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Communicating with participants during the conduct of multi-center clinical trials

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Abstract

Background: Communicating with trial participants is an important aspect of study conduct, relevant for informed consent and respect for participants. Group teleconferences are one means to convey information to trial participants. We used group teleconferences during an ongoing large-scale clinical trial to communicate important trial updates.

Methods: The National Institute of Neurological Disorders and Stroke Exploratory Trials in Parkinson's Disease Longitudinal Study-1 trial studied creatine for treatment of early-stage Parkinson's disease. A total of 1741 participants enrolled at 45 sites in the United States and Canada to take part in a double-blind randomized trial of 5 years of treatment with creatine versus placebo. The study leadership held two teleconferences with study participants and their caregivers after each of two pre-specified interim analyses, for a total of four teleconferences. Each agenda included a presentation by study leadership followed by an open question and answer period. Teleconference recordings were made available to all site personnel and trial participants. Recordings were reviewed and abstracted for themes and topics of the presentations, participant questions, and discussion. Number of participants, connection time for each participant, number of questions, and caller connection time were summarized using descriptive statistics. After the first teleconferences, participants who remained on the call until the end were invited to complete a voluntary, four-question survey about the teleconference process. During the second teleconferences, participants were notified of premature study closure.

Results: There were 258 callers for the first pair of teleconferences and 604 callers for the second pair of teleconferences. Study leaders answered more than 110 questions from study participants and caregivers across all calls. The most frequently asked question themes related to study drug, Parkinson's disease, side effects, future research, and data analysis. The initial teleconferences were well received by participants. Based on responses to the post-call survey, 98% (118/121) of participants found the call useful, 91% (115/127) were interested in future similar calls, 88% stated the call made them more likely to continue in the study (112/128), and 85% (90/106) were satisfied overall with study communications.

Conclusion: Teleconferences provide a convenient way to communicate with trial participants and can be used during the conduct of clinical trials to convey study progress and other information. For multi-site trials, teleconferences enable participants to engage directly with study leadership and to ask questions. Survey respondents were highly satisfied with the group teleconference experience. Future research is needed to determine whether teleconferences improve participants' satisfaction with clinical trial participation and improve retention.

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Communication, teleconference, recruitment, retention, research ethics, novel methodologies, clinical trial, participant engagement

Background

Successful clinical trials require engaged and informed participants. Most research about study participant communication focuses on decision making to participate, informed consent, and clinical trial results.[1–3] Few researchers have examined participant engagement regarding study progress during the conduct of an ongoing trial. Although clinical trial participants want to be informed about trial results at study closure,[4,5] and the majority of investigators are in favor of sharing results, many never learn their treatment allocation[6] or study results. For studies with lengthy follow-up, participants may want to be kept informed of study progress. Little is known about the interest in and impact of ongoing communication with participants during longitudinal studies. We employed and evaluated group teleconferences as a means of ongoing, central communication with interested participants in a longitudinal clinical trial.

Methods

The National Institute of Neurological Disorders and Stroke Exploratory Trials in Parkinson's Disease Longitudinal Study-1 trial studied creatine for treatment of early-stage Parkinson's disease. A total of 1741 participants enrolled at 45 sites in the United States and Canada to take part in a 5-year double-blind randomized trial of creatine versus placebo. Details of study methodology and trial results have been published.[7,8] Pre-specified interim analyses were conducted after 25% of the trial cohort completed 5 years of study participation and again after 50% of the trial cohort completed 5 years of study.

All study participants were invited to take part in teleconferences with study leadership (Karl Kieburtz, Coordination Center Principal Investigator, and Barbara Tilley, Statistical Center Principal Investigator). Caregivers were also able to take part in each teleconference. Following review by the Data Safety Monitoring Board, calls were scheduled to report findings from the first (March 2013) and the second (September 2013) interim analysis. After the second analysis, the study was prematurely terminated for futility.[8] Participants and caregivers were notified of premature study termination during the second set of teleconferences. Individuals who did not participate in the calls were notified of study closure by study site personnel, and the termination announcement was posted to a public website (http://parkinsontrial.ninds.nih.gov/netpd-LS1-study-termination.htm). Participants also received reprints of the primary study manuscript, once published. Two calls were conducted after each analysis, scheduled at different times of day to accommodate differing schedules. Participants were notified of the calls by study personnel at their respective sites. Each teleconference was conducted in two phases. First, study leadership presented an update on study progress, with callers in a listen-only mode. During the following question and answer period, callers' telephones were activated one-at-a-time by the moderator. Each teleconference continued until all questions were answered. Call participants were invited to complete a poll of four yes/no questions at the end of the March 2013 teleconferences, using touchtone pads to respond. Following each call, audio recordings were made available to all trial participants via compact disk and a link on the National Institute for Neurological Disorders and Stroke study-specific website.

