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Clinician Surrogates and Equipoise: an Analogy to Lawyers who Represent Themselves?

DESPITE THE apparent increase in our knowledge of the biology of cancer, the process of decision-making in cancer management has become much more complex, and, in many ways, a much less certain procedure. With the increasing sophistication of the design of clinical trials and the proliferation of the available treatment options, the choices facing clinicians and their patients have become increasingly complicated.

Recently, a greater level of attention has been directed to the study of the decision-making process among patients and clinicians, including the introduction of the clinician surrogate model [1]. This model involves the assessment of responses by disinterested medical experts to detailed questionnaires on controversial issues of medical management. It has been postulated that such experts may provide more useful information than is available from patient surveys regarding choice of available treatment and the ethics of clinical trials [2, 3]. With the burgeoning number of reports of such studies [2, 4–6], it appears that increasing resources are likely to be expended in the application of the model, and it is time to assess whether this work is likely to advance our knowledge.

The decision to treat a particular neoplasm in a certain way is predicated on a broad range of factors: those that pertain to the community, the tumour, the patient and the doctor. Community issues include the available resources and funding, attitudes to cancer, and the pattern and extent of competing health problems. Tumour-related factors include the biology of the disease *per se*, the range of available treatments and the likely outcomes of such treatment. Indices relevant to the treatment of an individual patient include age, sex, physical state, mental and cognitive function, education, the extent and nature of prior treatment, compliance in the treatment regimen, the patient's understanding of the disease and its prognosis, and issues pertaining to "informed" and "cognisant" consent (one should perhaps draw a distinction between the provision of information and the real comprehension and application of such information by the patient).

Based upon remarkably scant objective data, an increasingly stringent medicolegal approach has evolved with respect to the factors governing the choice of treatment, and in particular to the quality of informed consent. However, many of us have come to believe that informed consent may really be a medical oxymoron, and that most patients simply do not have the background or training to give fully informed and cognisant consent regarding all of the relevant issues [5, 7]. The patient's understanding of these issues will be predicated on the nature and format of information provided and on the methods of information transfer [8–11]. We have previously shown in a randomised trial of consent procedures that the combination of verbal discussion and a written information sheet produces a greater level of comprehension and retained information than verbal communication alone [12], an observation confirmed by others [11]. Of importance, this increased level of understanding was achieved at the expense of a significantly greater level of patient anxiety [12].

Therefore, against this background of the patient's anxiety,

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partial incompetence to assimilate all of the pertinent facts, and the high potential for personal loss or gain, it is not surprising that the clinician's preference or perceived preference often will dominate the decision-making process (notwithstanding the declaration of the patient's informed consent) [5, 10]. This is important as patients and clinicians may have very different concepts regarding the selection and likely outcomes of different treatments [5, 11].

Where a particular approach has been proven to be optimal (for example, the use of platinum-based chemotherapy for metastatic germ cell tumours [13, 14]), the choice of therapy is relatively uncomplicated in most cases. However, a more vexed issue arises when genuine uncertainty and controversy exist in the medical community regarding the optimal management of a malignancy—the situation of "equipoise" [15].

Amidst the proliferation of psychological and pyschosocial studies of patients with cancer, and of the issues that influence their choice of treatment and the outcomes of these choices, there has also been increasing interest in the factors that influence the oncologist in the clinical decision-making process, and in particular in the resolution of specific management problems where equipoise exists. A related issue is the impact of these factors on the clinician's decision to enter (or not to enter) patients on the available clinical trials [16] and the level of the clinician's compliance in effecting the requirements of that trial [17].

Many factors contribute to this process, including the attitudes and training of the clinician, the information and biases gleaned from programmes of continuing education, the resources available, and the pattern of practice (academic versus private practice versus public/hospital clinic). Also of importance is the specificity and sensitivity of the published literature as an index of the available knowledge about the outcome of cancer trials. Simes [18], advocating an international registry of clinical trials, has shown that there is often an editorial bias against the publication of negative results that may colour our opinions regarding optimal management. Similarly, Hillcoat [19] has discussed the phenomenon of data recycling, in which the impact of a set of data from a single study is expanded by its repeated citation in reviews that encompass data from other reviews (which, in turn, have also cited or tabulated the initial set of data).

Clinicians are heavily influenced by the way in which data are presented to them [8]. In a survey assessing attitudes to different treatments for lung cancer, outcomes were modified when data were presented in terms of probability of death versus probability of survival [8], confirming a similar outcome from a psychological study of lay people [9], as noted above. It thus appears that the framing of decisions, a function of the way in which the options are presented, heavily influences outcomes of such studies, irrespective of the nature of the survey population [9]. In the current climate of increasing impatience for success against cancer, it is common for presentations of data at clinical or scientific meetings to be biased, often with excessively optimistic or unrealistic interpretations of data, or by the exclusion from presentation or discussion of negative trial outcomes. The real impact on clinical practice of these biases from the literature and from programmes of continuing education has not really been assessed.

