Ways Ahead

Improving support for people with brain tumours

STUDY PROTOCOL

- Version 5, 02/03/2022
- IRAS Number: 269814
- Sponsors number: FO16173
- Funder's number: GN-000435

Newcastle University

THE BRAIN TUMOUR CHARITY

NHS
The Newcastle upon Tyne Hospitals
NHS Foundation Trust

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Signature: Date:

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Name (please print):

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Position:

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Chief Investigator:

Signature: Date:

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Name: (please print):

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A. KEY STUDY CONTACTS

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Funder(s)	The Brain Tumour Charity
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B. STUDY SUMMARY

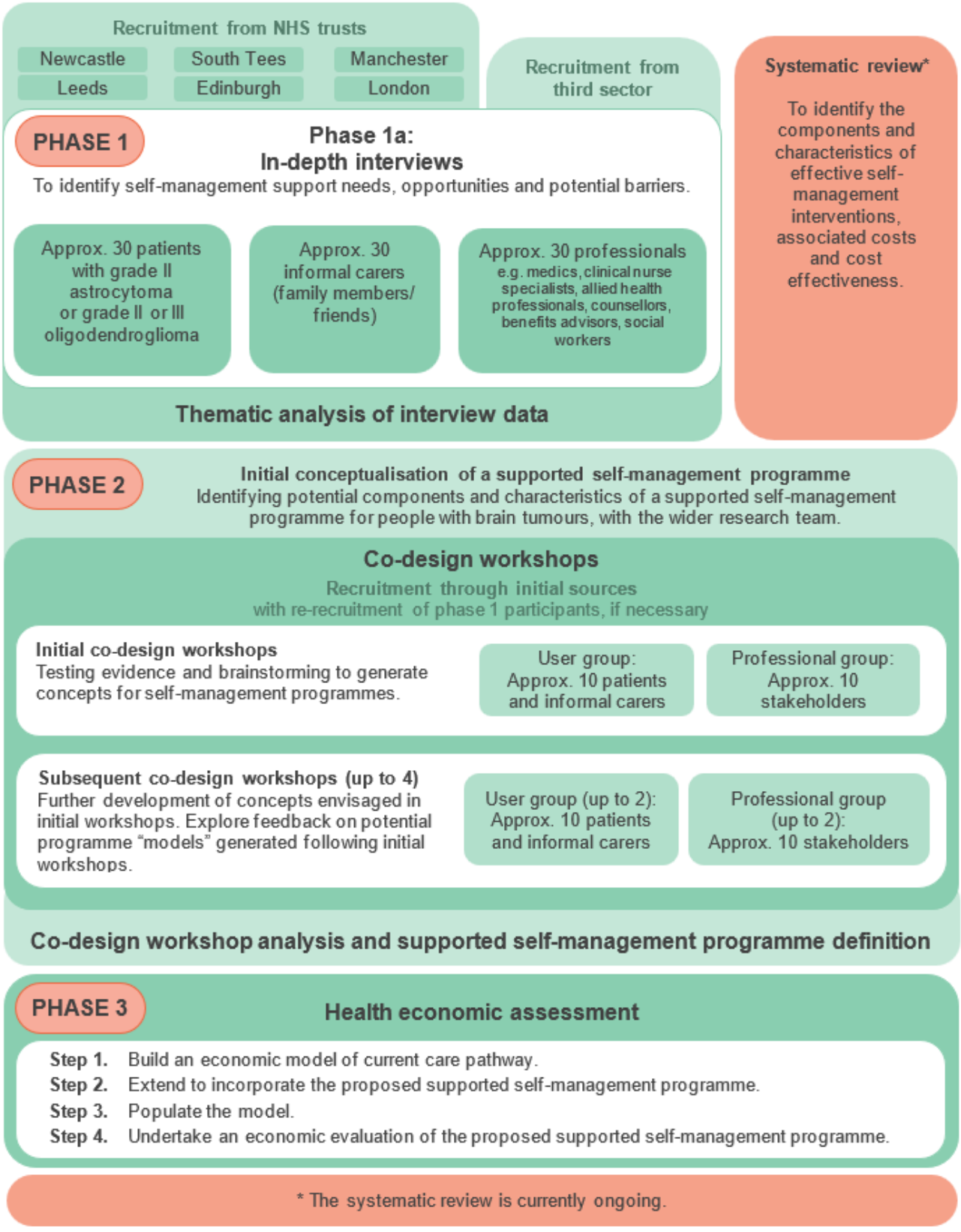
Study Title	Ways Ahead: Developing a supported self-management programme for people living with low- and intermediate-grade gliomas
Internal ref. no. (or short title)	Ways Ahead: Improving support for people with brain tumours
Study Design	This study will be conducted in three phases: Phase 1 will use qualitative methods to explore the self-management behaviours and support needs of adults living with low- and intermediate-grade gliomas, as well as the barriers and facilitators to self-management and implementation of a supported self-management programme. Semi-structured interviews will be conducted with approximately 30 people living with low- or intermediate-grade gliomas, 30 informal carers (family-members/friends) and 30 healthcare professionals. We will also conduct interviews with up to 15 cancer support professionals.

