When is an intervention ready to be tested in a randomised trial?

Primary care alliance for clinical trials (PACT) network

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Results from randomised trials showing effectiveness or lack of effectiveness of a particular intervention have the potential to influence clinical practice and policy. Many interventions that have appeared promising in observational studies have turned out not to be so when subjected to the rigorous evaluative methods of a randomised trial. As randomised trials are expensive and time consuming to undertake – and their results can be very influential – it is important that interventions tested in trials are actually ready to be tested. This is especially important if a trial is testing a new model of care or a complex set of interventions. There is little to be gained in finding out that a poorly developed intervention is not shown to be effective when tested in a randomised study. While there are numerous excellent texts and papers written about conducting and analysing trials, there is little in the way of written information to guide researchers as to when to test an intervention using a trial design.

Method

During the PACT workshop, a group of nine academics (including clinicians) discussed the thinking that goes into deciding when an intervention is ready to be tested in a randomised trial. We started by reviewing the details of an intervention delivered as part of a United Kingdom depression study[1] without knowing the actual study or the researchers. An assigned group 'note taker' kept an ongoing record of all suggestions made by the group. After half an hour of canvassing all issues that were important to the group members, we summarised and discussed the emerging points that group members saw as essential to good trial planning. The summary list was discussed and refined until all group members agreed upon the key elements necessary before an intervention is tested in a randomised trial.

Results

Our process of reflection upon a recent primary care trial, and the sharing of our own experiences and discussion, led to five key elements being identified as 'necessary' before undertaking a randomised trial to test an intervention. These elements are listed below. Many of the points are inter-connected and do not necessarily flow linearly. It should be noted that these suggestions are made only in regard to whether an intervention is ready to be tested and that all other methodological issues as outlined in the CONSORT statement[2] are considered. Also, such 'practical tips' should be seen in the context of the broader debate about the limitations of experimental methods for explaining how health interventions 'work' (as opposed to whether they are effective),[3] and thus the largely practical question of when a particular intervention is 'ready' to be tested in a randomised trial should be distinguished from the methodological question of whether this is the best way to assess its effectiveness.[4] A complex intervention is ready to be tested using a randomised trial design when:

1. **The intervention is based upon a theoretical framework of how it is effective**
   The group participants were forthcoming with examples they considered lacking in theoretical basis. There was a strong opinion that 'just having a good idea' was not good enough and many group members believed we could all increase the amount of time we spent understanding the theoretical basis for complex interventions.
   While Moulding et al[5] provide an overview of some key theories that may underpin the adoption of clinical guidelines, there is little theoretical work that underpins how many other models of care such as 'shared care', or 'case management' generate their supposed benefits.
2. **A detailed and complete description of the intervention**
   Developing a detailed description of the elements of a complex intervention was thought to be necessary in order to discuss the intervention with others. Most group members commented that an intervention needs to start as a draft, and that

a document or model needs to be developed and constantly updated as components are refined. Work by Grol[6,7] was suggested as a good starting point for planners of complex interventions. As a minimum, describing particular models of care or services will involve such information as the:

- number and specific type of clinical practitioners involved
- population or case mix served
- typical timing and location of clinician-patient encounters
- physical facilities necessary for care to be provided
- information and communication systems that support the model of care (eg. disease based registers, telephone triage systems), and
- access or referral arrangements to and from the model of care or service (eg. opening hours, appointment systems, discharge arrangements).

3. The intervention is acceptable to practitioners and patients

The need to spend time seeking the opinions of practitioners and patients early in intervention design was mentioned by every group member. Having a documented process for this and using methods such as interviews, focus groups and surveys were suggested as good ways to refine the intervention. Other group members mentioned the usefulness of study reference groups and steering committees for this phase of intervention development. Working out how the intervention would be implemented in the real world was a common theme mentioned by the group.

4. The barriers and facilitators to implementing the intervention have been identified and dealt with

A number in the group commented about the need to step back from the intervention being developed and identify the barriers and facilitators to practical implementation and revise the intervention accordingly. Identifying factors that can either enhance or prohibit the intervention's effectiveness is important for two reasons:

- understanding and addressing these factors gives the intervention the best chance of being effective, and
- 'effect modifiers' can be measured and analysed alongside the main outcomes.

Ultimately, understanding how a particular intervention interacts with different contextual factors allows the trial results to be more judiciously generalised to other settings (eg. different patient groups, other types of general practice settings).

5. The outcome measures chosen are clinically meaningful and directly relevant to the key components of the intervention

Chosen outcome measures need to be relevant to the prospective users of the research findings. Deciding upon outcome measures that mean something to researchers, practitioners, patients and policy makers can be very challenging. The group discussed the choices between:

- dichotomous outcomes (eg. depressed versus no longer depressed, hypertensive versus normotensive) which are easy to understand, and
- continuous outcomes (eg. changes in mean scores on a depression scale, reduction in blood pressure measurement in mmHg) which can be difficult to relate to real world outcomes. Discussing choice of outcome measures with practitioners and patients should be considered.

Discussion

This article reports on the outcome of a discussion between nine researchers and clinicians who have a special interest in randomised trials in primary care. We hope the 'five steps' will assist researchers (particularly those new to trial research) with their decision about when an intervention is ready to be tested.

Conflict of interest: this manuscript was accepted and edited by *AFP* staff members who have no university affiliations.

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