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Protocol for neuro-oncology anywhere 242: Pilot study evaluating telehealth and in-person assessments in patients with glioma receiving oral chemotherapy

Ugur Sener [a,b,*], Taylor Galloway [c], Bryan Neth [a,b], Joon Uhm [a,b], Sani H. Kizilbash [b], Jian L. Campian [b], Samantha Caron [b], William G. Breen [d], Eric Lehrer [d], Elizabeth Golembiewski [e], Sydney Schultz [f], Heather Hughes [g], Sue Steinmetz [g], Susan Geyer [h], Carolyn Mead-Harvey [i], Carey Huebert [j], William Tauer [j], Charles Mason [j], Terry C. Burns [k], Joshua Pritchett [b], Tufia Haddad [b]

[a] Department of Neurology, Mayo Clinic, Rochester, MN, United States of America
[b] Department of Oncology, Mayo Clinic, Rochester, MN, United States of America
[c] Clinical Trials Beyond Walls, Mayo Clinic, Rochester, MN, United States of America
[d] Department of Radiation Oncology, Mayo Clinic, Rochester, MN, United States of America
[e] Quantitative Health Sciences, Mayo Clinic, Rochester, MN, United States of America
[f] Pharmacy Services, Mayo Clinic, Rochester, MN, United States of America
[g] Oncology Clinical Research, Mayo Clinic, Rochester, MN, United States of America
[h] Clinical Trials and Biostatistics, Mayo Clinic, Rochester, MN, United States of America
[i] Clinical Trials and Biostatistics, Mayo Clinic, Scottsdale, AZ, United States of America
[j] Neurology Clinical Research, Mayo Clinic, Rochester, MN, United States of America
[k] Department of Neurosurgery, Mayo Clinic, Rochester, MN, United States of America

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ABSTRACT

Care at high volume centers is associated with an overall survival benefit for patients with glioma. However, access to these centers is challenging for patients who experience neurologic deficits, leading to loss of independence and rendering travel difficult. Patients with low socio-economic status (SES) often lack logistical resources for travel, leading to poorer outcomes. There is a critical need for scalable telehealth solutions to increase access to specialized care. The Neuro-Oncology Anywhere 242 study systematically compares telehealth and in-person neuro-oncology assessments, as decentralization of care delivery may enable glioma patients with neurologic deficits and low SES to access specialized care and experience improved health outcomes. The primary objective of this study is to assess patient satisfaction with care delivered as measured by institutional Press-Ganey survey scores obtained following telehealth and in-person assessments. A key secondary objective is to assess the completion rate of planned oral chemotherapy among patients with glioma within 28 days of telehealth visits compared to in-person visits. Chemotherapy adherence is evaluated using a novel digital pill diary that has been developed for this study. Other secondary objectives include preference for telehealth versus in-person evaluations as well as acute care utilization, neurologic impairment, and quality of life among participants after telehealth versus in-person visits. Successful demonstration of this will offer a strong scientific rationale to incorporate telehealth into interventional clinical trials to accelerate development of novel therapeutics unconstrained by geographic location, disability, or SES.
Trial registration id: NCT06625047.

* Corresponding author. Mayo Clinic, 200 First St SW, Rochester, MN, 55905, United States of America.
E-mail address: sener.ugur@mayo.edu (U. Sener).

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1. Introduction

Gliomas are the most common primary central nervous system (CNS) malignancy in adults, and they account for 26.3 % of all brain tumors [1]. Malignant brain tumors are associated with poor survival with a five-year survival rate of 35.7 % [1]. An average of 17,206 deaths per year are caused by malignant CNS tumors. In addition to this, gliomas are associated with a high symptom burden, with cognitive deficits, seizures, headache, dizziness, and motor deficits impairing quality of life throughout the course of illness [2].

Patients with glioma and their caregivers also experience significant productivity loss and financial burden both as a direct result of the condition and care management needs [3,4]. Patients with glioma frequently require extended unpaid time off or become unable to work, often causing them to acquire debt related to their medical care [4]. Malignant glioma care is also associated with a significant financial toxicity, leading to substantial out of pocket costs in addition to lost days of work [5,6]. Given the short overall survival (OS), high symptom burden, loss of independence and productivity, and significant financial toxicity associated with gliomas, there is an urgent need to improve the clinical, economic, and quality of life (QoL) outcomes in this patient population.

