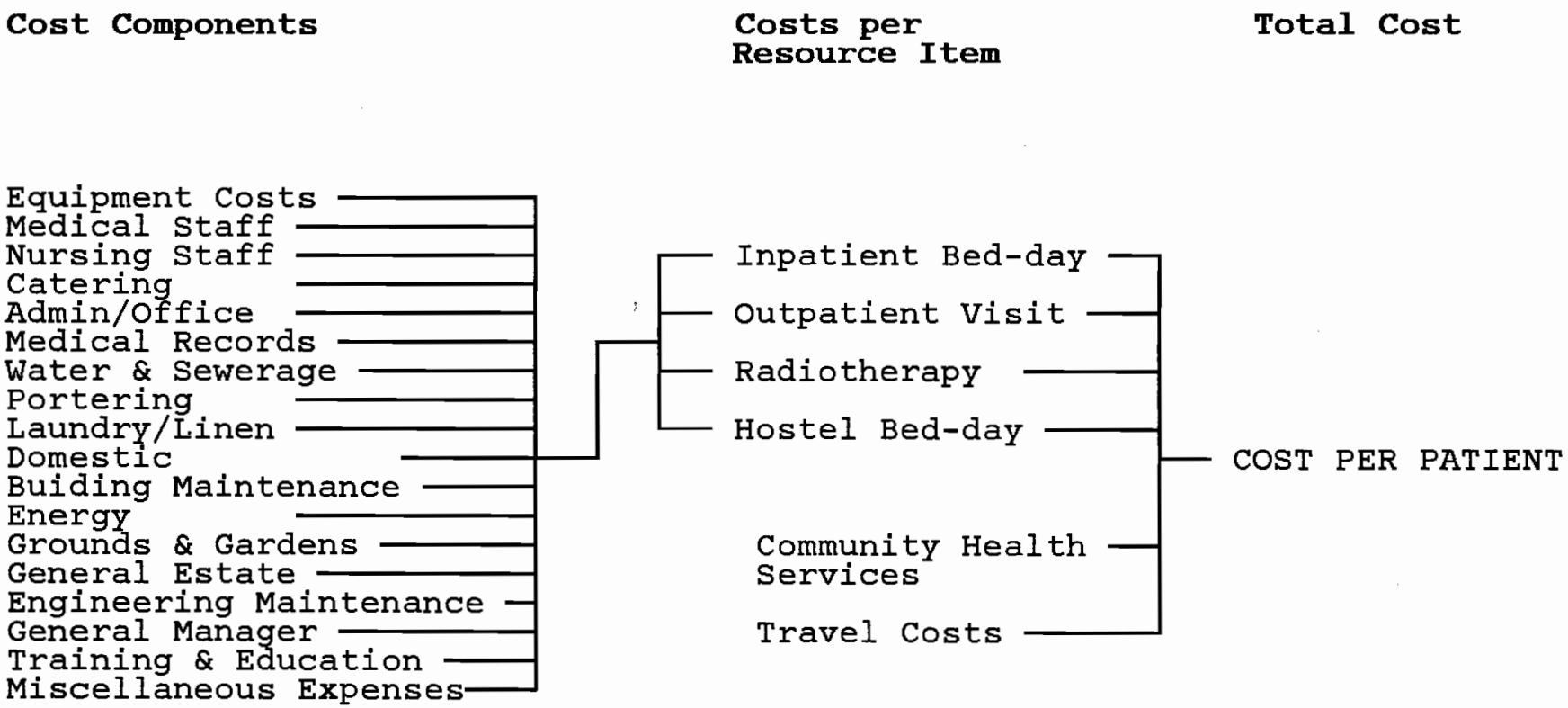
There are two principal methods which can be adopted to value resources:- the 'top-down' approach and the 'bottom-up' approach. The 'top-down' approach is the most simple but less exact method of costing and involves the deconstruction of aggregate data (e.g. a hospital catering budget) to a unit cost (e.g. a catering cost per bed-day). The 'bottom-up' approach is a much more exact method and involves aggregating each individual element of total resource use. For example, a bottom-up approach could be used to cost surgery, whereby the actual staff involved, the time taken for surgery and overheads consumed are estimated.