	Phase 2 will involve a series of online or face-to-face co-design workshops. At these workshops the findings from phase 1 and literature reviews will be presented and the groups will work together to co-create a supported self-management programme for people living with low- and intermediate-grade gliomas. Subsequent workshops will explore participant feedback on potential programme "models" generated by the research team, following the previous workshops. Participants will discuss potential challenges around acceptability and feasibility. Phase 3 will involve an early health technology assessment of the prototype supported self-management programme. This will assess the range of impacts the proposed programme may have on healthcare delivery and patient outcomes. A micro-costing analysis will assess potential budgetary impact if the programme was rolled-out as part of routine survivorship care. For comparison, the current care pathway for low- and intermediate-grade gliomas will be mapped, guided by clinical opinion, patient feedback, and nationally available data. An economic model will be developed to estimate possible changes in resource use and clinical and quality of life (QoL) outcomes for the programme relative to current practice. The model will produce preliminary estimates adopting both cost-consequence and cost-utility approaches.
Study Participants	Adults with low- or intermediate-grade gliomas Informal carers - family-members/friends (e.g. spouses, parents) who support people living with low- or intermediate-grade gliomas Healthcare professionals who care for people living with low- or intermediate-grade gliomas (e.g. clinical nurse specialists, psychologists, speech and language therapists) Cancer support professionals (e.g. counsellors and benefits advisors working for cancer charities who may have contact with people with low or intermediate-grade gliomas) Other stakeholders (e.g. commissioners)
Planned Sample Size	Phase 1 • Approximately 30 adults with low- or intermediate-grade gliomas • Approximately 30 family-members/friends • Approximately 30 healthcare professionals • Up to 15 cancer support professionals Phase 2 • Up to 20 adults with low- or intermediate-grade gliomas • Up to 20 family-members/friends • Up to 20 healthcare professionals, cancer support professionals and other stakeholders (e.g. commissioners)
Planned Study Period	January 2020 to January 2022

Research Aim and Questions	The aim of this research is to develop a theory-based supported self-management programme to improve quality-of-life in people with low- and intermediate-grade gliomas. This aim will be informed by the following research questions: What self-management strategies are currently used by people living with low- or intermediate-grade gliomas? What are individual-level barriers to, and enablers of, self-management for people living with a low- or intermediate grade glioma? What self-management support do people with low- or intermediate-grade gliomas want and how do they want it to be delivered? What system-level factors would help or hinder implementation of a supported self-management programme for people living with low- or intermediate-grade gliomas? Is it possible to co-produce, with patients, informal carers and professionals, a prototype self-management programme? What are the range of costs and benefits of implementation of a supported self-management programme for people living with low- and intermediate-grade gliomas?

KEY WORDS: Low- and intermediate-grade gliomas, brain cancer, self-management, programme, patients.

C. STUDY FLOWCHART



D. STUDY PROTOCOL

Ways Ahead: Developing a supported self-management programme for people living with low- and intermediate-grade gliomas

1 BACKGROUND

A primary brain tumour and its treatment can adversely impact many aspects of patients' lives and quality-of-life (QoL). Self-management – a person's active participation in rehabilitation to minimise adverse effects of illness and promote survival, health and well-being - can improve QoL in people with long-term conditions, including cancer. The potential for self-management has not previously been investigated in adult brain tumour patients. This project aims to develop a theory-based supported self-management programme to improve QoL in people with a particular type of adult primary brain tumour – low or intermediate grade gliomas.

