# Recruiting Patients to Cancer Trials

## Paper Prepared for the Prostate Cancer Clinical Studies Group

### 1. The Problem

1.1. There is general agreement that the recruitment of patients to clinical trials is a problem. So common is the phenomenon that it is enshrined in Lasagna's Law, which states that clinical trials systematically overstate the number of patients available for a trial. Recruitment to cancer trials is no exception. A recent UK study (Campbell et al 2007) suggests that something like one third of trials fail to recruit to their original target within the specified time. Where the problem is not addressed, however promising the new treatment looks, or how sound the trial design, the trial will fail, without enough patients to power it up.

1.2. Despite the clear importance of the issue, there appear to be remarkably few studies of patient recruitment to trials in the UK. My speculation is that the issue does not of itself excite the interest or play to the skills of those clinicians and/or scientists who dominate the world of clinical trials. There are very few studies exploring the issue which meet the standards of a Cochran systematic review. The two studies which do (Mapstone et al, 2009 and McDaid et al, 2006) conclude that it is not possible to predict the effect of specific recruitment interventions with any degree of certainty. However if one looks more generally at non RCT studies then these paint a reasonably agreed and coherent picture of the barriers to recruitment of patients to clinical cancer trials.

### 2. This Review

In undertaking this review I began by searching the literature on recruitment of patients to clinical trials in general using data bases like PubMed, Medline, Embase to establish the boundaries of the problem. I then focussed on cancer trials and particularly prostate cancer clinical trials. There is very little literature on recruitment to prostate cancer clinical trials in the UK, and much of the US literature focuses on the specific problems of recruiting Afro Caribbean and Hispanic men. A notable UK exception is the paper by Donovan et al 2002, published in the BMJ (The ProtecT study). Having extracted what appear to be the main issues from these papers, I then discussed them with various members of the NCRI Consumer Liaison Group.

### 3 Clinical Design of Trials

3.1. The primary driving force in designing a clinical trial is that the design will produce scientifically valid, reliable and significant results. However, the design of the trial is not wholly unrelated to patient recruitment. If the design positively inhibits the recruitment of sufficient patients then it is a 'bad' design because the trial will not produce significant results.

3.2 The evidence from studies of cancer trials shows that:

- Whilst patient recruitment protocols are developed for good scientific reasons, they often effectively disenfranchise large numbers of patients
- Clinical trials which are designed with all arms active are more attractive to patients than those which are designed with a placebo arm
- Open trials are viewed more favourably by patients than blinded trials.

## 4. Patient Recruitment Strategies

4.1. Just as there is no magic bullet in the treatment of prostate cancer, because of factors such as: the variation in the nature of the disease; the characteristics of the patient population; the context of their treatment - the same is true of patient recruitment. Although one can identify a range of strategies which report success with specific groups of patients in specific contexts, there does not appear to be a simple mechanical relationship between a specific intervention and patient recruitment that will invariably improve recruitment.

4.2 So, a useful way of looking at recruitment strategies is to see them in terms of factors which generally appeal to patients and therefore encourage them to enrol, and factors which tend to worry patients and therefore discourage enrolment. This approach of enhancing the appeal factors and reducing those factors which deter patients could form the basis of a general strategy for successful recruitment.

4.3 It has been identified that patients are <u>more likely</u> to be recruited to a trial if they believe:

- that such engagement is the only way to receive the new treatment
- that in a trial they will be given the attention of acknowledged experts in their condition
- that through the trial they will learn more about their condition
- that their condition will be more closely monitored in a trial.

4.4 Just as there are factors which encourage patients to enter clinical trials. So there are factors which deter many patients. The majority of factors which inhibit patients relate to their <u>understanding</u> of what it means to be in a clinical cancer trial. This understanding is hampered by vocabulary frequently used when introducing the idea of participation in a trial. What can be done to improve patient understanding? The first and vital step would appear to be to recognise it as a potential problem.

4.5 A number of qualitative studies show clearly how some patients interpret terms and concepts in quite different ways from the interpretations assumed by the medical fraternity. Classic examples include: “watchful waiting” - translated by some patients as “wilful neglect” or “no treatment” (Donovan at al, 2002). In this particular case the literature suggests that “active monitoring” might be a better term. The literature identifies several specific terms which cause patient worry:

- *Randomisation* is a technical concept and studies show that lots of patients find it difficult to understand. There is also the view held by some patients that it means that the consultant does not know what the best treatment is for a particular patient.
- Though the term *equipoise* is probably not used with patients, the underlying idea may be communicated and can suggest to patients that the clinician does not know what the best treatment is.
- Some studies indicate that the terms *experimental* (an "experimental treatment") is not helpful as patients may form the view that they are being treated like guinea pigs.

4.6 The qualitative studies of patient recruitment also seem to show the following:

- Patient leaflets need to be developed with patient/consumer representatives and they need to be piloted. Patient understanding invariably improves when this is done.
- Patients need time to discuss what it means to be in a clinical trial, and some evidence suggests that facilitated group discussion with other patients can be effective. Those recruiters with specific training in soft communication skills seem to do better than the untrained (Jenkins and Fallowfield, 2005).
- There does not appear to be any difference to recruitment success whether the main recruiter is a clinician or a nurse.
- Classic recruitment strategies like personalised letters, reminders by letter, phone or email appear to have minor positive effects.

