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ORIGINAL RESEARCH

Patient, Relative and Staff Experiences of Clinical Trial Participation in Neurooncology: "Maybe You Can Also Show the Positive, No Matter How It Ends"

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Purpose: There is a lack of evidence regarding how patients with malignant brain tumor and their relatives experience participation in neurooncological clinical trials. Similarly, insights from the perspective of trial staff caring for this group of patients are missing. This study aims to investigate patient, relative and trial staff experiences regarding participation in clinical neurooncological trials.

Methods: Within a qualitative exploratory study, 29 semi-structured interviews with brain tumor patients, relatives and trial staff were conducted and analyzed using reflexive thematic analysis (RTA) by Braun and Clarke. A patient researcher and patient council were involved in data analysis and interpretation.

Results: Four themes were developed reflecting significant aspects of the trial experience: 1. "It all revolves around hope"; 2. "Trial participation: experiencing unique medical care"; 3. "Everyone's roles are changing"; 4. "Communication as a possible area of conflict". Experiencing trial participation and general medical treatment were found to be interconnected to such a degree that they were often not meaningfully distinguished by patients and relatives.

Conclusion: In addition to assessing traditional endpoints for patient outcomes, we recommend increased emphasis on investigating the impact of the "soft" components constituting trial participation. Due to the interconnectedness of medical treatment and trial participation, we recommend further investigation in comparison to experiences in regular care. A deeper understanding of trial participation is needed to inform improvements for patient experiences and staff satisfaction alongside medical and scientific progress.

Plain Language Summary: The treatment options available to patients with (malignant) brain tumors are currently very limited. Therefore, patients are sometimes offered to participate in a clinical trial. This means that they receive an experimental treatment (eg new medicine) for which it is not yet clear whether it works better than regular medical care. Currently, little is known about how this group of patients, their relatives and the hospital staff who care for them experience the participation in these clinical trials – which is what we aimed to explore in our study reported here.

Based on interviews with patients, relatives and staff, we found that:

- trial participation mainly revolves around hope;
- trial participation entails experiencing unique medical care;
- trial participation significantly changes the previous roles of patients, relatives and staff;
- trial participation intensifies communication as a possible area of conflict.

By providing information on how patients, relatives and staff make sense of their trial experiences, this study constitutes an important addition to the traditional focus of clinical trials on medical and scientific endpoints (eg progression-free survival). This may help clinicians and researchers involved in cancer research and treatment to understand why "unsuccessful" trials can still be perceived as positive by patients or how hopeful communication may support their patients even when perceived as "unrealistic" from the clinicians' perspective. An in depth understanding of trial participation from the perspective of those affected is needed for improved care experiences alongside medical and scientific progress for cancer treatment.

Keywords: cancer research, brain tumor, qualitative research, care experiences

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Introduction

Malignant brain tumors belong to the tumors most difficult to treat, with limited established therapies available.[1,2] This underscores the need for new therapeutic approaches and concepts. Due to clinical and basic research, knowledge about this heterogenous group of tumors constantly increases.[1–3] Growing scientific insights give rise to new therapeutic targets with a shift towards targeted molecular therapies.[2,4] The most promising new therapeutic approaches progress into clinical trials.[1–3]

Patients with malignant brain tumors have to cope with the heterogenous consequences of a neurological disease and cancer, sometimes called the "double threat".[5] Malignant brain tumors often cause a high symptom burden, including cognitive deficits,[6] and therefore far-reaching impact on all aspects of life.[7–11] The overall burden of disease is high for patients and their social environment.[8,9,12] Previous research showed that malignant brain tumor patients have complex needs, eg regarding communication and information provision.[13,14]

Participation in clinical trials can come along with diverse challenges, but also benefits.[15,16] Due to limited therapeutic options, treatment may be considered to take place in an interventional trial. However, despite the high unmet need, trial options remain sparse and trial participation is possible only for a minority of patients. Little is known on how this group of patients and their relatives experience participation in clinical neurooncological trials. Similarly, published insights from the perspective of trial staff caring for this unique patient group are sparse.

To this purpose, we aimed to investigate patients', relatives' and staffs' perspectives and experiences on participating in a clinical neurooncological trial. This could help improve trial recruitment[17] in addition to improving patients' and relatives' care experiences as well as staff satisfaction during trial participation.

