GRIST: Growing Recruitment in Interventional and Surgical Trials

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Lancet editor Richard Horton amused many and outraged some by titling his commentary on the dearth of randomized trials 'Surgical research or comic opera'.[1] The sad fact is that 15 years later, the story is much the same: few patients enter randomized controlled trials of surgery. The need for 'fair tests'[2] has never been more pressing, as innovators of new technologies promote their advances while health services worldwide fail to contain and reduce costs. Disinvestment in ineffective or less effective treatments has proved difficult for National Institute for Health and Clinical Excellence (NICE).[3] but is essential to make way for better treatments. Low grade observational evidence is often sufficient to keep existing practices going, but higher quality evidence is needed to discontinue them. To borrow from Muir Gray on changing practice for interventions with a poor balance of good and harm, it's easier to 'stop them starting' than to 'start them stopping'.[4] There is a sound argument for surgeons taking greater ownership for the problem and the solution.

Two years ago in December 2009 the National Institute of Health Research (NIHR), Comprehensive Clinical Research Network (CCRN) with the National Cancer Research Institute (NCRI) and National Cancer Research Network (NCRN) provided funding for a National Working Party for Recruitment to Interventional Trials (NWPRIT) with a two year working term. There is now progress to report, and a vision for the future. It is little wonder that the vision includes rebranding of the group with the acronym GRIST standing for Growing Recruitment in Interventional and Surgical Trials, a mission statement encapsulating the intention of the project.

One of the obstacles to recruiting patients into trials is restrictive regulation surrounding clinical research. Doctors enjoy considerable freedom to try out new ideas in clinical practice – provided they only evaluate within an uncontrolled cohort study.[2] Somewhat paradoxically it has been made more difficult to do better quality research. To undertake more structured research calls for additional training in 'Good Clinical Practice' (GCP) required of clinical staff before they actively contribute to trials. NWPRIT has introduced GCP training, targeted at surgeons, and built this into trial launch days. Over 150 clinicians have been accredited for GCP with more prompted to take up GCP training locally, or online.

GCP seeks to ensure adherence to protocols, avoidance of bias in allocation and reporting, avoidance of any form of coercion, and to set standards for ethical behaviour. The philosopher Martyn Evans proposed that there was a public duty to be involved in medical research and that 'patients participating in the shared benefits of publicly funded health care enjoy the benefits of treatments tested on previous patients. Future patients similarly depend on treatments tested on present patients'.[5] Fallowfield and colleagues have found most patients were willing to take part in medical research (91% of about 1,000 participants). Randomization was an obstacle for half, but an obstacle at least partly overcome by better explanation.[6] The Mesothelioma and Radical Surgery Trial (MARS) was confidently predicted to be bound to fail to recruit, but the target of 50 patients, to demonstrate feasibility, was reached. In the event there were sufficient patients to show, that in this instance, less treatment was better than more.[7] The often stated

objection that patients will not accept randomization may have been overstated.[2]

One certain obstacle to randomization may be the first person to propose a treatment to a patient, if it is a doctor or nurse with an evident belief in one or other arm of the trial. Winding the tape back, to a point when uncertainty should have been declared, is not easy. One solution is that the treatment options are presented by a neutral individual, specifically trained in that role, and that uncertainty is explicitly acknowledged. The lesson was learned a long time ago when, for the first time, patients were asked to accept allocation to angioplasty or surgery in the RITA (Randomized Interventions in the Treatment of Angina) trial.[8] Recruitment was difficult until a body of 'RITA nurses' were recruited to introduce the trial even-handedly. Research Network and the Bowel Disease Research Foundation provide joint funding to 16 UK units who receive one session per week (approximately £3,000 per annum) to fund a nurse specialist in coloproctology who are there to recruit to surgical trials. In nine units, trials were opened for recruitment as a result and over 100 additional patients have been recruited to portfolio trials as a direct consequence of this activity.

NWPRIT provided a 'trials clinic' which succeeded in helping chief investigators of trials in urology, breast, colorectal, and head and neck surgery to turn things around. The working party has also identified trials which could not be salvaged – itself an important outcome. Wasted effort is spared and resources can be redirected.

It is clear that the vast majority of patients being treated within surgical units are not being approached for participation in prospective clinical trials. Increasing clinical and public awareness is therefore a priority. Examples of good initiatives have been identified. Queen Elizabeth Hospital, with the University of Birmingham, have devised a pamphlet which is now sent to all patients who are attending the hospital for surgical procedures explaining that they are attending a hospital actively engaged in research. This initiative has support from the Integrated Research Application System (IRAS). Patients are informed prior to admission that they will be approached for clinical trials and that, embedded within the hospital consent form, consent is easily provided by all patients who wish for surgical specimens to be used for research.

There is a powerful argument for placing clinical research at the centre of a high quality, patient-orientated surgical service. GRIST is motivated and well placed to help this happen. We have a responsibility to future patients to perform clinical trials that will improve practice. Without patient participation, there is nothing deliverable from all our efforts in framing research questions and designing studies. Growing recruitment into trials is an essential component.

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