The population of brain tumour patients is growing. Each year in the UK, more than 10,000 new primary brain tumours are diagnosed, making it the eighth most common cancer[1]. In the UK, malignant brain tumour incidence has risen by almost 40% since the 1970s. At the same time, survival has doubled; 5-year survival is now 60% for those aged 15-39 at diagnosis and 35% for those aged 40-49. These trends mean that there is a growing population of people, in particular younger adults, living with and beyond a primary brain tumour[1].

A brain tumour can have a devastating impact on patients' lives, and many of the problems and needs are specific to this form of cancer. Patients can experience a range of general cancer-related symptoms (e.g. fatigue, sleep disorders, pain) as well as specific problems and limitations due to the tumour and its treatment (e.g. cognitive limitations, seizures, visual impairment, changes in personality and behaviour, speech problems, mobility problems)[2-4]. These symptoms and problems are common, may occur in clusters and get worse as the disease progresses[5-7]. Cognitive deficits, in particular, increase as the disease progresses, hampering communication and decision-making[6]. Social roles change and patients may lose independence or become isolated[4]. As a result, patients' supportive care needs are multi-facetted and complex. However, these needs often go unmet, in part due to poor communication with, and information from, healthcare providers, as well as low referral to, and use of psychosocial services[6,8,9].

Since services do not meet patients' needs, family members often devote significant time and energy over months or years to performing caregiving tasks that may be physically, emotionally, socially or financially demanding[10]. As a consequence of the cancer, its treatment and side-effects, patients often have significant distress, depression and anger[11-13]. These, in turn, adversely impact on physical and psychosocial quality of life (QoL)[14,15]. Moreover, the consequences extend into the family, as carers too often have considerable psychological problems[6,12,16]. Indeed QoL in patients and their carers is significantly correlated[17]. Given this burden, it is essential to identify effective ways to empower and support adult primary brain tumour patients to manage specific problems, adjust to survivorship, and thereby optimise wellbeing and QoL.

There is a large and growing evidence-base indicating that self-management programmes can improve various clinical and psychosocial outcomes – including QoL, psychological wellbeing and healthcare utilisation – in people with long-term conditions[18]. Self-management is an "individual's ability to manage the symptoms, treatment, physical and psychosocial consequences and lifestyle changes inherent in living with a chronic condition"[19]. Patients who self-manage may feel more empowered and are better able to make informed decisions, navigate health systems, cope with treatment and treatment-related side-effects, and consequently, are more satisfied with care. However, to successfully self-manage, patients need a set of skills (such as problem solving, action planning/goal setting, communicating with healthcare providers), motivation and confidence. Self-management interventions or programmes seek to equip people with these skills and confidence, usually by improving self-efficacy (following Bandura's social cognition theory[20]).

Self-management is not – and should not be – the sole responsibility of the patient[21]. They need support from a network of health professionals, family and friends, and fellow patients[22]. Thus self-management programmes must consider what health professionals and health services can do to support people to self-manage, and how best to mobilise social resources[23]. It is, therefore, unsurprising that self-management strategies co-created with patients and providers are more likely to have positive effects[18].

Although somewhat behind many other conditions in relation to self-management, there is considerable potential for supported self-management in cancer. Most cancer survivors already use some form of self-management post-treatment and many survivors are willing to take an active role in dealing with the challenges of cancer[24-26]. To date, around 80% of self-management programmes in cancer have focused on specific problems such as fatigue or pain[27-29]. However adjustment-focussed programmes may be particularly valuable in the survivorship phase, as when primary treatment has finished, the patient and their family have less contact with oncology professionals and they have to adjust to the "new normal" of living with cancer[30]. There is emerging evidence that both problem-focussed and adjustment-focussed programmes can improve cancer survivors' self-efficacy, social, physical and psychological wellbeing and QoL[29,31-35]. However, the potential for self-management has not previously been investigated in adult brain tumour patients and there are no self-management programmes specifically for the group with low or intermediate grade gliomas.

2 RATIONALE

This research responds to NHS England's recommendations that cancer patients be provided with information and education to prepare for self-management, including advice on healthy lifestyles, information on managing the long-term side-effects of treatment, signposting to rehabilitation, work and other support services[36]. A 2017 survey found that less than 20 percent of cancer patients attended an NHS based self-management support event[37]. The same survey found that those with brain

cancer were among the least likely to receive ongoing health and wellbeing support, highlighting the need for interventions that address the specific needs of this group.

