

# Putting participants and study partners FIRST when clinical trials end early

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## Abstract

Between 2018 and 2019, multiple clinical trials ended earlier than planned, resulting in calls to improve communication with and support for participants and their study partners ("dyads"). The multidisciplinary Participant Follow-Up Improvement in Research Studies and Trials (Participant FIRST) Work Group met throughout 2021. Its goals were to identify best practices for communicating with and supporting dyads affected by early trial stoppage. The Participant FIRST Work Group identified 17 key

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recommendations spanning the pre-trial, mid-trial, and post-trial periods. These focus on prospectively allocating sufficient resources for orderly closeout; developing dyad-centered communication plans; helping dyads build and maintain support networks; and, if a trial stops, informing dyads rapidly. Participants and study partners invest time, effort, and hope in their research participation. The research community should take intentional steps toward better communicating with and supporting participants when clinical trials end early. The Participant FIRST recommendations are a practical guide for embarking on that journey.

## 1 | INTRODUCTION

Multiple high-profile Alzheimer's disease (AD) clinical trials ended earlier than planned between 2018 and 2019 due either to futility or safety concerns.<sup>1-5</sup> Although sponsors had communication plans in place, many research participants and their study partners first learned about the trials' early and abrupt endings through news coverage, rather than through direct communication from personnel at their study site.<sup>6</sup> Early termination of trials is not a new challenge in AD and AD and related dementias (ADRD) research.<sup>7,8</sup> However, participants' and study partners' understandable disappointment about the end of these trials—and how they learned about it—renewed calls from within the AD/ADRD research community to identify better ways to communicate with and support participants.<sup>9</sup>

This led to the creation of the Participant Follow-Up Improvement in Research Studies and Trials (Participant FIRST) Work Group, which first met in January 2021. The multidisciplinary work group had 31 members, including research participants and their study partners (i.e., knowledgeable informants who enroll in AD/ADRD research with the participant); clinical trialists and study personnel; as well as representatives from academia, industry, patient advocacy organizations, and the US National Institutes of Health (NIH). The goals motivating this work group were: (1) improving communication with research participants and their study partners when trials end early and (2) supporting those affected by early trial stoppage. To this end, members met regularly to describe the central issues, define the limitations of current approaches, and iteratively develop and refine recommendations.

Here, we outline opportunities identified by the Participant FIRST Work Group for improving communication and support across the pre-, mid-, and post-trial periods.

## 2 | EARLY TRIAL STOPPAGE

Based on regular reviews of accumulating data, an independent Data and Safety Monitoring Board (DSMB; sometimes also called a Data Monitoring Committee),<sup>10</sup> study sponsor, or principal investigator will make recommendations concerning the continuation, modification, or termination of a clinical trial.<sup>11</sup> We focus on termination of clinical trials here.

### 2.1 | Why trials end early

Why might a recommendation be made to terminate a trial early? There are three main reasons.<sup>12</sup> First, it may be due to a finding of benefit. In such cases, one arm of a study is found to be clearly superior to the other, and a decision is made that continuing to expose participants to the inferior arm (and to research-related risks) cannot be ethically justified. Second, it may be due to safety. Due to the occurrence of adverse events such as serious illness or death, risks to participants are determined to outweigh any potential benefits of participation. Once this determination is made, the study cannot continue due to ethical and regulatory requirements. Third, it may be due to futility. In these cases, interim analyses of study data suggest that there is unlikely to be a meaningful treatment effect even if the study were to attain its planned sample size, and so termination of the trial may be recommended for ethical reasons or to conserve the sponsor's resources, especially time and money.

Within clinical trials, a crucial challenge is to balance the interests of the trial participants with the longer term benefits to all patients in generating reliable conclusions rooted in data. While there are rich debates within the literature about how to best strike this balance, they are beyond the scope of this article.<sup>13-18</sup> Rather, our focus is on communicating with and supporting participants and their study partners<sup>19</sup> after a decision to terminate a clinical trial is reached.

### 2.2 | Constraints on participant notification

Although direct notification of participants about early stoppage of clinical trials is an essential step in study termination, participants and their study partners may learn of early stoppage from a press release or news coverage. In part, this is due to the sometimes-underappreciated legal context of federal securities laws. Most clinical trials on AD/ADRD are conducted by large pharmaceutical companies that are public companies. In the United States, public companies are subject to various obligations under the federal securities laws, which are enforced by the US Securities and Exchange Commission (SEC).<sup>20</sup> Similar laws exist in the European Union and other jurisdictions, though our focus here is the United States.

