ELSEVIER

Social Science & Medicine 61 (2005) 685–695

SOCIAL SCIENCE & MEDICINE

www.elsevier.com/locate/socscimed

Patient preferences in randomised controlled trials: Conceptual framework and implications for research

Peter Bower[a,*], Michael King[b], Irwin Nazareth[c], Fiona Lampe[d], Bonnie Sibbald[d]

[a]*NPCRDC, 5th Floor, Williamson Building, University of Manchester, Manchester M13 9PL, UK*
[b]*Department of Mental Health Sciences, Royal Free and University College Medical School, UK*
[c]*Department of Primary Care and Population Sciences, Royal Free and University College Medical School, UK*
[d]*National Primary Care Research and Development Centre, University of Manchester, Manchester M13 9PL, UK*

Available online 17 February 2005

Abstract

Patient preferences have recently been highlighted as a potential threat to the validity of randomised controlled trials (RCTs). Although there have been significant methodological and statistical developments in relation to these issues, comparatively little attention has been paid to the development of a conceptual model concerning preferences and their effects on decision-making. This article describes the development of such a model, which was undertaken in parallel with a systematic review of the empirical data concerning preference effects. The model describes the concept of preference in terms of theoretical concepts from the psychological and economics literature, and describes a preliminary model of the development and operation of preferences in the context of RCTs. The paper then examines the implications of the model for informed consent and recruitment procedures. Key issues for future research are also outlined.

Keywords: Randomised controlled trials; Preference trials; Methodology; Informed consent

Introduction

Preference-n. a sentiment, or frame of mind, induced by the erroneous belief that one thing is better than another (*Ambrose Bierce—The Devil's Dictionary Bloomsbury*)

The most reliable evidence concerning the effectiveness of health care derives from randomised controlled trials (RCTs) (Sibbald & Roland, 1998). However, there is current interest in the effects of *preferences* for particular interventions on the results of RCTs. Preference effects are traditionally minimised by *blinding* (Day & Altman, 2000; Schulz & Grimes, 2002). However, RCTs are increasingly being used to evaluate interventions that are less amenable to blinding, such as surgical or psychosocial interventions. In these cases, preferences may have important methodological implications. Preferences may interact with random assignment to influence outcome. Patients randomised to their non-preferred intervention may suffer what has been termed *resentful demoralisation* (Cook & Campbell, 1979), which in turn may lead to worse outcomes, either directly (through refusal to adhere to treatment) or indirectly (through a negative placebo-like effect) (Janevic et al., 2003). If such preference–assignment interactions are of significant magnitude, randomising patients with preferences may reduce internal validity by providing a biased estimate of the true effect of an

*Corresponding author. Tel.: +44 161 275 7638; fax: +44 161 275 7600.
E-mail address: peter.bower@man.ac.uk (P. Bower).

0277-9536/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.socscimed.2004.12.010

intervention (Torgerson & Sibbald, 1998). In addition, if patients with preferences do not enter RCTs because of the risk of being randomised to a non-preferred intervention, the results may not be representative, threatening external validity (Britton et al., 1998).

At present, there is disagreement over the magnitude of such 'preference effects', and the optimal way of dealing with the methodological issues raised (Janevic et al., 2003). Some authors have proposed that RCTs should continue to randomise all patients, but that preferences should be measured so that they can be examined in the analysis (Torgerson, Klaber-Moffett, & Russell, 1996). Others propose a more fundamental change (e.g. the 'comprehensive cohort design'), where patients without preferences are randomised, but those with preferences are offered their preferred intervention and followed up in the same way as randomised patients (Brewin & Bradley, 1989). Such an approach has significant implications for trial design, sample size and costs.

Given the current uncertainty, the optimum way of assessing the current evidence concerning preference effects may be through a systematic review of RCTs where a comprehensive assessment could be made of the empirical evidence for the hypothesised effects of preferences on recruitment and patient outcome. Such an empirical review was completed by the present authors (King et al., 2004). However, given the complexity of issues surrounding preference effects, examination of empirical data alone was felt to be insufficient without parallel development of a conceptual framework concerning the nature of preferences, to assist in the interpretation of the results. This conceptual framework is the focus of the current paper, which seeks to:

(a) describe a general model of the development and operation of preferences
(b) consider the implications of this model for RCT methodology

Methods

The databases searched for the empirical review were Medline, Embase, PsycInfo, Cinahl, AMED, and the Cochrane Library. Themes relating to preferences were translated into thesaurus terms and their equivalent text words and phrases (the lack of a precise thesaurus term to describe the concept of preference across all databases hindered the development of the search strategies). These searches were combined with a methodological filter to capture study designs relevant to the empirical review. Database searches were supplemented with hand searching of key journals, contacting experts who had published preference studies, and searching through reference lists.

The development of a conceptual framework differed in form and function from the empirical systematic review (Ashcroft et al., 1997). Firstly, the aim was not to provide an exhaustive analysis of all the available literature, but to identify key papers of theoretical relevance. In addition, key processes used in traditional systematic reviews (i.e. explicit and transparent literature searching strategies, specific inclusion and exclusion criteria, and the application of study quality criteria) are not appropriate for the development of a conceptual framework, where issues of consistency and utility are paramount. Therefore, a less structured approach was taken to the development of the conceptual model. Relevant papers identified from the empirical study were used, but were supplemented with other sources, including the results of preliminary scoping searches undertaken for the main systematic review and the identification of key texts on related issues such as decision-making and trial design. Much of the literature retrieved derived from the disciplines of economics and psychology.

Results of the systematic review

As noted above, the conceptual review was conducted in part to assist in the interpretation of the results of the conventional review of empirical studies. Therefore, the results of the conventional review will be summarised first.