The comprehensive research conducted by the Brain Tumour Charity (and reported in "Losing Myself – the Reality of Life with a Brain Tumour") indicates that, for adults, living with and beyond a brain tumour has a substantial adverse effect on a range of issues that contribute to quality-of-life, including cancer-related symptoms, physical functioning, psychological wellbeing, and social relationships. The impact also extends to family members who live with, support and help care for patients.

The potential for self-management in adult primary brain tumour patients has not previously been investigated. This group's unique and complex needs suggests programmes developed for other conditions or cancers may not be suitable or easily transferable. This project will develop – for the first time - a theory-based supported self-management programme specifically designed to improve QoL in adult primary brain tumour patients.

The project is consistent with the objectives of the National Cancer Survivorship Initiative (NCSI), which moved the focus of cancer care from treatment delivery to recovery, health and well-being[38], and the English Cancer Strategy, which aspires to a recovery package being available to every person with cancer by 2020[39].

This research will focus particularly on a subset of brain tumours namely Low- and Intermediate-Grade Gliomas (LIGG), which are most commonly diagnosed in young adults in their 30s and 40s[40-43]. Though these tumours can usually be treated by surgical removal and, in certain cases, radio- and/or chemo-therapy, in almost all cases, LIGGs will progress to high-grade gliomas, which are terminal[44]. Consequently, life expectancy following diagnosis with a LIGG is limited to around 5-15 years, depending on the sub-type[42,43,45]. Living for extended periods with a terminal condition can affect people's ability to recuperate, cope with, and resume everyday activities, such as returning to work[46]. Therefore the development of a supported self-management programme could be very beneficial for this patient group, but to achieve this, their distinct needs and wants must first be understood.

3 RESEARCH AIMS AND QUESTIONS

3.1 AIM

The aim of this research is to design a prototype supported self-management programme to improve QoL in people with LIGGs.

3.2 RESEARCH QUESTIONS

To address the research aim, the study will ask the following questions:

- What self-management strategies are currently used by people living with low- or intermediate-grade gliomas?
- What are individual-level barriers to, and enablers of, self-management for people living with a low- or intermediate grade glioma?
- What self-management support do people with low- or intermediate-grade gliomas want and how do they want it to be delivered?

- What system-level factors would help or hinder implementation of a supported self-management programme for people living with low- or intermediate-grade gliomas?
- Is it possible to co-produce, with patients, informal carers and professionals, a prototype supported self-management programme?
- What are the range of costs and benefits of implementation of a supported self-management programme for people living with low- and intermediate-grade gliomas?

3.3 OBJECTIVES

The objectives of this project follow the research questions, namely, to:

1. Identify self-management strategies currently used by people living with low- and intermediate-grade gliomas.
2. Explore individual-level barriers to, and enablers of, self-management by people living with low- and intermediate-grade gliomas.
3. Identify health system/service-level factors that would help or hinder implementation of a supported self-management programme for people living with low- and intermediate-grade gliomas.
4. Co-produce, with patients, family-members/friends, healthcare professionals, and cancer support professionals, a prototype supported self-management programme.
5. Estimate the potential costs and benefits of implementation of a supported self-management programme for adult primary brain tumour patients, and assess how this programme would change the current routine supportive care pathway.

3.4 OUTCOME

The primary outcome of this research will be a prototype supported self-management programme for people with LIGGs. This prototype will be ready for testing in a subsequent study.

The study will also report findings on the needs of people with LIGGs in relation to self-management, including the potential barriers, motivators and facilitators. Alongside this, the system-level factors that may affect the implementation of a supported self-management programme will be identified, as will the potential costs (from both the NHS and societal perspectives) of implementation of a supported self-management programme.

4 STUDY DESIGN

The project will be guided by the MRC guidelines for development of complex interventions and NCSI guidance on designing self-management interventions for cancer survivors[47,48]. The theoretical underpinning will be provided by Normalization Process Theory (NPT) and the Theoretical Domains Framework (TDF) and related tools. NPT takes a “system” perspective and provides a foundation for understanding implementation processes in healthcare[49,50]. The TDF brings together multiple psychological and organisational theories to identify variables which influence

personal behaviours (e.g. knowledge, beliefs about capabilities) [51,52]. The Behaviour Change Wheel (BCW) [53] and Behavioural Change Techniques (BCTs)[54] taxonomy will be used to help start forming solutions to the problem of self-management in LIGG patients.