Under US securities law, withholding material information from those with financial interests in a public company is a crime. Favorable

or unfavorable business developments, such as the early termination of an important clinical trial, are examples of material information.<sup>21</sup> Information is material if there is a substantial likelihood that a reasonable investor would consider it important in making an investment decision and view the fact as altering the totality of available information.<sup>22</sup> If the early termination is determined to be material, this information must be disclosed on a timely basis. Such information is considered nonpublic until it is disseminated through recognized channels of distribution and investors have had reasonable time to react. The SEC recognizes several methods of disclosure, including press releases or press conferences.<sup>22</sup>

The dominant concern behind disclosure requirements is that withholding material information could lead to the crime of insider trading. Insider trading has been identified as a concern in health care broadly and in clinical trials specifically.<sup>23</sup> For example, the SEC has previously prosecuted clinicians involved in a clinical trial for insider trading after they used nonpublic information about early trial stoppage to sell stocks, thereby avoiding substantial financial losses.<sup>24</sup>

Public companies must promptly notify shareholders that a clinical trial is ending early, if that is deemed material information. These companies cannot tell research sites, participants, or study partners before they notify shareholders. Additionally, companies usually cannot directly contact participants and study partners; therefore, there is a natural delay in communication because study sites serve as crucial intermediaries, relaying the news. For an example of how notification of early stoppage plays out in practice, consider that at 7:00 am EST on March 21, 2019, Biogen issued a press release halting its Phase III aducanumab trials after independent analyses suggested the trials were unlikely to meet their primary endpoint.<sup>4</sup> Extensive news coverage followed.<sup>25,26</sup> Even as sites rushed to notify participants and study partners across the globe, some participant–study partner dyads (hereafter, “dyads”) inevitably learned about the trials’ early end by viewing electronic news feeds, turning on the TV, or reading the newspaper.<sup>9</sup>

Although private companies are not immune from scrutiny under federal securities law, they are not subject to the same disclosure requirements as public companies. When a clinical trial is funded solely by the NIH or a private foundation, it may be exempt from disclosure requirements. The disclosure requirements for any particular study should be determined in collaboration with the sponsor, funder, study personnel, and (as needed) legal counsel.

### 2.3 | Participant and study partner reactions

Although systematic data on participants’ experiences of early stoppage are lacking, there is anecdotal evidence that participants have a range of reactions when trials end.<sup>6,9,27</sup> Here, we highlight three reactions that came up frequently in the Participant FIRST Work Group’s discussions, as well as in work group members’ conversations with participants and study partners who were part of trials that stopped early.

Feelings of uncertainty, loss, and vulnerability were common. First, when a trial ends early, many participants and study partners describe

#### RESEARCH IN CONTEXT

1. **Systematic Review:** The Participant Follow-Up Improvement in Research Studies and Trials (Participant FIRST) Work Group met throughout 2021. Members included research participants and study partners; clinical trialists and study personnel; and representatives from academia, industry, patient advocacy organizations, and the US National Institutes of Health. The group’s goals were to identify best practices for communicating with and supporting dyads affected by the early stopping of Alzheimer’s disease/Alzheimer’s disease and related dementias clinical trials.
2. **Interpretation:** The group identified 17 recommendations spanning the pre-, mid-, and post-trial periods. These recommendations focus on prospectively allocating sufficient resources for orderly closeout; developing dyad-centered communication plans; helping dyads build and maintain support networks; and, if a trial stops, informing dyads rapidly.
3. **Future Direction:** Future work will assess the acceptability of these key recommendations to researchers and sponsors and their practicability in actual clinical trials, as well as measure their effect on participant and study partner satisfaction.

being plunged into uncertainty and having questions about “what comes next?” Second, individuals who enjoyed good rapport with their study team care for—and feel cared for in return by—study personnel. Often, these participants and their study partners looked forward to study visits as a chance to socialize and find support. When a trial ends early, valued relationships and interactions abruptly end, which creates a sense of loss. Third, for individuals with serious diagnoses like mild cognitive impairment or dementia, as well as for their study partners, having access to specialists and specialized care through participation in a clinical trial can promote health and foster feelings of security and safety. For some, the trial may be a means of gaining access to health care or expertise that isn’t otherwise available to them. Thus, the termination of a clinical trial may precipitate feelings of vulnerability for participants and their study partners.

