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Post-trial access to implantable neural devices: an exploratory international survey

Nathan Higgins ,[1] John Gardner,[2,3] Anna Wexler,[4] Philipp Kellmeyer,[5,6] Kerry O'Brien,[2] Adrian Carter[1,3,7]

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For numbered affiliations see end of article.

Correspondence to
Nathan Higgins;
nathan.higgins@monash.edu

ABSTRACT

Objectives Clinical trials of innovative neural implants are rapidly increasing and diversifying, but little is known about participants' post-trial access to the device and ongoing clinical care. This exploratory study examines common practices in the planning and coordination of post-trial access to neurosurgical devices. We also explore the perspectives of trial investigators on the barriers to post-trial access and ongoing care, as well as ethical questions related to the responsibilities of key stakeholder groups.

Design, setting, and participants Trial investigators (n=66) completed a survey on post-trial access in the most recent investigational trial of a surgically implanted neural device they had conducted. Survey respondents predominantly specialized in neurosurgery, neurology and psychiatry, with a mean of 14.8 years of experience working with implantable neural devices.

Main outcome measures Outcomes of interest included rates of device explantation during or at the conclusion of the trial (pre-follow-up) and whether plans for post-trial access were described in the study protocol. Outcomes also included investigators' greatest 'barrier' and 'facilitator' to providing research participants with post-trial access to functional implants and perspectives on current arrangements for the sharing of post-trial responsibilities among key stakeholders.

Results Trial investigators reported either 'all' (64%) or 'most' (33%) trial participants had remained implanted after the end of the trial, with 'infection' and 'non-response' the most common reasons for explantation. When asked to describe the main barriers to facilitating post-trial access, investigators described limited funding, scarcity of expertise and specialist clinical infrastructure and difficulties maintaining stakeholder relationships. Notwithstanding these barriers, investigators overwhelmingly (95%) agreed there is an ethical obligation to provide post-trial access when participants individually benefit during the trial.

Conclusions On occasions when devices were explanted during or at the end of the trial, this was done out of concern for the safety and well-being of participants. Further research into common practices in the post-trial phase is needed and essential to ethical and pragmatic discussions regarding stakeholder responsibilities.

WHAT IS ALREADY KNOWN ON THIS TOPIC?

Trials of implantable neurosurgical devices have increased dramatically in past decades; however, common practices in the provision of post-trial access to implantable devices are unclear, and the scope of post-trial responsibilities of key stakeholders remains uncertain.

WHAT THIS STUDY ADDS?

Our exploratory study is the first international survey of post-trial access to implantable neural devices. We report on investigators' recent experiences providing post-trial access to devices and the extent to which these arrangements were planned. We found device removal at the end of the trial to be uncommon; we also found almost unanimous agreement among investigators that there is an ethical obligation to facilitate post-trial access to neural implants.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY?

These findings emphasize the potentially lifelong implications of device implantation. Future qualitative research will be instrumental in understanding how investigators have navigated the complexities of providing research participants with continuing access to neural implants.

INTRODUCTION

Neurotechnology research has seen unprecedented investment in recent years. International brain initiatives have committed 7 billion USD to basic and translational neuroscience,[1] and industry spending exceeds 100 million annually.[2] As clinical trial activity continues to increase,[3 4] it is necessary to attend to ethical issues associated with such trials. Although there is a corpus of ethical scholarship on post-trial access to pharmaceuticals,[5] trials of innovative neurosurgical devices present unique challenges. While post-trial participants in pharmaceutical trials are often granted special access to the investigational drug directly from the sponsor, or off-label access through an authorized

prescriber if the drug has been approved for another condition, participants in neural implant trials often remain dependent on the research institute and multidisciplinary research team for ongoing care. These participants may require regular outpatient visits for device monitoring and adjustment, or inpatient stays for repeat surgeries for battery replacements, maintenance and new hardware components. The research centers facilitating these trials are typically large metropolitan university hospitals, creating high travel demands for those participants residing in regional or remote areas.

Over the past 5 years increasing attention has been paid to the unique features of neural implant trials that complicate the provision of post-trial access. Recent semistructured interview studies have found that ongoing access to deep brain stimulation (DBS) is not a guarantee,[6] and that participants often worry about who will be financially, clinically and logistically responsible for their ongoing clinical care.[7] Ethical commentaries[8] and journalist reports in *The New Yorker*,[9] *MIT Technology Review*,[10] *Nature News*[11 12] and *IEEE Spectrum*[13] have also called for attention to cases of device manufacturers discontinuing development or going bankrupt. Commentators have argued that, depending on the stage of device development, patients may be exposed to a range of harms, such as being required to undergo surgical removal of devices that continue to provide benefit, or being left with devices that are dormant or remain functional although with limited or no prospect of replacement or maintenance.