The search identified 34 RCTs described in 44 papers. Most (74%) were comprehensive cohort designs (Brewin & Bradley, 1989). There was no consistent approach to examining preference effects. There was some evidence that preferences could impact on external validity, although the effects were not consistent across studies or generally substantial in magnitude. There was evidence that preferences were related to outcomes in a proportion of studies, but the presence of 'preference effects' was again inconsistent both between and within studies, and even variable in direction (i.e. in some studies patients with preferences had better outcomes, and in some they were worse). Clearly, there is no simple 'preference effect', and the unexplained variation highlights the need for a clear understanding of the nature of preferences, the mechanisms by which they affect behaviour, and the possible influence of contextual factors such as the type of intervention, mode of delivery, and outcomes.

Definition

One dictionary definition of 'prefer' is 'to like something better than another: tend to choose' (Oxford University Press, 2001). This definition highlights the

fact that preferences in the context of RCTs involve two processes: an *evaluation* of an intervention in terms of its desirability; and a *choice* between alternative interventions based on that evaluation. In the model proposed in the current paper, the term 'preference' is restricted to the evaluation and is defined as the difference in the perceived desirability of two (or more) interventions within an RCT. This definition of preference relates to a preference between alternatives and is thus a relative quality.

In economics, the 'desirability' of an intervention can be understood in terms of the concept of *utility*, which refers to a measure of the satisfaction gained from the consumption of a good or service, such as health care (Drummond, Stoddart, & Torrance, 1997). Utility relates to choices between such goods and services, and this includes the notion of sacrifice of one option in order to receive another. In psychology, 'desirability' is most often represented by the concept of *attitude*, defined as 'a disposition to respond favourably or unfavourably to an object, person, institution, or event' (Ajzen, 1988).

Basing the current model of preferences on the concepts of utility and attitude suggests a number of key attributes. Both utility and attitude are concepts which are *global* and *unidimensional*, in that neither provide information on the basis of the evaluation. However, both these concepts are hypothesised to be *quantifiable* i.e. patients can be described as having a specific 'strength' of preference, which may vary from a slight preference which has little substantive importance, through to large preferences which have a major influence on behaviour.

A preliminary model of the development of preferences

The proposed model of the development of preferences is a four-stage model. The four stages are as follows:

1. The first stage concerns the source of preferences i.e. *information* received about interventions in an RCT.
2. The second stage concerns the *processes underlying judgements* about the desirability of the interventions.
3. The third stage concerns the result of these judgment processes, which is a global *preference* for an intervention.
4. The fourth stage represents *patient decision-making about randomisation*. When patients are offered participation in a standard RCT, this concerns the decision whether or not to enter the RCT. In comprehensive cohort designs, where only a proportion of patients will be randomised, this concerns whether patients will agree to be randomised, or choose to have a particular intervention.

The components of the model will be considered in greater detail below.

Judgements about the desirability of the intervention

In economics, individuals have different utility functions, and the arguments of those functions represent the attributes of a commodity that contribute to its overall utility (Mooney, 1994). The overall utility depends on the utility associated with each argument, multiplied by the probability (either objective or subjective) of that argument. In decisions about interventions made under conditions of uncertainty, subjective expected utility is the normative model within economics (Drummond et al., 1997; Wright, 1984) which suggests that preferences will be based on the individual utilities associated with the outcomes of each intervention, multiplied by the probabilities of those outcomes.

Similarly, models of the development of attitudes within psychology are generally based on expectancy–value theory, where 'a person's attitude towards an object is related to his beliefs that the object possesses certain attributes (expectancies) and his evaluations of those attributes (values)' (Ajzen, 1988). This is broadly analogous to the economic model. It should be noted that both these models highlight the importance of *expectancies*, which links with a candidate mechanism for the placebo effect (Crow et al., 1999). This may account for the indirect effect of preferences on outcome mentioned in the introduction.

The nature of expectancies

In economics, the *arguments of the utility* function have been traditionally limited to *outcomes*, because health care is seen as something that has no value in use, but only through the benefits derived from it (Donaldson & Shackley, 1997). Disbenefits such as side effects and other negative health status outcomes may be equally important in relation to some interventions.

Psychological models involve similar outcome expectancies, but also include expectancies about *process* issues (Crow et al., 1999; Donaldson, 2001; Holmes-Rovner et al., 2001), such as personal convenience or financial cost. Arguments have also been made within economics for extending the utility function to consider process issues (Scott & Vick, 1999; Vick & Scott, 1998; Ryan & Farrar, 2000; Donaldson & Shackley, 1997; Donaldson, 2001).

Expectancies concerning process issues will differ from outcomes in that the latter are uncertain, and thus involve notions of *risk* and patients' attitude towards risk (Drummond et al., 1997). In contrast, there may be little or no uncertainty related to the process of a defined intervention in an RCT.

One particularly important process expectancy highlighted by psychological theory is *self-efficacy* (Conner & Sparks, 1996; Bandura, 1997). This relates to the belief that particular behaviours required to use an intervention are within the capabilities of the individual. Self-efficacy is theoretically distinct from outcome expectancies, and there is good evidence that self-efficacy is an important predictor of health-related behaviour (Schwarzer & Fuchs, 1996). Self-efficacy expectancies may be of greater relevance in those interventions where the patient is a more active participant.

The nature of values

The second aspect of the expectancy–value calculation is the value patients place on particular processes and outcomes. Compared to the amount of research on the expectancy aspect of decision-making, values have received relatively little attention. This may be due to their inherently personal nature: 'who knows better than an individual what he or she prefers' (Fischoff, Goitein, & Shapira, 1982). Although both the expectancies and the values involved in the decision-making of an individual may be subjective, certain aspects of expectancy do have more objective referents (such as outcome expectancies that might be derived from research, or the known process attributes of an intervention). However, even if the process and outcome of interventions within an RCT are standardised, patient perceptions of the value of different aspects of process and outcome may vary in relation to their own characteristics and experience.

