WE'VE GOT A GROOVY THING GOIN' BABY... OR HAVE WE? INVOLVING WOMEN IN CLINICAL TRIALS

S Lockwood

Breast Cancer Action Group
Fairfield, VIC

Abstract

This paper explores how the number of women in clinical trials might be increased and the extent to which researchers, clinicians and women are jointly working to improve outcomes for women. It explores the issues from the perspective of women with breast cancer, but the arguments presented here are applicable to other diseases. It also considers the loss of trust in the research process that results from inappropriate promotion of results. The Women's Health Initiative trial is used as an example of how fear and loss of trust can ensue. Some mechanisms to improve trust are suggested, such as community information abstracts to complement the scientific information abstracts which are an integral part of every scientific paper.

Introduction

Women who have been diagnosed with breast cancer want the best possible treatment for themselves and other women with the disease. Clinical trials are an important mechanism for improving treatment outcomes, so women are very interested in the results of trials. Clinicians are also interested in improving outcomes through research. They also want better outcomes for their patients, but many of them are also interested in the intellectual challenges which research provides. Both women and clinicians have an interest in increasing the number of women in clinical trials.

Clinical trials have been very successful to date

In 2002, 84% of women diagnosed with breast cancer survived five years, whereas just 10 years ago this figure was 72%[1]. This is a great improvement, most of which is due to better detection and treatment. Much of the research providing these improvements has come from clinical trials.

But 30% of women diagnosed with breast cancer still die of it, and some of those who are cured suffer ongoing side-effects of their treatment, eg lymphoedema. It is therefore imperative that more work be done to improve outcomes. Both the effectiveness and safety of treatments must improve.

The only way to get improved outcomes faster is to increase the number of women participating in clinical trials. Greater numbers of women means faster results over a wider range of potential treatment options.

Encouraging more people to participate in clinical trials

The literature relating to encouraging patients to participate in clinical trials focuses on the fact that patients:

- don't understand the research process;
- find it difficult to deal with the concept of randomisation;
- feel that they are being used as guinea pigs; and, as a result
- may turn down the opportunity to participate in trials[2].

But there is another side to this litany of problems. Work done by the National Breast Cancer Centre surveying women who had been recently diagnosed and treated for breast cancer showed that most women were not invited to participate in a clinical trial. Only 6% of women were asked to participate, of these, half said yes. That is, 50% of women with whom a trial was discussed agreed to participate. So, while only 3% of women participated in trials, this was 50% of the women offered the chance to participate.

These figures indicate that the main problem is not with the women refusing to participate in a trial, but that so few women were asked in the first place. This experience is not unusual, and fits with data from other surveys[3,4].

But, where are the real impediments? Why aren't women being asked to be part of a clinical trial?

There are three options:

- more relevant trials;
- increased numbers of participants; and
- increased involvement of clinicians.

Perhaps there are too few trials. It is clear that there are many trials, but they all relate to areas of interest to research scientists and clinicians. Many of these are concerned with chemotherapy and different modes of delivering therapy. Although these are important questions, are they as important to women with breast cancer as they are to researchers? There are very few trials in radiotherapy and surgery and even fewer in the areas of psychosocial issues. The study of Australia's research into breast cancer which was carried out by the Kathleen Cunningham Foundation and the National Breast Cancer Centre entitled "Breast cancer research in Australia: current research and future priorities" demonstrated clearly that the views of women about what makes research projects worthwhile are very different from those of researchers or clinicians[5]. This situation will not have changed from 1996 when the study was done. So, there need to be more relevant trials. But relevant to whom - women, researchers, clinicians or all three parties?

Too few clinicians are involved in recruiting women to clinical trials. The actual numbers of clinicians involved with clinical trials in breast cancer is unknown in Australia. But it appears to be only a small proportion of the total number of specialists who are treating women with breast cancer. Overseas studies have shown that those specialists who are treating large numbers of women with breast cancer, or are working in larger specialty teams, are more likely to enrol women in trials[6]. It is hard to get the resources needed to support active involvement in clinical trials, most importantly access to data managers and study nurses. This may be the greatest barrier to more clinicians becoming involved. Perhaps the move to multidisciplinary teams and greater specialisation will lead to more clinicians offering women entry to clinical trials.

