Evaluating new treatments in psychiatry: the potential value of combining qualitative and quantitative research methods

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Summary
Clinical trials have been extensively used in order to explore the effectiveness of drug treatments for psychiatric disorders. Double-blind, randomized controlled trials provide the potential to explore the effectiveness of treatments free from the effects of bias and confounding factors. More recently clinical trials have been used in order to evaluate the effects of more complex interventions such as psychological treatments and alternatives to inpatient treatment. Clinical trials of complex interventions present several methodological challenges including the need to identify their mechanisms of action, problems ensuring the fidelity of the experimental intervention and variations in the effects that interventions have in sub-groups of people. We argue that some of these challenges can be met by incorporating qualitative research methods into the experimental evaluation of complex interventions. The benefits and some of the problems of combining methods are illustrated by examples of recent and ongoing research.

The value of clinical trials
Evidence based healthcare, a process which involves making clinical decisions on the basis of best available evidence is widely seen as a central component of efforts to improve the quality of health services (Sackett & Wennberg, 1997). Controlled trials and especially randomized controlled trials (RCTs) (collectively referred to in the rest of this document as ‘clinical trials’) continue to be seen as one of the key methodologies for ensuring that interventions that aim to improve health are assessed in an unbiased way (Greenhalgh, 1997; Harris et al., 1998). High quality clinical trials randomly allocate subjects to alternative interventions in a controlled environment (Pocock, 1983). In doing so they seek to measure the effects of experimental interventions free from the confounding effects of other factors that may influence findings in non-randomized studies.

The methodology of clinical trials was initially developed to investigate the effects of drug treatments. The earliest trials investigated the efficacy of antibiotics (e.g. MRC, 1948) and similar methods were subsequently applied to the evaluation of drugs used in the treatment of depression, schizophrenia and other psychiatric disorders (e.g. Leff & Wing, 1971). By comparing the effects of active drugs with placebos it may be possible to ‘blind’ patients and raters to which treatment a particular subject is receiving. So called ‘double-blind’ studies have the added potential of reducing the likelihood of observer and recall bias, which may effect the findings of studies where patients and raters know whether or not the subject has received the ‘active’ treatment (Day & Altman, 2000). It has been shown that clinical trials in which raters are not blind are more likely to demonstrate positive effects than those where raters are blinded to the treatment that patients receive (Shultz et al., 1995).

Many of the interventions, which have been developed for the treatment of mental health problems, are more complex than drug treatments. These include psychological treatments and novel forms of service delivery such as case management, home-treatment and assertive community treatment. Such ‘complex’ interventions tend to:

- comprise multiple inter-connecting elements;
- have mechanisms of action that are difficult to identify;
- have effects that depend on a range of factors including the actions of the practitioners who deliver them (MRC, 2000).

Difficulties encountered in clinical trials of complex interventions
Clinical trials of complex interventions face a range of methodological problems not shared by trials of...
simple interventions (see Table 1). For example, it is seldom possible to devise trials of complex interventions that are properly ‘double-blind’. While it is sometimes possible to ‘blind’ those assessing patient outcomes, blinding study participants who receive complex interventions is often difficult or impossible to achieve (Taylor & Thornicroft, 1996). In order to consent to take part in a study, patients need to be provided with information about the treatments on offer. Patients who agree to take part in a drug trial have to agree to take a tablet in a way that is specified by the study protocol. However patients taking part in a trial of a psychological intervention are required to play a more active part in their treatment. It is sometimes possible to devise a control treatment which is sufficiently similar to the experimental intervention to allow the patients to remain ‘blind’ (e.g. Sensky et al., 2000). However, as interventions become more complex, it is impossible to gain informed consent for patients’ participation without them (and the clinical teams involved in their care) having sufficient information to judge which group they have been assigned to. The effect of randomization on the person’s expectations and perceptions of the care they subsequently receive may impact on their willingness to engage in, and therefore benefit from, the treatment they are assigned to (Brewin & Bradley, 1989).

