Communicating Clinical Trial Results to Research Participants

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Background: Communicating clinical trial results to research participants is seldom accomplished in a timely or an effective manner.

Objective: To evaluate the effectiveness of a plan to communicate results in an industry-sponsored randomized controlled trial for Huntington disease.

Design, Setting, and Participants: Postal survey to research participants at 28 of 41 research sites (including 217 of 316 participants) in Canada and the United States.

Intervention: We communicated trial results by means of (1) a media release from the investigators within a day after a sponsor-issued press release; (2) a subsequent telephone call from the site staff to the participants; and (3) a conference call for research participants 2 weeks after the results were released.

Main Outcome Measures: Source and timing for learning study results and satisfaction with their communication.

Results: Of the 217 study participants surveyed, 114 (52.5%) responded. Most (73.1%) first learned the study results from their site’s telephone call, and 46.3% learned the results within 1 day of the sponsor’s press release. Participants reported high or complete satisfaction with the site telephone call (89.3%) and conference call (82.1%) but relatively low satisfaction with the sponsor’s press release (50.0%). Most respondents reported good understanding of the risks and benefits of the experimental treatment and the next steps for their participation.

Conclusion: Surveyed research participants learned of the clinical trial results soon after public release and highly valued the personalized and accurate communication efforts by the study investigators.

Arch Neurol. 2008;65(12):1590-1595

Despite exposing themselves to risk, volunteers in clinical trials are not routinely informed of trial results. Systematic efforts to communicate trial results to participants have been few, and their absence has led to high-profile public concerns about trial results, especially those showing a lack of benefit. In general, federal regulations and institutional review boards require disclosure only of information that may affect ongoing participation in a research study but not disclosure of research results at a trial’s conclusion. In addition, although sponsors are usually not required to inform research participants of results, commercial sponsors often must inform public investors in part to limit insider trading concerns.

In the absence of a legal mandate, investigators have recommended that providing both positive and negative clinical trial results be the “ethical norm.” Despite this recommendation, efforts to communicate results to research participants remain quite limited. Some participants never learn study results, although many would like to have that information.

We recently completed an industry-sponsored, multicenter, double-blind, randomized, parallel-group, placebo-controlled trial of an ω-3 fatty acid (eicosapentaenoic acid) in subjects with mild to moderate Huntington disease (TREND-HD) that consisted of a 6-month placebo-controlled phase followed by a 6-month open-label phase. During the study, the investigators and sponsor developed a communication plan to release the results of the placebo-controlled portion of the study to research participants in a timely and personalized manner. We then surveyed research participants to evaluate the plan’s effectiveness based on the timing and method of learning the results and their satisfaction with different parts of the plan.
We compared baseline characteristics using Fisher exact tests for categorical outcomes and *t* tests for continuous outcomes for research participants who were and were not surveyed and for participants who did and did not respond to the survey. We used an exact binomial test to examine no preference in the timing of participants learning study results. Satisfaction with the communication of study results was analyzed by dichotomizing the 5-point Likert scale and modeling the probability of being satisfied or completely satisfied as a function of communication source. Given that some participants rated multiple communication sources, a logistic regression model was fitted using generalized estimating equations, assuming a compound symmetry correlation structure. All statistical tests were performed at the 2-sided significance level of 5%, and no correction was made for multiple testing.

## METHODS

### COMMUNICATION PLAN

The communication plan, developed during the course of the trial and approved by the University of Rochester research subjects review board, had 3 principal elements. The first was a media release from the principal investigators posted on the Huntington Study Group's public Web site (huntingtonstudy.org) and e-mailed to members of the Huntington disease community. The second was a telephone call from site staff (the site coordinator or investigator) to research participants providing results and next steps for their participation. The third was a joint telephone conference call for the investigators, sponsor, and study participants to communicate study results. Participants in the clinical trial were informed in advance by postal mail of the approximate time (month) when study results would be released. The sponsor and investigators held a 90-minute joint telephone conference call for the investigators, sponsor, and study participants providing results and principal safety findings. The investigators were asked to telephone study participants to inform them of the results and their next steps. The next steps for trial participants were to stop taking study medication and to schedule a closeout visit with their site within approximately 1 month. On April 25, 2007, the Huntington Study Group issued a separate media release indicating the preliminary results of the study. On May 8, 2007, the study sponsor issued a press release making public these results. Later that same day, investigators received via e-mail a summary of the study's results that included results of the primary and secondary measures and principal safety findings. The investigators were asked to telephone study participants to inform them of the results and their next steps. The next steps for trial participants were to stop taking study medication and to schedule a closeout visit with their site within approximately 1 month.