These participant reactions are an important signal, indicating an imbalance in the partnership between participants and researchers. Participants and study partners invest time, effort, and hope in their research participation, and they ought to be treated with care and respect. Moreover, the experiences of today’s participants may influence tomorrow’s prospective participants and their willingness to enroll in the next AD/ADRD clinical trial. There is a real urgency to address this issue, which prompted the Participant FIRST Work Group to develop recommendations to help research teams communicate with and support research participants.

**TABLE 1** Summary of the Participant FIRST Work Group's recommendations

Pre-trial	<ol style="list-style-type: none"> <li>1. Sponsors and funders should provide resources and funding in the study budget to ensure orderly trial close-out.</li> <li>2. Sponsors or principal investigators should ensure that the communication plan developed for the trial addresses the possibility of early stoppage.</li> <li>3. Study personnel must address the possibility of early stoppage during the informed consent process.</li> <li>4. General information about early stoppage should be available to members of the public.</li> <li>5. Study personnel should encourage participants and study partners to build and sustain their support networks.</li> </ol>
Mid-trial	<ol style="list-style-type: none"> <li>6. Study personnel should regularly check and update contact information for participants and study partners.</li> <li>7. Study personnel should remind participants and study partners that clinical trials might end early.</li> <li>8. Sponsors and principal investigators should anticipate and proactively address participants and study partners' questions and concerns when there is news from related clinical trials.</li> </ol>
Post-trial	<ol style="list-style-type: none"> <li>9. If a sponsor announces early stoppage via a press release, that press release should explicitly address participants and study partners.</li> <li>10. The sponsor or principal investigator should communicate news of early stoppage to site investigators and study personnel.</li> <li>11. Upon learning of early stoppage, study sites should initially contact participants via e-mail as soon as possible.</li> <li>12. As soon as possible after the initial notification e-mail is sent, study personnel should call participants and study partners and personally inform them that the trial has stopped.</li> <li>13. Sponsors, principal investigators, and study sites should consider leveraging social media to disseminate consistent information about early stoppage to participants and study partners.</li> <li>14. Sponsors and principal investigators should collaborate with patient advocacy organizations to support participants and study partners when trials end early.</li> <li>15. Sponsors should prepare answers to FAQs and disseminate them broadly.</li> <li>16. Site investigators should invite participants and study partners to a personalized close-out meeting to cover information like participant arm assignment.</li> <li>17. Sponsors or principal investigators and sites should collaborate to ensure top-line results are shared with participants and study partners.</li> </ol>

### 3 | RECOMMENDATIONS

The Participant FIRST Work Group's recommendations (Table 1) are divided into three time periods: pre-trial, mid-trial, and post-trial. Responsibility for implementing these recommendations may be assigned to the clinical trial sponsor (i.e., an organization that initiates and takes responsibility for a clinical trial, often holds the investigational new drug application to the US Food and Drug Administration), funder (i.e., an organization that provides financial support for a clinical trial), principal investigator (i.e., the individual responsible for the preparation, conduct, and administration of the entire clinical trial), site investigator (i.e., the individual responsible for the conduct and administration of the clinical trial at a particular study site), or study personnel (i.e., individuals who interact or intervene with research participants under the supervision of the site investigator, such as research nurses or coordinators). We acknowledge that when responsibility is distributed over many stakeholders, accountability is also diffused; however, this is unavoidable given the scale of many clinical trials and the infrastructure necessary to conduct them. Ideally, clear communication and coordination among these stakeholder groups, along with well-defined roles and responsibilities, will produce timely, seamless, effective support for participants and study partners impacted by

early stoppage. Ultimately, broader infrastructural mechanisms may be necessary to clarify roles and responsibilities to promote timely, effective communication with respect to early termination of clinical trials.

In AD/ADRD research, participants are generally required to enroll as part of a dyad with a study partner. Therefore, the work group recommendations embrace the needs of both participants and study partners. Further, in formulating these recommendations, work group members were mindful that clinical trials are conducted in a variety of settings, from academic institutions to independent research clinics. These sites have different organizational structures and different resources available to them. Recommendations are meant to be feasible across settings.

#### 3.1 | Pre-trial recommendations

##### 3.1.1 | Recommendation 1

Sponsors and funders should provide resources and funding in the study budget to ensure orderly trial close-out. Study budgets should account for the possibility of early stopping from the outset, as

**TABLE 2** Template for initial e-mail notifying participants and study partners the trial has ended early

Dear [Participant and/or Study Partner],

Thank you for being a valuable partner in [Trial Name]. We are writing to inform you this trial has been ended early by [Sponsor]. A press release explaining this decision can be found at [link to press release on sponsor's website].