Three of four teleconferences were recorded, two after the first interim analysis and one after the second interim analysis. The fourth was not recorded due to technical problems. Research personnel reviewed recordings in their entirety and abstracted themes and topics from presentations, participant questions, and discussions. Number of teleconference participants, connection time for each participant, number of questions, and teleconference length were summarized using descriptive statistics.

Teleconferences were hosted, moderated, and recorded by a commercial vendor (Encounter Collaborative, Portland, Oregon). Approximate teleconference costs included US$1000 per hour per 150 open telephone lines, plus an additional US$150 per hour related to monitor costs and US$50 for each recorded call.

The Institutional Review Board of the University of Rochester (home of the coordination center) and of each trial site approved the teleconference format and concept. Participants were instructed when notified of the teleconferences and again at the beginning of the teleconference not to share identifying information in order to maintain confidentiality.

Results

Teleconferences were held on 14 and 28 March 2013 to present the Data Safety Monitoring Board's conclusions and recommendations from the first interim analysis to 258 callers. At the time of these calls, there were 1398 active trial participants. Two teleconferences were held on 11 September 2013 to present the Data Safety

Table 1. Participant questions.[a]

Question theme	No. of questions		
	First interim analysis calls	Second interim analysis/ study closure calls	Total
Study drug	15	5	20
General questions about PD	7	7	14
Side effects	9	3	12
Future and other ongoing research	3	9	12
Data and statistical analysis	8	2	10
Study group assignment and blinding	5	2	7
Safety concerns	5	2	7
Rationale for study drug, sample size, and study design	3	3	6
Results	0	6	6
Post-study drug availability	2	1	3
Transparency and data sharing	3	0	3
Funding sources for PD research (current and future)	1	2	3
Study eligibility	2	0	2
Study measurements and assessments	1	1	2
Dropouts and withdrawals	1	1	2
Terminology clarification	1	0	1
Study communications	1	0	1
Study timeline	1	0	1
Study impact	0	1	1
Total	68	45	113

PD: Parkinson's disease.

[a]Question themes and numbers were abstracted from three recorded calls. The 11 September 2013 afternoon call was not recorded due to technical problems.

Monitoring Board's conclusions and recommendations from the second interim analysis to 604 callers. At the time of these calls, there were 1339 active trial participants. For recorded calls, the call durations were 77, 57, and 106 min. Approximately, 89% (n = 230) of callers remained on the first set of teleconferences longer than 10 min, and 95% (n = 572) remained on the second set longer than 10 min. Median participant connection times were 75 min (97% of total call time, range: <1–77 min), 57 min (100% of total call time, range: <1–57 min), and 50 min (47% of total call time, range: <1–106 min) for each recorded call, respectively.

During the opening 5–10 min of each teleconference, lead investigators described their roles in the trial, expressed appreciation to trial participants, explained the context of the trial within Parkinson's disease research, described the study design and outcome measures, and reported progress with enrollment. The concept and statistical approach to the interim analysis were also reviewed: (1) Are there sufficient data to conclude benefit of the study drug? (2) Is there an indication that the study drug is unsafe? (3) Are there sufficient data to conclude futility? In the first pair of teleconferences, participants were informed that the interim analysis had not identified a reason for the study to be terminated; thus, the study would continue as planned. In the second pair of teleconferences, participants were informed that the study was being terminated for futility.

Following the presentations by the lead investigators, the remainder of the call was devoted to answering questions from participants. Data abstracted from the recorded teleconferences are presented in Table 1. There was no disclosure of participant identity during any teleconference. Topics addressed included explanations, in laymen's terms, of the rationale for the selection of the study drug, trial design, sample size, clinical assessments, data protections, confidentiality, and statistical concepts. Topics also included complex concepts such as blinding, differences between symptomatic and disease-modifying therapies, stages of pharmaceutical development, regulation of nutritional supplements versus drugs, and supply chain processes.