As the bottom-up approach is the more exact method, it is being used to cost a sample of the most important resource variables - for example, radiotherapy staff costs during treatment. However, as the bottom-up approach is both time consuming and, in many instances, not feasible, the top-down approach is being used in the costing of all other resources used.

Table 1 Methods of Deriving Unit Costs

Resource Item	Method of Costing	Data Required	Source of Data
Radiotherapy			
– Equipment Costs	Top–down	Cost of equipment No. of treatments p.a.	Medical physics department Radiotherapy department
– Radiotherapy Staff	Bottom–up	Staff involved Time per treatment Overtime payment method No. of treatments per overtime session	Observation of treatment/questionnaire Observation of treatment Staff questionnaire Staff questionnaire
– Consultants	Bottom–up	No. of consultants Proportion of time spent on treatment No. of treatments p.a.	Consultant questionnaire Consultant questionnaire Radiotherapy department
– Technicians	Bottom–up	Overtime payment method No. of treatments per overtime session	Staff questionnaire Staff questionnaire
– Overheads	Top–down	Overhead budgets Information on allocation bases No. of treatments p.a.	Unit finance department Various Radiotherapy department
Hospital Inpatient/Outpatient			
– Nursing Staff	Bottom–up	Nursing staff No.of bed–days/outpatient visits p.a.	Senior nursing officer Senior nursing officer
– Consultants	Bottom–up	No. of consultants Proportion of time spent in ward/clinics No. of bed–days/outpatient visits p.a.	Consultant questionnaire Consultant questionnaire Senior nursing officer
– Overheads	Top–down	Overhead budgets Information on allocation bases No. of bed–days/outpatient visits p.a.	Unit finance department Various Senior nursing officer
Community Resources	Top–down	Cost per visit	Various
Travel	Top–down	Cost per mile	Various

Figure 1: Method of Deriving Cost per Patient



The use of community health and social services is being assessed from two sources – the patients and their GPs. GPs are asked to provide information relating to surgery consultations and home visits and also referrals to other services such as district nursing and home helps. The same questions are asked of the patients and part of the analysis will be to investigate variation in reported use of services.

Information on the travel and personal costs to the visitors of the patients is also being gathered from a sample of patients. The need to limit the quantity of data collected prevented this from being incorporated into the trial for **all** patients, but will provide a useful source of additional information.

The data collection points for the resource data coincide with the collection of clinical data, but are limited to the first two years of follow up. Although it is possible that the effects of late toxicity due to radiotherapy may not be evident until four years after the start of treatment, it is unlikely that any significant variations in resource use will occur after two years. However, it would be possible to include estimates of costs associated with any severe late events on a retrospective basis at the end of the trial, as long as the incidence of these is recorded.

Details of travel and hospital resources are recorded weekly during treatment; radiotherapy resources at the end of treatment; community and hospital resources at 3, 6, 9 and 12 months; and hospital resources continued at 3, 6, 9, 12, 18 and 24 months.

3.3 Method for Collecting and Analysing Quality of Life Data

There are two main methods of obtaining quality of life data: (i) from conducting interviews, and (ii) from using questionnaires. Within the context of multicentre clinical trials, it would be extremely costly to undertake interviews. This, together with the fact that quality of life assessments were not the primary focus of the CHART trial, led to the decision to use questionnaires. Self-report, rather than observer rated, questionnaires were used as it has been shown that there are significant differences between a patient's assessment of his or her quality of life, and that made by the doctor or the patient's relatives[13]. Self-report questionnaires designed for use with cancer patients were examined for item coverage, time to complete, ease of scoring, use in other cancer trials, and the clinical recommendations of experts[14]. Consequently, the decision was made to use the Hospital Anxiety and Depression Scale[15] as a measure of psychological state, and the Rotterdam Symptom Checklist[16] to provide an assessment of performance status, physical and psychological complaints.