We know you will likely have many questions. It may take time for us to answer all your questions, but we are committed to sharing what we know, as soon as possible. Right now, we are gathering additional information to share with you. Someone from our team will be following up by phone [define time frame for call] to answer your questions and discuss next steps.

In the meantime, please contact [identify a site investigator, study coordinator, etc.] at [e-mail and/or phone] if our team can assist you.

Having support is important, so please consider sharing this e-mail with those in your support system, such as family members, friends, a physician, faith leader, or others. If you are interested in support resources, here are a few options: [links to disease-specific advocacy organizations or other appropriate groups].

Respectfully,  
[Site Investigator]

adequate preparation begins pre-trial, continues throughout a trial, and extends into the post-trial period. For example, close-out budgets should cover a research coordinator's time for some pre-specified period after the trial ends to ensure participants have a contact person and advocate at the study site. Given the importance of treating participants with respect, funders should consider requiring plans for orderly trial closeout to be proposed as a condition of funding.

### 3.1.2 | Recommendation 2

Sponsors or principal investigators should ensure that the communication plan developed for the trial addresses the possibility of early stoppage. Being prepared is essential for communicating with and supporting participants. All communications should be clear and accessible to participants with cognitive impairment, culturally sensitive, and available in participants' preferred language(s). This article contains model language throughout, recognizing that it will need to be tailored for use in any particular clinical trial and should be translated to account for participants' diverse language needs across study sites, such as in multinational clinical trials. Tailoring may best be accomplished by soliciting input from an advisory board that includes representative participants and study partners.<sup>28</sup> These individuals may offer insights into what information they would like and how they would like to receive it, which should inform the development of the communication plan.

An essential piece of the communication plan is an e-mail to notify dyads that the trial has ended early. The goal of this e-mail would not be to provide comprehensive information about early stoppage but rather to reassure participants and study partners that study personnel recognize that there will be many questions and will follow up soon. For sample text see Table 2. We suggest that this neutral text be pre-approved by an institutional review board (IRB) and saved for use if and only if the trial stops early. This pre-approval would allow for rapid notification, if needed (see recommendation 11).

### 3.1.3 | Recommendation 3

Study personnel must address the possibility of early stopping during the informed consent process. Throughout our discussions, work group members emphasized the importance of educating participants and study partners about early stoppage and, as appropriate, about the federal securities laws that shape the dissemination of news that a trial is being terminated. Education should begin in the consent process, and written information should be included in both the consent document and study brochure. Sample language is found in Table 3.

### 3.1.4 | Recommendation 4

General information about early stoppage should be available to members of the public. In addition to providing trial-specific education, it is also helpful to refer participants and study partners to resources such as the National Institute on Aging's website (<http://www.nia.nih.gov>), which offers extensive clinical trials information for members of the public, including a discussion of early stoppage.<sup>29</sup> The work group recommends that patient advocacy organizations also link to or post information about early stoppage on their websites, as they can be an important source of information and support for research participants or those considering research participation. For examples, see the Alzheimer's Association (<http://www.alz.org/whentrialsend>) and the Association for Frontotemporal Degeneration (<http://www.theaftd.org/research-clinical-trials/clinical-trials/>) websites.

### 3.1.5 | Recommendation 5

Study personnel should encourage participants and study partners to build and sustain their support networks. The pre-trial period is an opportunity for participants and study partners, should they choose, to build and sustain their support networks and supportive relationships—beyond the relationships formed with individuals

**TABLE 3** Template language for consent document and study guide*Consent form*

If there is any news relevant to your participation, the study team from [Study Site] will inform you and your study partner as soon as possible via e-mail and then by phone to discuss pertinent information and next steps. This may include new information about safety, modifications to the study protocol, or early stoppage of the study. If you would like more information about why a study may end earlier than initially planned, please see the study guide.

*Study guide*

An important obligation for any clinical trial is to protect and promote the well-being of participants like you. There are many ways that study teams accomplish this. In this study, we have a Data and Safety Monitoring Board (DSMB), a group of independent experts including [statisticians, clinicians, and a research ethicist]. The DSMB will periodically review data as they are collected and then make recommendations to the study sponsor and investigators as to whether the study can continue, should be modified, or should end early. A study may end early for many reasons. For example, the DSMB may conclude the intervention is working so well the study does not need to continue, or it may conclude that the intervention is not working or is harming participants. Even if a study ends early, your participation is valuable because it advances our knowledge and can help patients in the future.

