Provider-reported challenges and barriers to referring patients to neuro-oncology clinical trials: a report from the Society for Neuro-Oncology member survey

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Abstract

Background. Whereas much information exists in general oncology regarding the barriers to clinical trial referral, those specific to neuro-oncology are not yet well known. Trial barriers lead to lower patient accrual, which can lead to less-efficient clinical trials and slower improvement of the standard of care, which may negatively effect patient outcomes. Thus, the aim of this study was to determine the clinical trial referral barriers that are specific to neuro-oncology to improve trial accrual rates.

Methods. An electronic survey was completed by 426 Society for Neuro-Oncology members, of whom 372 are included in this report. Descriptive statistics, including frequencies, means, and proportions, were used to characterize our survey sample.

Results. Only 22% of participants reported that their center tracks referrals to clinical trials inside as well as outside their own institution, with an estimate of less than 30% of patients referred. The most commonly reported provider-referral barrier was finding ongoing trials in the patient’s geographic area. Providers also perceived that while considering participation in a trial their patients may not qualify for any trials, and if they do, may be unable to travel to the study site for follow-up. Additionally, practice location and provider and institution type all influenced referral patterns.

Conclusion. Efforts should be made to broaden trial availability and eligibility criteria, improve trial referral tracking, and ensure patients and their caregivers understand the goals and importance of clinical trials to reduce barriers and improve trial participation.

Keywords

clinical trials | neuro-oncology | provider-reported | referral barriers

Clinical trials are imperative in translating basic research findings into the clinical setting to improve survival and quality of life among cancer patients, yet only around 3% to 5% of such patients actually participate in one during the course of their illness. In the brain tumor population, a 2002 report by Chang et al found that 20% of patients enrolled in their Glioma Outcomes Project, which prospectively followed malignant glioma patients throughout the course of their disease and treatment, were participating in a clinical trial for their disease. To enroll in a clinical trial, a patient must first be diagnosed with cancer, screened for relevant trials, and be
found eligible for specific trials. Patients must then be offered a trial slot by the provider, decide to participate, and lastly, enroll in a trial. Thus, a patient’s decision to enroll in a clinical trial is only one instance in a long, multistep process that can be complicated by the challenges and barriers providers face when considering referring their patients for participation in a clinical trial.\(^1,^2\) In oncology clinical trials it has been noted that there are distinct patient, provider, and institutional barriers and concerns that complicate referral.\(^3\) Notable patient challenges and concerns include the logistical challenges and costs associated with trial enrollment, lack of awareness, eligibility, and limited access to available trials, mistrust of clinical trials and their merit, and a lack of discernable personal benefit from participation.\(^4\) Provider and institutional barriers and concerns include limited staff and financial resources, restrictive trial eligibility criteria, limited actively accruing trials,\(^5\) inconvenience for the clinician, an altered relationship between providers and their patients, and a possible physician role conflict between researcher and care provider.\(^2,\,^6-^10\) Trial barriers ultimately lead to lower patient accrual, which can lead to less-efficient clinical trials and slower improvement of the SOC, which negatively affects patient outcomes.\(^1\)

In 2016 the National Brain Tumor Society (NBTS) conducted an online survey of patients and their care partners concerning patient attitudes, perceptions, and participation in clinical trials. The NBTS survey, which included 1463 participant responses, showed that only 21% of brain tumor patients actually participated in clinical trials after diagnosis, despite 53% of patients reporting that they explored information about clinical trials and 42% of patients recalling being informed about clinical trials by their medical team. The top reasons for not participating in brain tumor clinical trials were cited as that 1) the patient’s doctor did not recommend participation in the trial, 2) the patient did not qualify for the trial, and 3) the patient did not know where to find a clinical trial. Less than 5% of participants in the NBTS survey reported concerns about cost, placement in a placebo group, or concerns about the experimental nature of a trial as reasons for not participating.

One of the major initiatives of the Society for Neuro-Oncology (SNO), a multidisciplinary, international organization dedicated to promoting advances in neuro-oncology, is to improve clinical trial accrual. To assess the concerns, challenges, and barriers that exist in neuro-oncology clinical trial referral, a prospective evaluation through a physician-based questionnaire was desperately needed.\(^2\) Thus, SNO, in collaboration with multiple organizations including the patient-outcomes team in the Neuro-Oncology Branch of the NIH, and the NBTS, developed a provider-reported survey that was distributed to the SNO membership to identify the unique barriers and challenges that exist in neuro-oncology clinical trial referral and enrollment.

### Methods

The study was reviewed by and determined to be exempt from the NIH Institutional Review Board. The Provider Survey on Clinical Trials was completed online by those on the SNO mailing list (including SNO members and meeting attendees). The survey consisted of 44 questions on participant characteristics (demographic and center information), institutional patient care patterns including clinical trial referral and management, and perceived provider and patient barriers to neuro-oncology clinical trial referral and enrollment. Participants were informed of the confidentiality of their responses prior to completing the survey. The survey was sent out to members via an email link using SurveyMonkey on 3 days (February 27, 2018; March 13, 2018; and April 17, 2018) and data collection was closed April 20, 2018.

IBM SPSS Statistics version 24 was used to analyze descriptive statistics from the provider dataset. This included analyses of the mean, median, SD, range, and frequency of responses from the overall sample and specific subgroups. The subgroup analyses conducted assessed responses across geographic regions (United States of America [USA], Europe—including Israel, and other global regions), self-identified institution type (academic medical research centers and other institutions), and neuro-oncology profession type (adult and pediatric neuro-oncologists).

