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Comments and Critique

Confirmed Dissent and Informed Consent

IN A perfect world two conditions would be necessary before it was acceptable to randomise a patient into a clinical trial. Firstly, perfect equipoise on behalf of the doctor concerning the treatments on trial when faced with a individual patient in the consulting room and secondly, perfect equipoise by the patient, having been fully informed about the choices on offer and completely understanding the potential harm and benefits of the randomised options. Looked upon in that way randomised controlled trials are either impossible or unethical and much of the criticism trialists have faced over the past 10 years or so from armchair ethicists or the lay public reinforce that view. Yet without randomised controlled trials it is impossible to accumulate reliable evidence of harm and benefit in the treatment of chronic diseases with a variable natural history [1]. This has led in the past, and for that matter, to a large extent today, to treatments being determined according to the whim or prejudice of the individual clinician, producing a variability which in itself is unacceptable and in some parts of the world has led to a cottage industry of second opinions. In these circumstances, it would be quite inappropriate to apportion all wisdom to one or other side and the appropriate response is to recognise that uncertainty is inevitable and the more veracious the authority, the more likely he is to vocalise this uncertainty. However, for most of us, it is intellectually and humanistically unacceptable to continue to live with such uncertainty without taking practical steps to resolve the dilemma. The mere fact that a national or trans-national trial of treatment is launched is an indication of a "consensus of uncertainty" amongst the leaders of the profession. The problems are bad enough with diseases that have been recognised since the dawn of civilisation but become even more acute with the identification of new conditions with an uncertain natural history as for example AIDS or screen-detected duct carcinoma *in situ* (DCIS). The latter has to be recognised as a new condition which has only been identified as a result of the implementation of the National Programme for Breast Cancer Screening using modern mammographic techniques. Two papers in this current issue of the *European Journal of Cancer* address the problems from the patients' and profession's point of view, resulting from the launch of the United Kingdom Co-ordinating Committee for Cancer Research (UKCCCR) trial of the management of screen-detected DCIS.

Mrs Thornton, a patient diagnosed with this condition and invited to take part in the trial, is performing a valuable service by highlighting the agonising dilemma a woman faces when the uncertainties of the natural history and treatment for this condition are described at the time she is recovering from the shock of a "positive" mammographic screen.

A number of separate issues are raised by Mrs Thornton; the scientific integrity of the trial itself, the principles of screening and the other more important generic issue of informed consent and the process of recruitment into a multi-centre trial.

We wish to concentrate most of this commentary on the latter issues but we must declare our interest by stating categorically that we support this trial and in fact, are actively involved.

The criticisms of the scientific integrity of the trial are dealt with by Joslin and Fentiman in this issue (pp. 430–431) and the need for continued randomisation of radiotherapy has been commented on by Recht [2].

We believe that the public has a right, and for that matter, a duty to involve themselves in these discussions as well as the right to challenge professional dogma, but we cannot accept the fact that this right extends to challenging the "consensus of uncertainty" of our professional leaders. Any patient can of course develop a prejudice against any form of therapy and has the clearly defined privilege of refusing offers of that treatment. No doubt an informed and intelligent lay person with selective citations from the literature, could also come up with a degree of scientific justification to underwrite their prejudice, but it becomes a bizarre twist of medical history when therapeutic dogma should be imposed on the profession who are laudably expressing the educated doubts of the group.

"The limited data available on DCIS, particularly with regard to the potential promise (and disadvantage) of breast conserving therapy does not warrant dogmatism concerning the merits of the different treatment options, particularly in relation to patient sub-groups. Hence it is important to increase the awareness of both physicians and patients as to the value of the data that will be gathered from these trials and to alert them as to how little information there is to support at present, any one treatment option as best". This quotation, from a consensus meeting organised by the EORTC in Leuven in September 1991 surely says it all [3].

Mrs Thornton then goes on to criticise the trial as being in some way a breach of the principles of screening formulated in 1968 by the World Health Organisation, which includes that the natural history of the disease should be well understood before screening is undertaken and implies that the launching of the trial is in some way a failure to observe the principles contained within the Forrest report. Surely, this is not a criticism of the trial, but a criticism of a programme of screening that identifies a condition of uncertain natural history. It could even be argued that the more scientific approach would be a natural history study whereby screen-detected DCIS was observed without any therapeutic intervention. There is indeed a good deal of justification for such a study as it has been estimated that perhaps only between 1 in 5 or 1 in 3 of screen-detected DCIS will in a woman's natural lifetime progress to the invasive disease [4]. Yet you can imagine the public outcry if such a study was suggested; akin to the furore that followed the natural history

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study of carcinoma *in situ* of the cervix carried out in New Zealand a decade or two ago [5].