## 5. The Role of clinicians and health service staff

5.1 Clinicians and health staff are invariably involved, either directly or indirectly in the recruitment of patients to cancer trials. The UK evidence does not suggest that either party (doctors or nurses) is superior as far as achieving adequate recruitment is concerned, although both appear to be more effective if they have been trained in relevant communication skills ( Jenkins and Fallowfield, 2005). There is some evidence to suggest that trials with a dedicated trial manager recruit best, all other things being equal.

5.2 Clinicians tend to be more supportive of trials when they regard the trials as addressing an important question at a timely point. They also tend to be more favourably disposed towards a trial when it is firmly grounded in existing clinical practice and where the results could easily be incorporated into future practice.

5.3 Various studies have illuminated some of the factors which inhibit the disposition and the abilities of clinicians as trial recruiters:

- Perceived difficulties over informed consent and problems in explaining the concept of randomisation. More generally an unknowing or unwitting use of terminology that patients do not understand.

- The evidence suggests that some clinicians do not like having open discussions with patients that embrace the notion that there is uncertainty over the 'best' course of treatment (the equipoise problem): some even suggest that this jeopardises the doctor-patient relationship. This is particularly the case for those clinicians who have a lack of awareness of on-going clinical trials and who have a strong preference for a particular treatment arm.
- More prosaically, clinicians tend to be very busy people and recruiting patients to a trial inevitably makes even more demands on their time. Some clinicians report that they see few rewards in such activity.

## 6. Contextual patient variables

6.1. Many patients are ignorant about the availability of relevant trials because nobody has brought them to their attention and they have not read about them.

6.2 Studies like that of Slavin et al.(1955) strongly indicate that the majority cancer patients who know about trials are either enthusiastic or uncertain about the prospects of joining a trial. Only a small minority say that they are unwilling to participate. This is an important finding because it indicates that there is a significant pool of patients who could, in principle, be recruited by the appropriate actions of clinicians and health staff.

6.3 The relationship between a patient and their clinician/nurse is important. Relationships which are marked by a caring attitude, personal warmth and trust seem to be beneficial to the recruitment act.

6.4 Discussion with Consumer Liaison Group members suggests that patient convenience is a more important factor than most formal studies have suggested. Key factors here are:

- the proximity of trial centres to patients and ease of transport and parking;
- the frequency of visits required, particularly in relation to work and other commitments.
- the quality of the environment in which patients have to wait and be treated – this is also thought to be a factor in whether patients are willing to persist with their involvement .

## 7. Conclusions

7.1 The recruitment of patients to clinical cancer trials is a significant issue on which there is surprisingly little research and certainly little which looks specifically at prostate cancer trials in the UK.

7.2 Despite the paucity of research and the inconclusive results of systematic reviews, the evidence from the available studies is strongly suggestive of the barriers to patient recruitment and of the factors which are likely to encourage patients to enrol.

7.3 Finally, a major issue in recruitment is patient understanding of clinical cancer trials. Where this can be improved – by engaging 'consumers' in the drafting of publicity

material, by the focused training of recruitment staff, and by giving time and careful consideration to the recruitment process, then the prospects for suitable recruitment are likely to be improved.

**Professor Ian Jamieson, September 2012**

**References**


Campbell,M.K., Snowdon,C., Francis,D., Elbourne,D., McDonald,A.M., Knight,R., Entwistle,V., Garcia,J., Roberts,I., and Grant.A. (The STEPS Group)(2007), 'Recruitment to Randomised Trials: Strategies for Trial involvement and participation study. The **STEPS** study' *Health Technology Assessment*, 11, 48.

Donovan,J., Mills, N., Smith,M., Brindle,L., Jacoby,A., Peters,T., Frankel,S., Neal,D., and Hamdy, F (2002) 'Improving the design of randomised trials by embedding them in qualitative research: ProtecT (prostate testing for cancer and treatment) study' *BMJ*. 2002 October 5; 325(7367): 766–770.

Cox,K (2002), 'Informed consent and decision-making: patients' experiences of the process of recruitment to phases I and II anti-cancer drug trials'. *Patient Education and Counseling* Vol 6: 2, pp.31-8 January

Fallowfield,L., Ratcliffe,D., and Souhami,R. (1997), 'Clinicians' attitudes to clinical trials of cancer therapy', *European Journal of Cancer*. Nov.33 (13), pp.2221-9

Jenkins,V and Fallowfield,L. (2000), 'Reasons for accepting or declining to participate in randomized clinical trials for cancer therapy'. *British Journal of Cancer*. 2000 June; 82(11): 1783–1788.

Jenkins,V. And Fallowfield,L. (2005), 'Discussing randomised clinical trials of cancer therapy: evaluation of a Cancer Research UK training programme', *British Medical Journal*, 330: 400-3.

McDaid,C., Hodges,Z., Fayter,D., Stirk,L. And Eastwood,A. (2006), 'Increasing participation of cancer patients in randomised controlled trials: a systematic review.' *Trials*, 7:16

Mapstone,J., Elbourne,D., and Roberts,I.G. (2009), 'Strategies to improve recruitment to research studies (Review). *The Cochrane Library*, 2009, Issue 4

Slavin,M.,Mossman,J., Bowling,A., Leonard,R., Steward,W., Harper,P., McIllmurray,M., and Thatcher,N. (1955), 'Volunteers or victims: patients' views of randomised cancer clinical trials', *British Journal of Cancer*, 71,1270-1274.

Watson,J., and Torgeson,D.J. (2000), 'Increasing recruitment to randomised trials: a review of randomised controlled trials'. *BMC Medical Research Methodology* 2006, **6**:34 doi:10.1186/1471-2288-6-34