Despite increasing scholarly and journalistic attention to these issues, common practices in the post-trial phase of neural implant trials remain unclear. Clinical trials registered to databases such as Clinicaltrials.gov seldom contain information about plans for post-trial access.[14] A recent review of 45 journal publications of DBS trials found that only four described ethical considerations related to study termination and only three reported actual details about explantation and continued access.[15] Sankary *et al*'s qualitative study of DBS participants provided some insight into study exit protocols, noting that nine participants had the device explanted at the end of the trial, seven of whom had to undergo explantation as part of the study protocol.[7] While studies such as this are well equipped to capture the nuances of stakeholder experiences and attitudes towards post-trial access, there is a need for larger, survey-based research to begin documenting the broad current state of practice in the field of implantable neural device research.

Relatedly, it is typically not sustainable for the gamut of post-trial responsibilities to be borne solely by the research team given the costs, specialist expertise and time commitment involved in maintaining the functionality of a neural implant. Lázaro-Muñoz *et al*'s recent interview study of DBS investigator and patient experiences emphasizes a need for greater attention to the extent to which post-trial arrangements are planned for before trial recruitment, as opposed to dealt with during or after the trial on an ad hoc basis.[6] There is general agreement among basic scientists and engineers,[16] trial participants[7 17] and trial investigators[6 18] that participants should be assured ongoing access to the implant and appropriate care. Elsewhere scholars have argued that post-trial responsibilities should be distributed among trial stakeholders, namely the research team, trial participants, institutions, governments, sponsors and private healthcare insurers.[19–21] However, there is a paucity of work examining how post-trial responsibilities may be distributed among these stakeholder groups, given the diversity of post-trial practices across countries and regions where regulatory and funding requirements may have an influence.

The pace of neural device innovation needs to be accompanied by studies on post-trial practices that can inform the development of guidance for trial investigators. Here, we define 'post-trial access' as provisions offered to trial participants that would facilitate continued individual benefit from the investigational implant. We use 'post-trial access' (rather than related terms 'post-trial care' and 'continuing access') owing to its history of use in international ethical documentation (eg, Declaration of Helsinki) and research scholarship.[5] Building on previous semistructured interview studies investigating participant experiences and perspectives on post-trial access to DBS,[6 7] we conducted the first international survey of post-trial practices in neural implant research. A broader, exploratory study of this kind—capturing trials varying by funding source, geographic location and IDEAL stage (Idea, Development, Exploration, Assessment, Long-term study)[22]—will serve as a crucial initial step in charting the state of current practices in this quickly advancing field.

To this end, we surveyed an international sample of neurosurgical device investigators on (a) whether research participants continued to have access to these devices and (b) whether these post-trial arrangements were planned for prior to the commencement of the trial. We also asked investigators to (c) give their ethical perspectives on the planning and coordination of continuing access, including any barriers or facilitators they may have encountered.

MATERIALS AND METHODS

Recruitment

Clinical trial investigators were contacted via email to complete an online survey about the most recent interventional (ie, not observational or retrospective) trial of a therapeutic implantable neural device they had been involved in. On the IDEAL framework of surgical innovation,[22] eligible investigators were those who had recently worked on a device trial from stage 1 (Idea; First in-human) to stage 3 (Assessment; High-quality RCTs, Pivotal studies). To identify investigators potentially eligible to complete our survey, we completed a systematic search of PubMed articles, and a systematic search of trials listed on the International Clinical Trials Registry Platform (ICTRP) in October 2021. For the PubMed search, articles (n=813) were screened by title and abstract, with the names and