### SURVEY

To evaluate the plan's effectiveness, we developed a 13-question postal survey asking study participants to indicate when they first learned the study results, their information sources, and their satisfaction with those sources (on a 5-point Likert scale, where 1 indicates completely dissatisfied and 5, completely satisfied). They were also asked to rate how well they understood the study drug's reported risks and benefits and their next steps for study participation (on a separate 5-point Likert scale, where 1 indicates strongly disagree [with a statement that they understand] and 5, strongly agree). Finally, they were asked to indicate which statement better describes their preference: “It is important to me that results of clinical studies undergo a thorough review period before I am informed, even though it may delay my learning the results of the study” or “It is important to me to learn the results of a clinical trial as soon as possible, even though it may prevent a thorough review.” Sites that submitted the survey to and received approval from their respective institutional review boards in a timely manner were included in the results.

### STATISTICAL ANALYSIS

We summarized survey responses using descriptive statistics. We compared baseline characteristics using Fisher exact tests for categorical outcomes and *t* tests for continuous outcomes for research participants who were and were not surveyed and for participants who did and did not respond to the survey. We used an exact binomial test to examine no preference in the timing of participants learning study results. Satisfaction with the communication of study results was analyzed by dichotomizing the 5-point Likert scale and modeling the probability of being satisfied or completely satisfied as a function of communication source. Given that some participants rated multiple communication sources, a logistic regression model was fitted using generalized estimating equations, assuming a compound symmetry correlation structure. All statistical tests were performed at the 2-sided significance level of 5%, and no correction was made for multiple testing.
ing the teleconference, which was principally aimed at study participants and their caregivers. Approximately half of the call was devoted to opening remarks from the principal investigator and sponsor and half to answering the questions of study participants (2 study participants asked questions) and their caregivers (5 caregivers asked questions).

SURVEY POPULATION

Of the 41 sites (6 in Canada and 35 in the United States) participating in this clinical trial, 28 (5 in Canada and 23 in the United States) participated in the survey, which was completed between June and November 2007. These 28 sites accounted for 217 of the total trial population (68.7%). The baseline characteristics of the population surveyed were generally similar to the overall study population, with the exception of a greater occurrence of depression in the surveyed population (comparisons are given in the Table). Of the 217 study participants surveyed, 114 (52.5%) responded. Respondents were older, received a diagnosis at an older age, and had a shorter trinucleotide repeat length, less suicidal ideation, and better total functional capacity (Table).

TIMING AND SOURCE OF INFORMATION ABOUT STUDY RESULTS

Nearly half (46.3%) of the study participants reported learning the study results within 1 day of the sponsor’s public release (Figure 1). The telephone call from site investigators was the most common initial (73.1%) and overall (82.4%) (data not shown) source of information about study results. Traditional media out-

**Figure 1.** Time when survey respondents learned of study results, which were first released April 24, 2007 (n=114). Percentages sum to more than 100 because some participants selected multiple responses for this question.

**Figure 2.** Proportion of survey respondents who first learned study results from each information source (n=114). Percentages sum to more than 100 because some participants selected multiple responses for this question. HD indicates Huntington disease.
lets (eg, newspaper, television/radio, and general Web sites) were uncommon sources of information for this study (none was used as the initial source of information; newspaper and television/radio were each used by 10.0% of participants as a later source of information).

Study participants reported high levels of satisfaction or complete satisfaction with the telephone call (89.3%) and conference call (82.1%), but relatively low levels with the sponsor’s press release (50.0%) (Figure 3) (P < .001 for the telephone call vs press release; P = .03 for the conference call vs press release). Most respondents reported agreement or strong agreement with having a good understanding of the study drug’s risks (84.5%), the study drug’s benefits (83.0%), and their next steps for concluding research participation (78.0%). Most study participants (59.4%; P = .06 for testing equal preference) tended to prefer that results undergo a thorough review before being informed, even if the review delayed their learning of the results.