Methods

Research Design

An inductive qualitative exploratory study including semi-structured interviews was conducted, utilizing a critical realist framework.[18] Medical Faculty of Heidelberg University's ethics commission approved the study (S-037/2021). All participants provided informed consent, including for publication of anonymized quotes. For improved clarity, we use "trial" to refer to clinical neurooncological trials and "study" when referring to our qualitative study reported here.

Setting & Research Team

The study was conducted at the Department of Neurology at Heidelberg University Hospital. RT and LB were responsible for data collection and analysis. RT is a medical student new to qualitative research and LB a social scientist with approximately 10 years' experience in qualitative research. Neither was involved in patient care. CG is a senior physician with >5 years' experience in neurooncological care. WW is the medical director of the Department of Neurology with > 25 years' experience in neurooncological care and clinical trials. During data analysis, the team was joined by a patient researcher.

Participants & Recruitment

To gather diverse perspectives, we applied a purposive sampling strategy for all three subgroups of our participant group. Patients and relatives were recruited from two ongoing clinical trials: NCT Neuro Master Match N2M2 and AMPLIFYing NEOepitope-specific VACcine Responses in Progressive Diffuse Glioma (AMPLIFY-NEOVAC).[19,20] This made it possible to include the perspective of newly diagnosed patients as well as patients further in the disease trajectory with relapses. Staff was purposively sampled to cover all relevant disciplines involved in the interdisciplinary care of neurooncological trial participants. We used Malterud's model of information power to constantly evaluate the size and composition of the participant group during the research process.[21]

Data Collection

Data collection took place between April and July 2021. The semi-structured interview guides were developed based on literature research and expertise on clinical trials provided by experienced colleagues in preliminary informational

conversations. All interviews were conducted by RT. Due to covid-19-pandemic safety precautions, some interviews were conducted face-to-face, while others were conducted by videoconference or by phone. Whenever possible, interviewees could choose their preferred setting. All interviews were audio-recorded and transcribed verbatim. Demographical information was gathered on age, gender, marital status, tumor type and other characteristics (see Tables 1–3).

Data Analysis

Data analysis was conducted according to reflexive thematic analysis (RTA) by Braun & Clarke. RTA fits the study's experiential focus, is suitable for interview data and recommended when aiming for actionable outcomes.[18,22] Following the six phases of RTA, while continuously discussing the analytic developments in the team, four themes were developed. During data analysis, it became apparent that even though data collection was focused on trial participation, patients' and relatives' answers often did not clearly distinguish between trial participation and regular medical care or disease experience in general. In reporting our results, we specify whether information refers to trial participation and/or medical care, or whether a clear distinction is not possible based on the information provided.

Patient and Public Involvement

Starting in the planning phase, the Patient Council of the Department of Neurology was regularly updated by the research team and invited to provide feedback. The interview guide was piloted with two volunteers from the Patient Council eg for harmful questions and to reflect aspects such as length and atmosphere of the conversation. During data analysis, the research team was joined by a patient researcher – a neurooncological patient at the department who had not experienced a trial participation and was not involved as a study participant in the current study. In ongoing meetings, study methods and analytic content were discussed. The comparison and complementation through personal insights expanded the analytic perspectives.

Table 1 Demographic Information – Relatives

Age in Years (Minimum, Maximum, Average)	**33–71,5 Years (54,2 Years)**
Gender	
Male	3
Female	5
Diverse	0
Relationship to patient	
Spouse	4
Partner	1
Child	1
Sibling	1
Friend	1
Housing situation	
Lives with patient	6
Does not live with patient	2
Carer for patient	
Yes	2
No	6

Table 2 Demographic Information – Staff

Age in Years (Minimum, Maximum, Average)[a]	**29–60 Years (43 Years)**
Gender	
Male	3
Female	12
Diverse	0
Occupation	
Physician	11
Study nurse, social worker, other[b]	4
Medical specialties	6
Neurology	9
Radiology and radiooncology	1
Neurosurgery	1
Work experience in years (minimum, maximum, average)	3–42 years (14 years)
Trial experience in years (Minimum, Maximum, average)	0,25–24 years (10,6 years)
Length of employment at UKHD in years (minimum, maximum, average)[c]	2–32 years (13,4 years)

Notes: [a]One information is missing because only age margin has been declared; [b] Not further specified to ensure anonymity; [c] One information is missing.
Abbreviations: UKHD, University Hospital Heidelberg.