Care at high volume centers is associated with improved outcomes for glioma patients, with >30 % longer OS for patients who receive their care at specialized centers [7]. Moreover, length of hospital stay and re-admission rates were significantly less at high volume centers. However, access to specialized neuro-oncology care is often challenging for patients with glioma due to neurologic deficits and lack of resources, which make travel impractical or difficult [2,8–10].

With the COVID-19 pandemic, telehealth adoption increased, including tremendous growth of video-enabled, telehealth visits within our institutional neuro-oncology practice. For individuals with glioma who have difficulty with travel due to neurologic disability and/or low SES, telehealth represents an attractive option for access to specialized neuro-oncology care [11]. From 2019 to 2021, telehealth utilization rates within the cancer practice at our institution were highest for our neuro-oncology group at a level of 52 % of all ambulatory visits, compared with 20–27 % for other solid tumor groups, underscoring the extensive experience of our neuro-oncology clinic in the delivery of cancer care via telehealth for patients with CNS malignancies [12].

While guidance for the conduct of telehealth assessments is available for the neuro-oncology practice, the impact of this care delivery model on patient outcomes remains unassessed for patients with glioma receiving chemotherapy [13]. To address this gap, this institutionally funded pragmatic clinical trial evaluates patient satisfaction with telehealth versus in-person assessments for individuals with glioma undergoing chemotherapy with temozolomide. The study also evaluates chemotherapy completion rates, acute care utilization, visit modality preference, health related quality of life, and neurological impairment following telehealth versus in-person assessments. Our central hypothesis is that neuro-oncologic assessment for patients undergoing chemotherapy with temozolomide for treatment of glioma is safe, feasible, and associated with patient satisfaction similar to in-person evaluations.

2. Materials and methods

2.1. Study design

In this single site pragmatic clinical trial, patients with glioma intended to undergo chemotherapy with temozolomide are evaluated after video-enabled telehealth and in-person visits (Fig. 1). The study measures patient satisfaction with care delivered, chemotherapy completion rates, acute care utilization, health related quality of life, and neurological disability following telehealth versus in-person assessments. The study was approved by the Institutional Review Board (IRB). The trial was activated on October 7, 2024. Planned accrual is one year from study open.

2.2. Eligibility

Patients age ≥18 years with a diagnosis of glioma requiring adjuvant chemotherapy with temozolomide are eligible for enrollment. The tumor diagnosis for such patients is designated by ICD-10 code C71.9, 'Malignant neoplasm of the brain,' which includes glioblastoma (GBM), astrocytoma, IDH-mutant, and oligodendroglioma IDH-mutant, 1p/19q codeleted. Patients are required to have an ECOG Performance Status or 0, 1, or 2 and Karnofsky Performance Status (KPS) of ≥60, as well as expected survival ≥6 months in the opinion of treatment team at the time of enrollment. Participants must be able to complete patient experience surveys on their own or with assistance from a caregiver. Participants who do not have devices that permit telehealth visits will be provided with tablet devices to facilitate appointments for the duration of the study. Individuals with uncontrolled and/or intercurrent illness or other conditions limiting safety of or compliance with study proceedings

