TESTING TREATMENTS

HOW PATIENTS CAN JEOPARDIZE FAIR TESTS OF TREATMENTS

Involving patients in research is not always helpful in promoting fair tests of treatments. A survey of researchers in 2001 revealed some very positive experiences resulting from involving patients in clinical trials but it also laid bare some very real problems. These mostly resulted from everyone's lack of experience of this type of collaboration. First, there were often substantial delays in initiating research. There were also concerns about conflicting interests and 'representativeness' of some patients who had not yet appreciated the need to avoid bringing only their own interests to trial management meetings.[5]

Many of these problems seemed to arise from patients' understandable lack of knowledge about how research is done and funded. Desperate circumstances sometimes provoke desperate efforts to access treatments that have not been adequately evaluated and may do more harm than good, even to patients who are dying. We have already referred to the way that lobbying by patients and their advocates for 'compassionate' release of 'promising' new drug treatments for AIDS had its downside: it delayed the identification of treatments directed at outcomes that mattered to patients. More recently, counterproductive and misinformed advocacy, by both individuals and patient groups, has affected t he p rescribing o f drugs for multiple sclerosis and breast cancer.

In the mid-1990s, interferons were introduced to treat patients with the relapsing-remitting form of multiple sclerosis on the basis of scant evidence of benefit. Very quickly, patients with all forms of multiple sclerosis clamoured for these costly drugs, and healthcare services agreed to fund their use. Interferons became an accepted standard treatment for this debilitating disease. As a result, we will never know how to give interferons appropriately in multiple sclerosis – the research was never done and it is now too late to turn the clock back. However, with the passage of time one thing has become abundantly clear – interferons have nasty side-effects, such as 'flu-like' symptoms.

Herceptin (trastuzumab), as we explained in Chapter 1, p9-12, is not a wonder drug for all women with breast cancer. Firstly,

PESTER POWER AND NEW DRUGS

'New drugs by their very nature are incomplete products, as full information about their safety, effectiveness and impact on costs are [sic] not yet available.

It is worth noting that enthusiastic support for what is "new" is not the sole preserve of newspapers and can often easily be seen in other media outlets and among the medical and scientific communities.

"Pester power" is a concept normally associated with advertising aimed at children. The question to be asked in this context is, are we witnessing patient pester power or quasi direct-to-consumer advertising, where awareness is raised about new products and patients, charities and indeed clinicians then demand that these products be made available? If this is the case, we need to know more about who is driving this type of marketing, its actual impact on clinician and consumer behaviours and whether it is permitted within the existing regulatory code of practice.'

Wilson PM, Booth AM, Eastwood A et al. Deconstructing media coverage of trastuzumab (Herceptin): an analysis of national newspaper coverage. *Journal of the Royal Society of Medicine* 2008:101:125-32

its effectiveness depends on a particular genetic make-up of the tumour, which is present in only 1 in 5 women with breast cancer. On top of that, the drug has potentially serious side-effects on the heart. Yet patient advocacy, fuelling a media frenzy, led politicians to go with the flow of public opinion: use of Herceptin was officially endorsed with scant regard for the existing evidence or acknowledgement that further evidence concerning the balance of benefits and harms was still awaited.

Patients' organizations: independent voices or not?

Another less well known conflict of interest exists in the relationship between patients' organizations and the

INVOLVING CITIZENS TO IMPROVE HEALTHCARE

'The confluence of interest between advocacy groups, those who sell treatments, and those who prescribe them makes for a potent cocktail of influence, almost always pushing policy makers in one direction: more tests, more procedures, more beds, more pills. . .

As someone reporting in this field for more than a decade, I sense that what's often missing from the debate is a voice genuinely representing the public interest. Sponsored advocacy groups are quick to celebrate a new treatment or technology but slow to publicly criticise its limited effectiveness, excessive cost, or downright danger. And, like many journalists, politicians tend to be unnecessarily intimidated by senior health professionals and passionate advocates, who too often lend their credibility to marketing campaigns that widen disease definitions and promote the most expensive solutions.

The emergence of new citizens' lobbies within healthcare, well versed in the way scientific evidence can be used and misused, may produce a more informed debate about spending priorities. Such citizens' groups could routinely expose misleading marketing in the media and offer the public and policy makers realistic and sophisticated assessments of the risks, benefits, and costs of a much broader range of health strategies.'