Information about interventions

Information about interventions may derive from a number of sources (both from within and outside the RCT context). According to the preliminary model, this information will lead to various expectancies about the process and outcome of an intervention.

A critical distinction in the present context concerns the *validity* of these different expectancies, which in turn relates to the nature of the information on which they are based. Some authors have cautioned that a distinction needs to be made between *informed choices*, in which 'patients rely on the estimates of the size of risks and benefits of proposed interventions, as reported in reliable overviews' and *subjective preferences*, 'in which patients ignore the available evidence and prefer to rely on prayer, on a hunch, or the advice of friends, relatives or seers for a decision' (Silverman & Altman, 1996, pp. 173–174).

There is sufficient evidence of patient (and professional) difficulty in making sense of important issues such as risk to provide some support for such a crude distinction (Wright, 1984; Edwards & Bastian, 2001), and preferences may be related to mistaken views or misinformation that simply do not reflect the actual process or outcome associated with interventions (Kerr et al., 2003). Strict distinctions between 'valid' and 'invalid' may be especially relevant for process expectancies, because interventions have certain objectively defined process attributes, and patients' understanding and knowledge of these can be assessed relatively easily and compared against the actual process.

However, a number of caveats exist to any distinction concerning the validity of preferences. Importantly, any distinction between preferences made on the basis of the validity of the underlying expectancies may not influence the eventual impact of those preferences, because the strength of the preference may be critical, not the 'validity' of the expectancies on which it is based.

However, patient preferences may differ from those 'reported in reliable overviews', yet still be rational, for a number of reasons. RCTs are ideally conducted where there is *clinical equipoise* i.e. where a rational, informed person has no preference between two available interventions (Chard & Lilford, 1998), and where the choice between two interventions cannot be made on the basis of health outcomes. However, clinical equipoise does not take into account differences in the process of intervention. In addition, patients' outcome expectancies may be based on *personal subjective* expectancies, such as the belief that an intervention is particularly suited to them as an individual, which might contradict research evidence suggesting that the *average* effect is zero. Thirdly, the proposed expectancy–value model has two sources for preferences: expectancies and values, and as noted earlier the latter are inherently subjective (Fischoff et al., 1982). This has important implications for changing preferences through information. Some preferences may be responsive to information, as factually incorrect expectancies may be relatively easy to address. However, some preferences may be less amenable to change through provision of information, since the preference may be determined more by the value associated with that aspect of the intervention.

In summary, the relationships between expectancies, values and preferences are complex, and there are a number of cases where simple distinctions between 'informed' and 'uninformed' preferences are unhelpful. It may make more sense to distinguish 'informed expectancies', where there is evidence that patients have received sufficient information, clear inaccuracies have been corrected, and patients have had time to consider this information in order to make a judgement based on their expectancies and the values they place on them. However, the precise definition of 'informed expectancies' is likely to be controversial.

Decision-making about randomisation

The earlier definition of preferences and the preliminary model both make a distinction between patients' preferences and actual decision-making about randomisation. Preferences are generally expected to influence decisions about randomisation, but not determine them. In one RCT, 82% of patients willing to enter a comprehensive cohort study agreed to be randomised, but 80% reported having a preference after randomisation (Ashok et al., 2002). Distinguishing between preferences and decisions is important: when patients make randomisation decisions that conflict with their preferences, those preferences could still influence outcomes, and thus threaten the validity of the trial.

It is beyond the scope of the present paper to consider the wide variety of influences that may impact on decisions to take part in an RCT (Hjorth, Holmberg, Rodjer, Taube, & Westin, 1996; Verheggen, Nieman, & Jonkers, 1998; Ross et al., 1999; Senore et al., 1999; Taylor, Margolese, & Soskolne, 1984). However, the current model proposes that the decision to agree to randomisation can be understood as a second expectancy–value calculation. Participation in the RCT will have utility for patients, one source of which is the strength of their overall preference, multiplied by the likelihood of receiving a particular intervention (i.e. 50% in a 2 arm RCT).

An important contextual effect on this calculation concerns the availability of the preferred intervention outside the RCT (Janevic et al., 2003). If the intervention is available outside the RCT, then the issue is one of potential loss of access, and associated loss of utility, if patients agree to randomisation. If the intervention is not available outside the RCT, then the issue is one of potential gain.

This basic model suggests an important distinction. Some influences on patient decisions about participation in an RCT may cause patients to make a decision in contradiction of preferences by compensating any potential utility loss with additional utility gains from elsewhere. For example, patients may gain utility through engaging in an altruistic act, such as agreeing to be randomised to promote scientific knowledge (Holmes-Rovner & Wills, 2002). However, if patients' decisions about randomisation are not compensated with other utility gains, then the decision may be more problematic, especially if it represents coercion.