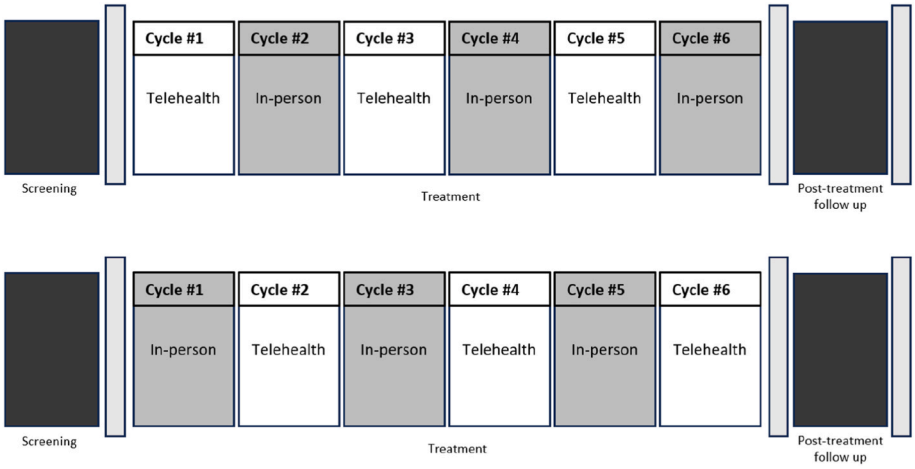

Fig. 1. Trial Schema*
*Participants may start the study with an in-person or telehealth visit. As they continue the study, they alternate between in-person and telehealth visits, which is standard clinical practice for individuals receiving chemotherapy with temozolomide for glioma at the study institution. Participants complete up to six chemotherapy cycles while on study. In the event of disease progression or intolerable toxicity requiring chemotherapy discontinuation, subjects end their participation in the study.

are not eligible. Individuals unable to swallow tablets or had known hypersensitivity to temozolomide are not eligible.

2.3. Recruitment

Study staff review the electronic health record (EHR) for patients with glioma intended to undergo standard of care chemotherapy with temozolomide. Eligible patients are approached by the study team members, who describe the study, answer questions, and explain requirements for participation. Eligible patients may also be approached by phone calls and patient portal messages. Interested patients eligible for enrollment provide remote electronic or written informed consent and are registered to the trial.

2.4. Interventions

Temozolomide is frequently prescribed for treatment of gliomas including glioblastoma, IDH-mutant astrocytoma, and oligodendroglioma [14–17]. Temozolomide is an oral chemotherapy agent. In the adjuvant setting, following initial surgical intervention and radiation therapy for gliomas, it is most frequently administered in 28-day cycles, in which patients take the medication during days 1–5 of each cycle [15]. Temozolomide is typically well tolerated, with common toxicities including nausea, constipation, and fatigue [18]. However, this chemotherapy can cause significant hematologic toxicity, requiring careful clinical monitoring during treatment [18,19].

During temozolomide treatment, the institutional practice is to complete tumor response assessment visits every other cycle to ensure there is adequate tumor control to justify further treatment. Toxicity assessment visits are completed at the end of cycles in which no tumor response assessment is performed to ensure that any hematologic or other adverse effects of therapy are adequately managed before treatment continues. Since patients with glioma frequently reside far from our center or experience neurological difficulties that render travel difficult, the institutional practice is to perform the toxicity assessment visits via telehealth. However, patient satisfaction with telehealth visits has not been prospectively evaluated in this setting. Further, chemotherapy adherence and acute care utilization following telehealth visits as compared to in-person visits has not been evaluated.

Based on our existing practice, we designed a pragmatic clinical trial for patients with glioma intended to receive temozolomide. Participants are evaluated either by video-enabled telehealth services or in person at the end of each cycle. Patient satisfaction with care delivered is assessed through Press-Ganey surveys delivered to participants digitally. Chemotherapy completion is assessed using a digital pill diary developed for this study and confirmed by clinicians during visits. Treatment-related and other adverse events experienced by participants are tracked. Acute care utilization, as defined by emergency department visits or days of inpatient hospitalization, is tracked digitally following each type of visit. Laboratory assessments to monitor hematologic toxicity can be completed at our institution or at any location of the participant's choosing and transmitted digitally for review.

Participant performance status and neurological status as determined by the Neurological Assessment in Neuro-Oncology (NANO) is assessed at the end of every cycle [20]. The NANO scale involves assessment of behavior, level of consciousness, language function, visual fields, facial strength, upper and lower extremity strength, coordination, sensation in upper and lower extremities, and gait. All domains, except visual fields and sensation, can be evaluated by telehealth even in absence of a medically trained individual with the patient. Accordingly, the full NANO scale assessment is completed during in-person visits and domains other than visual fields and sensation are evaluated during telehealth visits. Participant quality of life is measured digitally by the validated European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 survey, which is a 30-item questionnaire that is specifically designed to evaluate cancer patients [21,22].