Workers at the Ontario Cancer Institute have been active in addressing some of these issues, and in particular in the application of the clinician surrogate model. For example, Moore *et al.* [4] have studied patterns of practice among urological oncologists in some detail. Historically, as has occurred for most cancers, the management of urological malignancy has been governed by approaches based on "rational empiricism"—innovative approaches have been developed from hypothetical, preclinical or clinical models, assessed objectively and, if apparently successful, have been introduced into clinical practice. In the latter part of this century, randomised clinical trials have been effected for most urological cancers, as reviewed elsewhere [20]. However, accrual to these studies has often been lower than projected, presumably hampered by a range of biases of the referring clinicians [21]. Using the clinician surrogate model, Moore and colleagues [2, 4] have attempted to discover how clinicians themselves would wish to be treated, to determine whether their opinions are influenced by those of their peers, and to discern what impact this could have on the entry of patients into clinical trials.

In an initial study [4], a questionnaire describing six clinical problems in genitourinary malignancy was sent to urologists in Britain, Canada and the USA and to radiation oncologists and medical oncologists in the USA who were known to practise genitourinary oncology. The clinician surrogates were asked to define how they would wish to be treated for each of the clinical problems. Added questionnaires (describing the same clinical problems, but set in the context of patient management rather than the surrogate setting) were sent to 81 Canadian urologists. In general, subjects selected their own modality of treatment as part of management whenever feasible. A wide range of views were expressed regarding the selection of optimal treatment. Major geographical differences were defined between the practice of genitourinary oncology in Britain, Canada and the USA, with greater conservatism being manifested in Britain (especially with regards to chemotherapy and radical surgery). Another feature of interest was an apparent reluctance of the clinicians to participate in clinical trials as surrogate patients, in contrast to their willingness to enter patients into these studies. In a subsequent study [2], questionnaires were again sent to the clinician surrogates who received the initial survey. On this occasion, three of the clinical problems were again presented, and details of the responses from the previous survey were included. The surrogates were asked to select treatment for themselves, and whether they would agree to be randomised on the relevant clinical trials. This survey showed a similar pattern of response to the previous one, and was interpreted to show that the clinicians were aware of the extent of controversy on these management issues but retained their own biases, and that they were reluctant to enter themselves as the subjects of randomised clinical trials.

While these data are interesting, it is difficult to know how to interpret them, as discussed by the authors [2]. Most of the radiation and medical oncologists were selected as experts in genitourinary cancer on the basis of having published a paper on genitourinary malignancy within the preceding 3 years. Whether they can be regarded as truly expert in genitourinary cancer on this basis is a moot point. Although the group spent an average of 39% of their time in the practice of genitourinary oncology, 28% spent 20% or less of their time in this discipline, and the way in which subjects defined the percentage of their time in this work was not described. Furthermore, there was a great potential for selection bias as only about 60% of the surveyed population responded to the questionnaires. It is unlikely that Dr Moore and colleagues, who have been instrumental in improving the precision of our assessment of clinical trials, would accept data from a phase II or III trial in which

40% of the potential denominator was unavailable for analysis. In addition, there is no clear evidence that the results of the survey (e.g. the apparent reluctance of the surrogates to participate in clinical trials) represents a real phenomenon, as opposed to an artefact of the model. There is also no evidence that the reported reluctance of the surrogates to enter themselves into clinical trials has any valid implications for the ethical or design issues pertaining to these clinical trials.

Parenthetically, it is interesting that a group of clinicians, who apparently were not prepared to enter randomised trials and who were not influenced by the decisions of their peers (nor presumably by the clinical literature), empirically supported this model as useful in the design and evaluation of clinical trials, as well as in the consideration of relevant ethical issues [2].

The validation of such studies remains a critical and difficult issue, and it will not be easy to conceive a trial design that will allow these observations to be confirmed objectively. Nevertheless, before we accept the information gleaned from this approach, we must resolve several important questions: (1) What evidence is there that the answers from clinician surrogates have real implications for patient management and the ethics of design of clinical trials? (2) Do such surrogate studies really reflect patterns of practice and the opinions of the clinical population, especially in the context that a significant proportion of the survey group does not participate in the assessment? (3) What constitutes the appropriate selection for participants in such studies? (4) What methodological flaws contribute to biases in the study design? (5) Is there any evidence that we would treat ourselves or our families more appropriately or effectively than our patients? The aphorism that "the lawyer who represents himself has a fool for a client" could equally apply in the practice of medicine.

Some tools of clinical pyschology are highly imprecise by their very nature and because of the endpoints being evaluated. There is a great risk that clinician surrogate studies actually reflect the application of quantifiable and reproducible statistical methods to ill-defined or non-quantifiable psychological endpoints. We must be careful not to accept a lesser level of stringency of evaluation in these studies than would be appropriate for more conventional scientific trials. The investigators who are developing these approaches must now provide more information regarding their validity as models of the clinical decision making process. The clinical community has the responsibility to await such data before adopting their conclusions.

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