Factors Influencing the Participation of Older People in Clinical Trials – Data Analysis from the MAVIS Trial

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Abstract: Background: Older people are less likely to be included in clinical trials. Little is known about factors influencing older people’s decisions about participating in clinical trials. Objectives: To examine the views of older people about participating in clinical trials. Methods: Postal questionnaire to 801 participants who had completed the MAVIS nutrition trial, aged 65yrs and older. Closed and open questions sought participants’ views about factors important to them when deciding to take part in a trial, features of the MAVIS trial they liked and disliked and changes they would suggest. Results: 540 (59% of MAVIS trial participants) returned the questionnaire. The most important reasons reported for taking part in the trial were helping the research team and medical knowledge, and helping other older people. Participants valued good communication with the trial staff and good organisation. Participants reported concerns about swallowing pills and taking a placebo. Participants reported that future participation in trials could be influenced by poor health status. Limitations: This questionnaire surveyed older participants who had taken part in a randomised controlled trial. It did not elicit the views of people who had withdrawn or never decided to take part in the trial. Conclusions: Older people report altruistic reasons for taking part in trials. Simple trial designs, which minimise demands on participants and maintain good communications should be preferred. Explaining the need for older people, despite poor health, to participate in trials may help the generalisability of clinical trials.

Key words: Randomised controlled trial, patient participation, older people, nutrition.

Background

The randomised controlled trial (RCT) is widely accepted as the most powerful method to evaluate the effectiveness of new health technologies. However, low accrual and retention of participants can restrict the value of the trial, reducing the statistical power and generalisability (1, 2). A recent review reported that 31% of trials funded by the UK Medical Research Council and National Health Service Research and Development Health Technology Assessment Programme that recruited participants between 1994 and 2002 did not achieve their original recruitment target (3). Older people, in particular, are less likely to be included in RCTs, restricting generalisability further (4).

Studies which have examined factors influencing trial recruitment have often focussed on cancer trials (1, 2, 5, 6) or hypothetical trials (7). Trial recruitment is influenced by clinician and patient factors. Clinician barriers identified (1, 2, 5) include time pressures and constraints, lack of staff and training, concern about the impact on the clinician-patient relationship, concern for the patients, loss of professional autonomy, and lack of reward and recognition. Barriers to participant accrual and factors influencing participation in RCTs include the extra demands of the study (e.g. additional procedures and appointments), patient treatment preferences and treatment uncertainty (1, 2, 5). Factors affecting older people’s views on taking part in RCTs have seldom been examined.

The aim of this study was to explore the factors that influence older people to take part and remain in randomised trials through surveying participants who had completed a randomised controlled trial investigating the effect of multimineral and multivitamin supplements on infections, known as the Mineral And Vitamin Intervention Study (MAVIS trial) (8).

Methods

The MAVIS trial design

The MAVIS trial was a randomised, double blinded placebo-controlled trial which investigated the effect of a multimineral and multivitamin supplement on infections, health service use and quality of life in 910 community-dwelling people aged 65yrs and older in the Grampian region of Scotland. Full details of the trial are provided elsewhere (8). Grampian Research Ethics Committee gave approval for the study. All older people covered by the general practices involved were eligible to take part, unless their general practitioners (GPs) had indicated that they were too unwell to be contacted, or they already took vitamin or mineral supplements. Eligible older people were recruited by mailing them an initial invitation from their GP. Those who indicated they were interested returned a reply by post and were invited to an appointment in the GP’s surgery.

Participants were asked to take one tablet a day for one year. They were also asked to record daily in a diary whether they had an infection and any contact with primary care for infection. At the end of each month participants returned the
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diary by post to the trial office, together with a questionnaire about trial tablet consumption over the last seven days. Ten percent of participants were also randomly selected to take part in a tablet count at six months and one year, requiring them to return unused tablets at these time points. Questionnaires for the Euroqol (EQ-5D) (9) and Short-Form-12 (SF-12) (10) were completed at the GP visit and sent out at six months and one year.

Participants also completed digit span forwards (11) and verbal fluency (12) cognitive function tests at recruitment, and then by phone at one year. Two researchers were involved in recruitment (a research nurse and a research dietitian). Both researchers conducted the subsequent cognitive function tests by phone. Participants were also phoned shortly after recruitment to check that there were no concerns about the study. The two researchers or trial secretary also phoned participants if diaries or questionnaires were not returned after one postal reminder, or if there were queries about information provided in the diaries.

