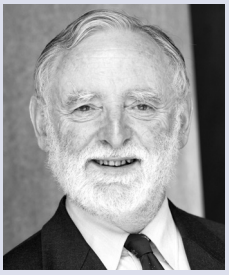
CLINICAL TRIALS: BENEFITS AND CHALLENGES



A Coates AM

CEO, The Cancer Council Australia

International Breast Cancer Study Group

Australian New Zealand Breast Cancer Trials Group

Sydney, NSW

Clinical trials provide the evidence basis for rational decision-making in medical therapeutics. They provide benefits to participating patients, future patients, the community, third party payers (such as governments and private health insurers) and to participating clinical researchers.

Benefits

Patients participating in clinical trials receive treatment under rigorously defined, ethically scrutinised protocols. There is some evidence that such patients survive longer than similar patients treated with similar regimens outside trials[1]. While these assessments may be subject to bias, they may also reflect a better standard of care because of the clear guidelines and rigour of documentation required by the trial process. Interestingly, Joffe and Weeks recently noted and objected to the view of American oncologists (and especially paediatric oncologists) that benefit to the patient was a legitimate purpose of clinical trials[2]. Early access to new and more effective treatments is another potential benefit highly sought after by patients. Although many patients in phase I trials may receive ineffective low doses, Horng et al concluded that the consent forms used did not offer inappropriate inducements to trial participation[3]. Satisfaction of helping future patients is another, purely altruistic motive for trial participation.

Evidence from earlier trials is available to assist patients and their doctors in reaching treatment decisions. Such evidence includes benefits of treatment, side effects and impact of treatment on quality of life as judged by similar patients who have had similar treatment.

From the viewpoint of government and doctors, trials provide evidence to give security that the advice offered (and paid for) is appropriate, allowing preferential use of more efficacious, acceptable and economical treatment while (hopefully) discarding treatments shown to be ineffective.

Clinical discipline in the use of defined regimens, dose modifications and documentation may as noted above lead to better outcomes.

In short, trials tell us what works, such as screening for breast and bowel cancers, breast conserving surgery, adjuvant systemic therapy in breast cancer and bowel cancer, radiotherapy in breast, rectal cancers and chemo-radiotherapy for cancers of rectum, lung, head and neck, cervix and oesophagus. Trials also tell us what doesn't work. High dose methotrexate was once popular in many tumour types but comparative trials severely limited its applicability. An early attempt to justify government support for the costs of clinical trials as a good investment was based on this work. Laetrile was an "alternative" medication popular in the 1980s, and more recently we have seen the influence of clinical trials in reducing the use of high dose chemotherapy with stem cell support for breast cancer.

Challenges

Geography provides problems in multi-centre trials, especially if multiple time zones are involved, though modern communication is reducing this aspect of the problem.

Consumers reasonably want access to information about available trials, but apart from the United States, few countries provide reliable access to such information. Patient recruitment is highly variable, but generally low. There are many examples to support the claim that this is not due to patients being unwilling to participate, but rather to barriers at the doctor level[4].

Funding is a perennial problem – especially since research grants seldom cover the infrastructure costs of maintaining cooperative trials groups. Absence of such funding tends to deliver control of the agenda to those with money to pay for trials, largely the pharmaceutical industry, whose trials may be aimed more at commercial return from early registration of new agents rather than the broader approach to clinically important questions.

Consumer participation is important in trial design, conduct and interpretation. The Australian New Zealand Breast Cancer Trials Group for example has had consumer representation on its Scientific Advisory Committee for many years, and is also advised by a Consumer Advisory Panel.

So who benefits? Participating patients receive accurate treatment, and possibly better outcomes. Future patients have evidence to assist their decisions. Third party payers (government, private health insurers) gain knowledge about which treatments are effective, acceptable and cost-effective, while participating clinical researchers have the benefits of defined regimens, and benefit from early contact with new developments from other ongoing trials group research. Clinical trials are a good buy for patients, doctors and society.

References

1 DA Braunholtz, SJ Edwards, RJ Lilford. "Are randomized clinical trials good for us (in the short term)? Evidence for a 'trial effect'". *J Clin Epidemiol*, 54 (2001): 217-24.

2 S Joffe, JC Weeks. "Views of American oncologists about the purposes of clinical trials." *JNCI Cancer Spectrum*, 94 (2002): 1847-53.

3 S Horng, EJ Emanuel, B Wilfond, et al. "Descriptions of benefits and risks in consent forms for phase 1 oncology trials." *N Engl J Med*, 347 (2002): 2134-40.

4 PM Ellis, PN Butow, RJ Simes, et al. "Barriers to participation in randomized clinical trials for early breast cancer among Australian cancer specialists." *Aust NZ J Surg*, 69 (1999): 486-91.