### Results

#### Description of Overall Sample

The sample for this study originally consisted of 426 respondents, of whom 372 providers were assessed in the present analyses after 54 participants were removed because they either did not qualify for the survey because of limited involvement in direct patient care or they failed to provide responses to a large majority of the questionnaire (Fig. 1). The sample breakdown for each subgroup analysis can be seen in Fig. 1 as well. Because this survey was electronically distributed and completed internationally, providers from more than 40 countries were represented, with most coming from the USA and Europe (Fig. 2).

Table 1 provides an overview of the demographic information and characteristics of the survey sample. The majority of providers were white men from the USA. There was also a relatively equal distribution of providers across USA regions. About half of the sample participants were adult neuro-oncologists, with another small subset self-reporting a focus on pediatric neuro-oncology. The remaining participants reported to be some other type of physician, including neuro-surgical oncologists, neuro-radiation oncologists, and neurologists, nurse practitioners, or other health care professionals, such as clinical research staff or physician assistants. Most of the providers have been working in the health care industry for 21 years or more and see around 101–300 patients per year. The large majority of providers worked at academic medical research centers with clinical trials occurring at their own center (Table 2). When provider characteristics were analyzed across geographic regions and institution type, results showed that the percentage of neuro-oncologists between the USA and Europe remained about the same,
and between academic medical research centers and other institutions. However, in other global regions there was a slightly higher percentage of neuro-surgical oncologist participants than in the USA or Europe.

**Provider Clinical Trial Referral Patterns and Institutional Referral Tracking Systems**

Providers reported having referred, on average, 28% of their patients to neuro-oncology clinical trials. Additionally, most adult neuro-oncologists spent 1 hour or less per week referring patients to clinical trials. As depicted in Table 2, though a majority of institutions tracked the number of patients seen who were referred for participation in a clinical trial within their own institution or network of institutions (66%), many did not have a system for tracking referrals to trials outside their institution or network of institutions. Also, many providers either did not know or claimed to not have any system to determine the percentage of patients referred to trials at their institution (37%).

**Clinical Trial Referral Beliefs, Sources of Information Among Providers, and Patient Inquiry**

A large majority of providers were either principal or co-investigators on a clinical trial (Table 1) and tended to feel that all clinical trials should either be referred or considered (Table 3). Only 33% of providers felt a trial should be entered or considered only if evidence existed of the trial’s efficacy in similar patients, whereas an even smaller subset expressed concerns about the scientific merit of trials to date. Providers reported to have accessed information regarding trials at their own institution multiple times per week while having done so only a few times per month for trials outside their institution. Clinical trial finder websites, word of mouth and colleagues, and conferences were found to be the main sources of information about clinical trials for providers (Table 3). Most providers also reported having used multiple sources to obtain information about clinical trials. Providers who reported having used clinical trial finder websites tended to rate their most frequently used site highly on its user-friendliness, with an average ranking of 7.4 out of 10. Less than half of clinicians reported that their patients usually ask about clinical trials. Those patients who do inquire about trials do so most frequently after tumor recurrence.

**Clinical Trial Availability and Recommendation Patterns**

Most providers claimed to have had clinical trials available for primary and/or recurrent WHO grade III/IV brain tumor patients and those with metastatic tumors, but not for patients with other tumor types or grades (Table 3). However, pediatric neuro-oncologists and providers from academic medical research centers were far more likely to report having a trial available at their own institution for low-grade glioma patients than adult neuro-oncologists or providers from institutions other than academic centers, respectively. In line with the tumor types for which trials were available, providers indicated that they are more likely to recommend primary and/or recurrent WHO grade III/IV brain tumor patients to a clinical trial. These trials are most frequently recommended at the patient’s time of first diagnosis and/or after tumor recurrence or progression (Table 3).