Participants had frequent questions about study drug, target symptoms, and potential benefit, about how to take the study drug properly, and how to address missed doses. Some participants had inquiries about medication side effects and about study processes, including randomization procedures. Participants also asked conceptual questions about risk of developing Parkinson's disease, how to measure slowing of disease progression, the potential for differential effects of study drug in different people, subgroup analysis, reasons why people dropped out of the study, and about study activities. Participants also had the opportunity to reiterate and confirm their understanding of information presented at the start of the call and to place that information in the context of the future of the study.

Table 2. Poll responses: first pair of teleconferences.

Polling question	% Yes (valid n)
Did you find this conference call useful?	98% (121)
Have you been satisfied with communication from your study site and the sponsor of the LS-1 trial regarding the status of the study?	85% (106)
Would you like to have more calls like this scheduled in the future?	91% (127)
Does this conference call make you more willing to continue in this study?	88% (128)

"Valid n" represents the number of callers who responded to each question.

Table 2 shows the number of respondents who answered each of the four survey questions that were posed at the end of the first two calls. The number of participants who answered each question varied, but reflected a response rate of 41%–50% of the total number of callers. Of those who completed any portion of the survey, more than 90% found the call useful and were interested in participating in future, similar calls.

Discussion

Informing study participants about study methods, progress, and results is a prudent clinical trial practice.[9] Provision of such information demonstrates respect for the time and commitment of study participants, consistent with the principle of respect for persons defined in the Belmont Report on ethical principles and guidelines for the protection of human subjects.[10] Study participants also value receiving study results. In a comprehensive review of 15 research studies, a median 90% of respondents (range: 20%–100%) were interested in receiving this information.[11]

In this study, we actively engaged trial participants during an ongoing clinical trial to convey study progress. Trial leaders used the teleconferences to share information about enrollment, safety monitoring, and interim analysis. The teleconferences were also used to report important information about the future of the trial in a timely manner. The premature study closure announcement via teleconferences occurred with study participants the day prior to public press release and reached over 600 individuals.

Many research participants have limited understanding of clinical research, including measures for safety oversight, which can lead to reluctance to participate or remain engaged in studies.[12] The teleconferences allowed investigators to address the importance of study drug and medication adherence and the appropriate procedures for taking the study drug. Questions about safety and side effects provided context for discussion of safety monitoring and trial oversight. Teleconferences may serve as an extension of the informed consent process by providing updated information that allows participants to continue their evaluation of the risks and benefits of the intervention, upholding participants' right of autonomy.

Strengths of this communication approach include fostering connections between participants and study leaders. In addition, participants heard responses to other callers' questions, which enhanced the information gained beyond that which occurs between a single patient-investigator exchange. Teleconferences have the potential to motivate further discussion of concerns with site staff.

Risks of group calls include the possibility that participants may mention personal experience of perceived benefit, worsening, or adverse events, which could unduly influence other participants. Additionally, some participants sought specific medical advice that could not be dispensed in the absence of a clinical patient–physician relationship. For these callers, the need for contact with their physicians, site coordinator, and site investigator was emphasized. In addition, the audio-alone format of teleconferencing does not allow for use of visually presented material, such as figures or tables, but teleconferences may complement other strategies. Web-based formats may overcome this limitation but may limit participation based on access to technology. Where dysarthria or hearing impairments are significant concerns, teleconferences may not be the ideal format for question delivery and discussion. In this study, the anonymity of the callers precluded us from knowing what proportion were study participants versus caregivers. Even under assumptions that all callers were trial participants, the overall participation rate was low, which prevents us from generalizing the experience of motivated callers to the entire trial sample. For future group teleconference, better methods for notification of participants of the teleconferences and determination of optimal timing, frequency, and duration of calls should be investigated.

Periodic teleconferences were well received by call participants who answered the end-of-call survey. There was a high degree of satisfaction with the call, and participants were engaged in terms of remaining on the call and asking questions. The majority of survey respondents reported that this kind of communication encouraged them to continue in the study, suggesting that periodic teleconferences have the potential to enhance retention. This finding is particularly important for clinical research studies with long follow-up periods. Teleconferences can be used to convey important study information, including achievement of study milestones. Future research is needed to determine how best to optimize content and to determine whether group teleconferences promote study engagement and retention.

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Declaration of conflict of interests

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