Patient preference randomised controlled trials in mental health research

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Summary The relationship between psychiatric patients' preferences for different treatments and the outcome of interventions is unclear, as the few relevant trials have tended to be underpowered. Strong patient preferences result in patients refusing to enter a trial. This leads to bias and limits generalisability, and the patient preference randomised controlled trial (RCT) design has been proposed as an alternative. Limitations and advantages of patient preference RCTs are discussed.

Declaration of interest None.

Randomised controlled trials (RCTs) are widely accepted as the definitive method for comparing the efficacy of specific treatments. However, RCTs were originally developed for drug interventions rather than for the complex interventions that are common in psychiatry. Randomised controlled trials involve a range of potential confounding factors such as patient perceptions, experiences and preferences, and the views of carers and how these interact with the patient's views and social stigma. The influences of patient preferences on outcome are considered here, as psychiatric patients often have strong treatment preferences, which have traditionally been ignored by investigators. The advantages and disadvantages of patient preference RCTs are also discussed.

EFFECT OF PREFERENCES ON OUTCOME

The relationship between patient preferences and the outcome of interventions is unclear. The few relevant trials in the literature have tended to be underpowered. Statistical tests of the influence of patient preferences on the effectiveness of interventions are interaction tests, which have low power and therefore may not provide evidence of interaction even when the latter is present. Interaction tests require relatively large numbers of patients, but are not usually the prime focus of RCTs. Therefore the sample sizes of published RCTs were not calculated with these in mind.

There is some evidence to suggest that patient preferences do not affect outcome. For example, a study comparing day hospital and in-patient treatment for rehabilitation of alcohol-dependent patients found no significant differences in relapse or psychosocial outcomes between individuals with a preference for one of the treatment settings (who selected their treatment) and those without such a preference (who were randomised) (McKay *et al*, 1995). However, it is difficult to draw conclusions from this study as follow-up rates were very low, ranging from 10% to 70% in the different treatment settings. Similarly, a study that compared cognitive–behavioural therapy, non-directive counselling and general practitioner care found no significant differences in outcome (assessed by Beck Depression Inventory scores) between participants who were randomised to each treatment and those who received their preferred treatment (Ward *et al*, 2000). However, all outcomes were self-rated, and a conservative approach to data analysis was adopted by using the last observation carried forward. Chilvers *et al* (2001) randomised patients with major depression to generic counselling or antidepressant treatment in primary care, and investigated the effect of patient preference by offering a choice of treatment to the patients who were not randomised. They found that patients who chose counselling did better than those who were randomised to it, although the power of the study for detecting interactions was low. A recent systematic review of the effect of patient and physician intervention preferences on randomised trials found some evidence that patient preferences influence outcome in a proportion of trials, but the evidence for moderate or large preference effects was much weaker in large trials and after accounting for baseline differences (King *et al*, 2005). Therefore these studies do not demonstrate conclusively any consistent effect of preference on outcome, but they do show that preferences exist and that the characteristics of patients who have preferences may differ from those of patients who consent to randomisation.

Strong patient preferences result in patients refusing to consent to enter a trial and undergo randomisation. This leads to bias, as the absence of these patients may restrict generalisation of the findings and may weaken the external validity of the results (Torgerson & Sibbald, 1998; King *et al*, 2005). If patients with strong preferences are recruited and randomised, and it is not possible for them to be blinded to treatment, as is often the case in complex interventions in psychiatry, participants who are not randomised to their treatment of choice may be disappointed and suffer from 'resentful demoralisation' (Bradley, 1996), which has implications for compliance, whereas those who are randomised to their preferred treatment may have a better outcome irrespective of the efficacy of the intervention.

The patient preference RCT paradigm or comprehensive cohort design (Brewin & Bradley, 1989) has been proposed as an alternative to the conventional RCT. Patients with treatment preferences are allowed their desired treatment without randomisation and those who do not have particular preferences are individually randomised in the usual way.

Treatment trials that include patients who are not willing to be randomised allow trialists to estimate the representativeness of the randomised sample. If randomised patients resemble non-randomised patients, the patient preference trial provides greater evidence of the external validity of the trial results. The analysis should also include at least one comparison between the two randomised arms alone, and therefore the power calculation will need to take this into consideration at the planning stage. The sample size is therefore larger than in a conventional trial. The randomised component must be as large as a standard RCT, and the number of non-randomised patients must be sufficient to allow comparison of the effect of each treatment for individuals who express a preference for that treatment with the effect for those who do not, and

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also comparison of individuals who are willing to be randomised and those who are not. This is a reflection of the fact that the sample size must be large enough to allow interactions between treatment and prognostic factors to be investigated (Schmoor *et al*, 1996). Analyses that include the non-randomised groups should be treated as observational studies, with known confounding factors adjusted for in the analysis (Torgerson & Sibbald, 1998). The use of randomised status (agreeing to randomisation or not) as a covariate might also be helpful (Olschewski & Scheurlen, 1985).