Limitations of the proposed model

Fig. 1 shows a more detailed version of the model. As noted earlier, the proposed model is based on generic models of decision-making within economics and psychology, although it does not exhaust the full range of models even within those disciplines. For example, alternatives have been offered, such as prospect theory

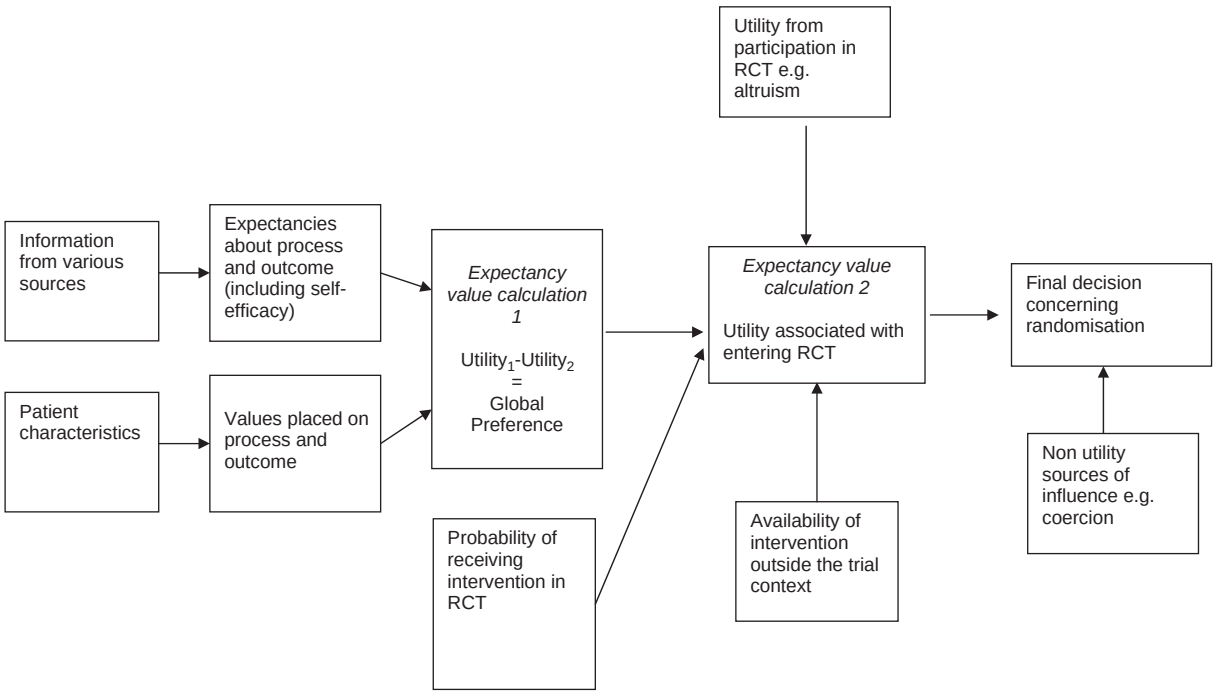

Fig. 1. A model of patient preference and decision-making.

(Kahneman & Tversky, 1979) and regret theory (Loomes & Sugden, 1982). Particular models may have relevance in particular contexts, depending on the type of intervention, patient population and outcome.

Models of decision-making developed within economics are generally normative models, in that they are concerned with how people might *best* make decisions, not how they actually do make them. Their relevance to routine decision-making has been questioned (Naylor & Llewellyn-Thomas, 1998; Dolan, 1997). Psychological models also have this normative basis, although the addition of variables such as self-efficacy represents an attempt to provide more descriptive models. However, the image of the *rational*, *individual* decision maker still dominates models from these disciplines. Each of these attributes has important limitations.

In contrast to the focus on *rationality*, research has indicated that there may well be an important emotional component to decision-making that is overlooked by normative models (Feather, 1982). This may be especially important in certain disorders, such as the influence of negative mood on perceptions of the probability of benefit or harm in depressed patients (Shafir & LeBoeuf, 2002). In addition, certain interventions may raise particular emotions which may have a profound effect e.g. surgery (Ubel & Loewenstein, 1997). Some of these emotional influences may be captured by the current model. For example, depressed patients may have an increased expectancy of the likelihood of negative effects of an intervention, which would decrease their perceived preference according to Fig. 1. Alternatively, if an aspect of an intervention is particularly feared (e.g. surgical procedures), that could be captured by a particularly high negative value being associated with that attribute. However, it is unlikely that the full range of possible emotions of relevance in decision making about interventions (such as disappointment or anxiety concerning uncertainty) can be adequately captured or understood in such terms (Ubel & Loewenstein, 1997), and generally, expectancy–value theories have viewed emotion as a peripheral issue rather than a central determinant of decision-making (Feather, 1982). Future developments may need to place emotions in a more central position in the model.

Secondly, the image of the *individual* decision-maker may pay too little attention to the social context in which decisions are made. Decisions about interventions may involve influences from professionals, peers and family (Kuczewski & Marshall, 2002; O'Connor et al., 2002). The influence of professionals is especially interesting, as there is an issue of the possible operation of *professional preferences*, which may be mediated through interaction with patients, as well as more directly. At present, the model considers social influences as occurring either through the provision of information (which determines expectancies), or through other sources of influence on the randomisation decision (e.g. coercion). Again, this is unlikely to do justice to the full range of possible social influences, which may include complex issues concerning social roles, power and authority (Kuczewski & Marshall, 2002). Such social influences may be particularly important in particular contexts (e.g. vulnerable or disempowered groups) or with certain types of interventions (e.g. those which can have an impact on the wider family).

Finally, the current model is a static one, in which preference formation and decision-making are seen as relatively discrete events. However, little is known about the *stability* of preferences over time. Current models of preference effects hypothesise that preferences developed before receiving an intervention will have potential influences after the intervention is received. However, it is possible that initial expectancies and values will change after experience with the intervention, which has very important implications for preference effects. This is likely to be especially important in relation to novel interventions where previous patient experience is lacking, and the gap between expectancy and experience may be particularly marked.

Patient preferences in RCTs—preference elicitation and informed consent procedures

The model developed in the previous section suggests that patients entering an RCT can be characterised along three distinct dimensions.

1. whether the expectancies on which preferences are based are 'informed';
2. whether patients have preferences or are in a condition of equipoise;
3. whether patients are willing to accept randomisation.