*Where the intellectual property is owned by a public company include:*

In some cases, you may learn that the trial has ended through the news media before the study site is able to notify you personally. This is the result of legal requirements. If the study ends early for any reason, [Sponsor] is legally required by the [US Securities and Exchange Commission] to announce this decision promptly to its shareholders, which it typically does via a press release. Additionally, [Sponsor] is prohibited from telling the study sites, study team, research participants, or anyone else prior to that public release of information. We understand this is not ideal, and we want you to know that your contributions to this research are very important. The research team will notify you via e-mail and then by phone as soon as possible to discuss the end of the trial and next steps. If you experience delays in receiving information from your study site after the press release is issued, you can also contact the study site directly. For more information about what happens when a trial ends, see the [National Institute on Aging website or patient advocacy websites].

*Where the intellectual property is owned by a private company or academic investigator include:*

The study site will notify you via e-mail and then by phone as soon as possible to discuss the end of the trial and next steps. For more information about what happens when a trial ends, see the [National Institute on Aging website or patient advocacy websites].

*For all:*

Our study team encourages you continually to be in conversation with your support network about your research participation. Some people share information about their research participation with family members, friends, a physician, a faith leader, or others. If the study ends early, these individuals can serve as valuable sources of support for you.

at their site—that will persist past the trial's end. To this end, site investigators and study personnel should highlight opportunities throughout the trial.

Study personnel can encourage dyads to discuss their research participation with family members and friends, or with trusted others such as a primary care clinician or faith leader. Study personnel may, for example, provide participants with pamphlets about the study that address common questions and concerns and that might stimulate supportive conversations. The work group recognizes that some participants and study partners may be reluctant to discuss their research participation with others, given the stigma of AD/ADRD,<sup>30</sup> and this should be respected. Research participants and study partners (if they are also care partners) might be referred to support groups, whether at the study site or elsewhere. Or, the study site might connect dyads with community-based services and supports or clinicians if they identify unmet needs.

It is important to identify disease-specific patient advocacy organizations; these patient advocacy organizations can serve as a resource for dyad members and should be seen as partners in supporting participants and study partners (see, e.g., recommendation 14). Sponsors or principal investigators may wish to connect with national organizations, while site investigators or study personnel might connect with local chapters to learn about their offerings. Some patient advocacy organizations have materials available in multiple languages. Goal may simply be to make dyads aware of resources available to them.

Social media and online forums such as AlzConnected (<http://www.alzconnected.org>), a message board for persons with AD/ADRD and their caregivers, offer additional places where participants and study partners might find connection and support. Budget and resources permitting, clinical trials might also offer online portals where participants and study partners can share their experiences with one another. Concerns have previously been expressed about how online communication might introduce bias or otherwise affect the integrity of a clinical trial, though strategies to mitigate such risks have been detailed elsewhere.<sup>31</sup>

## 3.2 | Mid-trial recommendations

### 3.2.1 | Recommendation 6

Study personnel should regularly check and update contact information for participants and study partners. Study sites must maintain current contact information—including phone numbers, e-mail addresses, and mailing addresses—for research participants and study partners to allow for timely study-related communication, including but not limited to notification of early stopping. Confirmation of contact information might be conducted as a routine part of study visits, such as upon arrival and check-in. Sites should also proactively document and use participants' preferred means of communicating with site investigators or study personnel.

### 3.2.2 | Recommendation 7

Study personnel should remind participants and study partners that clinical trials might end early. Work group members noted that while dyads ought to be reminded about the possibility of early stoppage, it is important not to undermine their confidence in and commitment to the ongoing clinical trial by overemphasizing this point. Communication regarding early stoppage might, as an example, be conveyed to participants and study partners as part of broader education about trial designs, including information about periodic review of trial data for evidence of safety, benefit, or futility.

### 3.2.3 | Recommendation 8

Sponsors and principal investigators should anticipate and proactively address participants and study partners' questions and concerns when there is news from related clinical trials. When a clinical trial ends early, participants, study partners, investigators, and study personnel in that trial are affected. Individuals involved in other trials may also be affected and will reasonably have questions or even concerns about the implications for their own research participation. For instance, if one trial has stopped early for reasons of safety, participants in a trial evaluating a similar drug (e.g., another anti-amyloid therapy) may worry about their own safety or wonder if their study will also end early. Therefore, sponsors and principal investigators should work with site investigators and study personnel to support dyads enrolled in their study if a related study ends. This recommendation applies to other "big" news that may come out over the course of a trial, such as approval of a similar drug by the US Food and Drug Administration, or news coverage of participants in another trial experiencing severe adverse events.