Table 3 Demographic Information – Patients

Age in Years (Minimum, Maximum, Average)	**39–70 Years (56 Years)**
Gender	
Male	4
Female	2
Diverse	0
Marital status	
Unmarried	1
Married	4
Divorced	1
Working/ employed at time of interview	
Yes	2
No	4
Diagnosis	
Glioblastoma WHO-grade IV	5
Astrocytoma WHO-grade II	1
Karnofsky-Index	
100%	1
90%	2
80%	2
70%	1
In need of care	
Yes	0
No	6

(*Continued*)

Table 3 (Continued).

Age in Years (Minimum, Maximum, Average)	39–70 Years (56 Years)
Number of neurosurgical operations	
1	4
2	1
3	1
Number of tumor progressions at time of interview	
0	3
1	1
2	2
Patients with prior trial participation	0
N2M2 participation	4
Standard-of-care	2
APG101	1
Palbociclib	1
Amplify participation	2
Avelumab	1
Patient in analogue treatment[a]	1

Notes: [a]No further information provided due to privacy protection.
Abbreviations: WHO, World health Organization; N2M2, NCT Neuro Master Match study.

Results

General Results

We conducted 29 interviews with an average duration of 65 minutes with 6 patients, 8 relatives and 15 staff members. Of these, 13 interviews were conducted on site, 7 via video-conferencing, and 9 via telephone. Further information is provided in Tables 1–3. In the following, we report the four themes resulting from our RTA. As indicated above, we report these themes with a research focus on trial participation but regarding some aspects there was a high inter-connectedness of patients' and relatives' experiences of trial participation and their medical care in general. Quotes were translated from German to English by RT and LB.

It All Revolves Around Hope

Our analysis showed hope to be one of the most salient factors for trial participation for patients as well as for relatives; the central motivator for their decision to participate. This primarily included hope for own advantages but was also often mentioned as hope for benefits for future patients.

> My decision to participate? (…) That there might be an advantage for me as well as for science (…). That if it doesn't help me, science advances by getting new insights because of me [and] my illness (…). Interview-04-patient

One facet of hope was associated with experimental treatment arms, showing that some patients and relatives perceived them to be superior to standard treatment. While for many patients and relatives, hope contributed to the decision to participate, the participation itself also generated new hope for patients and relatives. This seemed to initiate a type of chain reaction, for example when hope was sustained by positive experiences such as MRI controls without disease progression. However, negative experiences such as worsening physical limitations and disease progression could also disappoint hopes.

> When they saw something [on the MRI] already six months [after surgery], it was like a punch to the gut. Interview-11-relative

But this did not necessarily mean that all hope was lost, as several patients and relatives described maintaining hope even after multiple setbacks.

> Now I just hope that after the fourth time, it will get thwarted a bit. Interview-05-patient

Hope influences how patients, relatives and staff interact, and is in turn influenced by these interactions. Staff interviewees were aware of the importance of hope but also expressed that there should not be – what they call – "unrealistic" hope (interview 13-staff). Navigating between these poles, they try offering an information-based frame while also attempting to not take away hope with actions or words. All staff interviewees identified this as a challenging balancing act and explained the need for a personalized, situational approach for patients and relatives.

> That's definitely the balancing act between honest communication, not taking away hope in therapy, but simultaneously not raising false hope. There is no standard way, it depends extremely on the patients and relatives and [in] every new conversation you have to figure out what fits for them and how much you communicate. Interview-26-staff

Some physicians emphasized that in addition to shaping current interactions, this balancing act could also affect how patients and relatives would handle their disease in the future. For example, they explained that information-based but hopeful conversations mastering the balance at the beginning of the disease could provide a good foundation for patients and relatives later processing worsening stages of disease. This importance was also shown by patients' and relatives' negative reactions to perceived imbalances regarding hope.