Each of these individual dimensions highlights a potential problem for the effective administration and interpretation of RCTs. If expectancies do not meet some criteria for being 'informed', then recruitment and randomisation of patients may be unethical. If patients do have strong preferences, then outcomes may be biased if these interact with outcomes. Finally, if patients refuse randomisation because of their preferences, then recruitment to the trial may be both delayed and biased. In addition, the *combination* of these dimensions can define particular types of patients who may raise particular issues. For example, any patient who does not have 'informed' expectancies is problematic from an ethical standpoint, but if they are in equipoise and agree to randomisation they are not problematic for those solely concerned about

recruitment. Among patients with 'informed expectancies', those who are not in equipoise but agree to randomisation are potentially problematic both ethically and in terms of interpretation of the results, but do not cause difficulties for recruitment. Identifying such types of patients may be important when interpreting RCT data.

Informed consent and 'informed expectancies'

As noted above, any informed consent procedure should ensure that patients at least meet the criteria for 'informed expectancies', as broadly defined earlier. In the context of preference effects, one of the most basic issues relates to those patients who enter RCTs with clearly inaccurate expectancies (i.e. ideas about the process of an intervention that do not reflect the actual intervention they will receive). In these cases, such problems may be addressed by provision of more detailed information during informed consent procedures, making sure that the information is understandable to patients and unbiased. A recent study described how ostensibly neutral descriptions (i.e. 'watchful waiting') could be interpreted negatively by patients as an expectancy of relative neglect (Donovan et al., 2002b), and pilot qualitative research may assist in these cases (Halpern, 2002). The major technical limitation in such cases may relate to concerns about the ability of patients to comprehend information relating to interventions (Ubel, 2002; Say & Thomson, 2003). There may be limits to the utility of written information alone (Tinsley, Bowman, & Ray, 1988), and more complex approaches (such as multimedia or interactive presentations) might be more helpful, especially where interventions are novel. There is also an obvious agenda relating to the training of clinicians and researchers involved in informed consent procedures (Towle & Godolphin, 2001).

In the psychological therapy literature, significant effort was expended in developing placebo psychological therapy interventions, and it was deemed necessary to check that both the active therapy and the placebo were perceived by patients as equally potentially efficacious (Parloff, 1986; Tinsley et al., 1988). Therefore, an additional step might involve checking the effects of information by assessing patient expectancies before and after the provision of information to ensure it has had the desired effect.

A gold standard model of the sequence and content of informed consent procedures in cancer trials has recently been described. This sequence involves *bearings* (developing a shared understanding of the illness); a discussion of standard treatment outside the trial, followed by processes of *amplification* (discussion of information received about the standard treatment), *declaration* (of the clinician's treatment recommendation) and finally *enunciation* (patient articulation of their decision concerning standard treatment). This is then followed by a discussion of the clinical trial and the interventions available within that, with the same sequence of events followed by *enactment* of the decision (Brown, Butow, Ellis, Boyle, & Tattersall, 2004; Brown, Butow, Butt, Moore, & Tattersall, 2004).

The complexity of this model highlights a distinction that has been made between *patient education materials* (which seek to provide information and increase knowledge) and *decision support* (which seeks to provide information, clarify values, and augment skills in decision-making) (O'Connor et al., 2002; Elwyn & Charles, 2001). Traditional informed consent procedures may have been more concerned with the former, whereas decision support in the context of RCTs might involve a specific preference elicitation interview, involving systematic consideration of stages 2 and 4 in the model described earlier. Stage 2 would involve systematic assessment of the utility associated with each intervention, with assessment of the expectancies and explicit integration of expectancies with patient values. Stage 4 would involve a specific check that the decision about randomisation reflects these preferences, and has not been vulnerable to coercion or other influences. Such an approach could be placed within the structure of the model informed consent procedure discussed above, and would require specific skills on the part of the professionals involved (Elwyn & Charles, 2001). Only patients without a preference between alternative interventions, or with only minor preferences within reasonable boundaries (Lilford et al., 2001; Chard & Lilford, 1998), would be judged as eligible for randomisation. Such a model approaches formal decision analysis (O'Connor et al., 2004; Ubel & Loewenstein, 1997) and there is no *theoretical* reason why such procedures could not be used, although the practical barriers are considerable. Key skills required for decision support have already been identified and may have important implications for informed consent procedures in the future (Elwyn & Charles, 2001).

There may be ethical concerns about modifications of informed consent procedures (e.g. specially designed information sheets) which have the *aim* (implicit or explicit) of increasing participation rates, because the assumption is that participation in the RCT is the optimal decision for the patient and that low rates of participation are suboptimal per se, as opposed to simply problematic for researchers (Lilford, 2003; Lilford et al., 2001). The definition of a 'good' outcome in terms of the decision-making problems faced by patients in RCTs is complex (O'Connor et al., 2002) and there is no reason why the perspectives of clinicians, patients and researchers should agree. A recent RCT of a controversial intervention used qualitative research to

examine the consent procedures, and iterative methods were used to further refine information sources used during consent procedures and to train researchers involved in allocating patients (Donovan et al., 2002b; Mills et al., 2003). This improved the percentage of patients willing to be randomised, but the authors themselves suggested that these improvements could reflect either better consent procedures or increasing coercion (although other confounds are possible in this study design). Nevertheless, the importance of encouraging expressions of equipoise in research staff has been highlighted (O'Connor et al., 2002; Zimbroff, 2001).

