Pragmatic trials in primary health care: what, when and how?

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The word pragmatic was first used in relation to trials by Schwartz and Lellouch in 1967, in a paper in which they argue that most therapeutic trials are inadequately formulated because there is ambiguity about which of two radically different kinds of problem they are designed to address. They explain what these two kinds of problem are by distinguishing between pragmatic trials that are designed to help choose between care options and explanatory trials that are designed to test causal research hypotheses, for example, to understand a biological process. In their 1998 paper entitled ‘What are pragmatic trials?’ Roland and Torgerson suggest that explanatory trials generally measure efficacy, the benefit a treatment produces under ideal conditions, while pragmatic trials measure effectiveness, the benefit the treatment produces in routine clinical practice.

In recent years, there has been a resurgence of interest in the distinction between pragmatic and explanatory trials with, for example, the publication of an extended CONSORT statement for pragmatic trials in 2008 and various articles in the Canadian Medical Journal and Journal of Clinical Epidemiology in May 2009, including discussion of the fact that some trials may have a mixture of pragmatic and explanatory elements so that it may be better to consider where trials sit on the pragmatic–explanatory spectrum (via the PRECIS tool) rather than using a strict divide between the two types. Zwartenstein and Treweek make a case for more pragmatic trials, suggesting that these are the types of trials that are most needed to answer relevant questions in health-related research but that they are still uncommon when set against the vast numbers of explanatory, usually drug, trials that have been conducted over the past 50 years.

Because of the nature of primary care, trials conducted in a primary care setting are almost always at the pragmatic end of the pragmatic–explanatory spectrum, hence the motivation for this editorial; those conducting and reporting these trials should understand the implications and pitfalls associated with these trials, which are somewhat different from those for trials at the explanatory end of the spectrum.

One of these implications is that those involved in identifying, recruiting and treating patients are often necessarily clinicians or other health services staff because this replicates, as far as possible, what happens in routine practice. In many trials, this places a considerable burden on clinicians in particular. In this issue, the study by Fletcher et al. exemplifies this for a trial conducted in a primary care setting, suggesting that decreasing clinician workload in ways that do not compromise the robustness of a trial may improve recruitment rates.

That pragmatic trials should reflect benefit produced in routine clinical practice means that these trials also need to include patients representative of those treated in routine clinical practice and that any intervention should be tested against whatever is usual care or best practice. These are common characteristics of trials in primary care, including those reported in Family Practice, are non-contentious and are usually relatively easily implemented.

Nevertheless, there are other aspects of pragmatic trials that bear closer examination, one of which is related to the definition and description of the intervention. In explanatory trials, the intervention is the therapy (usually a drug) itself and the aim is to assess efficacy; for example, in this issue White et al. report that, in largely explanatory trials, alendronate has been shown to be effective in reducing fractures. In routine practice, however, effectiveness is influenced not only by efficacy but also by the extent to which the therapy is acceptable to patients, who always have the option of refusing all or part of the therapy. In assessing effectiveness via a trial within a routine care setting, this option must be retained, and thus, the intervention is more correctly defined as the ‘offer’ of the therapy rather than the therapy itself. In addition, if a therapy is already used in routine practice, a pragmatic trial may not be designed to evaluate the effectiveness of a therapy at all but to evaluate measures designed to increase effectiveness; in most of the trials reviewed in White et al., intervention and control patients received identical medication but the intervention group received, for example, extra feedback on biomarkers or motivational interventions. Clarity in defining and reporting the exact nature of any intervention in a pragmatic trial is important to enable correct interpretation of the results. Interventions in pragmatic trials are often
complex and there is evidence that complex interventions are frequently not reported with sufficient detail to allow their replication. This diminishes the value of the results for researchers and clinicians.

The issue of bias also bears closer examination in pragmatic trials. That the avoidance of bias is a key quality criterion for all trials is indisputable. What bias means and how a pragmatic trial should be judged in relation to bias are more open to debate. Criteria for judging bias have their genesis in the field of drug trials, many of which, we have already established, are explanatory. The CONSORT movement has translated general criteria for avoiding bias into easily accessible statements against which trial reports can be assessed. One example is the issue of blinding. In a drug trial, for which placebos can be manufactured, it is considered good practice for all those involved in the trial to be blinded to which intervention group a patient is in, and this is usually relatively straightforward to do. In these circumstances, referring to a trial as ‘blinded’, although not strictly correct (since a trial is an inert entity incapable of being blind or unblind), is fairly unambiguous. In pragmatic trials, however, this is not the case. Dependent on the intervention it may be impossible to blind certain groups of individuals involved in the trial. This is the case for the interventions reviewed in White et al., where the authors acknowledge the impossibility of, for example, blinding participating physicians to an educational or motivational intervention. In fact it has been argued that in some trials in routine practice, knowledge of the intervention by clinicians delivering the intervention and/or by patients receiving the intervention is a valid part of the intervention and therefore blinding is undesirable. There is a question mark, therefore, over whether unblinding per se constitutes potential bias. Nevertheless, simple checklists, such as the Jadad quality scoring system, used by White et al., do not allow for such considerations and all the trials in their review scored low for blinding. This low-quality assessment may not be appropriate for pragmatic trials. This is not to say, however, that investigators should ignore the issue of blinding but rather that in pragmatic trials it needs to be considered more carefully. The extended CONSORT statement for pragmatic trials acknowledges this in suggesting that for these trials investigators should either state that blinding was carried out or explain why it was not. It is also helpful for these trials to avoid such terms as ‘single blind’ and ‘double blind’ in favour of stating which groups out of those delivering the intervention, patients and those assessing outcomes were or were not blind. In particular, conducting a trial to assess an intervention in routine practice does not exempt investigators from trying as much as possible to blind outcome assessors to allocation status since outcome assessment is clearly part of the research process not part of routine practice.

A further characteristic of many pragmatic trials is that some element of the intervention being evaluated may be aimed at clinicians or other health professionals or health service staff, which often necessitates a cluster-randomized design, for example, one of the trials on biomarker feedback reviewed in White et al. Those conducting such trials should be aware of their complexities particularly regarding bias and generalizability; these have been discussed elsewhere.

In summary, while some judgements about the quality of trials are appropriate across all trials, other aspects such as maximizing recruitment, defining and describing the intervention, the potential for bias and choice of design need careful consideration for trials at the pragmatic end of the pragmatic–explanatory spectrum. Various publications in recent years have highlighted some of the relevant issues and bear close scrutiny by those conducting and reporting these trials.

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References