Twenty years ago medical paternalism and the naive trust of the lay public conspired either to disguise uncertainty or to encourage randomised controlled trials where consent to randomisation was not explicit in the protocol [6]. Since then there has been a dramatic swing in the attitudes of both the profession and the public which need to be encouraged and yet is in danger of swinging so far to the other extreme as to paralyse progress.

Mrs Thornton's intervention is a valiant attempt by an individual patient, mercifully free of ideology, trying to grapple with the problem and share with the doctors the burden of uncertainty. One of the two options are available in such circumstances; the patient can take the doctor's best advice, which in her case was to join the DCIS Trial, or make her own decisions regarding treatment. Surely, it is better to have confidence in a doctor who is truthful and therefore admits having doubts, rather than one who either withholds the truth or expresses an unjustified confidence in one therapeutic approach which is not shared by the leaders of the profession. Involvement in a clinical trial does not deny a patient a choice. Indeed paradoxically the opposite is nearer the truth. The misplaced confidence of the inexpert clinician for one regimen alone denies that aspect of choice which should be the privilege of all our patients.

Perhaps the most difficult issue faced by Mrs Thornton and many like her, concerns the practicalities and timing of obtaining informed consent for entry into a multi-centre trial [7]. One of us (MB) has recently been involved in making a video, illustrating the problems of communication when seeking recruitment into a trial [8]. In this film a premenopausal woman with early breast cancer was shown being given the diagnosis together with an explanation of the significance of involved axillary lymph nodes. She was offered breast conserving surgery and had explained that there was uncertainty as to the need for radiotherapy in her case. Because of the involvement of her axillary nodes the rationale for and toxicity of adjuvant systemic chemotherapy was explained in full detail. Uncertainty as to the additional need for ovarian suppression lead to the offer of entry into a trial organised by the Cancer Research Campaign investigating the value of a luteinising hormone releasing hormone (LHRH) agonist. During the interview the dismay and perplexity on the face of the patient was almost too great to bear watching. That this was the first of three scheduled interviews, before a final agreement as to treatment, with or without randomisation would be arrived at, did not lessen the conclusion that the patient found this an unbidden and hurtful experience. The fact that the "patient" was an actress made it no better, as one would judge the reality even less tolerable to witness.

Abandoning the use of euphemism to hide the truth of the diagnosis has been generally welcomed. Now is the time for both public and profession to face up to the fact that denying uncertainty, although more comfortable in the short term cannot serve the best interests of current or future patients. Yet it appears we are dammed if we try to hide the truth and dammed if we are over-zealous in describing the truth. It is thus extremely difficult, as Mrs Thornton herself points out, to find the middle ground, between the old paternalism and the new model autonomy.

Perhaps it would be more realistic for us to recognise that there is in fact no middle ground, but that the requirements of each individual patient are different. Some would, no doubt, welcome the return of old-fashioned paternalism whereas others cherish the relatively new found right of autonomy. Indeed, an individual patient may, particularly at a stressful time such as following diagnosis, long for the benefits of a paternalistic doctor in whom she can have absolute trust and confidence whilst at other times, when feeling less vulnerable, seek all the advantages of self determination. It is not helpful, however, for one group to impose their needs on another suggesting an unacceptable degree of ethical imperialism. We do need to continue to grapple with these complex issues in an atmosphere of mutual understanding so that the patient receives the "best" care, including treatment decisions that are made from a reliable scientific base.

Sadly, there is no simple solution to these agonising dilemmas but we salute the courage of Hazel Thornton to bring the issues into the public domain. She is not a professional ethicist, ideologist or doctor basher but in our view represents the true voice of the worried and perplexed women who offer themselves as "well" to the screening programme only to emerge as "diseased".

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1. Green SB, Byar DP. Using observational data from registries to compare treatments: the fallacy of omnimetrics. *Stats Med* 1984, **3**, 361–370.
2. Recht A. Radiotherapy and ductal carcinoma *in situ* of breast. *Lancet* 1992, **340**, 312.
3. van Dongen JA, Holland R, Peterse JL, *et al.* Ductal carcinoma *in situ* of the breast: second EORTC Consensus Meeting. *Eur J Cancer* 1992, **28**, 626–629.
4. Nielsen M, Thomsen JL, Primdahl S, *et al.* Breast cancer and atypia among young and middle-aged women: a study of 110 medicolegal autopsies. *Br J Cancer* 1987, **56**, 814–819.
5. McIndoe WA, McLean MR, Jones RW, *et al.* The invasive potential of carcinoma in situ of the cervix. *Obstet Gynaecol* 1984, **64**, 451–458.
6. Baum M, Houghton J, Zilka K. Ethics of clinical research: lessons for the future. *Br Med J* 1989, **229**, 251–253.
7. Thornton HM. Breast Cancer Trials: a patient's viewpoint. *Lancet* 1991, **339**, 44–45.
8. Fallowfield LJ, Hall A. Communications skills for oncologists. Cancer Research Campaign, 1992.