However, the adoption of more complex informed consent procedures may also have untoward effects. It may mean that patients without pre-existing preferences develop preferences during this procedure. Although much of the relevant research has been conducted in laboratory settings and may not be generalisable, there is evidence that preferences may not have an independent existence, but may be 'constructed' by the nature of their elicitation (Fischoff, Slovic, & Lichtenstein, 1980; Shafir & LeBoeuf, 2002; Fischoff et al., 1982), and vulnerable to so-called 'framing effects' such as the order of presentation of information (Donovan et al., 2002b). Although it may be assumed that providing information would increase the proportion of 'well-informed' people who have no strong preferences and thus are eligible to be randomised (McPherson & Chalmers, 1998), more complex preference elicitation techniques might *reduce* the sample willing to be randomised (Lilford, 2003; Lilford et al., 2001). There is some evidence from RCTs of informed consent procedures that there is an optimal level of information, and that increasing amounts of information can reduce recruitment rates (Edwards, Lilford, Thornton, & Hewison, 2003). Furthermore, the external validity of studies might be reduced if patients in the RCT have more information, and thus different preferences, from those who receive the intervention in routine care settings. However, where framing issues and other potential effects raise a tension between the methodological and ethical issues in an RCT, it is expected that ethical issues will generally take precedence in the current context of health care research.

The results of the empirical review in the context of the preliminary conceptual model

As noted previously, the empirical review found that the presence, magnitude and direction of preference effects were inconsistent. The development of the conceptual model has indicated some candidate hypotheses, which may account for this variation. For example, it is possible that measures of preference included in previous studies have failed to consider both process and outcome issues, which would make measures less valid and potentially mask preference effects. Studies (such as comprehensive cohort designs) which use a single dichotomous measure of preference may have failed to consider variation in the *strength* of preference, as preference effects may only occur when preferences are particularly marked. Initial preferences may also be a poor predictor of outcomes if they change rapidly with initial experience of the intervention, and there has been little consideration of the *stability* of preferences in the context of such experience. Finally, the model suggests that patients may agree to randomisation even if they have preferences concerning the interventions. Failure to identify such patients during the analysis would also tend to attenuate relationships.

Conclusion

As noted earlier, the model is proposed as a general framework for conceptualising preferences in RCTs and is not definitive. Further theoretical and empirical work is required to extend and test it. Nevertheless, the model has some utility in encouraging consideration of the complex issues concerning the nature and impact of preferences, and the implications for RCT design.

The research agenda relating to preferences is significant in scope. One obvious need is for further qualitative research on the process of preference formation and decision-making in RCTs (Donovan, Brindle, & Mills, 2002a; Featherstone & Donovan, 1998; Mills et al., 2003), with a specific focus on issues such as emotions and social context which are neglected in the model. Such work might be usefully complemented by quantitative approaches such as discrete choice experiments (Ryan & Farrar, 2000) to further illuminate the processes by which patients judge alternative interventions and weigh up the importance of process and outcome issues.

It is beyond the scope of the present review to consider issues of preference measurement in any detail, but accurate assessment of the impact of preferences is obviously dependent on valid and reliable methods of measurement. The current model has provided some indication of important issues to consider in the development of measures.

Whatever future research is conducted, it is also necessary to acknowledge that the issue of preferences in RCTs highlights one of the key tensions at the heart of health care, between the desire to provide interventions of proven efficacy and cost effectiveness, and the current emphasis on patient choice. In both routine health care delivery and the context of RCTs, it is necessary to find a balance between increasing patient autonomy and choice, and ensuring that the delivery of essential research evidence is not hampered.

Acknowledgements

The authors would like to acknowledge Rosalind Lai, Medical Librarian, Royal Free and University College Medical School, and Martin Chandler and Maria Morou, research assistants, Department of Mental Health Sciences, Royal Free and University College Medical School, for their assistance with the review, and the referees and editor for their comments on an earlier draft. The systematic review on which this paper was based, was funded by the United Kingdom Health Technology Assessment Program, Grant 98/26/03.

References

Ajzen, I. (1988). *Attitudes, personality and behaviour*. Milton Keynes: Open University Press.

Ashcroft, R., Chadwick, D., Clark, S., Edwards, R., Frith, L., & Hutton, J. (1997). Implications of sociocultural contexts for the ethics of controlled trials. *Health Technology Assessment*, *1*(9).

Ashok, P., Kidd, A., Flett, G., Fitzmaurice, A., Graham, W., & Templeton, A. (2002). A randomized comparison of medical abortion and surgical vacuum aspiration at 10–13 weeks gestation. *Human Reproduction*, *17*(1), 92–98.

Bandura, A. (1997). *Self-efficacy: the exercise of control*. New York: W.H. Freeman and Company.

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

Britton, A., McKee, M., Black, N., McPherson, K., Sanderson, C., & Bain, C. (1998). Choosing between randomised and non-randomised studies: a systematic review. *Health Technology Assessment*, *2*(13).

Brown, R., Butow, P., Butt, D., Moore, A., & Tattersall, M. (2004). Developing ethical strategies to assist oncologists in seeking informed consent to cancer clinical trials. *Social Science and Medicine*, *58*, 379–390.

Brown, R., Butow, P., Ellis, P., Boyle, F., & Tattersall, M. (2004). Seeking informed consent to cancer clinical trials: describing current practice. *Social Science and Medicine*, *58*, 2445–2457.

Chard, J., & Lilford, R. (1998). The use of equipoise in clinical trials. *Social Science and Medicine*, *47*(7), 891–898.

Conner, M., & Sparks, P. (1996). The theory of planned behaviour and health behaviours. In M. Conner, & P. Norman (Eds.), *Predicting health behaviour: research and practice with social cognition models* (pp. 121–162). Buckingham: Open University Press.

Cook, T., & Campbell, D. (1979). *Quasi-experimentation—design and analysis issues for field settings*. Chicago: Rand McNally.