## 3.3 | Post-trial recommendations

### 3.3.1 | Recommendation 9

If a sponsor announces early stoppage via a press release, that press release should explicitly address participants and study partners. If early stopping will be announced in a press release, sponsors should work with their media team or press office to ensure that the press release addresses participants and their study partners. While press releases often thank dyads for their contributions to research, press releases should also anticipate that dyads will want to know "what happens next?" Sponsors might simply say that participants and study partners should expect their study site to be in touch soon with more information.

Some sponsors allow members of the public to sign up for e-mail alerts—for example, to be notified that a new press release has been issued. It may be helpful for study personnel to sign up for these e-mails as a backup form of notification (see recommendation 10), and some participants may wish to sign up. However, work group members gen-

erally advise against study sponsors and sites relying upon these e-mail alerts as the primary source of communication with participants, given the important role of study sites in communicating research-related information to dyads (see recommendations 11 and 12).

### 3.3.2 | Recommendation 10

The sponsor or principal investigator should communicate news of early stoppage to site investigators and study personnel. Participants and study partners are not the only ones taken by surprise and affected by early stoppage, and the relationships dyads have built with site investigators, research nurses, study coordinators, and others involved in the trial are very important. Therefore, site investigators and study personnel, especially those responsible for communicating with participants and study partners, should immediately be notified that the trial is ending. The reason for stopping should be communicated in a straightforward way and paired with additional information to assist site investigators and study personnel in answering participants' and study partners' questions consistently and correctly.

This communication has the benefit of ensuring that *all* study personnel, not just site investigators, are in possession of relevant information. By extension, it ensures that study personnel are equipped to notify participants, if appropriate, and to respond supportively to participants' questions or concerns. Work group members heard anecdotal reports of participants and study partners who inadvertently informed study personnel at their site that a trial had been terminated by reaching out for more information; when news of early stopping flows in this direction, it undermines trust in the research community.

### 3.3.3 | Recommendation 11

Upon learning of early stoppage, study sites should initially contact participants via e-mail as soon as possible. Although participants would prefer to be notified by phone (see recommendation 12), there was broad agreement amongst work group members that notification by phone may unfold too slowly, particularly if trial stoppage is covered by the news media. An e-mail can ensure that all dyads are notified simultaneously and receive consistent messaging. Moreover, the e-mail offers reassurance that the site investigator or study personnel will soon be in touch. As detailed in recommendation 2, a notification e-mail should be prepared and IRB approved in the pre-trial period to ensure rapid notification at this step.

When communicating with participants and study partners as a group, the site team should ensure privacy and confidentiality and not, for example, make identifying information such as names or e-mail addresses visible to other recipients. The work group acknowledges that older adults may not be online, and there are socio-economic and geographic disparities in internet access in this population.<sup>32</sup> Thus, it is important to know dyads' preferred communication channels and to identify the preferred means of connecting with participants or study partners who are not online. Even individuals who are online will not

regularly check e-mail. Therefore, it may be desirable to also send a text message prompting members of the dyad to check their e-mail; however, no sensitive information should be sent by text message.

### 3.3.4 | Recommendation 12

As soon as possible after the initial notification e-mail is sent, the site investigator or designated study personnel should call participants and study partners and personally inform them that the trial has stopped. Work group members agree that it is preferable for dyads to learn about early stoppage directly from someone at their study site, and the best method of notification is by telephone. Ideally, messaging will be consistent within and across study sites. To promote such consistency, sponsors or principal investigators should consider providing discussion points to guide these phone calls. Each study site should also consider identifying one or two point persons for trial-related communication; these individuals can be a resource for study personnel as well as a consistent point of contact for participants and study partners.

### 3.3.5 | Recommendation 13

Sponsors, principal investigators, and study sites should consider leveraging social media to disseminate consistent information about early stoppage to participants and study partners. Several work group members noted that social media sites (e.g., Facebook, Twitter) provide additional avenues to disseminate information about early stoppage, particularly given that social media use is relatively common among older adults and growing.<sup>32</sup> For example, a study site might retweet a sponsor's press release or post the body of the initial e-mail notifying participants that the trial has ended to its Facebook page. When considering use of social media, the ability to monitor and, if needed, to manage online activity, for instance, addressing misinformation or answering questions posted by participants and study partners, should be considered.