There will be three phases of primary research. We will employ qualitative methods across phases 1 and 2. For phase 1 we will use semi-structured interviews among four groups of participants (patients, informal carers, healthcare professionals and cancer support professionals), as this will provide understanding of "how and why" from the perspectives of the participants, providing explanations and understanding meanings, experiences, and processes. Phase 2 will involve co-production workshops which will seek to design the prototype supported self-management programme. We will follow the sequential and systematic co-design approach of O'Brien et al[55] to integrate scientific evidence, expert knowledge and experience, and stakeholder involvement. This approach will ensure that the intervention is relevant and useful for the target population, thereby maximising acceptability and effectiveness.

Phase 3 concerns an early health technology assessment of the prototype supported self-management programme. This will assess the range of impacts the proposed programme may have on healthcare delivery and patient outcomes. A micro-costing analysis will be undertaken to assess potential budgetary impact if the programme was rolled-out as part of routine supportive care. For comparison purposes, the current care pathway for low- and intermediate-grade gliomas will be mapped, guided by clinical opinion, patient feedback and nationally available data. An economic model will be developed to estimate possible changes in resource use and clinical and QoL outcomes for the programme relative to current practice. Model parameters will be informed by nationally available data, literature, and expert elicitation techniques consistent with best practice guidance. The model will produce preliminary estimates adopting both cost-consequence and cost-utility approaches. These estimates will assist in assessing the viability of the proposed programme structure and in highlighting areas where programme modifications may increase efficiency in outcomes.

4.1 DATA COLLECTION

Phase 1 – Semi-structured interviews

Three sets of semi-structured interviews will be conducted with: adult LIGG patients; family-members/friends who support an adult LIGG patient; and healthcare professionals involved in caring for adult brain tumour patients. An additional set of one-to-one or group interviews will be conducted with cancer support professionals involved in the support of adult brain tumour patients.

The interviews will be conducted by research staff and take place either by telephone, Skype (or a similar facility that allows video calls, such as Zoom), or face-to-face, as the interviewee prefers. Interviews will take place at the interviewee's preferred location (e.g. hospital, university, home, Maggie's centre). Interviews will be at a time convenient for the interviewee. In the event of a face-to-face group interview with cancer support professionals, a time and location will be arranged and agreed

with the participants involved. If related patients and family-members/friends participate, they will be interviewed separately (where this is possible) so that each can be fully open and honest. It is expected that the interviews will last 60-90 minutes, or as long as the participant wishes. Interviews will be recorded, with the interviewee's agreement, using a password encrypted audio recording device. If permission to audio-record is refused, the interviewer will take detailed notes.

Before the interview commences, the researcher will seek informed consent (see 6.4). This will include reminding the participant that we would like to audio-record the interview, that they are free to withdraw at any time, and do not have to answer any questions they do not feel comfortable answering (as stated in the study information sheets).

Participants will then be asked to complete a one-page "About You" form collecting some key demographic details such as age, relationship status and employment status. The demographic questions asked vary appropriately for the patients, family-members/friends, healthcare professionals and cancer support professionals, as these questions are asked to learn more about the person or people that are about to be interviewed. If the interviewee prefers, the interviewer will run through the questions with them and note the answers.

Interviews will be informed by topic guides, which will be used flexibly to allow interviewees to raise issues they consider important, and allowed to evolve as interviews progress to ensure sufficient depth is reached. Each interview and topic guide will commence with a couple of questions designed to ease participants into the discussion (e.g. questions about themselves and their circumstances). The interviewer will ask "headline" open-ended questions for each area of interest on the guide; they will also develop a range of sub-questions and prompts to explore the issue in more depth. If necessary, the interviewer will rephrase a question to aid a participant's understanding.

The topic guides for patients and family-members/friends will be informed by the TDF. The patient topic guide will cover: the impact of the brain tumour on health and wellbeing; understanding and views of self-management; self-management strategies the individual currently uses, and has previously used; other self-management strategies the individual might like to, or be willing to, use; experience of formal and informal support for self-management; difficulties experienced with, and barriers to, self-management; and what would help the individual better self-manage. Family-members/friends will be asked about: their views and attitudes towards self-management for their support recipient; their contributions to the support recipient's self-management; and barriers and facilitators to the support recipient self-managing. They will also have the opportunity to raise any issues they wish about their own support needs as someone involved in caring for an individual with LIGG. The topic guide for both healthcare professionals and cancer support professionals will cover: views on main areas of unmet needs among adult LIGG patients; potential for self-management among adult LIGG patients; own experiences of patients who have used self-management; what would be needed to successfully deliver supported self-management for adult LIGG patients. Participants will have an opportunity to raise at

the end of the interview, any topics they feel are important but that have not been captured by the questions asked.