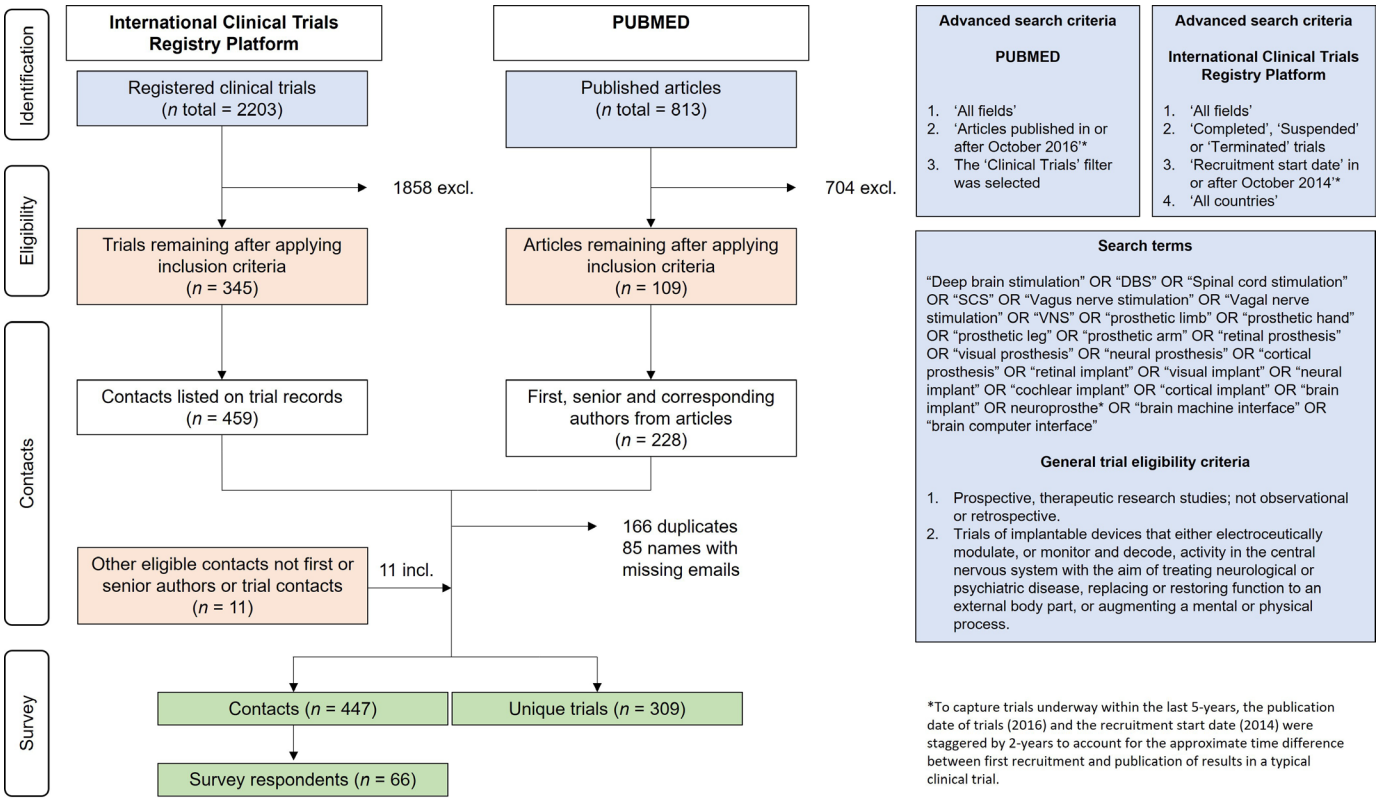

Figure 1 Systematic search of PubMed and the International Clinical Trials Registry Platform (ICTRP) with details of search terms and inclusion criteria.

emails of first and senior authors retrieved from articles that met eligibility. For the ICTRP systematic search, trial titles and descriptions were screened (n=2203), with the names and emails of 'Responsible Parties' collected from eligible trials. The search was pilot tested and calibrated prior to data collection. Search terms were identical for both searches, however several minor differences in search filters were introduced to tailor the search to each platform (figure 1). Together, the PubMed and ICTRP screens yielded 309 unique trials from the past 5 years. These searches were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and meta-analyses Scoping Review extension.[23] All PubMed articles and ICTRP trials and publications were screened by NH, with uncertain cases discussed with coauthors JG and AC.

Recipients were sent an initial email and two reminder emails and were encouraged to review the specified eligibility criteria (ie, senior trial investigators) before completing the survey. Survey responses from email recipients that did not meet a priori eligibility were excluded from the data set. Full details of inclusion criteria for trials, inclusion criteria survey respondents, search terms and screening results are found in figure 1.

Survey and analysis

The online survey contained 23 questions (21 multiple-choice, and 2 short-answer). The survey was hosted on Qualtrics and underwent several rounds of testing and revision by scholars and clinicians at our institute. Survey participants gave informed consent on the landing page of the survey. They were informed that participation was anonymous and any identifiable trial information (eg, names of institutions, device manufacturers) would not be reported in the results. Descriptive parametric statistics were used in the analysis of multiple-choice questions, and short-answer questions were analysed qualitatively, involving the inductive formation of a codebook related to barriers and facilitators of post-trial access.[24] Full survey details are found in online supplemental material. The study was approved by the University human research ethics committee.

Patient and public involvement

Patients and the public were not directly involved in collection or analysis of this data.