Moynihan R. Power to the people. *BMJ* 2011;342:d2002.

pharmaceutical industry. Most patients' organizations have very little money, rely on volunteers, and get little independent funding. Grants from and joint projects with pharmaceutical companies can help them grow and be more influential, but can also distort and misrepresent patients' agendas, including their

research agendas. The scale of this problem is difficult to gauge but a fascinating insight comes from a survey done to assess the level of corporate sponsorship of patient and consumer organizations working with the European Medicines Agency. This Agency coordinates the evaluation and monitoring of new drugs throughout Europe and, to its credit, has actively involved patient and consumer groups in its regulatory activities. However, when 23 such groups were surveyed between 2006 and 2008, 15 were shown to receive partial or significant funding from medicines manufacturers or pharmaceutical industry associations. Moreover, fewer than half of the groups accurately identified to the Agency the source or amount of funding that they received.[17]

In some cases patient organizations have been set up by drug companies to lobby on behalf of their products. For instance, one of the companies that makes interferon formed a new patient group 'Action for Access' in an attempt to get the UK National Health Service to provide interferons for multiple sclerosis (see above).[18,19] The message heard by patient groups from all of this publicity was that interferons were effective but too expensive, when the real issue was whether the drugs had any useful effects.

Bridging the gap between patients and researchers

We drew attention above to problems that can result from patients becoming involved in testing treatments, and ways in which they may unintentionally jeopardize fair tests. As with most things, good intentions do not guarantee that more good than harm will be done. Nevertheless, there are clear examples of the benefits of researchers and patients working together to improve the relevance and design of research. As a result, many researchers actively seek patients with whom they can collaborate.

In an example of the value of collaborative preparatory work, researchers explored with patients and potential patients some of the difficult issues involved in testing treatments given in an emergency. If therapies for acute stroke are to succeed, they need to be started as soon as possible after the stroke occurs. Because they were unsure of the best way to proceed, the researchers asked patients and carers to help them. They convened an exploratory meeting with a group of patients and health professionals, and

conducted focus groups involving older people. As a result, plans for the trial were clarified and patients helped the researchers to draft and revise trial information leaflets.[20]

This thorough preliminary research led to plans for a randomized trial which were endorsed promptly by the research ethics committee. The focus group participants had recognized the ethical dilemmas of trying to obtain informed consent from someone with an acute illness which may well have left them confused, or unable to communicate, even if not unconscious. They were able to suggest solutions that led to an acceptable trial design for all parties, and substantial improvements in the information leaflets.

Social scientists are increasingly involved as members of research teams to formally explore sensitive aspects of illness with patients and so improve the way in which trials are done. For a clinical trial in men with localized prostate cancer, researchers wanted to compare three very different treatments – surgery, radiotherapy, or 'watchful waiting' – and this presented difficulties both for clinicians offering the trial and for patients trying to decide whether to participate in it. Clinicians so disliked describing the 'watchful waiting' option that they had been leaving it to last, and describing it less than confidently because they had mistakenly thought the men asked to join the trial might find it unacceptable. Social scientists were asked to study the issue of acceptability to help determine whether the trial was really feasible.

The social scientists' results were a revelation.[21] They showed that a trial offering 'watchful waiting' would be an acceptable third option if described as 'active monitoring', if not left until last to be explained by the doctor when inviting the patient, and if the doctors were careful to describe active monitoring in terms that men could understand.

The research, bridging the gap between doctors and patients, had identified the particular problems that were presenting difficulties for both parties and that could easily be remedied by better presentation of the treatment options. One result was that the rate of acceptance of men invited to join the trial increased over time, from four acceptances in ten to seven in ten. This more

rapid recruitment meant that the effect of all these treatments for men with localized prostate cancer would become apparent earlier than would have been the case if the preparatory work had not been done. And, because prostate cancer is a common disease, many men stand to benefit in the future, earlier than they might have done.

WORKING COLLABORATIVELY BODES WELL FOR THE FUTURE

There are numerous ways in which patients and the public can become involved in testing treatments. As we have already outlined, they may be the prime movers – the ones who identify the gaps in understanding and the need to find new ways of doing things. Their input may be facilitated by researchers; they may be involved in some stages of the work but not others; they may be involved from the moment of identification of a specific uncertainty that needs addressing through to dissemination and implementation, and incorporation of the project's findings in an updated systematic review; and they may be involved in different ways within one project. Sometimes they initiate the work themselves. There is no hard and fast rule: the appropriateness of different strategies and approaches in a particular study will dictate those strategies chosen. As the localized prostate cancer trial described above illustrates, methods are evolving all the time. When patients and researchers work together they offer a powerful combination for reducing treatment uncertainties for the benefit of all. Various methods for enabling this joint working, suited to individual studies as appropriate, with endorsement and support from national research organizations, bode well for the future.