> (…) We also had conversations with an oncologist [at the previous treatment centre]. And these conversations were really awful. She took away our hope and left us distraught, so it was clear that [the patient] couldn't stay [at the previous treatment centre]. (…) From my perspective, these conversations were (…) ruthless. Almost worse than the actual situation (…). Interview-18-relative

Like staff, relatives also experience this balancing act in their interactions with patients.

Trial Participation: Experiencing Unique Medical Care

Experiencing unique medical care during trial participation profoundly shapes the experience of patients and relatives, often even beyond their participation. In addition to access to new medical approaches, almost all patients and relatives spoke about the outstanding personal care, eg having a small, stable group of contact persons, more conversations with staff, the possibility to speak to staff whenever needed, organizational support or the good relationship to staff. Especially the study nurses were mentioned regarding these positive experiences. This (perceived) quality of care already plays a role during decision making around potential trial participation, eg by staff highlighting how trial participation could involve those aspects of high-quality care provision mentioned above. Patients as well as relatives reported taking not only medical but also these personal care aspects into account for their decision.

> (…) That you (…) are closely monitored by the physician (…) or can speak with the physician in case of a question (….) and that you feel better taken care of, because you do have a lot of questions (…). You can ask these questions two or three days later (…) instead of two or three weeks later (….). Interview-02-patient

The perception that the experienced good care differs from other medical areas came up in contrast to inpatient care, experiences from other hospitals or experiencing care after the trial participation ended. Some patients and relatives spoke about their wish to have ongoing access to the same care services after trial participation.

> (…) I'd say it was a dramatic difference. During the trial we had one contact person, who we could always reach. (…) When he was inpatient (…) it all felt a bit more impersonal and the communication in general was more difficult. Interview-11-relative

The care during trial participation was one of the most prominent aspects about patients' and relatives' experiences, relevantly influencing their satisfaction with it. Even some patients whose participation ended earlier due to the progression of their disease, respectively their relatives, outlined a mostly positive view of trial participation because of the good care.

> They have done everything within human power. I would vouch for everyone. Interview-23-relative

Most of the staff talking about the above benefits of trial participation clarified afterwards that they did not mean to say that regular care is inferior. Instead, they explained that clinical trials often make additional resources available for patient care which lead to the perceived differences between regular and trial care.

> (…) Of course, it is an advantage that [patients] get "pampered" – that's what we call it nicely (…). That's just not possible in the daily routine. Not because [we] don't want it, but because (…) there's no staff for this. Interview-10-staff

Everyone's Roles are Changing

Trial Staff

The professional role of the trial staff is primarily influenced by the lack of curability of most malignant brain tumors, shifting their focus from aiming to cure to providing good care. Despite the specific and comparatively small medical field of neurooncology, the role of physicians in the outpatient trial setting gets more global, eg adopting tasks from other medical specialties such as general practitioners. In addition to this, most staff members described that the aspect of caring ("kümmern") matters a lot to the patients. Therefore, staff get involved in many non-medical issues and concerns.

> (…) You are also a general practitioner with this job. I have never treated as much nail mycosis as in neurooncology. [The fact that they have a brain tumor] is more important than everything else. And you also need a friendly ear for that, even when it's not the job. Interview-10-staff

Due to the trial setting with heightened frequency of appointments in comparison to regular care, trial staff often adopt the role of confidants and get to know more of the person behind the disease. To be able to remain healthy themselves, many staff interviewees described strategies they developed to distance themselves from their patients' fates.

> I have patients who I already see for years (…) and with whom I have a more intense relationship. And I frequently get asked if we could be on a first-name basis. (…) That's out of the question. (…) I always try to stay on a professional level. Interview-07-staff

Nevertheless, they experience individual stories which they take home from work or patients from whom they find it harder to distance themselves.

> As a mother, it's sometimes difficult for me when patients have kids. It is difficult not to think about how it goes when they come home and have to tell their three and seven-year-old kids that their mom is terminally ill. Interview-03-staff

In context of the changing medical role and professional obstacles, trial staff described different notions of what professionality in these roles meant to them, especially how much emotionality is part of it.