Participants can join the study at any time during their course of temozolomide treatment. Up to 6 cycles of temozolomide treatment is tracked for each patient. Individuals who complete planned therapy end their participation. Patients who choose to stop chemotherapy for any reason, experience disease progression that requires a change in treatment, or experience intolerable toxicity that requires treatment discontinuation end their participation in the study. Chemotherapy dosing is in accordance with temozolomide's United States Food and Drug Administration (FDA) label. Dose reductions or interruptions in chemotherapy are undertaken in accordance with usual clinical practice and temozolomide's FDA label, at the discretion of the treating clinician.

The starting visit modality is not randomized. Participants may begin the study with either a telehealth visit, or an in-person visit in accordance with the visit type that would have been scheduled for their routine clinical care regardless of study enrollment. This design avoids unnecessary travel to the study institution for participants who might be assigned to an in-person first visit that would have been otherwise evaluated by telehealth. The starting visit modality for each participant will be considered in evaluation of study outcomes.

2.5. Study measures

Study measures are completed according to the schedule in Table 1. Participants undergo performance status, NANO, and QoL assessments at baseline and after completion of every chemotherapy cycle. At the end of each chemotherapy cycle and at the end of study participation, patient satisfaction with care delivered, chemotherapy completion, adverse events, and acute care utilization are evaluated. At the end of treatment, participants are asked about visit modality preference. Patient satisfaction, adverse events, acute care utilization, performance status, NANO, and QoL assessments are also repeated at 30-day safety follow up.

2.5.1. Measurement of effect

Participants will be patients with glioma intended to undergo temozolomide. There will be up to 6 planned visits, performed at the end of each cycle of chemotherapy. The data used for assessment of study goals will be obtained during these visits. These visits include collection of the Chemotherapy Completion Assessment, Adverse Event Assessment, Performance Status Assessment, and NANO Assessment. Patient Satisfaction Assessment will be assessed by Press-Ganey surveys sent to participants at the end of each chemotherapy cycle. Visit Modality Preference will be assessed at the end of study for each participant by a survey.

2.5.2. Primary endpoint

The primary objective will be to determine patient satisfaction with care delivered as measured by institutional Press-Ganey survey scores obtained following telehealth and in-person assessments. These surveys include with Likert response scales (1–5, 1 = very poor, 5 = very good). Participants are asked to describe their visit experience by providing scores in multiple categories including ‘Likelihood of recommending practice to others,’ ‘Concern the care provider showed,’ ‘Provider's discussion of treatment options,’ and ‘Provider effort to include patients in decision-making.’ The surveys are delivered digitally upon completion of the associated visit and can be completed at any time prior to the next study visit. These institutional surveys have been utilized in other settings including evaluation of quality assurance for routine clinical practice. All participants who meet eligibility criteria who have signed a consent form and who have completed at least one cycle of temozolomide chemotherapy will be evaluable for the primary endpoint.

2.5.3. Secondary endpoints

Secondary endpoints include completion rate of planned oral chemotherapy, preference for telehealth versus in-person neuro-oncologic evaluations, acute care utilization days, neurologic impairment as

Table 1
Schedule of trial activities.

Tests and procedures[a]	Screening	Active Monitoring Phase							
	≤30 days prior to registration	End of Cycle 1	End of Cycle 2	End of Cycle 3	End of Cycle 4	End of Cycle 5	End of Cycle 6	EOS[b]	30-Day Safety Follow-up[c]
Window		±7 days	±7 days	±7 days	±7 days	±7 days	±7 days	±7 days	
Medical history and exam, height, weight[d]	X								
Patient Satisfaction Assessment		X	X	X	X	X	X	X	X
Chemotherapy Completion Assessment		X	X	X	X	X	X	X	
Visit Modality Preference Assessment								X	
Adverse Event Assessment		X	X	X	X	X	X	X	X
Acute Care Utilization Assessment		X	X	X	X	X	X	X	X
Performance Status Assessment[e]	X	X	X	X	X	X	X	X	X
NANO Assessment	X	X	X	X	X	X	X	X	X
Quality of Life Assessment	X	X	X	X	X	X	X	X	
Pregnancy Testing if applicable	X[f]								