LIMITATIONS

First, any comparison that uses non-randomised groups is unreliable because of the presence of unknown and uncontrolled confounding factors. Differences in outcome may be explained by differences in the baseline characteristics of participants in the randomised and non-randomised groups. A preference effect cannot be disentangled from possible confounding arising from differences between patients with particular preferences. An example of this might be previous treatment history, which could be associated with both preferences and the patient's perceptions of the effectiveness of the proposed treatment.

Second, patient preferences may change over time, both during the trial and subsequently. It is also unlikely that patients make decisions completely independently; clinicians are likely to play a part in the final decision.

Finally, it is likely to be difficult to determine how many patients will choose to enter each arm of the trial, and funding bodies may be reluctant to accept estimates of the cost and duration of the trial without the results of a pilot study specifically designed to elicit this type of information.

ADVANTAGES

First, these trials can recruit patients who would not otherwise have been recruited to the study because they would not have agreed to be randomised. Second, RCTs that incorporate patient preferences can provide greater evidence of the external validity of the trial results. For example, Ward *et al* (2000) compared patients who were not willing to be randomised (the patient preference arms) with those who were randomised, and confirmed the representativeness of the randomised sample.

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Collection of data on patient preferences may be useful to clinicians, and it may indicate whether a particular intervention is effective even in patients who are not highly motivated. For example, Moffett *et al* (1999) found that simple exercise classes could lead to long-term improvements in individuals with back pain who had not had a strong preference for the intervention. They asked patients what their preferences were before allocating them at the start of the trial. This had advantages over the usual patient preference design, as it demonstrated that preferences did not have an impact on outcome without needing the larger sample size that would have been necessary for a patient preference RCT.

ALL PATIENTS HAVE PREFERENCES

It may be argued that the best way of dealing with preferences is to measure and take account of preferences within the RCT itself. In such a design the strength and direction of patient preferences are elicited before randomisation, and all consenting patients are randomised, thereby retaining the rigour of the full randomised design. This design was used in a trial of physiotherapy treatment of back pain in which most patients expressed a preference but none of them refused randomisation (Torgerson *et al*, 1996).

More radically, Chalmers (1997) has challenged the bases of treatment preferences. He suggests that there is a widespread belief that new treatments are likely to be superior to existing alternatives. Patients therefore need to be given reliable information by clinicians and researchers, which would help to increase the proportion of well-informed people with no strong preferences who would thus be eligible to participate in randomised treatments.

In conclusion, collection of data on patient preferences may prove to be useful when evaluating mental health services. It may be part of a comprehensive cohort study examining the external validity of the population in an RCT, it may be part of an investigation of the effect of preferences on outcome, or it may be an investigation of patient choices, but all of these are important preference questions. Patient preference trials have been neglected in psychiatric research, but patient preference RCTs may prove to be a useful paradigm, and data on patient preferences are clearly an important part of mental health services research.

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REFERENCES

Bradley, C. (1996) Patients' preferences and randomised trials. *Lancet*, **347**, 1118–1119.

Brewin, C. R. & Bradley, C. (1989) Patient preferences and randomised clinical trials. *BMJ*, **299**, 313–315.

Chalmers, I. (1997) What is the prior probability of a proposed new treatment being superior to established treatments? *BMJ*, **314**, 74–75.

Chilvers, C., Dewey, M., Fielding, K., *et al* (2001) Antidepressant counselling for treatment of major depression in primary care: randomised trial with patient preference arms. *BMJ*, **322**, 772–784.

King, M., Nazareth, I., Lampe F., *et al* (2005) Impact of participant and physician intervention preferences on randomized trials – a systematic review. *JAMA*, **293**, 1089–1099.

McKay, J. R., Alterman, A. I., McLellan, T., *et al* (1995) Effect of random versus non-random assignment in a comparison of inpatient and day hospital rehabilitation for male alcoholics. *Journal of Consulting and Clinical Psychology*, **63**, 70–78.

Moffett, J. K., Torgerson, D., Bell-Syer, S., *et al* (1999) Randomised controlled trial of exercise for low back pain: clinical outcomes, cost and preferences. *BMJ*, **319**, 279–283.

Olschewski, M. & Scheurlen, H (1985) Comprehensive cohort study: an alternative to randomised consent design in a breast preservation trial. *Methods of Information in Medicine*, **24**, 131–134.

Schmoor, C., Olschewski, M. & Schumacher, M. (1996) Randomised and non-randomised patients in clinical trials: experiences with comprehensive cohort studies. *Statistics in Medicine*, **15**, 263–271.

Torgerson, D. J., & Sibbald, B. (1998) Understanding controlled trials: what is a patient preference? *BMJ*, **316**, 360–364.

Torgerson, D. J., Klaber-Moffett, J. & Russell, I. T. (1996) Patient preferences in randomised trials: threat or opportunity? *Journal of Health Services Research and Policy*, **1**, 194–197.

Ward, E., King, M., Lloyd, M., *et al* (2000) Randomised controlled trial of non-directive counselling, cognitive–behavioural therapy, and usual general practitioner care for patients with depression. I. Clinical effectiveness. *BMJ*, **321**, 1383–1391.

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