Crow, R., Gage, H., Hampson, S., Hart, J., Kimber, A., & Thomas, H. (1999). The role of expectancies in the placebo effect and their use in the delivery of health care: a systematic review. *Health Technology Assessment*, *3*(3).

Day, S., & Altman, D. (2000). Blinding in clinical trials and other studies. *British Medical Journal*, *321*, 504.

Dolan, P. (1997). The nature of individual preferences: a prologue to Johannesson, Jonsson and Karlsson. *Health Economics*, *6*, 91–93.

Donaldson, C. (2001). Eliciting patients' values by use of 'willingness to pay': letting the theory drive the method. *Health Expectations*, *4*, 180–188.

Donaldson, C., & Shackley, P. (1997). Does 'process utility' exist? a case study of willingness to pay for laparoscopic cholecystectomy. *Social Science and Medicine*, *44*(5), 699–707.

Donovan, J., Brindle, L., & Mills, N. (2002a). Capturing users' experiences of participating in cancer trials. *European Journal of Cancer Care*, *11*, 210–214.

Donovan, J., Mills, N., Smith, M., Brindle, L., Jacoby, A., Peters, T., Frankel, S., Neal, D., & Hamdy, F. (2002b). Improving design and conduct of randomised trials by embedding them in qualitative research: ProtecT (prostate testing for cancer and treatment) study. *British Medical Journal*, *325*, 766–770.

Drummond, M., Stoddart, G., & Torrance, G. (1997). *Methods for the economic evaluation of health care programmes*. Oxford: Oxford Medical Publications.

Edwards, A., & Bastian, H. (2001). Risk communication—making evidence part of patient choices. In A. Edwards, & G. Elwyn (Eds.), *Evidence-based patient choice* (pp. 144–160). Oxford: Oxford University Press.

Edwards, S., Lilford, R., Thornton, J., & Hewison, J. (2003). Informed consent for clinical trials: in search of the 'best' method. *Social Science and Medicine*, *47*(11), 1825–1840.

Elwyn, G., & Charles, C. (2001). Shared decision making: the principles and the competences. In A. Edwards, & G. Elwyn (Eds.), *Evidence-based patient choice* (pp. 118–143). Oxford: Oxford University Press.

Feather, N. (1982). Expectancy–value approaches: present status and future directions. In N. Feather (Ed.), *Expectations and actions: expectancy–value models in psychology* (pp. 395–420). Hillsdale: Lawrence Erlbaum.

Featherstone, K., & Donovan, J. (1998). Random allocation or allocation at random? Patients' perspectives of participation in a randomised controlled trial. *British Medical Journal*, *317*, 1177–1180.

Fischoff, B., Goitein, B., & Shapira, Z. (1982). The experienced utility of expected utility approaches. In N. Feather (Ed.), *Expectations and actions: expectancy–value models in psychology* (pp. 315–339). Hillsdale: Lawrence Erlbaum.

Fischoff, B., Slovic, P., & Lichtenstein, S. (1980). Knowing what you want: measuring labile values. In T. Wallsten (Ed.), *Cognitive processes in choice and decision behaviour* (pp. 117–141). Hillsdale: Lawrence Erlbaum.

Halpern, S. (2002). Prospective preference assessment: a method to enhance the ethics and efficiency of randomized controlled trials. *Controlled Clinical Trials*, *23*, 274–288.

Hjorth, M., Holmberg, E., Rodjer, S., Taube, A., & Westin, J. (1996). Physicians' attitudes towards clinical trials and their relationship to patient accrual in a Nordic Multi-Center Study on myeloma. *Controlled Clinical Trials*, *17*, 372–386.

Holmes-Rovner, M., Llewellyn-Thomas, H., Entwistle, V., Coulter, A., O'Connor, A., & Rovner, D. (2001). Patient

choice modules for summaries of clinical effectiveness: a proposal. *British Medical Journal*, *322*, 664–667.

Holmes-Rovner, M., & Wills, C. (2002). Improving informed consent: insights from behavioural decision research. *Medical Care*, *40*(9), V-30–V-38.

Janevic, M., Janz, N., Dodge, J., Lin, X., Pan, W., Sinco, B., & Clark, N. (2003). The role of choice in health education intervention trials: a review and case study. *Social Science and Medicine*, *56*, 1581–1594.

Kahneman, D., & Tversky, A. (1979). Prospect theory: analysis of decisions under risk. *Econometrica*, *47*, 263–291.

Kerr, C., Robinson, E., Lilford, R., Edwards, S., Braunholtz, D., & Stevens, A. (2003). The impact of describing clinical trial treatments as new or standard. *Patient Education and Counseling*, *53*(1), 107–113.

King, M., Nazareth, I., Lampe, F., Bower, P., Chandler, M., Morou, M., Sibbald, B., & Lai, R. (2004). *Conceptual framework and systematic review of the effects of participants' and professionals' preferences in randomised controlled trials*. Unpublished report to the NHS Health Technology Assessment Programme (project 98/26/03), Royal Free and University College Medical School, unpublished.

Kuczewski, M., & Marshall, P. (2002). The decision dynamics of clinical research: the context and process of informed consent. *Medical Care*, *40*(9), V-45–V-54.

Lilford, R. (2003). Ethics of clinical trials from a bayesian and decision analytic perspective: whose equipoise is it anyway? *British Medical Journal*, *326*, 980–981.

Lilford, R., Edwards, S., Braunholtz, D., Jackson, J., Thornton, J., & Hewison, J. (2001). Ethical issues in the design and conduct of randomised controlled trials. In A. Stevens, K. Abrams, J. Brazier, R. Fitzpatrick, & R. Lilford (Eds.), *The advanced handbook of methods in evidence based healthcare* (pp. 11–24). London: Sage Publications.