[a] Any additional tests such as laboratory evaluations or imaging as well as procedures may be ordered as needed for clinical care.
[b] EOS = end of study, may be combined with Month 6 or other visit as needed.
[c] At least 30 days after last dose of chemotherapy; NOTE: May coincide with EOS visit. If there is a clinical concern, additional blood testing may be done.
[d] Can be extracted from medical record/visit ≤30 days prior to registration.
[e] Include both ECOG and Karnofsky.
[f] For persons of childbearing potential only. Must be completed ≤8 days prior to registration.

measured by the NANO scale, and impact of chemotherapy management by visit modality in regard to quality of life measures in patients with alternating telehealth and in-person visits.

Completion rate of planned oral chemotherapy is defined as participant taking 5 days of chemotherapy as prescribed, among patients with glioma within 28 days of telehealth visits compared to within 28 days of in-person visits. Completion of the intended chemotherapy cycle following a telehealth or in-person visit will be assessed as the proportion of doses planned for a cycle that are completed. All participants meeting eligibility criteria who have signed a consent form and who have taken at least one dose of temozolomide will be evaluable for the endpoint.

All participants who meet eligibility criteria who have signed a consent form and who have completed at least one telehealth, *and* one in-person visit will be evaluable for the following endpoints. Preference for telehealth versus in-person neuro-oncologic evaluations among patients with glioma receiving oral chemotherapy will be assessed by a survey. The impact of telehealth-based chemotherapy management relative to in-person management with regards to quality-of-life measures will be evaluated using the EORTC QLQ-C30 questionnaire, evaluating change in quality of life 28 days after chemotherapy cycle relative to quality-of-life at baseline or measured at the end of previous cycle.

The remaining endpoints will be assessed in all participants meeting eligibility criteria who have signed a consent form and who have completed at least one telehealth, *or* one in-person visit. Acute care utilization days is defined as emergency department (ED) visits and days of hospitalization. For this evaluation, ED visits and days of inpatient hospitalization within 28 days of a telehealth visit will be compared to acute care utilization days within 28 days of an in-person visit. Neurologic impairment as measured by the NANO scale will be assessed as decline in the NANO exam score within 28 days of telehealth visits compared to decline within 28 days of in-person visits, relative to assessment at baseline or at the end of the previous cycle.

Safety and tolerability of temozolomide chemotherapy in patients with alternating telehealth and in-person visits will be evaluated by the incidence of reported adverse events based on the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v5.0. We will assess the type of adverse event, the grade of the event, and the perceived attribution to study treatment.

2.6. Adverse event evaluations

From the time of registration until less than or equal to 30 days after the administration of the last dose of study drug, or until a new anticancer treatment starts, whichever occurs first, the Principal Investigator (PI) is responsible for ensuring that all adverse events (AEs) observed by study team or provided by external sources are reported. After 30 days from the last administered dose of study drug, only adverse events that are attributed to the study drug (possible, probable, or definite) are required to be recorded on the adverse event forms.

The investigators are responsible for AE diagnosis or syndrome(s), if known (if not known, signs or symptoms), dates of onset and resolution (if resolved), severity, and assessment of the relationship to study treatment. Investigators are asked to determine the relationship of the AE with any study mandated activity, review laboratory test results and determine whether an abnormal value in an individual study subject represents a clinically significant change from the subject's baseline values and follow reported AEs until resolution.

3. Statistical analyses

This is a prospective single-arm pragmatic trial with decentralized elements to determine patient satisfaction with care delivered following telehealth and in-person assessments for individuals with glioma undergoing temozolomide chemotherapy. Through this trial, we will assess the feasibility, acceptance, and safety of telehealth-based chemotherapy management among patients with glioma. The trial outcomes will aid to develop, refine, and support future decentralized clinical trials with investigational products in this patient population. We seek to enroll 30 participants in this pilot study.

The analyses for primary endpoint, secondary and correlative outcomes will begin once all participants have completed the trial protocol procedures.

3.1. Analysis of the primary endpoint

The primary endpoint of this trial is to determine patient satisfaction with care delivered as measured by institutional Press-Ganey survey scores obtained following telehealth and in-person assessments.