The HADS generates two independent subscales each consisting of seven items. Unlike most others measures of anxiety and depression, the HADS does not include physical symptoms which might also be symptomatic of physical illness. This is one of the main reasons why this instrument is used frequently as a measure of psychological state in clinical trials. To determine the severity of anxiety and depression, the authors of the scale recommend a cut-off score of 8-10 for 'borderline' cases and scores of 11 plus to indicate 'caseness' (each item is scored from 0 to 3, thus the maximum score for each subscale is 21).

Analysis of the Rotterdam Symptom Checklist is less clear cut. There is no 'standard' version, although the most recent publication[16] recommends using 30 "core" items plus any other items relevant to the particular patient group being studied. The version used in the CHART trial contains the majority of the core items; the exception being that the items 'low back pain' and 'abdominal ache' have been replaced by 'pain'. Additionally, the items 'cough', 'coughing up blood', 'hoarseness' and 'restlessness' have been included to maintain comparability with the version being used in other UK MRC cancer clinical trials. Factor analyses of the Rotterdam Symptom Checklist have revealed two subscales: physical and psychological complaints; the latter contains eight items and has been shown to be relatively robust. The physical complaints subscale is less stable, and it is recommended that a broad physical subscale is used consisting of the items not contained in the psychological complaints subscale[16,17]. Each item is scored from 0 (not at all) to 3 (very much); thus the maximum score from the psychological complaints subscale is 24. Hopwood et al (1991)[18] used a threshold of 11 to differentiate between "high" and "low" scores on the psychological complaints subscale in a group of patients with advanced breast cancer. No data have been reported on the eight items which measure performance status.

Initially, the quality of life assessments were planned to coincide with the collection of the clinical data. However, after further consideration of the time at which quality of life changes were expected to occur and the potential burden on patients, the planned number of assessments was reduced from 16 to 10 to take place during the first 2½ years of the study.

Patients are asked to complete the questionnaires prior to treatment, three, four, six weeks after the start of treatment; three and six months after the start of treatment, and thereafter at six monthly intervals.

When completing the questionnaires, the patients are asked to respond according to how they have felt in the week prior to assessment. Thus in the head and neck trial, maximum reactions from the CHART treatment (estimated to appear at day 14/15 and become maximal over the subsequent 7–14 days) would be identified at the three and four week quality of life assessments, and in the bronchus trial (estimated worst reactions 6/7 days following completion of treatment and the subsequent 10–14 days), at the four and six week assessments.

3.4 Data Handling

A decision had to be made about whether to code and enter the data at York, or use the facilities at the Medical Research Centre Cancer Trials Office in Cambridge where the clinical data were being processed. The advantages of handling the data at York were:

- the availability of data entry facilities;
- no problem with data transfer between sites;
- no delay in data processing; and
- lower cost.

However, these advantages did not outweigh the benefits of processing the data at Cambridge:

- the Cancer Trials Office handle other MRC cancer clinical trial data, including quality of life information;

- processing at Cambridge places equal importance on the resource and quality of life data as on the clinical data;

- the data collectors only have to deal with one office vis-a-vis queries on the forms; and

- storage space was available at Cambridge.

The decision was made, therefore, to process the data using the Cambridge facilities and to build the associated costs into the proposal for the resource and quality of life elements of the trial.

3.5 Quality Assurance for Economic and Quality of Life Data

As mentioned above, visits to each centre took place at least annually to ensure that no problems were encountered with any of the data collection forms. In addition, the data collection staff were in contact by telephone in between visits. A workshop to explain the aims of the economic and quality of life elements of the trial was organised for the data

collectors and provided useful background information about the clinical trial, as well as the economic and quality of life elements.