Clinical trials of complex interventions may also encounter problems maintaining the fidelity of experimental interventions. Because complex interventions are inevitably multi-factorial and usually depend on the relationship between those who deliver and those who receive the intervention, ensuring that subjects allocated to experimental treatments all receive ‘the same’ treatment can be difficult to achieve. Variation in the content and application of experimental interventions can further weaken the external validity of trial findings. For example, in studies of brief versus standard inpatient care for psychiatric patients, results are impossible to interpret without knowing what other facilities (e.g. acute day hospitals, crisis intervention teams, etc.) were available in the study settings. Furthermore, in trials of novel forms of treatment, those delivering the intervention may have a level of commitment and enthusiasm for the treatment that is difficult to replicate (Taylor & Thornicroft, 1996).

If evidence suggests that an intervention is effective, it is important to determine which aspects of the intervention brought about these effects. In the development of new drug treatments, by the time clinical trials are undertaken, the drug’s mechanism of action has been well researched and is comprehensively understood. By contrast, complex interventions in psychiatry are usually introduced as such, rather than in a step-wise manner, so that it is usually impossible from basic trial data to determine which component(s) of the intervention were responsible for the outcomes recorded. Explanatory studies of complex interventions require a fundamentally different approach (Schwartz & Lellouch, 1967). Absence of knowledge about the explanatory components of an intervention can limit its generalizability and impedes its further development and refinement (Weaver et al., 1996).

### Attempts to modify traditional trial designs

Some of the problems faced when conducting clinical trials of complex interventions may be addressed by making modifications to traditional trial designs (Hotopf et al., 1999). If raters involved in baseline assessments are likely to become aware of which treatment the patient subsequently receives, independent ‘blinded’ raters need to be responsible for collecting follow-up data (Banerjee, 1998). ‘Patient preference trials’, in which only patients who have no preference between alternative interventions are randomized, have been recommended as a way of avoiding problems with patient expectations and motivation in trials of complex interventions (Brewin & Bradley, 1989; Chilvers et al., 2001). Quality control measures such as providing standardized training and monitoring the delivery of the intervention can help to ensure that standards of treatment (Kamb et al., 1996). While quality controls are a prerequisite for trials of complex interventions, they may be insufficient to allow comprehensive interpretation of study findings or generalizability of their results. For example, in psychotherapy trials, it is possible to measure the therapist’s technical competence (e.g. Shaw et al., 1999) but this does not equate with skill or experience, and hence it is not surprising the correlations between patient outcomes and (basic) therapist skills are often only modest.

Despite attempts to adapt trial designs to meet the challenges of evaluating complex interventions, problems persist. These include residual variation in the delivery of the interventions being assessed (Bryant et al., 1999), and the limited ability of quantitative research methods to adequately explore and describe the active ingredients of interventions. As a result of these and other concerns the view that clinical trials provide the best evidence on which to guide clinical practice is frequently criticized (Britton et al., 1998; Graham, 2000; Slade & Priebe, 2001). Some

### Table 1. Common problems with trials of complex interventions

<table>
<thead>
<tr>
<th>Problem</th>
<th>Examples</th>
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<tr>
<td>Concealment of allocated groups is difficult</td>
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<tr>
<td>Comparison groups are often not strictly comparable</td>
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<tr>
<td>Differential contamination of experimental and control groups by other treatments</td>
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<td>Quality assurance of treatments delivered</td>
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<td>Differential attrition from intervention groups</td>
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<td>Problems in defining robust outcome measures</td>
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<td>Attribution of change to the specific intervention</td>
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<td>Controlling for patient expectancies</td>
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Table 1. Common problems with trials of complex interventions
have argued that observational and other research methods form a better basis for the evaluation of health services. An alternative approach may lie in combining qualitative research with experimental designs in the evaluation and development of complex interventions (Stokols *et al.*, 1996; Murphy *et al.*, 1998).

**The value of qualitative research methods in the evaluation of complex interventions**

Qualitative research methods attempt to address research questions with a holistic perspective that ‘preserves the complexities of human behaviour’ (Black, 1994). They have been used extensively in medical research in order to explore the behaviour and interactions of those who deliver and receive healthcare (Murphy *et al.*, 1998). In doing so qualitative research methods may be particularly adept at exploring and describing the process and outcomes of psychological and other complex interventions used to treat mental disorders.