RESULTS

Demographic information

Seventy-two investigators chose to participate and completed the survey. Six survey responses were excluded because they did not meet inclusion criteria; one survey was excluded for reporting on a non-implantable neurotechnology, one for reporting on an implantable drug delivery pump and four others for reporting on the results of an observational trial, leaving n=66 survey responses. Two investigators reported on the results of the same trial of a sensory prosthesis; thus, results include n=65 unique trials from n=66 investigators. Investigators

Table 1 Trial device and indication

Device type	
Deep brain stimulation	35 (54%)
Spinal cord stimulation	14 (22%)
Sensory prosthesis (eg, retinal implant)	6 (9%)
Cortical brain-computer interface	6 (9%)
Peripheral neuroprosthesis	2 (3%)
Vagus nerve stimulation	1 (2%)
Other	1 (1%)
Closed-loop stimulation	
Yes	11 (17%)
No	48 (74%)
Other	1 (1%)
Unsure	5 (8%)
Indication*	
Pain (including neuropathic pain and headache)	15 (23%)
Major depressive disorder	14 (22%)
Movement disorders	12 (18%)
Traumatic brain injury/spinal injury/stroke	8 (12%)
Other psychiatric disorder	6 (9%)
Sensory impairment (other than pain)	4 (6%)
Obsessive-compulsive disorder	4 (6%)
Epilepsy	2 (3%)
Alzheimer's disease	2 (3%)
Obesity	1 (2%)
Other	8 (12%)
Approved for other indications or patient populations	
Yes	48 (74%)
No	15 (23%)
Unsure	2 (3%)

*Participants could select more than one option

Table 2 Trial location and funding

Trial phase	
First-in-human or early feasibility (phase 0)	22 (35%)
Pivotal (phase III)	13 (21%)
Other	9 (13%)
Unsure	3 (4%)
Randomized controlled trial	
Yes	32 (49%)
No	33 (51%)
Country(s)*	
Europe	
Netherlands	10 (16%)
Germany	7 (11%)
United Kingdom	6 (9%)
France	4 (6%)
Spain	3 (5%)
Other	3 (6%)
North America	
United States	26 (40%)
Canada	4 (6%)
Oceania	
Australia	7 (11%)
Asia	
Israel	1 (1%)
India	1 (1%)
China	1 (1%)
Egypt	1 (1%)
Primary funding source*	
Public funds	32 (49%)
Commercial or industry funds	28 (43%)
Institutional funds (eg, university, hospital)	15 (23%)
Private foundation funds	3 (5%)
Personal research funds	2 (3%)
Other	4 (6%)
Trial status (as of mid-2022)	
Recruiting	26 (40%)
Completed	22 (34%)
Terminated	10 (15%)
Active, not recruiting	6 (9%)
Suspended	1 (2%)

*Participants could select more than one option.

were psychiatrists (30%), neurosurgeons (21%), neurologists (11%), bioengineers (9%), neuro-otologists or audiologists (6%), pain specialists (5%) and other research professionals (18%), with a mean of 14.8±8.4 (SD) and a range of 41 years (2–43 years) working on trials of neural implants (table 1).

Trials were predominantly conducted in North America (46%) and Europe (51%), with five trials being conducted across multiple countries. The primary funding source for most trials was government grant funding, and a quarter (25%) listed multiple funding sources (table 2). Over half the trials were trialing DBS for new or understudied indications (54%); however, a significant minority (23%) explored implants that had not been approved for any indication. Just under half (49%) were controlled to include a period of blinded or sham stimulation, and a clear majority (81%) of devices were open loop (table 2).

Post-trial arrangements

Investigators who had worked on trials that had concluded (ie, completed, terminated or suspended (n=33)) provided details about whether participants underwent device removal at the end of the trial. None of these investigators reported that 'all' or 'most' (>50%) participants

had undergone explantation at the end of their trial. Two-thirds reported that 'all' participants remained implanted after the end of the trial, and the remaining third reported that 'most' trial participants had remained implanted (ie, some had the device explanted) either during or at the end of the trial. Notably, only one trial of an industry-funded, unapproved neural implant involved 'some' participants undergoing explantation during or at the end of the trial; most involving device removal were DBS (8 out of 11). The most common reasons for explantation were infection and non-response (45% each). One investigator reported that one trial participant underwent explantation for 'cosmetic reasons' and another due to 'device malfunction'. Another investigator reported that a participant underwent removal because they 'blamed DBS on psychiatric life problems'.

When trial investigators were asked which stakeholders contributed to post-trial access in the trial they had worked on, the research team was most frequently mentioned (73%), followed by the research institution (48%), and the trial sponsor (27%). Research team responsibilities overwhelmingly involved clinical follow-up, from care via the trial's clinical team and specialists to monitoring and adjustment of device stimulation parameters. Post-trial responsibilities were shared across more than one stakeholder group in 66% of trials.