Meetings were also held regularly with the staff at the Cancer Trials Office to ensure that there were minimal problems with the coding and processing of the data. Such meetings and visits are essential to ensure a high standard of data collection and processing, and should be allowed for in the design of studies which aim to collect resource and quality of life data.

In addition, it was decided to appoint a data monitoring committee for the study, to mirror the one for the clinical trials. This is a novel departure for economic and quality of life assessments and the committee's role, vis-a-vis the clinical trial Steering Group is still being defined.

In clinical trials the major functions of data monitoring committees are: (i) to assess the reliability and completeness of the data being collected and; (ii) to stop the clinical trial if it becomes clear that one treatment is superior to the other by a large amount.

At the present stage of the development of economic evaluation, it is difficult to foresee the Committee fulfilling the second function, as there is no well developed notion of what constitutes a quantitatively important difference in such studies[19].

However, the first function is equally as important for economic and quality of life data as it is for the clinical data. Also, the committee has played an important role in helping the research team to resolve some of the critical methodological issues. Perhaps this is the

most important role for data monitoring committees during a time when methods are still being developed and refined.

3.6 Liaison with Clinical Staff

This is crucial to the success of a project. It should be acknowledged that not all clinicians participating in a trial will be familiar with resource and quality of life information; furthermore such areas of investigation are not likely to be their primary focus of interest. It is essential, therefore, to ensure a two-way flow of information in the form of reports, and active participation on the trial Steering Committee.

Finally, and perhaps most importantly, at the outset of a trial, it should be recognised that the endpoints of the clinical trial and the resource and quality of life trial may differ. This has implications for the timing of data analyses and preparation of material for publication. This reiterates the need for collaboration on the design and timeframe of the trial at an early stage.

3.7 Data Analysis

The economic and quality of life assessments have generated considerable interest among the clinical researchers participating in the trials, who have been keen to discuss how the data will be reported and, more particularly, how they will be integrated with the clinical data.

It has been agreed that no resource or quality of life data will be reported in advance of the clinical report, since the decision whether or not to adopt CHART depends on all three data elements. Some of the major analytical issues are discussed below.

First, the economic and quality of life assessments will be made on an 'intent to treat' basis, as is the common practice in clinical studies. In addition all randomized patients included in this part of the study will be followed for the whole assessment period or to death. This means that procedures will be required to deal with missing data.

Secondly, although the main comparison will be between treatments (in all centres), comparisons will also be made between treatments within centres and between centres within treatments (with anonymity preserved). This is because we believe that the organization of radiotherapy services varies from place to place, and differences in the arrangements for providing CHART may influence resource use. Therefore it will be important to ensure that there are no confounding effects and that useful information on the relative efficiency of different arrangements for providing CHART is not lost. The latter could be very useful in determining how CHART should be provided if it is found to be the superior therapy overall.

Thirdly, the reporting of costs will be based mainly on descriptive statistics (e.g. mean, median, range, confidence intervals) as significance testing may be inappropriate (either because of lack of statistical power or because there is no agreed quantitatively important difference in costs). Furthermore, while total costs will be reported, these will also be sub-divided into: (i) the costs of delivering radiotherapy treatment; (ii) inpatient costs and costs

of procedures; (iii) costs of community health and social services and; (iv) travel costs falling on the hospital sector and on patients. This is because it is important to identify where the major cost differences lie and by whom they are borne.

Fourthly, the vast quantity of quality of life data will be summarized by comparing percentages of patients experiencing anxiety and depression, reporting 'high' levels of psychological and physical complaints, and being unable to undertake everyday activities. In addition mean or median scores will be presented for each subscale of the two questionnaires as appropriate.

Finally, the primary reporting of the results will be in the form of an array of the key cost and quality of life data, to supplement those on survival from the clinical trials[20]. If one treatment does not dominate the other for all three components, trade-offs are implied. Presentation of the array of data will enable particular decision makers (e.g. clinicians, managers, patients) to make their own trade-offs. However, if the trade-offs are complicated the outcome data (on length of survival and quality of life) will be synthesised into a single value. A number of alternative approaches to synthesising the data will be explored, including the use of an existing matrix of health state preference values to calculate years of life gained, adjusted for quality.