> You are in the role of the physician, not in the role of a friend, a neighbor, or the spouse. […] Patients for sure do not want to realize that I am sad or mad or desperate. That's not wat patients want and that doesn't help them at all. Interview-03-staff

> (…) The alternative is to avoid patients getting close to you. You build up a [protective shield] and you definitely don't learn anything about your patients. But the question is: does this kind of work satisfy me? And that's a clear "no" for me. Interview-10-staff

Reflecting their role in decision-making of patients and relatives, staff and foremost physicians commonly experience being asked for their personal opinion and advice. Despite their understanding that providing (medical) advice is part of their role, some staff described their impression that sympathies and trust in doctors may relevantly influence patients' decision on whether to participate. The assessment of this role aspect was supported by narrations of patients and relatives about their trust in doctors and following their recommendations regarding trial participation.

> (…) After the first conversation there was the trust that [my sister] thought that she wanted to do what [the doctor] suggests. (…) I think that she didn't challenge the decision. Interview-18-relative

> For sure we let ourselves be guided by what the doctor told us, that this may be the better way for us. Interview-11-relative

Through the lens of trial participation, this possible influence has a heightened ethical significance because it not only concerns the decision about standard treatment but also for experimental trial participation. This led to one person mentioning possible conflicts of interest inherent to being a physician (treating patients) and researcher (conducting trials).

Relatives

Relatives tend to play an active role during patient's trial participation. They described their self-conception as active, supportive, trying to be helpful. As part of this role, they may be engaged in managing the disease, trial participation, logistics, emotional support, as communicators but also as first responders to medical emergencies. As such, most relatives not only have to deal with the present situation but also have to plan for potential future events. One difficulty associated with this active role is finding a balance between being supportive but not becoming overprotective.

> I always pushed him a bit to go [to a therapist] (…). I don't want to infantilize my father. So when he wants something I'll help him to do so but when he doesn't stand behind it, I'll let him do his thing. Interview-11-relative

> (…) Too nice and courteous (…) when you get help with things you wanted to do on your own. Like a little child (…). After all, you want to shape your life on your own and you want to do things on your own. Interview-02-patient

One timepoint when relatives often play a crucial role is in the patient's decision about trial participation. According to staff, there are some relatives who are more reserved but most of them clearly express their opinion. This opinion is perceived by staff to have an influence on the patient's decision, sometimes even being described by staff as an exertion of influence. From the perspective of patients and relatives themselves, the descriptions are diverse and range from containing oneself, exchanging views to supporting the participation.

Trial Participants

When patients become trial participants, their role is mainly defined by attending trial appointments and individual interactions with trial staff. For patients, the aim to contribute to general scientific development was generally more important than the specific scientific aim of the trial they participated in. By taking on the role of a trial patient, some relinquished other needs in context of their disease, eg being able to try parallel or complementary therapies.

Being a trial patient leads to changes in other areas of life as well. The disease and its treatment dominate, and life must be adapted to it. Beside the time for the trial appointments, the time for recovering from them also limits the time contingent of patients.

> I always organized the two days after the trial appointment in a way that there wouldn't be any appointments. I just allowed myself to rest. During this time, I am not as fit as usual. I have to sleep a lot and recover. Interview-15-patient

This collides with the description of some patients of how important spending enough time with close ones becomes. How the trial participation changes the job-related role of patients differs widely. Especially self-employed patients and their relatives spoke about multiple difficulties while a patient with a more flexible job experienced less impact of the trial participation and the disease.

> [I] have to keep at least the most urgent things going, which is not that easy with this prognosis. I can't just tell everyone about it (…). I don't want my staff to pack their bags and go (…). I want to keep my staff, I have to offer them a perspective for the future. Interview-02-patient

Other patients had to deal with how their temporary inability to work may become permanent. All working patients had in common that they experienced new boundaries for their professional role.

Communication as a Potential Area of Conflict

Communication in the context of trial participation (and medical care provision in general) was experienced as complex, influenced by multiple factors, and the predominant area of possible conflict. One influencing factor is the individual point at which patients and relatives find themselves in processing the diagnosis and prognosis of their disease. Early in

this trajectory, patients as well as relatives described low capacity for receiving and processing information, eg leading to difficulties or even an inability to ask questions during conversations.

> (…) It's not just the surgery but also the diagnosis that disrupted my life. (…) There is no mental space left for the [trial information] (…). You're not the same person anymore. You're not as resilient and receptive anymore. Interview-22-patient

These limitations especially apply to time points when patients are approached for trial participation, meaning the necessity for processing complex information encounters limited reception, processing, and communication capacity.

