When Risks Outlast Benefit: Post-Trial Phase of Implantable Neural Device Trials and a Framework for IRB Considerations of Vulnerability

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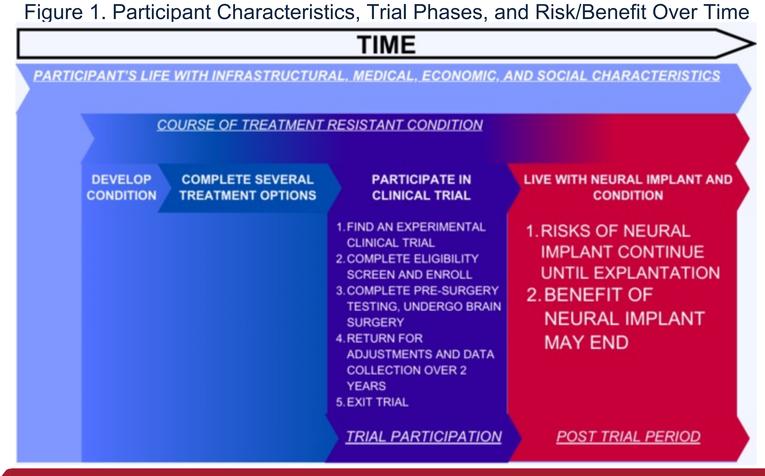
BACKGROUND

- Post-trial management of devices and participants is a pressing concern in the field of neural device implant research. Without any formal support or guaranteed continuing access to their experimental devices, participants who leave research protocols may lose the benefit of their implant or incur steep medical expenses without insurance coverage.
- This loss of device benefit can be especially harmful in participants exiting implantable device trials for treatment-resistant neurological conditions, who may lose access to effective treatment and experience rebound symptoms if they lose the benefit of their device (Vora et al, 2012).
- IRBs should require researchers to consider how certain characteristics in participants' lives (e.g. treatment resistant conditions, insurance that will not cover experimental care, lack of support) may impact the risk/benefit profile of a trial to its study population. By considering what kinds of vulnerability might impact the study population, researchers and IRBs can better identify measures that will decrease risk and protect benefit.
- Researchers and IRBs will not be able to fairly assess the risk/benefit profile of an experimental protocol without considering the position that participants will be in after finishing their trial participation.

Figure 1. Participant Characteristics, Trial Phases, and Risk/Benefit Over Time



METHOD

To help identify relevant characteristics that may impact the risk/benefit profiles of participants with treatment-resistant neurological conditions, we have reviewed relevant concepts from bioethics documents covering ethical trial design and conduct. We conducted a review of ethics guideline publications that consider participant vulnerability using these keywords: Risk/Benefit, Vulnerability, Neural Implant Device, Treatment-Refractory Disorders.

Texts Included in Review:

- Research Involving Persons with Mental Disorders that May Affect Decisionmaking Capacity
- Ethical and Policy Issues in Research Involving Human Participants: Summary, Volume 1, Volume 2
- Subpart A Of 45 CFR Part 46: Basic HHS Policy For Protection Of Human Subjects
- MRCT Center Post-Trial Responsibilities Guidance Document

Relevant Concepts Identified in Review

- Justice-Care Perspective
- Medical vulnerability
- Economic vulnerability
- Infrastructural vulnerability

FINDINGS

Justice-Care Perspective

"A justice-care perspective accepts respect, beneficence, justice, and integrity as fundamental ethical principles that guide the moral actions of scientists. The translation of these principles into moral actions is not, however, assumed to be achieved simply through a scientist's moral reflections, but must derive from expressions of mutual accommodation among scientist, participant, and caring others integrated into concrete practices. In addition, connectedness with, and caring for, those who participate in research need to be viewed as moral ends in their own right, rather than simply as a means to facilitate recruitment or maintain participant cooperation" (NBAC 2002, 31).