### 3.3.6 | Recommendation 14

Sponsors and principal investigators should collaborate with patient advocacy organizations to support participants and study partners when trials end early. The work group recommends that sponsors and principal investigators anticipate where dyads might turn for advice when a study ends. They can then share information about the trial's early termination, such as the frequently asked questions (FAQs) described in recommendation 15, with these organizations. This will prepare these organizations to share accurate, appropriate information with individuals who contact them. For example, the Alzheimer's Association and the Association for Frontotemporal Degeneration maintain hotlines for patients and families and facilitate support groups where questions about trial ending may arise. Patient

advocacy organizations might also be encouraged to share information on their websites or social media channels.

### 3.3.7 | Recommendation 15

Sponsors should prepare answers to FAQs and disseminate them broadly. Work group members, with additional input from current and past research participants and study partners, prepared a list of FAQs (Table 4). Sponsors may address these FAQs on their own website, share them with study sites to use in answering dyads' questions, or share them with patient advocacy organizations for use by hotline operators and support group leaders.

Patient advocacy organizations might post these FAQs—without answers—on their websites to prompt participants and study partners to think about what questions they might have for study personnel if their study ends and to encourage self-advocacy.

### 3.3.8 | Recommendation 16

Site investigators should invite participants and study partners to a personalized close-out meeting to cover information like participant arm assignment. A detailed checklist of points to cover during this close-out meeting is provided in Table 5. As with other materials, this information should be communicated to dyads in a manner that is accessible and that meets their needs and preferences. The checklist reflects the necessity of imparting information about the trial and any ongoing health considerations and also of addressing participants' and study partners' social and emotional needs.

While site investigators or their designees will conduct these meetings, they will need support from the sponsor or principal investigator to do this. For example, the work group recommends that sponsors or principal investigators provide sites with this checklist, modified as appropriate, and share information, such as a participant's study assignment, with sites to ensure the success of close-out meetings. It may be desirable to offer these meetings in person, or to consider other modalities like videoconferencing; choice of modality should be informed by dyads' preferences. As noted in the checklist, it is important to provide dyads with written materials that they can refer to after the close-out meeting.

It is possible that not all of this information will immediately be available when close-out meetings are conducted. If so, the site investigator or their designees should commit to following up with dyads and share a timeline for doing so, if possible. Participants and study partners may want to follow up with study personnel if they do not receive timely information.

### 3.3.9 | Recommendation 17

Sponsors or principal investigators and sites should collaborate to ensure top-line results are shared with participants and study partners.

**TABLE 4** Frequently asked questions (FAQs)

- Why did the trial end?
- What were the adverse events, and what do they mean for me? (Consider participants' age, genetic or biomarker risk profile, race, and ethnicity.)
- Did I experience an adverse event? Do I need to be assessed for a specific risk?
- When will I learn whether I was on an active drug or placebo? Or treatment versus control?
- Will I receive any of my personal results?
- What do my personal results mean for my diagnosis? (This is especially important for less common dementias for which diagnosis can take years.)
- What's the typical time frame for data to be released? Where can I access updates?
- What are the "top-line" or overall results from the study?
- What are the next steps for research of this treatment or intervention?
- Are there additional research opportunities that I might be eligible for? (e.g., Would I need to wait a certain amount of time before I am eligible for another study? Are there resources to provide more information on new trial opportunities?)
- Can I continue to receive the study drug or other intervention now that the trial has ended? Or, if I have not been receiving the study drug or other intervention, can I receive it now? If so, where and how can I get it?
- Where can I go to get more support? Am I able to talk to my physician about this, or is the information confidential?
- Whom should I contact if I have questions? Is my point of contact the pharmaceutical company, the study site, or someone else?
- Will I continue to have appointments at my study site?

