Introduction

Quality of cancer care is difficult to measure and is even difficult to define. As stated by Talcott (2003): “Few buzzwords can irritate me more than ‘quality of care’, especially when someone else’s standards are applied to my clinical work…” [1]. However, a reasonable starting point is to consider the following three points when questioning whether good quality of care is being offered to patients with cancer: (i) is the right treatment being given; (ii) is it being done well; and (iii) is the patient being treated in addition to the disease? We will use this framework in the present review, and will try to address each of these questions.

Is the right treatment being given?

Evidence-based medicine

The choice of therapy for a particular patient depends optimally on evidence that the treatment selected leads to better outcome and/or lower risk of side-effects compared with alternative management strategies. Multiple authors have developed classifications of evidence that can be obtained from clinical studies; although there is minor disagreement about the details of such a classification, a widely accepted grading of evidence is shown in Table 1. The highest level of evidence is derived from large, high-quality randomised controlled trials (RCTs) or meta-analysis. The lowest level of evidence derives from the opinion of an expert panel. As stated by Feinstein: “The opinion of experts has been a traditional source of all the errors throughout medical history” [2].

One type of study that is missing from Table 1 is that which is based on outcomes research, for example studies that use data from (usually large) populations that may compare outcomes following different management policies. Outcomes research has the limitation that the populations that are compared are not selected at random; therefore socioeconomic, genetic or environmental factors, and/or use or non-use of screening to detect disease may influence outcome in addition to the treatment given. However, even large, well designed randomised trials have limitations, as discussed below. These include the selection of a limited sample of patients, who may not be typical of others with the same disease, and the application of treatments under ideal conditions, which may not be applicable to a wider population. Large, well conducted outcome studies that take into account underlying differences in populations can provide a relatively high level of evidence regarding different strategies of management, and are complementary to RCTs.

Judging the quality of evidence

The relevance of a clinical trial to a given treatment decision depends not only on the type of trial (as classified in Table 1), but also on its quality. Judgement of quality can be separated into internal validity (how the trial was designed, executed and analysed) and external validity (external factors, such as its concordance with the results of related studies).
Internal validity

Some of the factors that are important in determining the internal validity of a clinical trial are listed in Table 2. First and foremost, the research question that is being asked in a pragmatic phase III study should be relevant to clinical decision-making. It is equally important that the outcome measures reflect benefit to patients and that the authors define explicitly the primary end point(s).

In a recent review of 510 abstracts describing RCTs presented at an American Society of Clinical Oncologists (ASCO) meeting, only 22% defined their primary end point explicitly [3]; the percentage may be higher in full reports, but definition of the primary end point would seem essential, even in the briefest abstracts. Failure to define the primary end point may allow post hoc analysis to be applied to whichever measure appears to favour a new treatment, and hence to artificial results [4, 5].

Common end points in cancer trials are tumour response, survival and (increasingly) a measure of quality of life (QOL). While tumour response may be a valid measure for evaluating the biological effect of a treatment, patients may have a significant reduction in tumour size without clinical benefit. Tumour response is also dependent on patient selection (patients with higher performance status are more likely to respond) and on the criteria used to measure response. Response to a given drug or drug combination may vary markedly from one patient to another, even if they have the same tumour type and stage of disease.

Survival is an appropriate measure of outcome, but there are relatively few treatments that have improved survival in adult patients with metastatic disease from common solid tumours [6]. In view of this, a single trial claiming improved survival must be viewed sceptically as it is quite likely to be a false-positive result, especially if the $P$ value is ‘borderline’. The factors that contribute to false-positive trials include publication bias in favour of positive trials (see below), the use of multiple significance tests in the analysis of the data (at least one may be positive by chance), and a low probability that a new treatment will be superior. It was shown by Parmar that if the true prevalence of clinical trials that compare strategies where there is a meaningful difference in survival is $\sim$10% (an arbitrary but not unreasonable estimate), and one designs an RCT with $\alpha=0.05$ and with 80% power to detect a positive result, then about one trial in every three reported as positive will actually be a false-positive [7]. For these reasons, any improvement in duration of survival needs to be verified in a second trial.

External validity

The reported results of a trial are more likely to be valid if they are consistent with clinical experience and with the results of related clinical trials. As discussed above, if true-positive trials are rare then false-positive trials will be common. If possible, positive results should be confirmed in a second trial before changes to standards of care are made.

Patients in clinical trials are often highly selected, with good performance status and near normal blood parameters, and so are frequently not representative of the general cancer patient population. Therefore, benefits seen in patients recruited to clinical trials are not necessarily generalisable to a less selected sample of patients with the same tumour type and stage.

