

### What is already known on this topic

Debate has focused on whether it is beneficial to withhold the artificial administration of fluids and food from patients with advanced dementia

### What this study adds

The course of dementia, the patient's quality of life, and the patient's current medical condition influence doctors' decision making more than advanced planning of care

Doctors try to create the broadest possible basis for the decision making process and its outcome, mainly by involving the family

withhold the artificial administration of fluids and food. Patients' living wills seemed of limited importance, but policy agreements were useful in the decision making process and for dialogue with the family. In the end the medical condition of the patient, the wishes of the family, and the interpretations of the patients' quality of life by their care providers were the most important criteria for withholding the artificial administration of fluids and food.

Doctors are constantly faced with uncertainties about what the patient wants. To reduce this uncertainty they try to create the broadest possible

basis for the decision making process and its outcome, mainly by involving the family.

The two illness trajectories had different contexts and concerned different professionals. The second trajectory was characterised by medical decision making by doctors. The first trajectory, characterised by care from nursing staff, seemed the most vulnerable to continuity of care, communication problems, and scarcity of staff.

We identified repeated patterns of decision making. We assume our findings are generalisable because the patterns were observed in two nursing homes in different regions and by two researchers working independently. Further ethnographic research is needed to confirm the generalisability of our findings.<sup>2</sup>

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## Informing participants of allocation to placebo at trial closure: postal survey

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### Abstract

**Objectives** To assess whether and how investigators of placebo controlled randomised trials inform participants of their treatment allocation at trial closure and to assess barriers to feedback.

**Design** Postal survey with a semistructured questionnaire.

**Participants** All investigators who published a placebo controlled randomised trial in 2000 in five leading medical journals, and a random sample of 120 trials listed in the national research register database.

**Main outcome measures** Number of investigators who informed participants of their treatment allocation at trial closure, methods for delivering the information, and barriers to unmasking treatment.

**Results** 45% of investigators informed either all or most participants of their treatment allocation, and 55% did not inform any participant or only informed those who asked. The main reasons for not informing participants were that the investigators never considered this option (40%) or to avoid biasing results at study follow up (24%).

**Conclusion** Further research is required to examine sensitive ways to communicate treatment information to trial participants.

### Introduction

In 1948 the Medical Research Council introduced a new experimental design to deal with therapeutic uncertainties.<sup>1</sup> The randomised controlled trial aimed to ensure the absence of systematic differences between treatment and control groups.<sup>2</sup> Placebos—surrogates for a control group receiving no treatment—were gradually adopted to act as dummy therapies to mimic the experimental treatment in appearance but not in substance or chemical structure.<sup>3</sup> Placebos helped patient retention and allowed the consequences of attention, expectation, suggestion, and natural course to be separated from the effects of the experimental treatment.

In March 2001 the Department of Health issued a research governance framework to ensure that the public could have confidence in, and benefit from, quality research.<sup>4</sup> Although the report states that the principal investigator should feed back results to participants, it does not explicitly discuss unmasking treatment allocation. We examined the extent to which recently conducted trials conform to some of the recommendations of the research governance framework and whether investigators of placebo controlled clinical trials inform participants of their treatment arm.



This is an abridged version; the full version is on [bmj.com](http://bmj.com)

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## Methods

We searched Medline to identify all placebo controlled randomised clinical trials published in 2000 in five leading medical journals: *Annals of Internal Medicine*, *BMJ*, *JAMA*, *Lancet*, and *New England Journal of Medicine*. Our search strategy was based on the fourth report developed by the NHS Centre for Reviews and Dissemination (see [bmj.com](http://bmj.com)).<sup>5</sup> We also searched the national research register.<sup>6</sup> We were able to select a random sample of commercially funded and non-commercially funded trials. We sent the investigators a letter outlining our aims, along with a short semistructured questionnaire. To increase the response rate we sent out letters to coauthors and two reminders.

## Results

Overall, we identified 92 placebo controlled randomised trials. By using the term “placebo” in the national research register, we identified 1973 completed trials. We selected a random sample of 60 commercial and 60 non-commercial trials.

The total response rate was 66% (139 of 212). Of the investigators who responded, 23% (32 of 139) were unable to complete the questionnaire (see [bmj.com](http://bmj.com)). These were mostly investigators of trials published in the register. One hundred and seven investigators completed the questionnaire. Of these, 48 informed either all (n=40) or most participants (n=8) of their treatment allocation; 53 did not inform any of their participants, and 6 informed only those who asked.

Investigators of trials selected from the national research register or commercially funded trials were less likely to inform participants than investigators of trials published in a leading journal or investigators of trials not funded commercially (see [bmj.com](http://bmj.com)).

### Informing participants of treatment arm

Participants were generally informed in person (23 of 48, 48%), by post (12 of 48, 25%), or by telephone (4 of 48, 8%). In five cases more than one method was used and in four cases investigators did not indicate how they informed patients. Information about treatment arm (in person or by telephone, n=32) was usually delivered by a nurse (8, 25%), the investigator (7, 22%), a doctor (5, 16%), or more than one professional (12, 38%). The most common method for informing those randomised to placebo was to simply tell them they were in the placebo arm (54%) or to give them a common definition of placebo effects (21%) (table).

A few investigators advised patients to follow up this result with their doctor or gave them the opportunity to ask questions or to discuss the option of

the active treatment. In one instance the investigator did not know because “the actual message was given at the discretion of the physician.” Some of the studies used a crossover design and patients were simply told they received both a placebo and an active treatment. In one of these studies, patients were also told that if they responded to placebo this probably resulted from being in a trial and the positive effects of placebo. In three cases, investigators explained the effect as a result of spontaneous remission.