After the end of the trial all participants who had not withdrawn or indicated they wished no follow-up were given details of their trial allocation and the results of the trial by post (801 of the 910 randomised). They were then sent this reply-paid follow-up questionnaire by post, which contained closed and open questions about taking part in RCTs. No postal reminders were sent out for this questionnaire.

Follow-up questionnaire

The questions asked were informed by the findings from Prescott and colleague’s systematic review (1, 2) and consultation with Professor Vikki Entwistle from the University of Dundee. Closed questions asked about motivating factors for taking part in a trial, health professional involvement, randomisation, use of a placebo, and filling in questionnaires. Quantitative methods were used to analyse participants’ responses to closed questions in the questionnaire. Categorical data were analysed using Chi-squared tests. Two-sided statistical significance was at the 5% level. For dichotomous variables odds ratios (ORs) are presented with 95% confidence intervals (CIs) for the proportion of participants responding to the closed questions that were asked (active treatment vs blinded placebo). When comparing response rates for the proportions answering the closed questions between the treatment groups, non-responders were not included in the analysis. Participant data were stored, manipulated and analysed using SPSS version 11.5.1.

The open questions focused on participants’ experience of the trial specifically asking “Would you consider taking part in a research study again, if asked?” We also looked at aspects that they liked by asking: “Are there things that you liked about the study?” Aspects that respondents disliked were also of interest, respondents were asked: “Are there things that you disliked about the study?” Respondents’ recommendations on how to improve the trial were also sought by asking: “Is there anything that you would have changed about the study?”

Content analysis, a systematic method for assigning text to content categories (13) was used by PF to analyse the data given in response to open questions from the questionnaire. Responses from all open questions were read and reread, and the categories were generated through close inspection and comparison of the data. A second researcher (SM) assisted with analysing a sample of responses for each question to enhance the reliability and reproducibility of the coding. The coded data set was then entered into an Access database. The themes of the analysis are illustrated using representative quotations.

RESULTS

Five hundred and forty (59%) of all 910 MAVIS trial participants returned the questionnaire. Participants responding to the questionnaire did not differ by gender, type of residence or smoking status from all those randomised to the trial. However, they averaged one year younger than those recruited to the trial (data not shown). There was no statistically significant difference in proportions responding to the questionnaire between different arms of the trial [OR 1.12; 95% CI (0.83, 1.51); p = 0.450] see Table 1.

Table 1
Flow chart of MAVIS trial participants

<table>
<thead>
<tr>
<th></th>
<th>Active treatment arm N (%)</th>
<th>Placebo arm N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total N randomised</td>
<td>456</td>
<td>454</td>
</tr>
<tr>
<td>N sent questionnaire</td>
<td>402 (88)</td>
<td>399 (88)</td>
</tr>
<tr>
<td>N responding to questionnaire</td>
<td>266 (58)</td>
<td>274 (60)*</td>
</tr>
<tr>
<td>Aged ≥85</td>
<td>5 (2)</td>
<td>8 (3)</td>
</tr>
<tr>
<td>Sex female</td>
<td>132 (50)</td>
<td>125 (46)</td>
</tr>
<tr>
<td>Sex male</td>
<td>134 (50)</td>
<td>149 (54)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>32 (12)</td>
<td>26 (10)</td>
</tr>
<tr>
<td>Lives in the community</td>
<td>259 (97)</td>
<td>271 (99)</td>
</tr>
<tr>
<td>Lives in a nursing home</td>
<td>7 (3)</td>
<td>3 (1)</td>
</tr>
</tbody>
</table>

* OR 1.12; 95% CI (0.83, 1.51); p = 0.450

Closed questions

There were no statistically significant differences in response rates to the closed questions between active and placebo arms of the trial, see Table 2. Overall, 86% of those responding to the survey reported that helping the research team was very important to them when deciding to take part in a study like MAVIS. Seventy-two percent of people rated helping other people like themselves as being an important issue when deciding to take part in a study like MAVIS.

Under half of the people reported that being asked to take part by a doctor was very important to them. Whereas being asked by a nurse was rated to be less important when deciding to take part in a study. Thirty-four percent of respondents from the active treatment arm and 40% from the placebo arm reported that reducing their risk of illness was important to them when deciding to take part in a study.