Perhaps recruitment will continue to depend on those few clinicians who have a direct interest in trials research. Some clinicians who are very supportive of clinical trials are able to recruit half their patients into trials[7]. Until more clinicians choose to become involved, it will be difficult to recruit increased numbers of women to participate in trials.

Despite the fact that so few women actually participate in clinical trials, larger numbers of Australian women are recruited than in many other countries. The ANZ Breast Cancer Trials Group provides a focus for Australian involvement in both

national and international trials. Australia has a significant involvement in international trials through its collaborations with the International Breast Cancer Study Group, the Breast International Group, and other international groups.

But perhaps there also needs to be some direct requests from the women themselves to participate in trials. This would encourage clinicians to become involved and encourage women to look for those clinicians who are interested in further research. The proposed national register of clinical trials and protocols will assist women to know what trials are available through different clinicians. This will be an effective tool to enable women to make their own choices about which trials might be of interest to them and approaching their clinicians to see if participation might be possible. This tool will only be effective if it includes consumer summaries. Similarly the New South Wales Directory of Breast Cancer Treatment and Services shows those clinicians who participate in trials. Again this gives women the option to choose clinicians who have an interest in improving practices through clinical trials.

It appears that many of these factors may be related. Trials that appear to be relevant to clinicians, researchers and participants are capable of attracting more recruits than those that are of interest to fewer participants.

Sentinel node biopsy trial in Australia: The SNAC trial

In 1998, women in Australia identified lymphoedema as one of the key problems facing women who have been treated for breast cancer. As a result of this concern, the National Breast Cancer Centre held a summit in Adelaide in February 2000. This included discussion of the need for more research in this area. At the same time, the Royal College of Surgeons in Australia was developing a proposal to conduct a clinical trial to ascertain the value of sentinel node biopsy in comparison with standard axillary clearance. It was possible to combine the two needs. One of the advantages of sentinel node biopsy is its potential to reduce the need for axillary clearance, and hopefully the incidence of lymphoedema. This trial has been enormously successful. It has encouraged surgeons to become actively involved in a clinical trial and has given them an opportunity to learn and perfect new techniques. Women find the trial of interest because it has the potential to reduce lymphoedema. It is also of interest to breast nurses, occupational therapists and physiotherapists.

To date, 478 women and 35 surgeons are participating in 26 centres[8]. This trial has recruited very quickly because it is of interest to all parties. It is a great example of how a trial can be successful if all those interested in the outcome get together, work up the proposal, arrange funding and help sell the concept.

So what can we learn?

From these experiences, we know some of the factors that encourage recruitment into clinical trials. They are:

- design win-win trials;
- use end points that are meaningful to participants;
- involve consumers in all aspects of trial design and management;
- educate and resource clinicians; and
- empower people – they are participants, not just subjects.

The other side of the coin – loss of trust

Asking individual women to participate in any sort of research is like asking them to take a leap into the unknown. Any new trial assumes, on the basis of the best evidence available, that the alternative treatment being offered is at least as good as current best practice, and offers a real prospect of improvement. But until the results of the trial are available, this is an assumption. It may be that the results of the trial do not show this, and it may be that the participants in the trial are actually at risk from some factor(s) that are not yet known. For this reason, consumer participation in research and clinical trials depends on trust. Women must be prepared to trust the researchers and clinicians to be offering them a new treatment that is, on balance, likely to work. But this trust is developed before the woman is ever diagnosed with breast cancer. It develops through years of experience, largely through stories in the media.

In 2002, a selection of research stories given prominence by the media were:

- breast self-examination doesn't work;
- breast screening doesn't work; and
- hormone replacement therapy (HRT) causes breast cancer.

These stories undermine the confidence the public has in the research community. These stories suggest that it doesn't matter what you do to try and find your breast cancer, that examining your breast is no good, and that if you go to the screening service, they won't find it either. So all the messages about finding breast cancer early – being the best way of avoiding dying from this disease – have been eroded by the work of research scientists. Similarly, the outrageous stories that were associated with the "increased risk of breast cancer because of the use of HRT" just infuriated women. HRT has been a "life-saver", physically and psychologially, for many women and now they find that their risk of breast cancer is supposedly so high that they will have to suffer in other areas of their life to avoid developing breast cancer. The views about the value of research were totally overwhelmed by the fear that was engendered in the community by the way in which the results were provided. This story came directly from the researchers and not from the media[9]. With stories such as these, trust is being eroded.

