Experimental treatment approaches and first-in-human Phase 1 trials are ethically complex. These studies create challenges for informed consent, impose burdens and risks to subjects and may offer little or no prospect of clinical benefit. Similarly, these studies create ethical concerns for investigators, coordinators and study staff. These issues are understudied in the field of regenerative medicine generally and in the Huntington’s disease (HD) population specifically.

An anonymous survey of HD patients and family members regarding attitudes and concerns about participation in a study that involved stem cells, gene therapy and neurological implantation was approved by the Institutional Review Board at UC Davis. The survey was offered on the HDSSA website from September - December 2014. Descriptions of adult stem cells, gene therapy and neurostimulation were provided in the introduction to the survey. Respondents were asked a series of sociodemographic questions followed by open-ended questions. Respondents who completed sociodemographic questions and at least one open-ended question were included in the analysis. We conducted a mixed methods analysis using quantitative and qualitative approaches to analyze participant responses.

Sociodemographic data were sorted and analyzed with descriptive statistics. Open-ended questions were assessed by a multi-disciplinary team of five individuals including a movement disorders neurologist, a study coordinator with a degree in linguistics, and three bioethicists with backgrounds in philosophy, rhetoric and medical anthropology. After individually test-coding open-ended questions, the team discussed and agreed upon a standard codebook, with which two team members independently coded all open-ended responses. The coders and another team member then reconciled all coding by consensus.

Of 268 respondents, 209 met our inclusion criteria and were separated into either Group 1: Individuals at risk or genetically tested for HD (n = 116) or Group 2: Family members or care providers (n = 93) (Figure 1). Respondents were largely Caucasian (96%), and more likely female (69%), with mean age of 52 years (range 18 – 79) and drawn from throughout the US (Table 1, Figure 2). Regarding attitudes about participation in a first-in-human trial for HD, 67% of individuals from Group 1 responded positively compared to 92% from Group 2 (Figure 3).

For Group 1, roughly one third were diagnosed with HD, one third were gene positive and not yet diagnosed, and one third did not know their HD gene status (Figure 4). Seventy-seven percent of these respondents had previously participated in research (Figure 5). Most respondents (72%) reported no ethical concerns regarding experimental approaches to the treatment of HD, and 67% indicated willingness to consider participation in such a study. The most important reason cited for considering participation in a Phase 1 study was to find a cure for HD (62%), and this was also cited as the most important benefit for study participation (57%). The most common perceived burden of participation in a first-in-human trial included concerns about access (38%), and the second most cited concern was fear of adverse effects in 31% (Table 2).

Group 2 respondents were primarily spouses or partners (46%), followed by parents (22%), other relatives (15%), and care providers (11%) or siblings (6%). Sixty-five percent of these respondents had no ethical concerns regarding experimental approaches to the treatment of HD, with 57% expressing support for the decision of a family member who wished to participate in such a study. Group 2 respondents were more likely to express safety concerns and specific types of adverse events (including death) than were those from Group 1. Perceived burdens related to participation were logistical (39%) followed by psychological/emotional burden (20%) and physical risk (10%) (Table 2).

The goal of this survey was to explore attitudes and concerns of HD patients and family members about potential participation in a first-in-human experimental approach to treatment of HD utilizing gene-modified stem cells modified delivered by neurostimulation implantation. Results showed a broad support for participation in such a study from both patients and family members. The chief ethical challenge identified by both groups was concern for the source of stem cells, with some respondents expressing concern about the use of embryonic stem cells. Both patients and family members identified concerns about the potential risks of such a trial, and some raised concerns about the safety of neurostimulation implantation. Few respondents reported any ethical or safety concerns about gene therapy. While family members and caregivers were largely supportive of the decision by a loved one to participate in such a trial, they expressed more specific concerns about potential risks, including psychological, functional and medical side effects and possible death. The burden of study visits and logistics was important to both groups. Post-trial support for participants was identified as an important concern by family members. Both patients and family members reported potential benefits of study participation, including advancing scientific knowledge, taking an active stance against the disease, and helping others affected by HD. Additional thoughts from respondents included gratitude, support, remarks on urgency, and sharing of personal stories.

Limitations of this study included the survey format, which prevented respondents from seeking clarification about sources of stem cells, details of gene therapy and neurostimulation delivery of therapy. Strengths of the survey include a large response rate from a broad range of patients and family members directly affected by HD.

As basic research discoveries are translated to experimental treatments for HD it is our ethical responsibility as researchers to understand the beliefs and motivations of participants regarding these approaches. An appreciation for these ethical challenges inherent to this type of approach enables the investigators and participants to bridge communications gaps through a well informed consent process.

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