Phase 2 – Co-production workshops

We plan to hold up to six co-production workshops to generate ideas for the operationalisation of a supported self-management programme, and gather feedback on designed prototypes. Workshops with patients and family-members/friends will be separate to workshops with health professionals, cancer support professionals, and other stakeholders (e.g. commissioners). We aim to involve approximately 10 participants in each workshop.

The workshops will be facilitated by members of the research team; other members of the team will also be in attendance and participate in discussions and activities. Workshops will take place online or face-to-face in neutral locations (see 5). It is expected that each workshop will last up to three hours, if face-to-face, or 60-90 minutes, if online. Workshop discussions will be recorded using a password encrypted audio recording device.

Before each workshop commences, the researchers will seek informed consent from all participants, reminding them that the workshop discussions will be audio recorded (as stated in the study information sheets). Care will be taken to ensure that participants understand that discussions taking place within the workshop are confidential. The researchers will ensure an atmosphere which is welcoming and non-judgemental, to ensure participants feel that their views and opinions are valued.

In the workshops, evidence on self-management among LIGG patients will be presented and assessed; this will include the findings from the interviews in phase 1 and a systematic review on self-management interventions for cancer survivors which the research team is currently undertaking (*see section C for study flowchart*). Ideas for what would be useful and what is needed to improve self-management in LIGG patients will be generated by workshop participants. Participants will brainstorm how an intervention should be designed, where and how it should be implemented, and the relevant components.

Subsequent workshop(s) will explore participant feedback on potential programme “models” generated by the research team, following the previous workshops. Participants will discuss potential challenges around acceptability and feasibility.

Several activities will be used at each workshop to engage participants, ensure workshops are interactive and interesting, and to facilitate discussion and engagement amongst participants.

Following completion of the co-production workshops, we may disseminate a PPI survey, informed by the workshop findings, through social media or the Brain Tumour Charity networks. This survey may include options to indicate preferences for intervention design, components, and mode of delivery.

Phase 3 – Health Technology Assessment

The objective of the early-stage health technology assessment is to assess the feasibility of the proposed supported self-management programme i.e. the

intervention. This involves developing an EXCEL-based economic model that compares resource utilisation and outcomes from the routine supportive care pathway i.e. standard of care, with the proposed intervention. In order to understand the standard of care comparator pathway, a pragmatic review of the literature in the cancer survivorship area coupled with expert elicitation techniques from a range of stakeholders will be undertaken. This will involve overlap with phase I and II data collection methods as well as further independent evidence gathering (e.g. focussed discussions or a brief survey with health professionals who care for patients with LIGGs).

The intervention pathway will include resource utilisation associated with the delivery and follow-up of the supported self-management programme and expected clinical and quality of life outcomes. The programme characteristics will be costed using a micro-costing framework itemising each identified component of the implementation and sustainability of the programme. Resource utilisation consistent with the programme features will also be costed using national reference costing approaches. Expected changes to resource utilisation and disease-specific and quality of life outcomes will be explored through expert elicitation techniques guided by available evidence on self-management programmes for cancer survivors. An EXCEL-based expert elicitation tool will be created and presented at the last co-design workshop to ascertain consensus on the range and effect size of expected outcomes.

4.2 DATA ANALYSIS

Phase 1: With interviewees' consent, interviews will be audio-recorded. The recordings will be transcribed verbatim by a transcription service approved by Newcastle University and who have signed a confidentiality agreement. The study co-ordinator will de-identify all transcripts so as to ensure anonymity of participants. The abovementioned also applies to audio-recordings from the co-production workshops. Analysis of the interviews will occur in parallel with data collection to ensure that any new issues raised are explored in subsequent interviews. The first few interviews in each set will be independently coded by two team members, with discussion and agreement of emerging codes and themes. These will be applied to the remainder of the interview set. Coding will be facilitated by NVivo software. Each set of interviews will be analysed separately. Thematic analysis within the Framework approach will be used[56,57]. Self-management strategies used by patients and family-members/friends will be identified and classified following Yun et al[58] and Dunne et al.[59]. In the patient interviews, the TDF will be used to identify which domains influence the self-management behaviours participants describe using. For analytical rigour, the classification of belief statements to the TDF domains will be discussed and agreed within the team. We have previously successfully used this analytical approach to identify the determinants of various cancer-related behaviours[60-62]. This will be the first time it has been used to understand influences on self-management among survivors of cancer diagnosed in adulthood. For the healthcare professional and cancer support professional interviews, the NPT will be used to identify key service/system issues, which might help or hinder implementation of a supported self-management programme; we have previously successfully used this framework to identify issues in implementation of alternative models of cancer follow-up[63].