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**Fig. 1** Sample Size Breakdown. In this study, 426 individuals provided consent and began the survey. Of these 426, 16 responded “no” to a question about their involvement in direct patient care and were prompted to the end of the survey. Thirty-eight additional participants did not answer any questions besides their profession and were removed because of insufficient data. The statistical analyses were conducted on a final sample of 372 participants. Three separate subgroup analyses were then conducted as well.
Fig. 2  Maps of the Locations of Providers Globally and in the United States of America (USA). Providers were primarily located in the USA (230 providers), whereas others were located in Europe (57 providers) and other global regions (72 providers). On the map of the USA, states from which a provider participated are shown in blue. Darker hues on the global map represent larger volumes of participants.
| Table 1  | Provider Demographics and Characteristics |
|----------|------------------------------------------|
|          | Overall | Academic Medical Research Center | Other Institutions | Adult N.O. | Pediatric N.O. | USA Providers | Europe Providers | Other Global Regions Providers |
| Gender   |         |                                   |                    |           |               |              |                  |                                |
| Female   | 162 (44)| 136 (45)                          | 24 (41)            | 69 (42)   | 9 (43)        | 106 (47)     | 28 (49)          | 24 (34)                        |
| Male     | 204 (55)| 164 (54)                          | 34 (58)            | 94 (57)   | 11 (52)       | 119 (52)     | 29 (51)          | 47 (66)                        |
| Prefer not to identify | 3 (1) | 2 (1) | 1 (2) | 1 (1) | 1 (5) | 3 (1) | - | - |
| Missing  | 3        | 2 | - | 2 | 1 | - | - | 1 |
| Race/Ethnicity (Select All That Apply) |         |                                   |                    |           |               |              |                  |                                |
| Asian    | 57 (15) | 46 (15) | 9 (16) | 21 (13) | 1 (5) | 25 (11) | - | 27 (38) |
| Black/African American | 6 (2) | 5 (2) | - | 5 (3) | - | 6 (3) | - | - |
| Hispanic/Latino | 15 (4) | 8 (3) | 6 (10) | 9 (5) | 2 (9) | 9 (4) | - | 6 (8) |
| White    | 263 (71)| 221 (73) | 37 (64) | 115 (70) | 17 (77) | 172 (75) | 53 (93) | 32 (45) |
| Other    | 32 (9)  | 25 (8) | 7 (12) | 16 (10) | 2 (9) | 20 (9) | 4 (7) | 7 (10) |
| Missing  | 3        | 2 | - | 2 | - | - | - | 1 |
| Country/Region |         |                                   |                    |           |               |              |                  |                                |
| United States of Americaa | 230 (64)| 187 (64) | 35 (61) | 111 (70) | 9 (41) | - | - | - |
| Northeast | 61 (27)| 52 (28) | 7 (21) | 26 (24) | 4 (44) | - | - | - |
| Midwest  | 47 (20)| 42 (23) | 3 (9) | 18 (17) | 3 (33) | - | - | - |
| South    | 66 (29)| 50 (27) | 15 (44) | 37 (34) | 2 (22) | - | - | - |
| West     | 50 (22)| 42 (23) | 8 (24) | 27 (25) | - | - | - | - |
| Puerto Rico | 1 (<1)| - | 1 (3) | - | - | - | - | - |
| Missing  | 5        | 1 | 1 | 3 | - | - | - | - |
| Europeb | 57 (16)| 49 (17) | 8 (14) | 23 (14) | 9 (41) | - | - | - |
| Other global regionsc | 72 (20)| 57 (19) | 14 (25) | 25 (16) | 4 (18) | - | - | - |
| Missing  | 13       | 11 | 2 | 7 | - | - | - | - |
| Provider Type |         |                                   |                    |           |               |              |                  |                                |
| Neuro-surgical oncologist | 71 (19)| 58 (19) | 12 (20) | - | - | 30 (13) | 13 (23) | 23 (32) |
| Neuro-radiation oncologist | 32 (9)| 24 (8) | 8 (14) | - | - | 16 (7) | 4 (7) | 12 (17) |
| Neuro-radiologist | 1 (<1) | 1 (<1) | - | - | - | 1 (<1) | - | - |
| Neuro-oncologistd | 166 (45)| 138 (45) | 24 (41) | - | - | 111 (48) | 23 (40) | 25 (35) |
| Pediatric neuro-oncologiste | 22 (6)| 21 (7) | 1 (2) | - | - | 9 (4) | 9 (16) | 4 (6) |
| Neurologist/Epileptologist | 6 (2)| 5 (2) | 1 (2) | - | - | 1 (<1) | 3 (5) | 1 (1) |
| Primary care provider | 1 (<1) | 1 (<1) | - | - | - | 1 (<1) | - | - |
| Palliative counselor | 1 (<1) | - | 1 (2) | - | - | - | 1 (2) | - |
| Neuro-oncology nurse | 6 (2)| 3 (1) | 3 (5) | - | - | 4 (2) | 1 (2) | 1 (1) |
| Social worker | 1 (<1) | - | - | - | 1 (<1) | - | - | - |
| Table 1 Continued | Overall | Academic Medical Research Center | Other Institutions | Adult N.O. | Pediatric N.O. | USA Providers | Europe Providers | Other Global Regions Providers |
|-------------------|---------|----------------------------------|-------------------|-----------|----------------|---------------|-----------------|-------------------------------|
| Nurse practitioner | 21 (6)  | 18 (6)                           | 3 (5)             |           |                | 19 (8)        | 1 (2)           | 1 (1)                         |
| Physician assistant | 5 (1)   | 5 (2)                            |                   |           |                | 5 (2)         |                 |                               |
| Clinical research staff | 18 (5) | 12 (4)                           | 4 (7)             |           |                | 16 (7)        | 1 (2)           | 1 (1)                         |
| Basic scientist | 2 (1)   | 1 (<1)                           | 1 (2)             |           |                | 2 (1)         |                 |                               |
| Other | 19 (5)  | 17 (6)                           | 1 (2)             |           |                | 14 (6)        | 1 (2)           | 4 (6)                         |
| Missing | -       | -                                | -                 |           |                | -             |                 |                               |
| Length of Time Working in Healthcare | Less than 5 years | 26 (7) | 24 (8) | 2 (3) | 13 (8) | 1 (5) | 17 (7) | 2 (4) | 7 (10) |
| 5-9 years | 63 (17) | 51 (17) | 10 (17) | 30 (18) | - | 42 (18) | 7 (12) | 11 (15) |
| 10-15 years | 74 (20) | 59 (20) | 11 (19) | 40 (24) | 4 (18) | 45 (20) | 10 (18) | 17 (24) |
| 16-20 years | 62 (17) | 50 (17) | 10 (17) | 27 (16) | 2 (9) | 37 (16) | 10 (18) | 12 (17) |
| 21+ years | 146 (39) | 119 (39) | 26 (44) | 55 (33) | 15 (68) | 88 (38) | 28 (49) | 25 (35) |
| Missing | 1       | 1                                | -                 | 1         | 1             | -             |                 |                               |
| Yearly Caseload | Don't see patients | 14 (4) | 10 (3) | 3 (5) | 4 (2) | - | 13 (6) | - | - |
| 1-50 | 63 (17) | 49 (16) | 14 (24) | 28 (17) | 10 (45) | 30 (14) | 13 (23) | 18 (25) |
| 51-100 | 67 (18) | 58 (19) | 9 (15) | 29 (18) | 7 (32) | 34 (15) | 12 (21) | 19 (27) |
| 101-300 | 158 (43) | 138 (45) | 20 (34) | 67 (41) | 5 (23) | 107 (48) | 23 (40) | 23 (32) |
| Greater than 300 | 63 (17) | 49 (16) | 13 (22) | 35 (21) | - | 40 (18) | 9 (16) | 11 (15) |
| Missing | 7       | -                                | -                 | 3         | 6             | -             | 1                |                               |
| Are You a Principal or Coinvestigator on a Clinical Trial? | Yes | 255 (74) | 222 (75) | 32 (68) | 136 (88) | 20 (91) | 155 (72) | 44 (83) | 46 (74) |
| No | 88 (26) | 73 (25) | 15 (32) | 18 (12) | 2 (9) | 60 (28) | 9 (17) | 16 (26) |
| Missing | 29 | 9 | 12 | 12 | - | 15 | 4 | 10 |