Planning for post-trial access

Investigators were asked two 'yes'/'no' questions about the planning of post-trial access in their trials. They were first asked whether they had included plans for post-trial access in the consent agreement, and in the trial protocol submitted to institutional review boards (eg, ethics applications), funding agencies (eg, grant applications), regulatory agencies (eg, investigational device exemption applications) and non-government funders. Overall, 88% reported that plans had been included in the trial protocol submitted to an IRB, which was higher than the number of investigators who reported that plans had been included in the consent agreement (77%). Investigators were next asked whether they had been required by oversight bodies to include post-trial plans. Over half of investigators reported that they had been required by their IRB to include plans (53%), whereas far fewer were required to include plans in submissions to

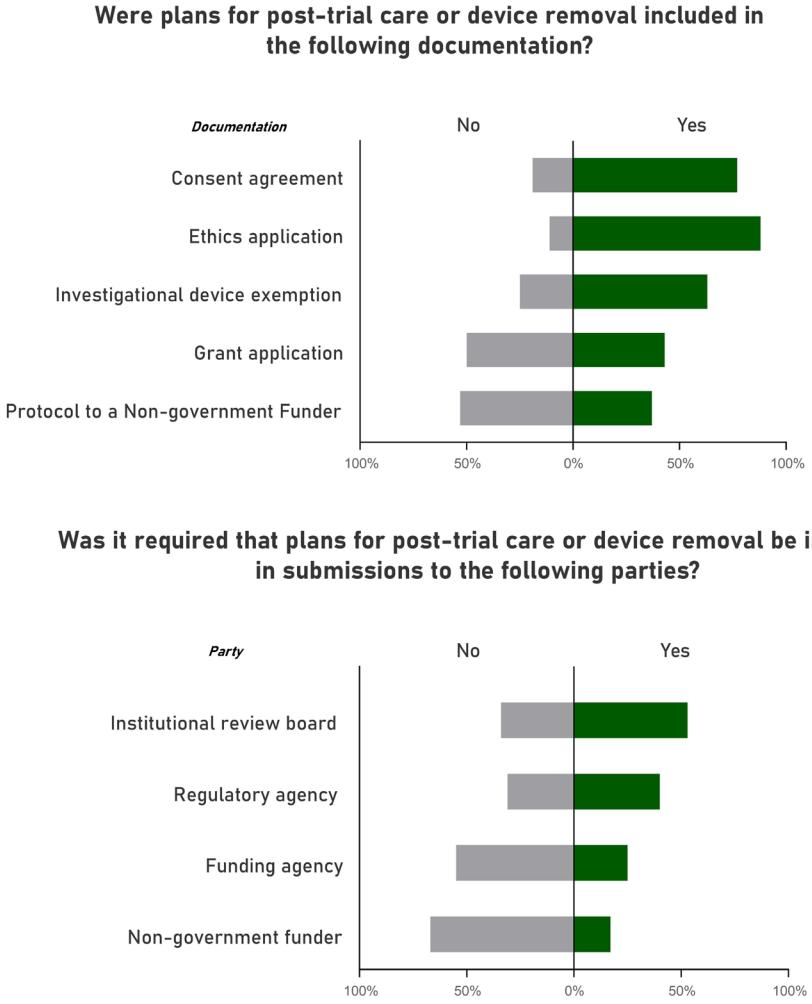

Figure 2 Proportion of researchers that included post-trial plans (top panel) and were required to include plans (bottom panel) for post-trial access in trial protocol submissions to parties.

non-government funders (in trials that received funding from non-government funders) (17%) (figure 2).

Barriers and facilitators to post-trial access

Investigators were asked two open-ended questions about their experiences coordinating post-trial access, namely the greatest 'barrier' they had encountered and the greatest 'facilitator or aid'. Among those who described barriers to post-trial access, almost half (47%) referred to a lack of resources:

> Despite some of these successful partnerships and genuine attempts to solve this dilemma, significant challenges related to costs remain (neuropsychologist 1, DBS trial)

Of those expressing concerns about resourcing, most referred specifically to funding (77%), whereas the remainder (23%) described logistical difficulties with maintaining access to clinical infrastructures or specialist expertise:

> Patients still need to have physical access to the center (neurosurgeon 1, DBS trial).
>
> …very few clinicians in the country have clinical experience or understanding [of] the device being used for psychiatric indications [which] places indefinite burden of care and education on research team (neuropsychologist 2, DBS trial).

Several investigators (16%) described some issues arising due to inadequate collaboration or poor communication between stakeholders, creating scenarios of uncertain responsibility:

> Device manufacturers not providing gratis devices for the life of the patient (neurosurgeon 2, DBS trial).
>
> Biggest concern is identifying who is financially responsible for elective device removal if the participant elects to have the device removed years after the trial end (neurologist 1, Cortical BCI trial).

For some (14%), these challenges instilled a strong sense of personal responsibility to ensure participants continued to receive care:

> I do the only thing I can do, which is steal a bit of funding from my current grants to help support those who have been participants in the past. And I will probably continue to do that. But eventually I may not have grants, or I might retire or die (bioengineer 1, peripheral neuroprostheses trial).