Patients and relatives described a wide range of informational and communicational needs, which also changed over time and over the course of the disease. Both patients and relatives spoke about consciously limiting or changing their own communication despite their needs, eg because of their wish to minimize burden for others or because of negative reactions from their surroundings.

> (…) Generally, people get quite annoyed quickly. At some point, I stopped talking about my disease. I just tell them how beautiful the world is. Interview-16-patient

> You don't want to drag others down with you. (…) Imagine you get visitors, you're excited about it and after ten minutes the conversation is about my wife's disease. Interview-21-relative

During the interviews, patients as well as relatives spoke about their wish to hear the truth about their situation, demanding honest communication by their attending staff. But at the same time, they would like for this truth to be conveyed as positively as possible.

> [The] conversation was quite negative. (…) I am in favor of talking about everything as it is, but maybe you can also show the positive (…), the possibilities, and that there are things left that you can still do. No matter how it ends. Interview-22-patient

Conversations in the context of the disease and trial participation can often be emotional. In these moments, staff sometimes experienced that these emotions and feelings of patients and relatives were displayed outwards and projected onto them. They experienced this as another aspect increasing complexity and communicational demands on trial staff. It is therefore not surprising that – as was the case for hope – trial staff primarily spoke about the need for an individual communicational approach, getting to know and responding to the communicational needs of patients and relatives. They try to meet them at their individual knowledge level, convey necessary medical knowledge step by step over time, stating that educating their patients about their condition is an ongoing, never-ending process. In addition, trial staff outlined that every point in time has its suitable topics to talk about. Many examples mentioned by staff made it clear that they aimed to communicate honestly yet carefully, consciously and selectively choosing their words.

> I think patients [and] relatives are quite attentive (…). That means that you need to communicate carefully, maybe that's the wrong word, but thoughtfully (…). Interview-24-staff

As trial staff cannot predict an individual patient's most likely outcome, they carefully display a spectrum of possibilities. They try to shape their incremental communication in a way that it is neither too positive, too negative, nor too anticipatory. All of this is an expression of their awareness of the potential impact of their communication on patients' and relatives' wellbeing. It also outlines how pronounced communication skills are needed.

Discussion

This study examined the experiences of malignant brain tumor patients, relatives, and staff regarding clinical trial participation. We found the trial experiences to be shaped by hope, unique medical care, changing roles and communication challenges. As mentioned above, despite our study's focus on trial participation, we observed that the experiences of trial participation and receiving medical treatment are highly intertwined. Based on our results we conclude that improving care experiences requires understanding trial experiences, and vice versa.

Summary and Comparison to Other Studies

It All Revolves Around Hope

We extracted hope as one of the most essential aspects of trial participation for patients and relatives. In particular, we identified hope as an important driving factor for trial participation. This confirms findings by Knifed et al who described that one third of their interviewed brain tumor patients indicated hope for treatment of their condition as their reason to enroll in the trial.[23] In addition, our results showed a type of chain of hope, starting with hope as the reason for trial participation, continuing with the resulting hope from participation, and thereby generating more hope over the course of participation. This confirms and expands on findings by Sutton that trial participation encouraged hope in brain tumor patients.[24] Our findings regarding the relevance of hope for patients also reflect and highlight the relevance of therapeutic misconception,[25,26] as do our findings of a generally rather blurred distinction between trial and regular medical care experience. This may be especially relevant when thinking about new trial concepts such as umbrella trials, which are highly relevant for state-of-the-art brain tumor research.[27,28]

Staff interviewees of our study often presented being informed versus being hopeful in an either-or-context. But in our analysis, we found that these conditions often existed in parallel – even though they could differ in their character and, depending on the situation, one could be perceived as more important than the other. From Cavers et al it is known how important it is for brain tumor patients and relatives to hope despite adverse circumstances.[29] This also indicates that being informed and yet hopeful does not have to be contradictory. However, participants in the mentioned study consisted of patients with low grade as well as with high grade brain tumors. Findings outside the neurooncological focus also support our findings that being informed and being hopeful can co-exist.[30–33]

Trial Participation: Experiencing Unique Medical Care

We found that the special care provided during trial participation crucially shapes the care experience and satisfaction of patients and relatives. Sutton also outlined a high level of patient satisfaction with the care received during trial participation. She named this as a major benefit of trial participation and showed the positive impact on patients' quality of life.[24] We confirmed in our study that satisfaction was particularly linked to the personal care provided by trial staff. These findings are in line with other studies emphasizing that the unique care crucially shapes the experience of oncological and non-oncological patients' trial participation.[34–40] Finally, most of the interviewed oncologists by Murphy et al outlined that they thought trial patients would receive better care.[39] However, it should be noted that our study did not assess whether quality of care or health outcomes were better within the scope of trial participation compared to regular care.