Infrastructural Vulnerability

"Although IRBs, researchers, and subjects often take them for granted, there are many protections and resources that contribute importantly to the safety of the research subject. When a consent form asks subjects to call a listed telephone number if they have a question or complaint, those phrases presuppose access to a telephone system… When an investigational drug regimen has to be skillfully administered, the researchers may be assuming the availability of skilled health care professionals and a responsible independent local review mechanism. At the structural level, essential political, legal, regulative, institutional, and economic resources may be missing, leaving the subject open to heightened risk" (NBAC 2001b, 177).

Potential infrastructural issues that may increase the risk of a participant losing device access in the post trial period include device manufacturer closure and a lack of universal healthcare.

Medical Vulnerability

"First, clinical trials should take far more seriously the needs of medically vulnerable research subjects… researchers should also be required to consider how they might provide maximum therapeutic benefit for patients who have run out of options. And, second, we need to consider the fair entitlements of research subjects who are disadvantaged in economic and other ways. It is a worry that we may be tolerating unfair arrangements in the context of clinical research that we would not find acceptable elsewhere" (NBAC 2001b, 178).

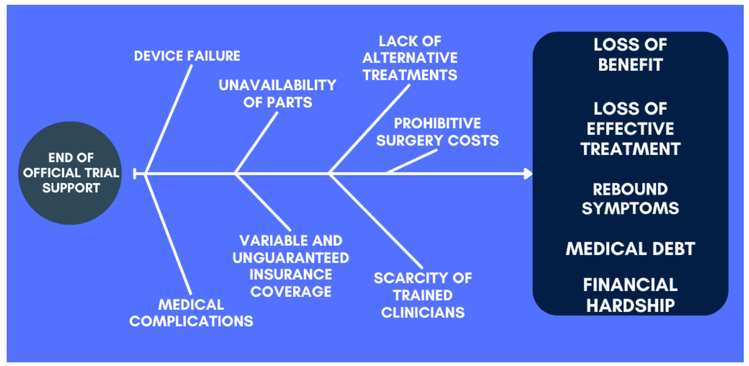
Patients often find experimental neural implant trials because their conditions are treatment resistant, they are experiencing treatment search fatigue (Zuk et al. 2021), and/and they feel that their other treatment options are limited. A participant who loses access to their neural implant device may lose access to their only effective treatment option.

Economic Vulnerability

"Prospective participants might have an economic vulnerability when they have the cognitive capacity to consent but are disadvantaged in the distribution of social goods and services such as income, housing, or health care. This type of vulnerability heightens the risk that the potential benefits from participation in the research study might constitute undue inducements to enroll, threatening the voluntary nature of the choice and raising the danger that the potential participant's distributional disadvantage could be exploited" (NBAC 2001a, 117).

Economic insecurity could increase participant risk in the post trial period by forcing a choice between taking on high medical costs without assured reimbursement or losing access to the device.

Figure 2. Post Trial Risk Factors and Potential Harms



CONCLUSION

Suggested IRB Requirements for Neural Implant Protocols for Treatment Resistant Neurological Conditions

IRBs should require that experimental protocols include post trial care management plans (PTMP) considering:

1. different vulnerabilities that may impact the study population
2. the ways those vulnerabilities may shape the risk/benefit profile of an individual's trial participation
3. how a participant's risk/benefit profile might change during and after trial participation
4. strategies to mitigate inequitable augmentations of risk and/or loss of benefit in the post-trial period.

Other Questions for Researchers Writing Experimental Neural Device Protocols for Treatment Resistant Neurological Conditions

1. Has the research team consulted any current or past trial participants in the design of their PTMP (Johnson et. al 2024)?
2. Has the research team built any mechanisms for ongoing contact with past participants (e.g. maintaining phone line or connecting participants to psychological support resources) (Sankary et al. 2022)?

It is important that as neural implant research grows and advances, the research community invests time and manpower providing support to past participants and gathering more data on post-trial care needs. IRBs can promote this work by requiring neural implant research protocols to put real effort towards study population involvement and PTMP development.

SCAN FOR REFERENCES

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