**Abbreviations:** N.O., neuro-oncologist; USA, United States of America.

Table numbers are reported in n (%) format and the Other Institutions group was composed of providers from community hospitals, regional hospitals, a cancer center, a hospice facility, outpatient clinics, and other free-response reported institutions. Percentages also may not add correctly because of rounding. Participants can be in multiple groups (provider type, global region, and institution).

- USA regions were determined according to USA census–recognized regions.
- Israel was included as part of the Europe subgroup.
- Canada was included in the Other Global Regions subgroup.
- *Neuro-oncologist* includes medical oncologists as well as specialized neuro-oncologists because the 2 physicians play the same role depending on the geographic location where the patient is being treated.
- Some neuro-oncologists may have been pediatric neuro-oncologists who did not specify this specialization. The members of this group, however, did self-identify as *pediatric neuro-oncologists.*
Table 2  Center Characteristics

| Center Type                        | Overall | Academic Medical Research Center | Other Institutions | Adult N.O. | Pediatric N.O. | USA Providers | Europe Providers | Other Global Regions Providers |
|------------------------------------|---------|----------------------------------|-------------------|------------|----------------|---------------|------------------|-----------------------------|
| Community hospital                 | 10 (3)  | —                                | —                 | 2 (1)      | —              | 5 (2)         | 2 (4)            | 3 (4)                      |
| Academic medical research center   | 304 (84)| —                                | —                 | 138 (85)   | 21 (95)        | 187 (84)      | 49 (86)          | 57 (80)                    |
| Regional hospital                  | 38 (10) | —                                | —                 | 17 (10)    | 1 (5)          | 22 (10)       | 5 (9)            | 10 (14)                    |
| Hospice                            | 1 (<1)  | —                                | —                 | 1 (1)      | —              | 1 (<1)        | —                | —                          |
| Cancer center                      | 1 (<1)  | —                                | —                 | —          | —              | 1 (<1)        | —                | —                          |
| Outpatient clinic                  | 6 (2)   | —                                | —                 | 4 (2)      | —              | 4 (2)         | 1 (2)            | 1 (1)                      |
| Other                              | 3 (1)   | —                                | —                 | —          | —              | 2 (1)         | —                | —                          |
| Missing                            | 9       | —                                | —                 | 4          | 8              | 8             | 1                | 1                          |
| Clinical Trials at Center          | Yes     | 348 (97)                         | 296 (99)          | 49 (86)    | 155 (98)       | 22 (100)      | 218 (99)         | 54 (98)                    |
|                                    | No      | 11 (3)                           | 3 (1)             | 8 (14)     | 3 (2)          | 3 (1)         | 1 (2)            | 7 (10)                     |
| Missing                            | 13      | 5                                | 2                 | 8          | 8              | 9             | 2                | 2                          |
| Does Your Institution Track the Number of Patients Seen Who Are Referred for Participation in a Clinical Trial? | Yes, within our institution or network of institutions | 164 (44) | 137 (45) | 23 (39) | 78 (47) | 5 (23) | 114 (50) | 20 (35) | 24 (34) |
|                                    | Yes, within our institution and to trials outside of our institution or network | 82 (22) | 69 (23) | 11 (19) | 34 (20) | 12 (54) | 49 (21) | 22 (39) | 9 (13) |
|                                    | No      | 80 (22)                          | 65 (22)           | 15 (25)    | 41 (25)        | 4 (18)        | 38 (17)          | 10 (18)                    |
|                                    | I don't know | 45 (12) | 32 (11) | 10 (17) | 13 (8) | 1 (5) | 29 (13) | 5 (9) | 9 (13) |
|                                    | Missing | 1                                | 1                 | —          | —              | —             | —                | —                          |
| What Percentage of Neuro-Oncology Patients at Your Institution Are Referred for Clinical Trials? | Mean (SD) | 28 (26) | 28 (25) | 21 (24) | 28 (25) | 26 (21) | 30 (87) | 12 (20) | 11 (20) |
|                                    | Median (range) | 20 (0-100) | 20 (0-100) | 10 (0-100) | 20 (0-100) | 20 (5-80) | 10 (0-1000) | 5 (0-100) | 4 (0-100) |
|                                    | I don't know | 139 (40) | 119 (41) | 18 (34) | 49 (30) | 5 (28) | 92 (46) | 15 (31) | 26 (44) |
|                                    | Missing | 21                               | 14                | 6          | 4              | 4             | 31               | 9              | 13              |

**Abbreviations:** N.O., neuro-oncologist; USA, United States of America.
Table numbers are reported in n (%) format unless otherwise stated. Percentages also may not add correctly because of rounding. Participants can be in multiple groups (provider type, global region, and institution).
Provider-Reported Challenges and Barriers to Clinical Trial Referral and Participation