Specifically, we will compare scores obtained following each cycle of temozolomide chemotherapy as patients alternate between telehealth and in-person visits. Each participant will be intended to receive up to 6 cycles of temozolomide chemotherapy with three associated telehealth and three in-person visits.

We hypothesize that the telehealth/remote visits will be preferred by patients vs. the in-person assessments, and thus, the satisfaction scores for the telehealth cycles will be better than those associated with the in-person assessments. We will calculate the mean score associated with the three telehealth visits vs. the mean score associated with the three in-person visits for each patient. With a sample size of 30 patients, we will have 80 % power to detect an effect size of 0.53 standard deviations (i.e., Cohen's $d = 0.53$) using a two-sided, two-sample paired t-test ($\alpha = 0.05$). We will also graphically evaluate potential patterns of change associated with these scores over time for the telehealth vs. in-person visits and quantitatively evaluate these using repeated measures mixed effects models to further evaluate potential influence of a time element with the satisfaction scores for telehealth vs. in-person assessments.

3.2. Analysis of secondary endpoints

We will assess the completion rate of planned oral chemotherapy, comparing proportion of doses planned for a cycle that are completed for the telehealth vs. the in-person cycles for patients. Similar to the primary endpoint analyses, we will evaluate and compare the average completion rates for telehealth vs. in-person assessment cycles across patients. We will consider the completion rate to be problematic if the difference in these mean rates for a given patient is 10 % or more. With 30 patients, we will have 80 % power to assess if the true rate of patients with this concerning differential in completion rates is 10 % or more (vs. the null hypothesis that at most 1 % of patients will have a concerning differential in completion rates), with $\alpha = 0.05$. Here, we will consider the telehealth regimen to not compromise therapy completion rates if at most 1 of the 30 patients has this concerning differential in completion rates. Otherwise, we will conclude that we will need to ascertain if there are other approaches we need to incorporate in future trials to improve completion rates for those cycles associated with telehealth visits.

Preference for telehealth versus in-person neuro-oncologic evaluations will be evaluated using a survey at the end of study, where patients are asked to report visit preference as in-person, telehealth, or no preference.

Acute care utilization days, defined as emergency department evaluations and days of hospitalization within 28 days of telehealth visits compared to those within 28 days of in-person visits, will be summarized. Acute care utilization data will be collected via participant and surveys and validated by study staff. In addition, participants will be asked about acute care utilization during the previous 28 days at each study visit. We will use repeated measures models with a Poisson model to estimate the numbers of days in each cycle that acute care was utilized. We will then be able to assess an incidence risk ratio to determine how the number of days with acute care utilization compares between telehealth vs. in-person cycles. To do this, we will utilize generalized estimating equation (GEE) models for a Poisson (count-based) endpoint with repeated measures.

Neurologic impairment will be measured by the NANO scale at each visit with rate of neurological decline within the 28 days following telehealth assessments compared to neurological decline within the 28 days following in-person assessments. These will be summarized graphically to assess patterns and differences based on telehealth vs. in-person assessments, as well as quantitatively in a manner similar to that described for the primary endpoint.

Quality of life measures will be obtained using the EORTC QLQ-C30 survey following each chemotherapy cycle. Similar to the other electronic patient reported outcome (ePRO) endpoint measures described above, we will assess quality of life as measured by the EORTC QLQ-C30, a 30-item questionnaire that is used to assess the quality of life of cancer patients, completed at baseline and at the end of each chemotherapy cycle. We will use similar graphical and quantitative approaches to compare the scores for these ePRO assessments and corresponding scores between cycles associated with telehealth vs. in-person assessments.

4. Discussion

CNS tumors are associated with a high symptom burden and neurologic disability [2,8], leading many patients to experience loss of income and often accumulation of debt related to medical care [4–6]. CNS tumors are also associated with poor survival [1]. There is a clear need for novel therapeutics but few patients with glioma enroll in clinical trials. Key limitations are the geographic-, disability-, and low socioeconomic status-associated challenges, and paucity of neuro-oncology specialists that constitute barriers to access in-person evaluations often required for clinical care and trial participation [23]. Access to innovative clinical trials and specialized neuro-oncology care is limited to studies enrolling participants with high performance status and ability to travel to academic centers.