### Reasons for not informing participants of treatment arm

Overall, 53 investigators never informed any of their trial participants about treatment allocation. The most common reasons were that they never considered this option (21, 40%) or that they wanted to avoid biasing results at study follow up (12, 23%), often referring to studies that were still ongoing. Eight investigators wanted to avoid extra costs and six wanted to avoid both extra costs and administrative work. Six investigators believed that participants did not need to know; two explained that this was because of the crossover nature of the study. In three cases participants had died, and in single instances participants were not informed to avoid interfering with the doctor-patient relationship, as it was “rather old news,” to avoid distressing or upsetting patients, and because it was not part of the methodology. Difficulty in contacting patients was highlighted in two studies. In one case patients came from an isolated community in Kenya and it would have been difficult to trace them after discharge. In another case the sample was based in Sri Lanka, and participants lived more than 125 miles (200 km) from the research facility. Many of the patients were poor and did not have a postal address. Follow up was considered pointless as previous attempts had a less than 20% success rate.

Of the 53 investigators who did not inform participants, most (75%) would consider informing participants of their treatment allocation once the study was completed in future studies.

### Informing participants of study findings

Many (67%; 32 of 48) of the investigators who did inform participants, also informed or would inform all or most of them of the study results. In trials where participants were not informed of their treatment arm, 9% of investigators (5 of 53) informed them of study results.

Although investigators were not directly asked about reasons for not informing participants of study findings, several did give an explanation. Reasons included that the study was ongoing and results were being analysed, the results were “too distant in time” and “rather old news,” it was difficult to trace patients, the results were unclear, none of the patients asked, they were never asked by their sponsors, and most of the uninformed participants were dead.

## Discussion

Patients need to be treated as participants rather than subjects by increasing their involvement in the trial process. Consumer involvement has been shown to help priorities and to refine trial questions, improving

Method for informing participants about treatment allocation at study closure

Method for informing participants	No (%) of participants (n=48)
Told they were in placebo arm	26 (54)
Told they were in placebo arm and given common definition of placebo effects	10 (21)
Told they received active treatment and placebo in crossover study	4 (8)
Told placebo response derived from positive effects of being in trial	4 (8)
Told placebo response derived from positive effects of placebos	2 (4)
Told placebo response derived from positive effects of both being in trial and placebos	3 (6)
Told placebo response derived from natural or spontaneous remission	3 (6)
Data on how patients were informed not given	8 (17)

the quality of patient information and making the study more relevant to patients' needs.<sup>7, 8</sup>

During the informed consent procedure patients are told that they may receive a placebo; this is usually described as a harmless inactive substance or an inactive dummy drug. We found that the most common method of informing patients in the placebo arm was to simply tell them that they were in this arm, without giving possible explanations for this effect. Just as knowing that patients have a 50% chance of being randomised to a placebo has been shown to influence health outcomes, it is possible that the placebo response may be disrupted when the treatment is unmasked to patients who have responded.<sup>9</sup> Unmasking the allocation of placebo may be a source of confusion and disappointment to patients and may even damage clinical relationships and have negative effects on patients' health, particularly in placebo surgery. For this reason, feedback should be handled sensitively. A recent trial evaluating the effects of antidepressants found that when placebo responders were told that they were receiving a placebo their mood deteriorated.<sup>10</sup> Within a month 70% of the patients needed antidepressants.<sup>11</sup> In another study, 50 patients with depression who responded to placebos over a 10 day single blind trial were randomised in a double blind way to either continue taking placebos for six weeks or to stop treatment. Half in each group relapsed at six weeks.<sup>12</sup> Therefore unmasking had no effect.

To avoid negative thoughts, misconceptions, or mistrust in health professionals, patients must be well informed. They could be told about the various debates on the therapeutic effectiveness of placebos, but that there is growing evidence for the healing effects of psychological and social factors, such as positive expectations and good patient-doctor relationships.<sup>13, 14</sup>

### Practical and research implications

A major gap is apparent in the literature examining patient understanding of placebos and their effect. Research should examine whether and how treatment should be disclosed to patients and the risks that disclosure may have on measured outcomes. Assessing context effects such as treatment preferences and the level of enthusiasm for trial participation may encourage a participant partnership approach in trials. It may also decrease the likelihood of disrupting placebo responses. Such research would therefore aid the development of effective and sensitive ways to communicate trial and treatment information to participants.

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### What is already known on this topic

Information is poor on the nature, extent, and effect of informing participants of placebo controlled randomised trials about their treatment allocation at trial closure

Less than 50% of participants receiving placebo are informed about their treatment allocation

### What this study adds

No standard procedure is available for informing patients of their treatment arm or of study results at trial closure

Effective and sensitive ways of communicating treatment allocation to participants are required, as is information on the effects on placebo responders

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### Corrections and clarifications

#### Minerva

Our electronic processing system allowed an author's name to "drop off" the authorship details accompanying a Minerva photograph (19 October p 912). B J Burgess is a specialist registrar in accident and emergency medicine at Southend Hospital, Westcliff-on-Sea, Essex SS0 0RY.

*The SCOFF questionnaire and clinical interview for eating disorders in general practice: comparative study*  
In the graph of a receiver operating curve in this article by Amy J Luck and colleagues (5 October, pp 755-6), the label for the x axis should have read "1 - specificity" [not "specificity"].

#### Whooping cough—a continuing problem

In this editorial by N S Crowcroft and Joseph Britto (2002;324:1537-8), we inadvertently failed to include Dr Crowcroft's statement of his competing interests. The following statement should have appeared with the article: "NSC has participated in epidemiological studies jointly funded by the Public Health Laboratory Service and Aventis Pasteur and GlaxoSmithKline, which manufacture various pertussis vaccines and which may gain or lose from the conclusions of this editorial."