**Overall Challenges and Barriers**

In terms of overall recommendation challenges and barriers, the survey addressed providers’ own concerns as well as the challenges they believed patients face when considering participation in a clinical trial. The most frequently selected challenges that providers have encountered during their careers in recommending participation in a clinical trial to their patients were that the patient may not be able to stay for treatment at the academic site, the patient may not be able to attend frequent follow-up as required, there may be no slot available for the patient in a multicenter trial, and it may be difficult to find trials near the patient geographically (Supplementary Table 1). In this survey, providers first selected a particular challenge encountered during their years of practice and then subsequently ranked how commonly seen the challenge was. The challenge that was selected and ranked as the most common for the overall sample was difficulty finding ongoing trials in the patient’s geographic area (Supplementary Table 1).

Providers were also queried about patient concerns and challenges, with the most frequently appearing challenges including that the patient may be concerned about the experimental nature of a clinical trial, the patient may be concerned about being placed in a placebo or control group, the patient may not qualify for a trial, and the patient may not understand the concept of a clinical trial (Supplementary Table 1). The patient participation challenge that was selected and ranked as the most common was that patients simply may not qualify for a trial. Overall, 92% of providers felt their patients encountered more than one challenge when considering participation in a clinical trial.

**Challenges and Barriers by Geographic Region: USA, Europe, and Other Global Regions**

After considering the overall sample, challenges and barriers were then evaluated separately based on geographic region including: the USA, Europe (including Israel), and other global regions. Supplementary Table 1 displays each geographic region’s most frequent provider concerns and the differences between each region and the overall findings. Providers from the USA reported many of the same concerns and challenges seen in the overall sample. However, financial concerns for the patient, such as lack of insurance coverage, was a more frequent barrier to trial referral in this group. Unlike USA providers, those from Europe and other global regions more frequently reported difficulty finding ongoing trials in the patient’s geographic area, limited staff resources, and a lack of awareness of any trials for which the patient met eligibility requirements (Supplementary Table 2). Both institutional groups, just as in the overall report, identified some challenges with financial concerns for the patient, such as lack of insurance coverage, as well. For the academic medical research center subgroup, the provider challenge that was selected and ranked as the most common was a tie between having no slot available for the patient in a multicenter trial and patients not being able to stay for treatment at the academic site. For the other institutions subgroup, difficulty finding ongoing trials in the patient’s geographic area was the most common challenge, which matched what was identified in the overall sample.

Providers from academic medical research centers reported the same frequent barriers identified in the overall sample, but with some differences in frequency. However, those providers not from academic medical research centers more frequently reported challenges with finding ongoing trials in the patient’s geographic area, limited staff resources, and a lack of awareness of any trials for which the patient met eligibility requirements (Supplementary Table 2). Both institutional groups, just as in the overall report, identified some challenges with financial concerns for the patient, such as lack of insurance coverage, as well. For the academic medical research center subgroup, the provider challenge that was selected and ranked as the most common was a tie between having no slot available for the patient in a multicenter trial and patients not being able to stay for treatment at the academic site. For the other institutions subgroup, difficulty finding ongoing trials in the patient’s geographic area was the most common challenge, which matched what was identified in the overall sample.

Differences in Challenges and Barriers Between Adult and Pediatric Neuro-Oncologists

It has commonly been identified that pediatric patients may be referred to academic centers and clinical trials more frequently than adult patients with cancer and therefore may face different challenges and barriers. In this study, to address these issues specifically, neuro-oncologists were categorized

The most frequently appearing patient concerns from providers from all 3 regions matched those seen in the overall sample. However, there were some differences, with providers from Europe identifying that patients might be too sick to travel; the USA participants identifying patient concern about cost and/or insurance coverage; and those from other global regions reporting that patients might not adhere to the protocol of a clinical trial. As seen in the overall report, European and USA providers felt the most common participation challenge for patients was that they simply may not qualify for a clinical trial. Providers from all 3 geographic regions felt patient concerns about placement in a placebo or control group and about the experimental nature of a clinical trial were also common challenges.
Table 3  Clinical Trial Referral Beliefs, Trial Availability, Patient Inquiry, and Provider Recommendation Patterns