**TABLE 5** Checklist for personalized trial close-out meeting

- **Express thanks.** Thank the participant and their study partner for participating in the trial and contributing to scientific advancement; acknowledge the time and effort involved in participating. If the trial ended early for reasons of harm or futility, express that a negative trial isn't a failure because we learn from negative trials, too.
- **Validate feelings.** Recognize that participants and study partners may react to the news of early stoppage with a range of emotions, and honor those reactions. The emotions they experience may differ depending on why a trial stops. For example, participants may feel disappointment or fear if a trial ends for futility or harm. They may feel satisfied or relieved if the trial ends for benefit. They may be anxious that their access to the research drug or other intervention will not be maintained.
- **Explain why the trial ended.** Provide participants and study partners with information about the reason(s) for early stoppage.
- **Disclose key information.** Share key information about the study generally and the participant specifically. If key information cannot be provided during the close-out, tell participants if they can expect to receive that information; if they can, address when, from whom, and how they will receive it. Key information includes:
  - "Top-line" or overall study results.
  - The participant's study assignment (e.g., randomization to active drug or placebo).
  - The participant's testing results (e.g., magnetic resonance imaging or positron emission tomography scan summary or images, genetic testing results, cognitive testing scores).
  - Adverse events or side effects that may require ongoing monitoring.
- **Outline next steps.** Provide information about what comes next. For example, will there be additional study visits? If so, when? What should participants do with extra trial-related medications they may have at home?
- **Discuss the possibility of ongoing access to the study intervention.** Talk with interested participants about whether it is possible—and, if so, how—to continue receiving the study drug or other intervention. For example, will there be an open-label extension? Will the sponsor approve requests for expanded access?
- **Encourage future research participation.** Ask if the participant would like information about other research opportunities.
  - Anticipate that participants will have questions about how their participation in the study that just ended may affect their eligibility for future studies (e.g., washout period; contraindications).
  - Consider inviting them to participate in a brain health research registry or connect them with resources like TrialMatch ([www.alz.org/trialmatch](http://www.alz.org/trialmatch)), an AD/ADRD clinical trial matching service maintained by the Alzheimer's Association, or the FTD Disorders Registry ([www.ftdregistry.org](http://www.ftdregistry.org)), a non-profit co-founded by the Association for Frontotemporal Degeneration and the Bluefield Project to empower people to both learn about frontotemporal degeneration research opportunities and to share their insights via survey-based research.
  - Participants and study partners may also be interested in learning about research-related roles such as openings on a patient/family advisory board or advocacy work.
- **Provide referrals to meet care needs.** Connect participants with clinical or psychological care, if needed.
- **Identify services and supports.** Equip participants and study partners with information about disease-specific advocacy organizations, support groups, or other relevant services and supports. Encourage participants and study partners to engage with their social networks for ongoing support.
- **Facilitate good-byes.** Recognize that many participants and study partners build relationships with study personnel over the course of a trial. Acknowledge that the end of a study can mean the loss of meaningful relationships, and facilitate good-byes. If individuals raise questions about what the trial's early end means for study personnel or the study site (e.g., Will there be layoffs? Will the study site shut down?), these should be answered truthfully.
- **Allow time for questions.** Ask whether the participant or study partner has any additional questions; provide contact information for study personnel, particularly if there is a new point person for communication, so that individuals can follow up if additional questions arise.
- **Allow time for feedback.** Inquire about what did or didn't work for the participant and study partner in the study generally and the close-out process specifically.
- **Provide written records.** Give participants written materials that address the points above; because the conversation might be stressful or emotional, the participant or study partner may not recall all of the details they are given.

There is an ethical obligation to demonstrate respect for research participants, one element of which is informing them of research results.<sup>33</sup> This obligation holds even when trials stop early. Work group members recommend providing a webinar or other public forum to share top-line results in an accessible manner (e.g., with captioning, in dyads' preferred language[s]) and to invite participants and study partners to submit questions in advance.

## 4 | CONCLUSION

The Participant FIRST Work Group's recommendations aim to assist the research community in taking intentional steps toward better supporting participants and study partners when clinical trials end early. Although the impetus for Participant FIRST was instances of early stopping in AD/ADRD clinical trials, the best practices outlined herein are not disease-specific and are therefore relevant to early stopping across other therapeutic areas.<sup>34</sup> Additionally, as these recommendations reflect a participant-centered approach to research, some lessons are applicable even beyond the early stopping context—for instance, when a study is paused due to a public health emergency like the COVID-19 pandemic—and could be used to improve communication and build partnership with research participants and study partners more broadly.

Culture change will require advocacy and commitment from sponsors, funders, principal investigators, site investigators, and study personnel. Notably, each of these stakeholder groups was reflected within the Participant FIRST membership; their respective contributions speak to a broad willingness within the research community to learn and improve: to put participants and study partners first when trials end early.

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## CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest. Author disclosures are available in the [supporting information](#).

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#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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