Publication bias can have a major influence on the evidence that is available from published studies. Even large RCTs are subject to publication bias. In a further study of the abstracts describing the 510 RCTs presented at an ASCO meeting, 26% remained unpublished 5 years later, with a significantly higher proportion of negative trials remaining unpublished (81% versus 68%; $P<0.001$) (see Figure 1) [15]. An example of the bias that this creates is that five large RCTs evaluating the use of interferon-α (IFN-α) in patients with renal cell cancer have been presented at ASCO in recent years. Two of these RCTs ($n=160$ and 350) showed a survival benefit for patients with...
metastatic disease and were published 1–3 years post-ASCO [16, 17]. However, three RCTs (n = 247, 283 and 270) evaluating the use of adjuvant IFN-α either showed no difference in survival or suggested a trend towards harm [18–20]. Two of these were published 2 and 7 years after presentation [18, 19], respectively, and the third study remains unpublished after 12 years [20].

Evidence-based guidelines

To assist oncologists in management decisions, several agencies have developed guidelines for the treatment of the more common cancers, based on a hierarchy of evidence from clinical trials [e.g. ASCO, National Comprehensive Cancer Network (NCCN), Cancer Care Ontario (CCO) and the French Standards, Options and Recommendations (SOR)]. These clinical guidelines are based on a review of the available evidence from clinical studies, and some of these groups also attempt to review the quality of the trials that provide the evidence. Recommendations for treatment are then based on the highest levels of evidence that are available.

To be successful guidelines need to be based on evidence, disseminated to all affected health professionals for critique, and implementation needs to include direct feedback on individual performance or general feedback on system performance. Finally, there needs to be accountability for performance [21, 22].

Several organizations have conducted audits to determine whether guidelines promote adherence to treatment recommendations and greater use of evidence-based care. For example, a study by Ray-Coquard et al. [23] reported on the impact of clinical practice guidelines in a regional cancer network in France. Medical records of patients with localized breast and colon cancer were examined from 1994 and 1996 (before and after implementation of guidelines in the cancer network) in four network hospitals, and in three hospitals that were in a region that did not have clinical practice guidelines. Medical decisions were analysed to assess compliance with clinical practice guidelines and to determine use of evidence from clinical trials. After introduction of the guidelines, hospitals in the network had a substantially higher number of decisions made according to guidelines and/or based on medical evidence, whereas the control hospitals did not (Table 3) [23].

Guidelines can increase evidence-based management and there is limited evidence to suggest that compliance with treatment guidelines can decrease economic costs and improve patient outcomes [21]. In Ontario, evidence-based guidelines are used to make decisions about whether or not to fund expensive new treatments.

Is cancer treatment being done well?

Even if management of patients complies with guidelines and with evidence-based medicine, the outcome remains dependent on how well treatment is delivered. Multiple studies (reviewed in Hillner et al. [24]) have shown that this depends on how frequently a practitioner or centre treats a particular cancer site [24–30]. For example, Hodgson et al. showed a negative correlation between both the need for colostomy and overall survival in relation to number of rectal cancer patients treated in Californian hospitals [28] (Table 4). While the relationship between outcome and volume is best defined for surgical procedures, it also applies to non-surgical treatment of cancer. Thus, the treatment of Hodgkin’s disease, testicular cancer, ovarian and breast cancer has been found to lead to better outcomes when delivered in cancer centres than when delivered in the community [24, 29, 31–34]. For example, in four studies of

---

**Table 3. Compliance rates for medical decision**

<table>
<thead>
<tr>
<th></th>
<th>Breast cancer exp tl (%)</th>
<th>Breast cancer control (%)</th>
<th>Colon cancer exp tl (%)</th>
<th>Colon cancer control (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline compliant (before practice guidelines)</td>
<td>12</td>
<td>7</td>
<td>14</td>
<td>39</td>
</tr>
<tr>
<td>Guideline compliant (after practice guidelines)</td>
<td>36</td>
<td>6</td>
<td>46</td>
<td>32</td>
</tr>
<tr>
<td>Supported by evidence (before practice guidelines)</td>
<td>64</td>
<td>45</td>
<td>74</td>
<td>71</td>
</tr>
<tr>
<td>Supported by evidence (after practice guidelines)</td>
<td>79</td>
<td>48</td>
<td>83</td>
<td>76</td>
</tr>
</tbody>
</table>

Adapted from Ray-Coquard et al., 2002 [23]. exp tl, experimental.

**Table 4. Relation of hospital volume to colostomy rates and survival for patients with rectal cancer**

<table>
<thead>
<tr>
<th>Quartile for hospital volume (n = 7257)</th>
<th>Colostomy rate (%)</th>
<th>30-day mortality (%)</th>
<th>2-year survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowest</td>
<td>37</td>
<td>4.8</td>
<td>77</td>
</tr>
<tr>
<td>Intermediate-low</td>
<td>35</td>
<td>2.9</td>
<td>81</td>
</tr>
<tr>
<td>Intermediate-high</td>
<td>32</td>
<td>1.6</td>
<td>83</td>
</tr>
<tr>
<td>Highest</td>
<td>29</td>
<td>1.6</td>
<td>84</td>
</tr>
</tbody>
</table>

Adapted from Hodgson et al., 2003 [28].
have demonstrated how improvement in pain control can be disseminated to as many patients as possible. Some centres of clinical trials. The evidence from clinical trials must also be important goals of cancer treatment, and important end points reverse) and communicate effectively with the patient.

aggressive treatment for small gains in survival, others the patient’s preferences regarding treatment (some will prefer and improves QOL [42]. He/she must take into account the relieves the side-effects of both the cancer and the treatment, only attempts to treat the tumour and to increase survival, but Treatment of the whole patient requires that the oncologist not to the disease?