The findings from a systematic review being undertaken by the research team (*see section C for study flowchart*) and the semi-structured interviews will be combined into a "theoretical model" of supported self-management in LIGGs. We will identify which influences on self-management are potentially modifiable to determine what needs to be done to change patients' self-management behaviours. The BCW[53] will be used to map the TDF domains contained within the theoretical model onto intervention functions that might be effective in changing self-management behaviours. For each of the relevant intervention functions, associated behaviour change techniques will be identified (from the BCT taxonomy[54]) (i.e. the techniques that can be used to overcome barriers to, and enhance enablers of, self-management). Following this behavioural analysis, the co-production workshops described in 5.1 will be conducted.

Phase 2: The research team will critically examine and evaluate workshop outputs, translating these into a design brief for the intervention (supported self-management programme) and intervention specification. This will detail the aim of the intervention, the design features it will include, and how these will be operationalised. This will constitute the prototype intervention. We will develop a logic model, providing a graphical/textual representation of how the intervention is intended to work, linking outcomes with processes and the underlying theoretical assumptions.

Phase 3: The disaggregated costs and benefits of implementing the self-management programme compared to the current care pathway will be analysed and reported consistent with a cost-consequence analytical framework. Costs will be reported in 2020 (£). An early health technology assessment including a deterministic cost-effectiveness analysis will also be highlighted using average costs and effects across both the intervention and the current care pathways; the base-case analysis will adopt an NHS healthcare payer perspective. Incremental cost-effectiveness ratios (ICERs) describing the ratio of cost difference to effectiveness difference for the range of outcomes identified will be estimated and reported for the base-case analysis along with a series of sensitivity and scenario analyses, including the adoption of a societal cost perspective. The net benefit of the intervention will also be examined and a summary of the drivers of uncertainty in costs and benefits will be presented.

5 STUDY SETTING

Patient, informal carer, and healthcare professional interviewees will be recruited through leading clinical centres across the UK. The sites which have currently agreed to participate are:

Newcastle upon Tyne Hospitals NHS Foundation Trust

Leeds Teaching Hospitals NHS Trust

The Christie NHS Foundation Trust

South Tees Hospitals NHS Foundation Trust

Guy's and St Thomas' NHS Foundation Trust

Western General Hospital, NHS Lothian.

We will apply to have the project adopted as a NCRI portfolio study to ensure collaborating sites (in England) have their service support costs covered. Should additional sites be needed to reach recruitment targets, they will be recruited.

The additional group of cancer support professionals will be recruited through cancer support organisations and charities, such as Maggie's Centre Newcastle, Brain Tumour Support, and The Brain Tumour Charity.

Participant interviews will take place over the phone, Skype (or another similar video-conferencing facility), or their preferred location (i.e. at the university, hospital, participant's home, or another place of their choice). Our previous work around co-design in cancer suggests that participants prefer neutral locations for co-design workshops. Therefore, where feasible, workshops will take place away from hospital or university premises (e.g. in Newcastle, workshops have previously been held at the Great North Museum or the City Library). Workshops may also be held online (i.e. over Microsoft Teams or Zoom).

6 SAMPLE AND RECRUITMENT

6.1 ELIGIBILITY CRITERIA

Since the focus is self-management in the survivorship phase, eligibility for the patient and informal carer interviews and workshop participation will be restricted to LIGG patients and their informal carers (i.e. close family/friends who have been involved in caring for LIGG patients). This group has been selected because: these tumours preferentially affect younger adults; treatments may involve observation, surgery, radiation and/or chemotherapy; and, although survival is longer than for high-grade gliomas, patients and their families live with knowing that the cancer will eventually progress and limit life[64,65].