| What Is Your Opinion About Clinical Trials? (Select All That Apply) | Overall | Academic Medical Research Center | Other Institutions | Adult N.O. | Pediatric N.O. | USA Providers | Europe Providers | Other Global Regions Providers |
|---------------------------------------------------------------|---------|---------------------------------|-------------------|-----------|----------------|--------------|----------------|-----------------------------|
| Clinical trials are a waste of time                           | 1 (<1)  | 1 (2)                           | 1 (2)             | 1 (2)     | 1 (2)          |              |                |                             |
| Few clinical trials have enough evidence to support recommendation | 11 (3)  | 6 (2)                           | 5 (9)             | 5 (3)     | 1 (5)          | 5 (2)        | 1 (2)          | 3 (4)                       |
| If there is evidence that a clinical trial may work for similar patients, then the trial should be entered or considered | 120 (33) | 96 (32)                        | 23 (40)          | 47 (29)  | 6 (27)         | 67 (30)      | 17 (30)         | 28 (40)                     |
| All clinical trials should be referred or considered           | 251 (69) | 218 (72)                        | 31 (54)          | 111 (69) | 15 (68)        | 165 (74)     | 42 (75)         | 38 (54)                     |
| Other                                                          | 18 (5)  | 15 (5)                          | 3 (5)            | 13 (8)    | 2 (9)          | 12 (5)       | 6 (9)           |                             |
| Missing                                                        | 10      | 2                               | 2                | 5         | 7             | 1            | 1               | 2                           |
| In the Last Year, for Which Patients Have You Had Clinical Trials Available at Your Institution? (Select All That Apply) | 18 (5)  | 15 (5)                          | 3 (5)            | 13 (8)    | 2 (9)          | 12 (5)       | 6 (9)           |                             |
| Primary grade I brain tumor                                    | 52 (15) | 52 (18)                         | 26 (17)          | 10 (45)  | 32 (15)        | 11 (20)      | 8 (13)          |                             |
| Primary grade II brain tumor                                   | 123 (36)| 117 (41)                        | 6 (13)           | 58 (37)  | 9 (41)         | 86 (40)      | 15 (28)         | 18 (30)                     |
| Primary grade III/IV brain tumor                               | 309 (90)| 269 (84)                        | 39 (83)          | 149 (96) | 18 (82)        | 202 (94)     | 47 (87)         | 48 (80)                     |
| Recurrent grade I brain tumor                                  | 55 (16) | 54 (19)                         | 1 (2)            | 29 (19)  | 11 (50)        | 40 (19)      | 11 (20)         | 3 (5)                       |
| Recurrent grade II brain tumor                                 | 117 (34)| 110 (38)                        | 7 (15)           | 58 (37)  | 13 (59)        | 91 (42)      | 15 (28)         | 8 (13)                      |
| Recurrent grade III/IV brain tumor                             | 256 (74)| 229 (80)                        | 26 (55)          | 126 (81) | 15 (68)        | 185 (86)     | 26 (48)         | 34 (57)                     |
| Metastatic brain tumor                                         | 185 (54)| 161 (56)                        | 23 (49)          | 88 (57)  | 6 (27)         | 142 (66)     | 17 (31)         | 19 (32)                     |
| Meningioma<sup>a</sup>                                         | 16 (5)  | 12 (4)                          | 4 (9)            | 5 (3)     | —              | 10 (5)       | 5 (9)           | 1 (2)                       |
| My institution does not have clinical trials available          | 6 (2)   | 6 (2)                           | 2 (4)            | 2 (1)     | —              | 3 (1)        | 3 (6)           | 2 (3)                       |
| Other                                                          | 23 (7)  | 23 (8)                          | 7 (15)           | 5 (3)     | 9 (41)         | 17 (8)       | 7 (13)          | 6 (10)                      |
| Missing                                                        | 29      | 17                              | 12               | 11        | 14             | 3            | 12              |                             |
| On Average, How Often Do Patients Inquire About a Clinical Trial? | 16 (5)  | 14 (5)                          | 1 (2)            | 11 (7)    | —              | 12 (6)       | 3 (6)           | 1 (2)                       |
| Always                                                         | 124 (38)| 106 (38)                        | 18 (38)          | 63 (42)  | 10 (48)        | 92 (44)      | 18 (35)         | 11 (18)                     |
| Usually                                                        | 124 (38)| 106 (38)                        | 18 (38)          | 63 (42)  | 10 (48)        | 92 (44)      | 18 (35)         | 11 (18)                     |
| Somewhat often                                                 | 92 (28) | 85 (30)                         | 7 (15)           | 43 (28)  | 6 (29)         | 59 (29)      | 12 (24)         | 17 (28)                     |
| When in the Disease State Do Patients Commonly Inquire About Clinical Trials? | Overall | Academic Medical Research Center | Other Institutions | Adult N.O. | Pediatric N.O. | USA Providers | Europe Providers | Other Global Regions Providers |
|---|---|---|---|---|---|---|---|---|
| Occasionally | 67 (20) | 51 (18) | 16 (33) | 28 (19) | 3 (14) | 35 (17) | 13 (25) | 17 (28) |
| Rarely | 25 (8) | 21 (8) | 4 (8) | 6 (4) | 2 (10) | 8 (4) | 5 (10) | 11 (18) |
| Never | 5 (2) | 3 (1) | 2 (4) | — | — | 1 (1) | — | 4 (7) |
| Missing | 43 | 24 | 11 | 15 | 1 | 23 | 6 | 11 |

| When in the Treatment Process Are You Most Likely to Recommend a Clinical Trial? (Select All That Apply) | Overall | Academic Medical Research Center | Other Institutions | Adult N.O. | Pediatric N.O. | USA Providers | Europe Providers | Other Global Regions Providers |
|---|---|---|---|---|---|---|---|---|
| At the time of first diagnosis | 246 (74) | 216 (77) | 29 (62) | 119 (76) | 17 (81) | 161 (80) | 34 (65) | 43 (67) |
| After surgery | 174 (53) | 148 (52) | 26 (55) | 85 (54) | 4 (19) | 111 (55) | 25 (48) | 29 (45) |
| If surgery is not a viable option | 111 (34) | 99 (35) | 12 (26) | 55 (35) | 3 (14) | 76 (38) | 16 (31) | 14 (22) |
| After standard treatment fails | 197 (60) | 170 (60) | 27 (57) | 102 (65) | 11 (52) | 124 (62) | 31 (60) | 32 (50) |
| After recurrence/progression | 219 (66) | 194 (69) | 25 (53) | 117 (75) | 10 (48) | 140 (70) | 36 (69) | 34 (53) |
| After metastasis | 104 (31) | 90 (32) | 14 (30) | 52 (33) | 3 (14) | 70 (35) | 17 (33) | 13 (20) |
| I do not recommend clinical trials to my patients | 1 (<1) | 1 (<1) | — | — | — | 1 (<1) | — | — |
| Missing | 41 | 22 | 12 | 10 | 1 | 29 | 5 | 8 |