**COMMENT**

In this industry-sponsored clinical trial, research participants with Huntington disease expressed high levels of satisfaction with personalized, timely, and accurate communication of study results. The participants preferred customized communications rather than announcements aimed at the public or at company investors. Survey respondents also reported a good understanding of the study drug’s risks and benefits as well as the next steps for concluding research participation. Whereas previous research has examined communicating research results by mail,17,18 most of the research participants in this study learned results through a telephone call from the site staff or a conference call with the study’s investigators and sponsor; both were well received. The conference call vehicle and format are novel approaches that provide for interactive communication among the study participants, investigators, and sponsor.

A previous study involving breast cancer treatment shared the results with only those individuals who indicated a desire to learn them;17 however, we sought to inform all research participants of our trial results. Among those surveyed in our clinical trial, few (<10%) indicated dissatisfaction with the communication of trial results by telephone or by teleconference. We did not disclose any results of genetic testing (eg, CAG repeat length), which was not the primary aim of the trial, to research participants.

The survey results are limited by a modest response rate, the use of a survey that has not been validated, clinical impairments in the study population, and a possible lack of generalizability to other disorders. Only 114 of the total 316 study participants (36.1%) responded to the survey, raising the question of response bias. Although respondents were slightly less affected by Huntington dis-
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Huntington disease affects cognitive function and could have affected the survey responses, but baseline Mini-Mental State Examination scores of study participants were appreciably higher than those that typically indicate competence to consent to treatment.30,31,20 Participants were also permitted to have someone help them complete the survey. To the extent that Huntington disease, a hereditary neurodegenerative disorder, is unique, the results of this study may not be readily generalizable to other medical conditions. However, the results at least may be applicable to other neurodegenerative conditions that affect cognition (eg, Alzheimer disease and Parkinson disease).

Although efforts to protect human research participants have appropriately focused on the recruitment, enrollment, and active follow-up phases of randomized controlled trials, relatively little investigative attention or regulatory concern has been directed to the needs of study participants at the conclusion of trials. Consequently, the obligation to disseminate research findings to research participants often falls through the cracks between institutional review boards’ and investigators’ responsibilities in the consent process, and from using a more evidence-based appraisal of clinical research practices. Our study suggests that addressing this need is feasible and highly valued by research participants.

Accepted for Publication: May 28, 2008.
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Author Contributions: Drs Dorsey and Beck had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Dorsey, Beck, Adams, Chadwick, de Blieck, McCallum, Stewart, Shoulson, and Huntington Study Group TREND-HD Investigators. Acquisition of data: McCallum, Deuel, and Huntington Study Group TREND-HD Investigators. Analysis and interpretation of data: Dorsey, Beck, Briner,
Deuel, Clarke, Stewart, and Shoulson. Drafting of the manuscript: Dorsey, Beck, McCallum, Clarke, and Shoulson. Critical revision of the manuscript for important intellectual content: Dorsey, Beck, Adams, Chadwick, de Blieck, Briner, Deuel, Clarke, Stewart, Shoulson, and Huntington Study Group TREND-HD Investigators. Statistical analysis: Beck. Obtained funding; Clarke and Shoulson. Administrative, technical, and material support: Adams, Chadwick, de Blieck, McCallum, Briner, Clarke, Stewart, Shoulson, and Shinaman. Study supervision: de Blieck and Shoulson.

Financial Disclosure: None reported.

Funding/Support: The TREND-HD Study and the communications effort were supported by Amarin Neuroscience Ltd.

Role of the Sponsor: The sponsor helped formulate and conduct elements of the communication plan. The sponsor was not involved in the collection, management, or statistical analysis of the data. Dr Clarke and Mr Stewart helped interpret the data and provided critical review of the manuscript for important intellectual content.

Previous Presentations: This study was presented as an abstract at the Huntington Disease Clinical Research Symposium; December 1, 2007; Boston, Massachusetts; and the abstract was published in Neurotherapeutics. 2008;5 (2):374-375.


REFERENCES


2. MacNeil SD, Fernandez DV. Offering results to research participants. BMJ. 2006; 332(7535):188-189.


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(Reprinted) Arch Neurol/Vol 65 (No. 12), Dec 2008 www.archneurol.com

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