Only 335 certified neuro-oncologists are available in the United States as of May 2025, underscoring the difficulty with access to specialized brain cancer care [24]. To circumvent barriers to in-person care, telehealth offers a viable alternative. Brain tumor patients are well-suited for remote care, as chemotherapy typically consists of oral regimens and symptom assessments as well as imaging review are feasible by telehealth [13]. Moreover, remote management has been an integral part of neuro-oncology practice since the COVID-19 pandemic [25].

From 2019 to 2021, telehealth visit rates at our institution were highest for neuro-oncology at 52 % compared with 20–27 % for other solid tumor groups [12]. Guidance for conduct of neuro-oncology telehealth assessments is available [13]. Telemedicine interventions have proven efficacy among patients with chronic conditions [26–29]. However, the comparative efficacy of telehealth neuro-oncology assessments to in-person evaluations remains unassessed [13]. The Neuro-Oncology Anywhere 242 clinical trial will address this by evaluating the feasibility, safety and acceptability of telehealth neuro-oncologic assessment that can be scaled to all glioma patients receiving oral chemotherapy. This contribution will provide scientific justification for its routine use in clinical care and clinical trials, thus demonstrating the feasibility of decentralized drug intervention trials for glioma patients.

The Neuro-Oncology Anywhere 242 clinical trial is innovative for its focus on the feasibility of neuro-oncologic telehealth assessments and remote adverse event monitoring among a population of patients with great need for access to highly specialized care and clinical trial opportunities. While telehealth assessments are routinely used in neuro-oncology practice, there is no prospective data evaluating their effectiveness in symptom management, acceptance by patients, and safety. Demonstration of preliminary efficacy with this pilot trial will provide a strong basis for future use in decentralized interventional trials. The decentralized oral chemotherapy management and symptom assessment approach developed herein also addresses health disparities by providing a solution to reach underserved patient populations.

Our long-term goal is to accelerate the development of therapeutically useful interventions to improve survival and quality of life outcomes for patients with CNS tumors in a setting that overcomes barriers and adapts to the needs of patients. If telehealth-based evaluations are determined to be feasible and satisfactory to patients in this trial, the study will provide objective support for routine use of digital health solutions in neuro-oncology care.

CRediT authorship contribution statement

Ugur Sener: Writing – review & editing, Writing – original draft,

Visualization, Project administration, Methodology, Investigation, Conceptualization. **Taylor Galloway:** Writing – original draft, Project administration, Methodology, Investigation, Conceptualization. **Bryan Neth:** Writing – review & editing. **Joon Uhm:** Writing – review & editing, Supervision. **Sani H. Kizilbash:** Writing – review & editing, Investigation. **Jian L. Campian:** Writing – review & editing, Investigation. **Samantha Caron:** Writing – review & editing, Investigation. **William G. Breen:** Writing – review & editing, Investigation. **Eric Lehrer:** Writing – review & editing, Investigation. **Elizabeth Golembiewski:** Writing – review & editing, Methodology. **Sydney Schultz:** Writing – review & editing, Project administration, Investigation. **Heather Hughes:** Writing – review & editing, Project administration. **Sue Steinmetz:** Writing – review & editing, Project administration. **Susan Geyer:** Writing – review & editing, Methodology. **Carolyn Mead-Harvey:** Writing – review & editing, Writing – original draft, Methodology, Investigation. **Carey Huebert:** Writing – review & editing, Project administration, Methodology, Investigation, Conceptualization. **William Tauer:** Writing – review & editing, Project administration. **Charles Mason:** Writing – review & editing, Project administration. **Terry C. Burns:** Writing – review & editing, Investigation. **Joshua Pritchett:** Writing – review & editing, Methodology, Conceptualization. **Tufia Haddad:** Writing – review & editing, Supervision, Methodology.

Ethical publication statement

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Ugur Sener has participated in professional services and activities for Merck & Co, Inc and Alexion Pharmaceuticals.

Data availability

No data was used for the research described in the article.

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