Despite the majority of investigators describing the post-trial phase as challenging, a notable minority (17%) mentioned they had not encountered any barriers when coordinating post-trial access to the device:

> No issue…but participants were connected to the research trial site system and continued to be part of that system (psychiatrist 1, DBS trial)

When asked about factors that had facilitated post-trial access, investigators frequently described scenarios where trial funding was sufficient to cover ongoing care:

> …industry sponsor [took] responsibility for lifetime guarantee for replacement of material for free (anesthetist 1, Spinal cord stimulation trial)

Although 17% described issues related to poor stakeholder collaboration as barriers, the same number (17%) acknowledged strong relationships both between stakeholders and within the research team:

> Excellent teamwork, entirely adequate clinical facilities, close collaboration with the company technical facilitators (neurosurgeon 3, Spinal cord stimulation trial).

Ethical perspectives on post-trial responsibility

Investigators were asked for their perspectives on three questions about post-trial responsibility. They were first asked to rate the degree to which they supported an ethical obligation to provide post-trial access to participants who individually benefited during the trial. Almost all respondents (95%) agreed there was an ethical obligation, with 82% answering 'definitely yes' and 13% 'probably yes'.

Next, investigators were asked whether the post-trial responsibilities of trial key stakeholders—research teams, participants, institutions, governments, sponsors and private healthcare insurers[6]—need to change. Investigators tended to indicate that sponsors and trial institutions should have more responsibility (79% and 67%, respectively), and that research participants should have either less (16%) or no change (51%) in how much responsibility they have for (their own) post-trial access and ongoing care (figure 3). A comparison between investigators from US and European-based trials revealed only a small difference in the belief that private healthcare (insurance) companies should have more responsibility (76% vs 64%, respectively). However, this difference was larger when comparing US and European investigators on the view that participants should have more responsibility (36% vs 17%).

Finally, investigators were asked if the inclusion of plans for post-trial access in trial protocol submissions should be a requirement. The majority (92%) responded either 'definitely yes' or 'probably yes' that it should be a requirement to include plans in submissions to IRBs. Although fewer investigators thought it should be required to include plans in submissions to non-government funders, over 70% still answered affirmatively.

DISCUSSION

Neurotechnology research continues to receive considerable commercial investment and billions from international brain initiatives. Trials of innovative neural implants present unique ethical challenges, and there is a

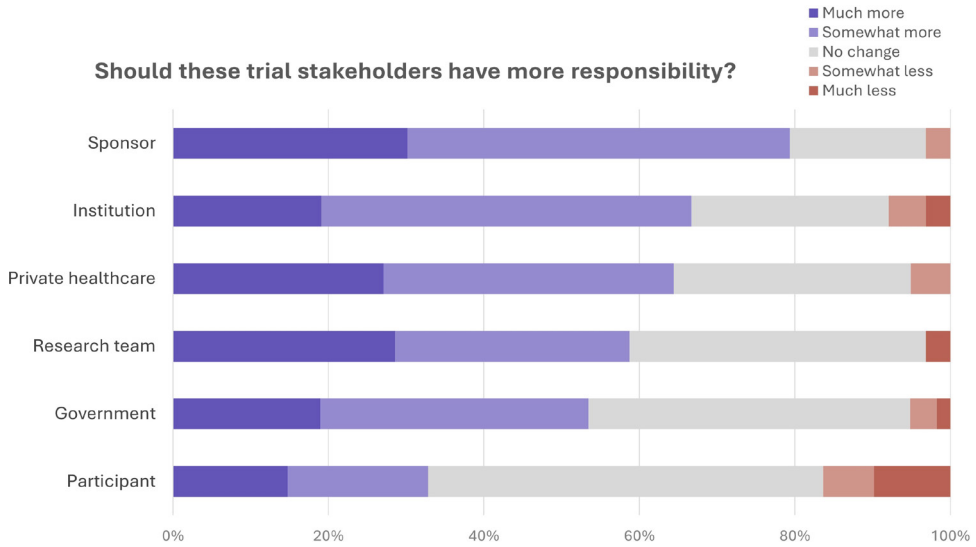

Figure 3 Investigator perspectives on whether trial stakeholders should have more, less or no change in responsibility for post-trial access.

particular need to attend to ethical concerns surrounding post-trial access and ongoing clinical care. While scholarly and journalistic attention to this topic has increased in recent years, common practices in the post-trial phase of neural implant trials remain unknown. This exploratory multinational survey aimed to explore common practices in the planning and provision of post-trial access to devices in this quickly advancing field.