It has long been argued that qualitative research methods have a particularly important role in ‘phase one’ or the pre-trial, modelling phase of the evaluation of a complex intervention (MRC, 2000). Qualitative methods used at this stage of an evaluation may help to identify variables for the study and help in the development of appropriate testable hypotheses. Less attention has been paid to the role of qualitative methods at later stages in the evaluation of interventions. However, qualitative research can perform three important functions in this context. First, collection and analysis of qualitative data within a trial may assist the process of examining the fidelity of the intervention. Second, in highly complex experimental studies (e.g. trials of case management) information about the process and interaction of the intervention elements can help identify ‘active ingredients’ and provide a more secure empirical basis for investigators to interpret their outcome data. Third, it may also provide an opportunity for post hoc analysis of factors associated with positive and negative outcomes both within and between study groups (e.g. Bradley *et al.*, 1999).

While clinical trials provide aggregate measures of effect, any intervention (but especially complex interventions) may produce very different effects in sub-groups of subjects. Attempts to explore these differences using sub-group analysis are problematic (Davies *et al.*, 2000). Qualitative research methods applied to experimental research may enable an exploration of the effects of interventions in sub-groups of people and enhance the explanatory power of the study (Powell & Davies, 2001). Similarly if results show no difference between experimental and control groups qualitative data may enable reasons for the apparent absence of effect to be explored (Murphy *et al.*, 1998). The potential benefits of using qualitative research methods in the ways described earlier are summarized in Table 2.

**Examples of the use of qualitative data collection collected in conjunction with clinical trials of psychiatric interventions**

The authors are currently involved in a number of studies that illustrate how qualitative research may be employed either to develop future trials or to enhance clinical trials that are undertaken concurrently.

**Qualitative research in advance of a trial: developing new interventions, testable hypotheses and appropriate outcome measures**

A key priority for mental health services is to develop effective methods for involving service users in the management and development of services. However, recent work completed by the team shows that models of user involvement (UI) remain undeveloped and that there is no significant evidence base relating to effectiveness. A further complicating factor that inhibits formal evaluation of UI is the absence of appropriate outcome measures. Outcome measures conventionally employed in the evaluation of psychiatric interventions (e.g. inpatient admission, symptomology) represent inappropriate outcome measures for UI. Even ‘patient satisfaction’ measures fail to adequately capture the quality of the users experience of care, user-sensitivity and empowerment. We are applying qualitative research methods

### Table 2. Potential benefits of qualitative research in the evaluation of complex interventions

<table>
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<th><strong>Pre-trial</strong></th>
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<tr>
<td>Qualitative research can help to identify the active ingredients of interventions</td>
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<tr>
<td>Contribute to the development and refinement of experimental interventions</td>
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<tr>
<td>Assist with the development and selection of appropriate outcome measures</td>
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<tr>
<td>Generate testable hypothesis for examination in the subsequent clinical trial</td>
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<tr>
<td><strong>During a trial</strong></td>
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<tr>
<td>Qualitative research methods can examine the fidelity of treatment delivered to those receiving experimental and control treatments</td>
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<tr>
<td>Provide further information about the active ingredients of interventions</td>
<td></td>
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<tr>
<td>Be used to explore interactions between subjects, interventions and those who deliver them</td>
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<tr>
<td><strong>Post-trial</strong></td>
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<tr>
<td>Qualitative research can be used to explore reasons for the positive (or negative) findings of a clinical trial</td>
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<tr>
<td>Provide further information about components of interventions that may lead to differences in patient outcomes</td>
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to study UI practice and identify a model of user involvement, which could potentially be assessed using cluster-randomized designs.