Another way to improve quality of care may be to recruit patients to clinical trials. Several studies have suggested that patients treated in clinical trials have a better outcome than patients who receive similar treatment but who are not in a clinical trial [38–40]. Studies have shown that patients with non-small-cell lung cancer, breast cancer and myeloma treated in trials had better survival than patients treated off study, even though they received similar treatments. The reasons for this benefit from inclusion in a clinical trial are unknown and a recent review suggests that it might be due to the failure to correct for confounding factors [41]: even after matching patients in a trial with others, there may be a bias for patients with better prognostic factors (e.g. performance status) to be recruited to trials (i.e. selection bias). Other possible benefits for patients on trials include better management of their disease, as they tend to have more frequent evaluation with potentially earlier detection of problems and better management of side-effects [38–40]. They are also more likely to maintain the scheduled dose and frequency of treatment. It is of great concern that well intentioned individuals in administrative or political positions are making it more difficult to recruit patients into trials, based on very rare incidents where clinical research has led to harm. These efforts may lead to greater harm, both immediate and long-term, if fewer patients are recruited to well designed clinical trials. The outcome of patients who are denied access to a clinical trial may be poorer, and future patients may be adversely affected because of failure to generate new evidence that is important for optimising cancer treatment.

Is the patient being treated in addition to the disease?

Treatment of the whole patient requires that the oncologist not only attempts to treat the tumour and to increase survival, but relieves the side-effects of both the cancer and the treatment, and improves QOL [42]. He/she must take into account the patient’s preferences regarding treatment (some will prefer aggressive treatment for small gains in survival, others the reverse) and communicate effectively with the patient.

Improving QOL and symptom control (e.g. pain, nausea) are important goals of cancer treatment, and important end points of clinical trials. The evidence from clinical trials must also be disseminated to as many patients as possible. Some centres have demonstrated how improvement in pain control can be achieved using institution-based programmes. For example, an education programme, the Zero Acceptance of Pain (ZAP) project, was implemented by Fortner et al. to educate clinical staff at the University of Memphis [43]. Experienced oncology nurses acted as ZAP coordinators in each clinic. Components included pocket pain management cards, self-report forms and patient pain journals. After participating in the ZAP programme, patients reported a decrease in their ratings for the worst pain in the last 24 h from 4.1 to 3.3 (P < 0.05) and in the level to which pain interfered with activities (from 3.7 to 2.9; P < 0.05), although the overall pain severity rating was not statistically significantly different [43], de Wit et al. also evaluated education of cancer patients with chronic pain. All patients received regular pain treatment and were then randomised to a pain education programme or no further intervention. Pain was significantly improved in the intervention group at 2 and 4 weeks, although the difference was not significant at 8 weeks [44] (see Figure 2).

Although management of pain may be improving, fatigue remains a largely unrecognised and poorly managed problem that effects QOL. A multicentre trial reported that cancer-related fatigue was “inevitable, unimportant and untreatable”. Incidence was reported to be 58%, as compared with 22% for pain and 18% for nausea and vomiting; however, most physicians never even asked their patients about fatigue [45]. There is much room for improved care of cancer patients through relief of fatigue; this is particularly important since many of the more aggressive cancer treatments, some of which may improve survival, also cause an increase in fatigue. There is emerging evidence that fatigue may be improved by exercise programmes [46–49] and by drugs such as methylphenidate [50].

Effective communication is an essential component of good cancer care. Several studies indicate that many patients leave consultations unclear about their diagnosis and prognosis, the management plan and the intent of treatment [51]. Not only do
patients report dissatisfaction with the level of communication with their health professionals, but oncologists acknowledge that their own training is insufficient in this area, and this adds to their own stress, lack of job satisfaction and burnout [51, 52]. Studies have shown that communication skills can be taught and are not something you ‘either have or you don’t’ [53, 54]. An RCT was performed that compared oncologists before and after training in communication. Doctors who had undertaken this training showed a higher use of open-ended questions, greater empathy, gave more appropriate responses to patient’s cues and used more psychosocial probing than they had before the course, or compared with a control group of doctors [53, 55]; all of these improvements were significant.

Conclusion

In this brief review we have emphasised that the achievement of high quality cancer care will require attention to multiple components of patient management. Elements of high-quality care include: use of evidence-based treatment, where evidence is gained from high-quality clinical trials; doing what we do often and hence do well; and recognising the need to treat the whole patient and not just the disease. Finally, patient treatment must be done well and with compassion.

References

51. Fallowfield L, Jenkins V. Effective communication skills are the key to good cancer care. Eur J Cancer 1999; 35: 1592–1597.