Most investigators who had worked on a completed trial of an implantable neural device reported that all participants remained implanted after the end of the trial; none reported that all or even 'most' had undergone explantation. While it is possible investigators were disposed to differing interpretations of 'after the end of the trial' (eg, primary completion date vs end of a follow-up period, recommended by FDA in the USA), the fact that devices remained implanted in the majority of trial participants underscores the importance of continuing participant access to specialist clinicians and healthcare infrastructures should they require device maintenance or elect to undergo device removal.

When devices were explanted during or at the conclusion of the clinical trial (roughly 33% of trial investigators reported that 'some' participants had undergone explantation surgery), this was done out of concern for the safety and well-being of participants. Infection and non-response were the most common reasons for explantation (both 45%). These reasons for explantation were consistent with the findings of a recent study of post-trial DBS participants; the authors found that participants' decisions to undergo explantation were often straightforward, and rarely conflicted with the recommendations of the research team.[7] None of the trials involved research participants undergoing explantation due to the manufacturer discontinuing development—scenarios that have greatly worried ethical commentators following the unfortunate removal of devices at the end of the NeuroVista trial despite some participants continuing to benefit.[8 11 12] Although this suggests that it is uncommon for investigators to recommend sample-wide device removal at the end of a trial (eg, manufacturer elects to discontinue development in an industry-funded trial), there have been several high-profile cases of manufacturers falling into bankruptcy and participants losing access after the device has been commercialised.[10 13] Given the relatively short time period covered by trials reported on in this study and the potentially lifelong implications of device implantation, it will be necessary for future investigations into post-trial outcomes to consider scenarios like this. To this end, we echo recent calls for the establishment of institutional device registries, which would enable tracking of therapeutic outcomes for participant–patient implanted with specific devices.[25]

It is also worthwhile emphasizing that device removal does not in many (perhaps most) cases constitute a *harm* to the participant or patient. Some devices are known to entail only temporary implantation with explantation written into the study protocol, such as DBS for poststroke hemiparesis.[26] Others are 'permanently' implantable (eg, cochlear implants, endovascular BCIs) that would sooner be left in and deactivated than explanted due to precipitous risks with removal.[27] Thus, factors such as the device and associated surgical procedure for explantation (eg, DBS vs endovascular BCIs), the target indication (acute vs chronic illness) and the *reasons* for explantation or continued implantation (eg, manufacturer bankruptcy vs reduction of immediate or foreseeable medical risks) ought to take primacy in how we evaluate and learn from cases of explantation in the context of research.

Consistent with previous investigator post-trial accounts,[6 28] there are a variety of challenges associated with the coordination of post-trial access. 'Resourcing' was a key barrier for our investigators, specifically the high cost of device maintenance and replacement and

ongoing access to specialists and specialist clinics for long-term support. Several diverted considerable time and research funds to ensure participants were not deprived of access to their devices. As neural implant research continues to grow; however, this ad hoc assumption of responsibility by investigators could become untenable. For example, as the current generation of precommercial brain–computer interfaces transitions from feasibility testing to multicenter pivotal trials—where sample sizes are larger to meet standards of safety and efficacy satisfactory for regulatory approval—individual investigators or health institutes may struggle to accommodate increasing post-trial participant loads.

One way to mitigate some of these challenges is to plan for post-trial arrangements before the trial has commenced. When asked whether they planned in the most recent trial they had conducted, 88% of investigators who completed our survey said they had included post-trial plans in the trial protocol submitted to their IRB, while only 77% had included plans in the consent agreement. Interestingly, this difference almost vanishes when for DBS trials only; DBS trials that included plans in IRB submissions almost always included these plans in the consent agreement, and vice versa. It is not obvious why trials of other device platforms may have included plans more often in submissions to IRBs than consent agreements, though reasons are likely to differ depending on the regulatory status of the device. For instance, two spinal cord stimulation trial investigators who had planned for post-trial access in the IRB protocol selected 'not applicable' for planning in the consent agreement. Given spinal cord stimulation has been used to treat chronic pain since the 1960s, these investigators may have been implanting existing patients with devices with novel stimulation parameters (eg, 10 kHz),[29] in which case, there may have been no need to explicitly outline ongoing access arrangements in the consent agreement if this was part of their regime of care.

Since post-trial access is not guaranteed, it is imperative that participants be fully informed about what will happen to their device after the end of the trial, from indefinite or lifetime access to partial access (eg, full access within a defined follow-up period, research funds used for a replacement battery only), to loss of access (ie, explantation or deactivation). While participants' concerns about ongoing access are often assuaged by their trust in the research team,[7] this trust should not negate the need for clear communication and understanding of post-trial plans. These plans should also reasonably account for contingencies. In multipayer systems such as the USA, investigators may be led to believe long-term care for DBS will be covered via preapproval notifications, only to have the insurance company switch and deny coverage.[30] Future studies should endeavor to uncover the reasons why some cases participants are sometimes not informed of post-trial arrangements in the consent agreement and identify any barriers that investigators may be encountering when attempting to plan.