Loomes, G., & Sugden, R. (1982). Regret theory: an alternative theory of rational choice under uncertainty. *Economic Journal*, *92*, 805–824.

McPherson, K., & Chalmers, I. (1998). Information about patients' preferences must be obtained first (letter). *British Medical Journal*, *317*, 78.

Mills, N., Donovan, J., Smith, M., Jacoby, A., Neal, D., & Hamdy, F. (2003). Perceptions of equipoise are crucial to trial participation: a qualitative study of men in the ProtecT study. *Controlled Clinical Trials*, *24*, 272–283.

Mooney, G. (1994). *Key issues in health economics*. Hemel Hempstead: Harvester Wheatsheaf.

Naylor, D., & Llewellyn-Thomas, H. (1998). Utilities and preferences for health states: time for a pragmatic approach. *Journal of Health Services Research and Policy*, *3*(3), 129–131.

O'Connor, A., Stacey, D., Rovner, D., Holmes-Rovner, M., Tetroe, J., Llewellyn-Thomas, H., Entwistle, V., Rostom, A., Fiset, V., Barry, M., & Jones, J. (2004). *Decision aids for people facing health treatment or screening decisions (Cochrane Review), Issue 2*. Chichester: John Wiley and Sons.

O'Connor, A., Tugwell, P., Wells, G., Elmslie, T., Jolly, E., Hollingworth, G., McPherson, R., Bunn, H., Graham, I., & Drake, E. (2002). A decision aid for women considering hormone therapy after menopause: decision support framework and evaluation. *Patient Education and Counseling*, *33*(3), 267–279.

Oxford University Press. (2001). *Concise Oxford dictionary*. Oxford: Oxford University Press.

Parloff, M. (1986). Placebo controls in psychotherapy research: a sine qua non or a placebo for research problems? *Journal of Consulting and Clinical Psychology*, *54*(1), 79–87.

Ross, S., Grant, A., Counsell, C., Gillespie, W., Russell, I., & Prescott, R. (1999). Barriers to participation in randomised controlled trials: a systematic review. *Journal of Clinical Epidemiology*, *52*(12), 1143–1156.

Ryan, M., & Farrar, S. (2000). Using conjoint analysis to elicit preferences for health care. *British Medical Journal*, *320*, 1530–1533.

Say, R., & Thomson, R. (2003). The importance of patient preferences in treatment decisions—challenges for doctors. *British Medical Journal*, *327*, 542–545.

Schulz, K., & Grimes, D. (2002). Blinding in randomised trials: hiding who got what. *Lancet*, *359*, 696–700.

Schwarzer, R., & Fuchs, R. (1996). Self efficacy and health behaviours. In M. Conner, & P. Norman (Eds.), *Predicting health behaviour: research and practice with social cognition models* (pp. 163–196). Buckingham: Open University Press.

Scott, A., & Vick, S. (1999). Patients, doctors and contracts: an application of principal-agent theory to the doctor–patient relationship. *Scottish Journal of Political Economy*, *46*(2), 111–134.

Senore, C., Battista, R., Ponti, A., Segnan, N., Shapiro, S., Rosso, S., & Aimar, D. (1999). Comparing participants and nonparticipants in a smoking cessation trial: selection factors associated with general practitioner recruitment activity. *Journal of Clinical Epidemiology*, *52*(1), 83–89.

Shafir, E., & LeBoeuf, R. (2002). Rationality. *Annual Review of Psychology*, *53*, 491–517.

Sibbald, B., & Roland, M. (1998). Why are randomised controlled trials important? *British Medical Journal*(316), 201.

Silverman, W., & Altman, D. (1996). Patients' preferences and randomised trials. *Lancet*, *347*, 171–174.

Taylor, K., Margolese, R., & Soskolne, C. (1984). Physician's reasons for not entering eligible patients in a randomised clinical trial of surgery for breast cancer. *New England Journal of Medicine*, *310*, 1363–1370.

Tinsley, H., Bowman, S., & Ray, S. (1988). Manipulation of expectancies about counselling and psychotherapy: review and analysis of expectancy manipulation strategies and results. *Journal of Counseling Psychology*, *35*(1), 99–108.

Torgerson, D., Klaber-Moffett, J., & Russell, I. (1996). Patient preferences in randomised trials: threat or opportunity? *Journal of Health Services Research and Policy*, *1*(4), 194–197.

Torgerson, D., & Sibbald, B. (1998). What is a patient preference trial? *British Medical Journal*, *316*, 360.

Towle, A., & Godolphin, W. (2001). Education and training of health professionals. In A. Edwards, & G. Elwyn (Eds.), *Evidence-based patient choice* (pp. 245–269). Oxford: Oxford University Press.

Ubel, P. (2002). Is information always a good thing? helping patients make 'good' decisions. *Medical Care*, *40*(9), V-39–V-44.

Ubel, P., & Loewenstein, G. (1997). The role of decision analysis in informed consent: choosing between intuition and systemasticity. *Social Science and Medicine*, *44*, 647–656.

Verheggen, F., Nieman, F., & Jonkers, R. (1998). Determinants of patient participation in clinical studies requiring informed consent: why patients enter a clinical trial. *Patient Education and Counseling*, *35*, 111–125.

Vick, S., & Scott, A. (1998). Agency in health care. Examining patients' preferences for attributes of the doctor–patient relationship. *Journal of Health Economics*, *17*, 587–605.

Wright, G. (1984). *Behavioural decision theory: an introduction*. Harmondsworth: Penguin.

Zimbroff, D. (2001). Patient and rater education of expectations in clinical trials (PREECT). *Journal of Clinical Psychopharmacology*, *21*(2), 251–252.