Everyone's Roles are Changing

Our findings illustrated how trial staff show increased efforts to act empathically in their professional role while staying healthy over time. These efforts appeared especially important in the neurooncological trial context, given more frequent and intimate contact between staff and patients as well as the often terminal prognosis. Their portrayed strategies and behaviour could be subsumed as emotional labour.[41] Regarding the potential influence of trust in medical staff on trial decisions, a Cochrane qualitative evidence synthesis also found that decision-making could potentially be influenced by health care professionals as prospective participants place great trust in them and their recommendations.[42] Finally, the potential confluence of different role aspects such as caretaker and scientist by trial staff is reflective of and inherent to more general questions associated with physicians being clinical investigators.[43] These aspects are also connected to the discussions about the concept of therapeutic misconception and therefore should be considered when designing clinical trials.[26,44,45]

As in our study, the oncological patients in the study of Sawyer et al spoke about how trial participation influenced other parts of their daily life. This included for example scheduling their life around the trial and the needed time for recovery.[46] Cox et al compared life during trial participation with life in a waiting loop.[47] From our study, it remains unclear if this finding is exclusive to trial participants or applicable to brain tumor patients in general. For example, the interviewed brain tumor patients by Halkett et al described changes in their private role because of their disease and Sterckx et al linked changing roles to the symptoms of the disease.[10,14] Considering the findings of our study, changes in patients' as well as relatives' roles may not only result from the trial or the disease itself but also from the format in which they receive tumor therapy. It seems plausible that the changes in roles could possibly be intensified by trial participation, especially because of the heightened

frequencies of trial appointments and the time needed for trial participation in general. This could be further explored by directly comparing the experiences of neurooncological patients with and without trial participation. In terms of holistic care of patients and their relatives and to better manage their expectations, it could be useful to include the potential impact of the above aspects on their life in the trial education.

Communication as a Possible Area of Conflict

Our study showed that time points when patients are approached for trial participation and need to process complex information often coincide with patients' limited reception, processing, and communication capacity. This result confirms findings described for other oncological patients in trial settings[48–50] and findings described for neurooncological patients outside of trials.[10,29,51,52] The need for honest but as positive as possible communication was also described in contexts of regular care for neurooncological and other oncological patients.[10,29,52–54] As Strang and Bergqvist concluded, truth is a complex, relative and dynamic concept.[53] In our analysis, the crucial point seemed to be the individual understanding – by patients, relatives and staff – of what honest and truthful communication includes. Like Malmström et al and others illustrated, and was also shown here, this could differ widely per person[30,33,55,56] opening up the potential for conflict when individual understandings differ. Reflecting the communicational approach of our staff interviewees in context of the existing literature, their general approach seems to be in line with what is currently known about the communicational needs of patients and relatives.