| To Which Patients Are You Most Likely to Recommend a Clinical Trial? (Select All That Apply) | Overall | Academic Medical Research Center | Other Institutions | Adult N.O. | Pediatric N.O. | USA Providers | Europe Providers | Other Global Regions Providers |
|---|---|---|---|---|---|---|---|---|
| Primary grade I brain tumor | 32 (9) | 28 (10) | 4 (8) | 12 (8) | 8 (38) | 17 (8) | 8 (16) | 4 (6) |
| Primary grade II brain tumor | 71 (21) | 64 (22) | 7 (14) | 32 (20) | 6 (29) | 41 (19) | 13 (25) | 12 (18) |
| Primary grade III/IV brain tumor | 204 (59) | 173 (59) | 30 (58) | 102 (65) | 11 (52) | 131 (61) | 28 (55) | 36 (55) |
| Recurrent grade I brain tumor | 49 (14) | 44 (15) | 5 (10) | 24 (15) | 10 (48) | 33 (15) | 9 (18) | 6 (9) |
| Recurrent grade II brain tumor | 88 (26) | 77 (26) | 11 (22) | 46 (29) | 9 (43) | 61 (28) | 13 (25) | 11 (17) |
| Recurrent grade III/IV brain tumor | 201 (58) | 174 (59) | 27 (53) | 101 (64) | 12 (57) | 133 (62) | 25 (49) | 35 (54) |
| Metastatic brain tumor | 122 (35) | 103 (35) | 19 (37) | 56 (35) | 5 (24) | 82 (38) | 18 (35) | 15 (23) |
| I recommend clinical trials to patients of all brain tumor types | 159 (46) | 137 (47) | 22 (43) | 76 (48) | 13 (62) | 104 (48) | 27 (53) | 22 (34) |
### Table 3 Continued

| What Sources Do You Get Your Information About Clinical Trials From Most Often? (Select All That Apply) | Overall | Academic Medical Research Center | Other Institutions | Adult N.O. | Pediatric N.O. | USA Providers | Europe Providers | Other Global Regions Providers |
|---|---|---|---|---|---|---|---|---|
| Research institute websites | 151 (48) | 121 (45) | 29 (67) | 74 (50) | 12 (57) | 101 (52) | 19 (38) | 26 (43) |
| Clinical trial finder websites | 216 (69) | 188 (69) | 28 (65) | 112 (75) | 16 (76) | 161 (83) | 21 (42) | 29 (48) |
| Conferences | 173 (55) | 151 (56) | 22 (51) | 81 (54) | 12 (57) | 102 (53) | 33 (66) | 31 (51) |
| Word of mouth or from colleagues | 188 (60) | 167 (62) | 21 (49) | 86 (58) | 14 (67) | 119 (61) | 31 (62) | 31 (51) |
| Industry representatives | 52 (17) | 41 (15) | 11 (26) | 20 (13) | 3 (14) | 21 (11) | 13 (26) | 15 (25) |
| Other | 14 (4) | 12 (4) | 2 (5) | 9 (6) | 1 (5) | 7 (4) | 1 (2) | 6 (10) |
| Missing | 57 | 33 | 16 | 17 | 1 | 36 | 7 | 11 |

**Abbreviations:** N.O., neuro-oncologist; USA, United States of America.

*Meningioma was written in and recategorized from free-text ‘other’ responses. Therefore, many other providers may have had meningioma trials at their institutions but failed to write it in as a free-response option.

Table numbers are reported in n (%) format. Percentages also may not add correctly because of rounding. Participants can be in multiple groups (provider type, global region, and institution).
into adult and pediatric provider subgroups. Results showed that adult neuro-oncologists faced similar challenges as the overall sample in recommending participation in a clinical trial to their patients. However, pediatric neuro-oncologists more frequently reported challenges with finding ongoing trials in the patient’s geographic area and time constraints than in the overall sample (Supplementary Table 3). As previously seen in the overall report, challenges with financial concerns for the patient, such as lack of insurance coverage, resonated both with adult and pediatric neuro-oncologists. Also, the provider challenge that was selected and ranked as the most common across profession types was difficulty finding ongoing trials in the patient’s geographic area. A few notable differences from the overall sample were identified when considering the most frequently reported provider-perceived patient challenges. Pediatric neuro-oncologists felt their patients feared being placed into a placebo or control group and faced greater challenges with language barriers than their adult counterparts did. Also, just as in the overall sample, adult and pediatric neuro-oncologists felt the most common participation challenge for their patients was that they simply may not qualify for a trial.

An additional analysis was conducted to better understand neuro-surgical oncologist referral beliefs and barriers. It was found that of the 79 (7%) total providers who reported limited staff resources to be a common challenge encountered in recommending participation in a clinical trial, 30 (40% of the total) were neuro-surgical oncologists and 10 (of the total 30) ranked this as a common barrier. Additionally, of the 57 (5%) who reported difficulty staying up to date on ongoing clinical trials, 25 (44% of the total) were neuro-surgical oncologists and 10 (of the total 17) ranked it as a common barrier. No other differences were observed between the overall sample and neuro-surgical oncologists’ top provider challenges/rankings or provider-perceived patient challenges/rankings.