The relative importance of the three components (i.e. survival, cost and quality of life) will depend on the outcome of the trials. Clearly if major differences in survival are observed, short-term differences in quality of life during treatment may be relatively unimportant and a larger difference in the costs of therapy could be justified. If the

differences in survival are small then the major decisions concerning the choice of therapy could turn on cost and quality of life.

4. CONCLUSIONS

This discussion paper has outlined some of the practical and methodological issues involved in the planning and organisation of a phase 3 clinical trial in which economic and quality of life components are incorporated. The main issues can be summarised as follows:

(1) It is clear that only some clinical trials will provide a suitable vehicle for economic and quality of life elements. There are both advantages and disadvantages to incorporating such assessments, and these should be weighed up when considering the design of the trial.

(2) It is essential that economists and those involved with quality of life assessments are involved in the detailed design of the clinical trial. This would ensure that full agreement is reached on the nature of the data to be collected, and the type of analyses to be undertaken.

(3) It is vital that all those involved in trials are aware from the outset that the timeframes for each element of the trial may differ. For instance in many cancer trials, the analysis of the clinical data may not be completed until the death of all patients in the trial, and/or after a sufficiently long follow-up period (say five years). However, it is likely that data about resource use and quality of life could be analysed at a much

earlier stage in the trial. This raises the issue of whether such data could be published before the final clinical report is prepared, at an appropriate stage to be decided by the trial Steering Committee. For example, in the CHART trial, an interim clinical analysis will be undertaken at the end of the recruitment period. At this stage a preliminary report on the economic and quality of life aspects will be prepared, with a subsequent input into the final clinical report. Those involved in economic evaluation and quality of life assessments are likely to be funded by several different sources on relatively short-term projects and, therefore, the motivation to publish as early as possible will be strong. Thus it is important that the coordination of publications is addressed at the outset.

(4) The choice of methods for data collection needs to take into account the staff available and the practical issues involved in the collection of a large volume of data. The implications of getting large amounts of low quality data should be considered when designing the trial.

(5) The need to ensure as high a standard as possible vis-a-vis data collection is essential if the trial is to be successful in achieving its objectives. In instances where the data collection staff are unfamiliar with resource and quality of life issues, training will need to be provided either on a group or individual basis. Regular contact with staff maintains the quality of the data collection process throughout the trial, and also ensures a good relationship between the data collectors and study co-ordinators.

(6) Finally, the resource implications of integrating additional elements into the clinical trial must be recognised. The benefits of including such assessments must outweigh the costs. It is not recommended that such elements are included in trials unless adequate resources are made available.

REFERENCES

(1) Berenson R, Holahan J. (1992). Sources of the Growth in Medicare Physician Expenditures. Journal of the American Medical Association,267, 687–691.

(2) Drummond, M.F. and Davies, L. (1991). Economic analysis alongside clinical trials: revisiting the methodological issues. International Journal of Technology Assessment in Health Care, 7, 561–573.

(3) Osoba, D., Aaronson, N. and Till, J. (1991). A practical guide for selecting quality–of–life measures in clinical trials and practice. In: Osoba, D. (Ed.). Effects of Cancer on Quality of Life. CRC Press Inc., Florida.

(4) Feeny, D., Labelle, R. and Torrance, G.W. (1990). Integrating economic evaluations and quality of life assessments in Spiker, B. (ed) Quality of Life Assessments in Clinical Trials, Raven Press, New York.

(5) Drummond, M.F. and Stoddart, G.L. (1984). Economic analysis and clinical trials. Controlled Clinical Trials, 5, 115–128.

(6) Dische, S. and Saunders, M. (1989). Continuous hyperfractionated accelerated radiotherapy (CHART). An interim report upon late morbidity. Radiotherapy and Oncology, 16, 67–74.