Strengths and Limitations

Several limitations have to be considered. First, due to the interconnectedness of trial participation and medical care from the patients' and relatives' perspective, a clear-cut differentiation was not always possible. From the clinical perspective and experience, some aspects reported here are not exclusively trial specific. However, while the impact of receiving a terminal prognosis may be similar for trial participants and regular patients, the experience of being a trial participant can only be meaningfully understood when considering the impact of receiving such a diagnosis. Therefore, while the experiences we displayed were gathered with a focus on trial participation, they comprise the holistic experience of patients with this particular disease, participating in a trial. The difficulty for participants to distinguish trial-specific information from their diagnosis and standard treatment was also reported by the Cochrane synthesis cited above,[42] and can therefore in itself be considered a result of this study. It could be beneficial for future research to specifically compare qualitative results for trial and non-trial experiences to not only support this clinical view but also to understand how these aspects might change due to trial participation. Second, our study was limited to the perspectives of trial participation at the department of neurology at Heidelberg University Hospital. We gathered and displayed important context information to enable readers to discuss transferability to other contexts. Another limitation is the proportionately smaller number of patients and relatives compared to staff given that brain tumors are a relatively rare disease. As we had to exclude some patients depending on their physical and mental condition, this might limit our conclusions eg regarding patients with reduced ability to communicate. Future research might benefit from examining and comparing the experiences of the three participant subgroups from multi center trials. Last, due to pandemic restrictions, the initial multi-method design, including observations before the interviews, had to be adapted. Observations may have enabled another analytic layer, analyzing the experience of the participants in relation to the observations. Nevertheless, RT was allowed to accompany a patient, their relative and staff during their appointments. This was not part of data collection but informed RT's perspective for analysis.

With the three different participant subgroups we gathered multiple perspectives on the experience of trial participation. This enabled us to investigate complex situations from different angles and to incorporate all phases of trial participation, which may not be visible to all subgroups. Another strength was the interconnectedness of the study team in the neurological clinic. It facilitated access and insights which would probably not have been offered in the same way for external investigators. Finally, our research team undertook different efforts to incorporate patient involvement over the whole course of our research project. As such, our project seems to be relatively advanced in terms of patient involvement in cancer research as compared to the published literature.[57] We believe that this helped conduct our analysis and interpretation close to its main stakeholders.

Scientific and Practice Implications

In terms of practice recommendations, the experience of good care seemed to have an important effect on the experience of trial participation, contributing to improved patient as well as relative satisfaction. According to staff, this is a consequence of the improved availability of resources, ie additional funding for clinical trials. We recommend future research to investigate in more detail the individual impact of the different "soft" components that constitute trial participation, eg faster access to the treating physician, dedicated study nurses, a more personal relationship with trial staff, and other aspects to be further explored. This could help inform the distribution of resources in regular care when fewer resources are available and thereby potentially increase satisfaction in other patient and relative collectives.

We reported that trial staff successfully manage the balancing act of hopeful communication but also that they experience it as challenging as they are aware of patients' and relatives' high expectations. We would recommend that hospitals investigate if services or trainings could be offered to support especially less experienced staff in mastering this balancing act and the handling of hope within the team. This could not only be beneficial for trials but also clinical practice. Trial recruitment and patients' as well as relatives' satisfaction could potentially be enhanced by intentionally addressing aspects that may become important regarding their trial experience, based on the patient experiences reported in this study, such as hope, quality of care but also time demands which possibly collide with other important focus areas in their life. This should not only occur at the start of the trial (when patients' information processing capacity may be low) but continuously throughout trial participation and progression of the disease.

For future research, we recommend to further examine aspects such as the different understanding of hope by patients, relatives and staff and its manifestations in their communication within the context of trial participation. As patients are asked to accept additional commitments within the scope of a trial with uncertain benefits of experimental therapies, this may lead to more specific challenges regarding the handling of hope compared to standard treatment. Another focus for future research might be to evaluate successful informal strategies already in use by trial staff to navigate working with these patients in the special circumstances of trials, and to identify best practices. This could enable hospitals to further develop support offers for their staff in work environments with growing demands and challenges. As brain tumors are entities with a low prevalence, larger studies could help to investigate whether our themes have the same relevance for other research centers and if opinions and experiences overlap, helping to identify center-specific factors. Future research might also benefit from reaching out to patients and relatives at different time points to gather insights into their thoughts and decision-making processes as they are happening and possibly changing. Given the interconnectedness of medical treatment and trial participation our results could be relevant beyond the trial setting. We would therefore recommend to explore and compare the experiences of neurooncological patients, relatives and staff to regular care or hospitals with less specialization. Based on our experiences with a patient researcher we would encourage future qualitative but also quantitative neurooncological research to incorporate patient representatives during the whole course of the research project. This can expand the analytic view and is associated with diverse other benefits as reported in the growing literature on stakeholder involvement.

Data Availability

While publication of anonymized quotes is permitted, the sharing of interview transcripts is not, as per the ethics committee's requirements. Reuse of interview transcripts outside the research team is also not permitted as per the ethics committee's requirements.

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