When asked about the ethics of post-trial access, investigators expressed overwhelming support for an obligation to provide post-trial access to participants. This aligns with previous studies that have found support among DBS researchers[6 18] and basic scientists and engineers[16] for an ongoing fiduciary obligation to provide ongoing care to participants. The results of this study also expand on these findings by identifying one of the conditions where investigators believe this obligation exists: when participants individually benefit during the trial, regardless of whether device efficacy had been demonstrated across the trial sample. As such, manufacturers and insurance companies should strongly consider incorporating the condition of 'individual benefit' into the eligibility criteria for ongoing coverage—a position accepted by many pharmaceutical companies.[31]

In discussions about post-trial access to pharmaceuticals, commentators have suggested that responsibilities be allocated according to the functional capacities of trial stakeholders,[20] and transition between stakeholders at critical junctions during the trial.[19] More recent discussions in neuroethics have seen 'mandatory planning' proposed as a means of holding investigators and manufacturers accountable. Most investigators in our study favored mandatory planning for post-trial access in submissions to oversight bodies, lending support to the notion that this would encourage investigators to the responsibilities of trial stakeholders in advance. Although broad support among investigators suggests this would be an effective way of improving clinical and research practices, questions remain about the practical implementation and scope of mandatory planning. While introducing required planning in grant applications might be relatively straightforward (and has to a limited degree already been instituted by the NIH in the USA), the concerted standardization of planning by IRBs would necessitate cross-institutional collaboration.

Future directions and limitations

Several avenues for future empirical research might meaningfully expand the descriptive and normative domains of the ethical issue of post-trial responsibility. First, studies might take a fine-grained approach to investigating the circumstances that give rise to explantation, considering factors contingent (eg, device safety, efficacy) and non-contingent (geographical location, device type) on trial outcomes. Second, engaging the perspectives of investigators, participants and industry professionals[32 33] will be essential to making sense of the complex trial factors, myriad stakeholder obligations and incentives, and tensions between duties of research integrity and clinical care. Finally, studies should explore the feasibility of proposed pragmatic solutions, such as device registries for long-term monitoring of participants or amending Consolidated Standards of Reporting Trials protocol reporting guidelines to become more feasible, enabling investigators to include information about post-trial arrangements in publications of results.[25]

There are limitations to this study. This was an exploratory study of recent clinical trials aimed at stimulating discussion about the issue of post-trial access to neural implants. Although we received 66 survey responses to 309 unique clinical trials, it is difficult to calculate an accurate response rate for several reasons. An unknown proportion of those contacted would have formed part of our intended study population. Some of those contacted for participation would not have met eligibility because they were not the trial investigators per se, but ineligible parties such as clinical administrators or research assistants. Thus, our findings should not be interpreted as prevalence estimates of post-trial practices for the field. Nevertheless, we achieved a reasonably high level of representativeness across key neural device types for an exploratory study of this nature (see online supplemental material). Other factors may have introduced bias into our sample. For instance, the survey and invitation email were written in English, so the sample was likely biased towards Western (English language) researchers and trials. Investigators were also able to respond with 'not applicable' or 'unsure' to several survey questions, in cases where the survey question was irrelevant to their trial or because they had forgotten the information since working on the trial. These limitations should be noted when interpreting the results and planning studies of a similar nature.

CONCLUSION

We surveyed international investigators about the planning and facilitation of post-trial access to neural implants, from established device platforms (eg, DBS) to precommercial technologies such as brain–computer interfaces and neuroprostheses. Our findings suggest device removal is an uncommon practice, and that when it does occur, it is often in the best interests of the participant rather than for financial or proprietary reasons. Investigators described a range of barriers to providing post-trial access; some went to great lengths out of a sense of personal responsibility for their participants, whereas others encountered little resistance thanks to robust healthcare infrastructures or good collaboration between stakeholders. Ultimately, investigators believe post-trial access is an ethical imperative but recognize the need for pragmatic initiatives that will, at the very least, enable them to anticipate barriers to post-trial access before they arise.

Author affiliations
[1]School of Psychological Sciences, Monash University, Clayton, Victoria, Australia
[2]School of Social Sciences, Monash University, Clayton, Victoria, Australia
[3]Monash Bioethics Centre, Monash University, Clayton, Victoria, Australia
[4]University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, USA
[5]University of Mannheim School of Business Informatics and Mathematics, Mannheim, Baden-Württemberg, Germany
[6]Medical Center—University of Freiburg, Freiburg, Baden-Württemberg, Germany
[7]School of Philosophical, Historical, and International Studies, Monash University, Clayton, Victoria, Australia

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ORCID iD
Nathan Higgins http://orcid.org/0000-0002-3412-8892

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