(7) Saunders, M., Dische, S., Hong, A., Grosch, J. et al (1989). Continuous hyperfractionated accelerated radiotherapy in locally advanced carcinoma of the head and neck region. Int. J. Radiation Oncology Biol. Phys., 17, 1–6.

(8) Van der Kogel, A. (1989). Continuous hyperfractionated accelerated radiotherapy (CHART). An editorial comment. Radiotherapy and Oncology, 16, 75–77.

(9) Saunders, M., Dische, S., Grosch, E., Fermont, D., Ashford, R., Maher, E., and Makepeace, A. (1991). Experience with CHART. Int. J. Radiation Oncology Biol. Phys. 21, 871–878.

(10) Morris, J. (1990). The Quality of Life of Head and Neck Cancer Patients: A Review of the Literature. Discussion Paper 72, Centre for Health Economics, University of York.

(11) Morris, J. (1991). Life after treatment – quality of life. Head and Neck, 13, 554–556.

(12) Drummond, M.F., Stoddart, G.L. and Torrance, G.W. (1987). Methods for the economic evaluation of health care programmes. Oxford, Oxford University Press.

(13) Slevin, M., Plant, H., Lynch, D., Drinkwater, J., Gregory, W. (1988). Who should measure quality of life, the doctor or the patient? British Journal of Cancer, 57, 109–112.

(14) Maguire, P. and Selby, P. (1989). Assessing Quality of Life in Cancer Patients. British Journal of Cancer, 60, 437–440.

(15) Zigmond, A. and Snaith, R. (1983). The Hospital Anxiety and Depression Scale. Acta Psychiatrica Scandinavia, 67, 361–370.

(16) de Haes, H., Van Knippenberg, F. and Neijt, J. (1990). Measuring the psychological and physical distress of cancer patients: Structure and application of the Rotterdam Symptom Checklist. British Journal of Cancer, 62, 1034–1038.

(17) Watson, M., Law, M., Maguire, G.P., Robertson, B., Greer, S., Bliss, J. and Ibbotson, I. (1992). Further development of a quality of life measure for cancer patients : the Rotterdam Symptom Checklist (revised). Psycho–Oncology, 1, 35–44.

(18) Hopwood, P., Howell, A. and Maguire, P. (1991). Screening for psychiatric morbidity in patients with advanced breast cancer: Validation of two self–report questionnaires. British Journal of Cancer, 64, 353–356.

(19) Drummond, M.F., O'Brien, B. (1993). Clinical importance, statistical significance and the assessment of economic and quality of life outcome. Health Economics; 2(3): (In press).

(20) Cox, D.R., Fitzpatrick, R., Fletcher, A.E., Gore, S.M., Spiegelhalter, D.J. and Jones, D.R. (1992). Quality of life assessment: can we keep it simple? Journal of the Royal Statistical Society (Series A), 155, 353–392.

APPENDIX: PARTICIPATING CENTRES AND PRINCIPAL CO-OPERATING CLINICAL ONCOLOGISTS

The Beatson Oncology Centre, Glasgow
Professor A. Barrett
Dr. Canney
Dr. MacBeth
Dr. Robertson
Dr. R.P. Symonds
Dr. H. Yosef

Mount Vernon Centre, Northwood
Professor S. Dische
Dr. M.I. Saunders

St. Mary's Hospital, Portsmouth
Dr. V. Svoboda

The Royal Infirmary, Bristol
Dr. H. Newman

Mersey Regional Centre, Clatterbridge,
Dr. B. Cottier

The General Hospital, Nottingham
Dr. D. Morgan

The Cookridge Hospital, Leeds
Dr. I. Rothwell

The Royal Marsden Hospital, London
Dr. J. Henk

Weston Park Hospital, Sheffield
Dr. M. Whipp

The Velindre Hospital, Cardiff
Dr. C. Gaffney