### Patient Registries, Print Material, Expanded Access, and Off-Label Information Among Providers

Most providers are willing to pursue expanded access (single-patient investigational new drug) to investigational agents (85%) and off-label access to medicines (91%) for their patients who are not eligible for clinical trials. Some of the reasons providers believe patients do not wish to share their data in patient registries are confidentiality concerns (55%), fear of misuse of their data (39%), and a lack of patient knowledge of where or how to find registries (36%). Many providers gave multiple possible reasons as to why patients may not wish to share their data. Additionally, most providers (76%) would allow an outside organization to make print materials available in their office about clinical trials for their patients.

### Discussion

This survey represents the first comprehensive evaluation of clinical trial referral barriers and challenges in neuro-oncology. SNO providers refer 28% of their patients to neuro-oncology clinical trials, aligning well with reported participation rates from Chang and colleagues and the general oncology population, as well as with the recent report by the NBTS (2016) in which 21% of patients reported having been referred. The results of this survey indicate that information about clinical trial availability and referral outside the provider’s own institution is limited. The majority of providers do not spend significant time on a full evaluation of trial availability or referrals outside their own institution. Overall, most institutions have trials available only for patients with newly diagnosed or limited recurrence high-grade gliomas.

When clinical trials are considered, there are challenges faced by the provider and identified in patients. The most common provider challenge was finding ongoing trials in the patient’s geographic area, whereas providers believe patients are most commonly concerned they may not qualify for a trial. Providers also frequently encountered referral barriers such as patients not being able to stay for treatment at the academic site, patients not being able to attend frequent follow-up as required, and having no slot available for a patient in a multicenter trial. Additionally, providers believe their patients may be concerned about the experimental nature of a clinical trial or about being placed in a placebo or control group, may not qualify for a trial, and may not understand the concept of a clinical trial. This highlights the need for a better system of tracking all referrals to clinical trials, regardless of whether they take place at the provider’s own institution. Providers should also have access to these data and analytics thereof. Finally, there is a need for a better system of efficiently disseminating comprehensive trial information to providers so they can be made aware of all options available for their patients.

There were some issues that differed based on the global region of practice, whether providers cared for adult or pediatric patients, and the setting, indicating that mechanisms to institute changes may vary based on these differences. The higher percentage of neuro-surgical oncologists observed in the other global regions subgroup compared with the USA or Europe may be consistent with practice patterns in which access to oncologists may be limited in these regions. Additionally, it is worth noting that not all US states were represented in this survey or even have any neuro-oncologists. Thus, the geographic barriers many patients are thought to face could be explained by the lack of access to neuro-oncology fellowship-trained physicians in their state of residence. Ultimately, the issues patients face in states without neuro-oncologists were not fully explored in this survey.

The provider-reported challenges of a lack of geographic diversity in trial sites and the need for patients to stay at the academic site for treatment are areas of concern that the community has been working to address through various efforts. For example, the American Society of Clinical Oncology-Friends of Cancer Research–led *Journal of Clinical Oncology* Special Series on Eligibility Criteria and efforts of nonprofit groups such as the Ronald McDonald House are aimed at decreasing the prevalence of these barriers. Further efforts should be made to ensure patients and their caregivers understand the goals and importance of clinical trials to compete with the USA or Europe may be consistent with practice patterns in which access to oncologists may be limited in these regions. Additionally, it is worth noting that not all US states were represented in this survey or even have any neuro-oncologists. Thus, the geographic barriers many patients are thought to face could be explained by the lack of access to neuro-oncology fellowship-trained physicians in their state of residence. Ultimately, the issues patients face in states without neuro-oncologists were not fully explored in this survey.

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ensure a lack of knowledge is not a barrier to participation. Increasing trial accrual rates and better educating patients about clinical trials are salient points, as this will allow for more-efficient trials that will improve the SOC more rapidly. Moreover, studies have reported that enrollment in clinical trials may hold a survival advantage for neuro-oncology patients,20,21 which makes reducing barriers a pivotal issue. A companion paper by Lee and colleagues22 in this issue provides practical guidelines for addressing the clinical trial referral barriers highlighted in this and the NBTS report. Future studies should continue to monitor referral and participation challenges and barriers and evaluate the impact of the recommended and implemented changes outlined in the Lee et al paper.

There are several limitations to this report. Providers self-selected to participate in this survey and the final sample may not be reflective of all practice patterns. The overwhelming majority of participants worked in academic medical research centers and self-identified as neuro-oncologists. Therefore, findings may not be applicable to issues identified by general medical oncologists who also provide care to these patients or by those practicing in regional or rural centers. Multiple providers from the same institution may have participated, leading to concerns about the overrepresentation of large academic centers’ experiences in this sample. The overrepresentation of academic providers in this survey cannot be understated. It is worth acknowledging that there are far more providers delivering care to neuro-oncology patients than are represented in this study. Also, the small sample size for some subgroups, such as pediatric neuro-oncologists, may have influenced results. Additionally, referral in Europe is complex because of issues of crossing geographical borders and language differences, which might have manifested in unique concerns that were not adequately explored in this survey. Finally, many questions in this survey asked providers what they thought about certain issues, and thus these responses are opinions. For instance, the provider-perceived patient challenges are the beliefs of providers themselves and not of patients, which may have led to biased responses.

Conclusions

The results of this survey indicate that the majority of patients with CNS tumors are not referred to clinical trials, and there is limited referral outside a provider’s own institution or tracking of clinical trial referral. Challenges and barriers to clinical trial referral and patient participation are numerous, and efforts to improve clinical trial access, broaden eligibility criteria, and better educate and support patients are needed to improve participation to ultimately enhance the care of this vulnerable patient population.

Supplementary material

Supplementary material is available online at Neuro-Oncology (http://neuro-oncology.oxfordjournals.org/).

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