**Qualitative data aimed at improving generalizability of study findings**

As many as 40% of Accident and Emergency department (AED) attenders have consumed alcohol prior to their presentation (Holt et al., 1980). While there is good evidence to suggest that brief interventions aimed at helping those who misuse alcohol can lead to reduced alcohol consumption (Wilk et al., 1997) the value of these interventions administered in the context of the emergency medical settings is unclear. Before an intervention can be offered to patients a system for identifying those who drink excessively needs to be established. A previous attempt to investigate the effects of an AED based intervention failed because only a small minority of patients who attended the department where screened for excessive drinking (Peters et al., 1998). A clinical trial is being conducted at St Mary’s Hospital where screening rates are far higher (Huntley et al., 2000). In parallel with the trial, qualitative data is being collected from in-depth interviews with staff in the AED in order to explore reasons for the high rate of screening that takes place. The rationale for the collection of this data is that, should the intervention prove to be effective, information about how to achieve high levels of screening will be at least as important as information about the intervention if this service is to be developed at other sites.

**Using qualitative research to assess the ‘active ingredients’ of complex interventions**

The value of case management for people with severe mental illness is one of the enduring controversies of community psychiatry (Tyrer et al., 1995; Marshall, 1996). Concerns about the efficacy of Care Programme Approach (CPA) and Care Management have led researchers to assess whether enhanced patient outcomes can be achieved by incorporating elements of Assertive Community Treatment (ACT), for which there is a secure evidence-base (Marshall et al., 2000). The recent UK700 case management trial (Burns et al., 1999) is the example par excellence of this trend. The UK700 study borrowed elements from the ACT model and tested the hypotheses that outcomes could be improved by reducing CPA caseloads to ACT norms of 10–15 patients. It was argued that this would enable more intensive casework with individual patients and encourage ‘assertive outreach’ (UK700 Group, 1999). Despite strong evidence that intervention fidelity was achieved (Burns et al., 1999) the main outcome findings (duration of hospitalization over 2 years) did not support the hypotheses. Burns et al. (1999) candidly acknowledge the pitfall of RCTs of complex interventions when they wrote: ‘We may not have measured those aspects of care which have most relevance to outcome’. We believe this problem to be solvable and one of our team (TW) is currently undertaking a multi-method analysis of process during the trial in which qualitative methods have been employed to identify factors and mechanisms influencing outcome.

**Qualitative data collection aimed at adding to the explanatory power of a trial**

Another recent clinical trial of case management compared two models of care delivered by mental health teams in an inner London Borough. The trial compared standardized measures of patient outcome among those randomized to either case managers working as part of a multi-disciplinary healthcare team or to care managers working with a separate team providing social services. In recognition of the importance of contextual factors in determining the treatment that patients receive and the effects that these factors can have on patient care, qualitative data was also collected through patient interviews and non-participant observation of meetings between patients and staff. This data will be used to generate hypotheses about reasons for positive or negative outcomes from the trial. It will enable exploration of the impact of factors, such as the impact of the trial on team working and financial and other constraints that influence the service that care managers provide.

**Potential obstacles to the collection and analysis of qualitative and quantitative data in the evaluation of interventions in psychiatry**

Despite increasing support for combining quantitative and qualitative research methods in the evaluation of interventions aimed at improving health (MRC, 2000), several factors may make this approach difficult to achieve (Baum, 1995). Researchers with expertise in qualitative and quantitative methods often have different academic backgrounds and may have a poor understanding of each other’s disciplines. Practical differences in the approach to data collection may complicate the study design. For instance, those collecting qualitative data are likely to require information about which treatment patients are receiving but this may effect arrangements for ‘blinding’ patients and those collecting quantitative data.

Issues concerning the synthesis and interpretation of data are yet to be fully considered. To what extent, and under what circumstances, can the findings of qualitative research inform (or even challenge) the analysis or interpretation of data from the trial? How
do we measure and assess the quality of trials that combine qualitative and quantitative methods? Such questions can only be addressed through conducting and reflecting on the results of further work that combines these methods.

Conclusions

There continues to be a need to extend the evidence base of psychiatry. Clinical trials should play a central part in generating evidence. By combining qualitative and quantitative research methods it may be possible to increase the explanatory power of trials. The collection and analysis of qualitative data can enable the active ingredients of interventions to be explored and provide a more complete description of the process of interventions that take place during a trial. In doing so, qualitative methods may help to ‘close the gap between discovery and implementation’ of new treatments (Jones, 1995) by providing a more complete picture of the content and effects of interventions used in the management of mental disorders.

References


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