The research industry, like all industries, helps create its own image in the community. Some responsibility for the stories that appear in the media has to lie with the media. And the media, as a general rule, are not exactly careful to ensure that the complete picture is presented to the public. So it is easy to blame the media, but, if the HRT results are representative of the way in which research results are publicised, some responsibility must rest with the research community.

Nurturing trust

We all must be very careful to nurture the trust between the community at large and the research community. There are many ways of doing this. Here are some suggestions.

Community information abstracts

Each research paper has a scientific information abstract that describes, in a form of code, the results of the research in such a way that other researchers can understand the results. In the current world, many of the research results are of interest to the general public. It seems appropriate for community information abstracts to be provided for some key articles. These community information abstracts would be of use to many different groups as well as consumers of health services. Journalists, general practitioners, policy makers, and others would benefit from a simplified version of the abstract written in normal, ie not coded, language. Some journals, such as the *Annals of Internal Medicine,* are already undertaking such a task with excellent results. The abstracts are clear, standardised and give the results in language that most people in the community can understand.

Awards for excellence in communicating the results of trials

In many areas of science there are awards for excellence in the public communication of science. Every year in Australia, the Eureka Awards acknowledge the role played by scientists and the media in presenting science to the general community. Similar awards could be put in place for excellence in communicating the results of medical research and in particular, clinical trials.

The outcomes of clinical trials are of interest to many members of the community. They are not just the domain of clinicians and researchers. Consumers have a role in the development of trials which can attract many more participants. Consumers can encourage the recruitment of more women to trials and they can play an important role in the delivery of the results of research. Consumers can also play a role in improving the trust between researchers, clinicians and the community. Consumer participation in all aspects of clinical trials will provide better outcomes for everyone.

Conclusion

An effective partnership between researchers, clinicians and consumers will ensure that clinical trials are more relevant, more available, and that we get results sooner and achieve our mutual objective of improving outcomes for women.

Let's get a groovy thing goin' together… so that others may groove for longer.

This paper, and the talk it originated from, is dedicated to Fairlie Howard, a breast cancer consumer with a great interest in clinical trials, who died of her disease in October 2002. She will be remembered always.

References

1 Australian Institute of Health and Welfare. *Australia's Health 2002*. AIHW, Canberra, June 2002.

2 PM Ellis, PN Butow, JR Simes, MH Tattersall, SM Dunn. "Barriers to participation in randomized clinical trials for early breast cancer among Australian cancer specialists." *Aust N Z J Surg*, 69, 7 (1999): 486-91.

3 MS Simon, DR Brown, W Du, P LoRusson, CM Kellogg. "Accrual to breast cancer clinical trials at a university-affiliated hospital in metropolitan Detroit." *Am J Clin Oncol*, 221 (1999): 42-6.

4 PN Lara Jr, R Higdon, N Lim, K Kwan, et al. "Prospective evaluation of cancer clinical trial accrual patterns: identifying potential barriers to enrollment." *J Clin Oncol*, 15, 19, 6 (2001): 1728-33.

5 A Marlin, S Redman, C Clarke, RI Clark, F Boyle. *Breast cancer research in Australia: current research and future priorities*. National Breast Cancer Centre, Kathleen Cunningham Foundation, Sydney, 1996.

6 CJ Twelves, CS Thomson, J Young, A Gould. "Entry into clinical trials in breast cancer: the impotance of specialist team. Scottish Breast Cancer Focus Group and Scottish Cancer Therapy network." *Eur J Cancer*, 34, 7 (1998): 1004-7.

7 Personal communication. J Chirgwin, September 2002

8 Personal communication. A McPhee, member of the SNAC Executive Committee, February 2003.

9 National Heart, Lung and Blood Institute. *NHLBI Stops Trial of Estrogen Plus Progestin Due to Increased Breast Cancer Risk, Lack of Overall Benefit*, Press Release, 9 July 2002.