6.1.1 Inclusion criteria

Patients will be eligible if they:

- Were diagnosed at 18 or older.
- Are in remission or stable on a watchful waiting approach.
- Have a grade II astrocytoma or a grade II or III oligodendroglioma.
- Have completed primary treatment (or be on observation).

Informal carers will be eligible if they:

- Are someone who currently supports, or has supported within the past 5 years, someone with LIGG (the index patient need not have participated in the study; they may also have passed away).
- Currently aged 18 or older.

Healthcare professionals will be eligible if they:

- Are a member of a relevant multidisciplinary team, involved in the care of brain tumour patients, i.e.
    - Medics (e.g. neurosurgeons, neuro-oncologists)
    - Clinical nurse specialists
    - Allied healthcare professionals (e.g. psychologists, physiotherapists, and occupational therapists)

Cancer support professionals will be included if they:

- Are involved in the support of brain tumour patients outside of NHS care pathways (i.e. counsellors, benefits advisors, and social workers).

6.1.2 Exclusion criteria

Patients will be excluded if they:

- Have severe psychological or social problems that would make it inappropriate to contact the individual (as judged by the referring member of the multidisciplinary team).
- Have communication difficulties, cognitive impairment, or memory difficulties that are so significant that these render them unable to take part in an interview.
- Are non-English speaking to the extent that they are unable to take part in an interview, as an interpreter will not be used.

6.2 SAMPLING

Phase 1 – Semi-structured interviews

Participant recruitment will continue until data saturation is reached in each of the three interview sets (patients, informal carers, healthcare professionals), defined as no new themes arising in the last three interviews[66]. For each set, 25-30 interviews are likely to be required for reasonable saturation, in accordance with Dworkin's sample size policy[67]. We aim to sample approximately six patients, six family-members/friends, and six healthcare professionals from each clinical centre.

Purposive sampling strata will be defined for each interview set to ensure sample heterogeneity and elicitation of a broad range of views and experiences. The sampling strata for healthcare professionals will be the clinical centre and discipline (clinician/nurse/AHP). The sampling strata for patients and family-members/friends will be: time since diagnosis; treatment modality(ies); and gender.

We also aim to interview up to 15 cancer support professionals from brain tumour support charities. For these individuals, we will seek a maximum diversity sample in terms of organisation and role.

Phase 2 – Co-production workshops

We will seek to obtain maximum diversity among co-production workshop participants.

6.3 RECRUITMENT

Recruitment of patients: phase 1

Identification and recruitment of patients will happen in collaboration with healthcare professionals within the collaborating centres. Two recruitment processes may be used, depending on what works best for the participating site.

Recruitment process 1: Potentially eligible patients will be identified from their medical records and provided with an information sheet either face-to-face at a clinic visit, or by post (by a specific study invitation letter or a routine clinical appointment letter).

If the individual would like to take part or find out more information, they can (i) indicate to someone in the clinical team that they are happy for their contact details to be passed to the study coordinator; (ii) contact the study coordinator directly by email or telephone (using a dedicated, secure, study email address and phone number, which will be provided on the information sheet). If a response is not received, a reminder letter, with an information sheet attached, will be sent by post. Following this, the recruiting member of the clinical team may also make a follow-up phone call to find out whether the person has been able to consider the study information and would be willing for their details to be passed onto the study co-ordinator.

Recruitment process 2: Patients may also be recruited via follow-up clinics. As above, eligible patients will be sent an invitation letter and information pack prior to a clinic visit, which will also inform them that at their next clinic visit, the researcher will be present and with their permission, will tell them more about the study. Where feasible in the running of the clinics, when eligible patients arrive at clinic, they will be asked by a member of the clinic staff if they would be happy for the researcher to briefly speak to them about the study. Meeting the researcher will help potential participants feel more at ease and for a rapport to be established.

If they agree to speak to the researcher, the study co-ordinator will ask if they have read the study information sheet or visited the study web page, will answer their questions and give them more details about the study. They will be asked if they would be happy to take part and arrange a time for interview, or if they would agree to be contacted by phone in a few days to ask if they would like to take part/arrange an interview. If so, the study co-ordinator will take their contact details. If not, the study co-ordinator will thank them for their time and they will be given no further information. On phoning the potential participants, the study co-ordinator will ask if they have any further questions and if they would like to take part. If so, a date and time for interview will be arranged.

For both methods of recruitment, patients will be informed that they are free to choose to refuse to participate and, if they do so, they will not be asked again. The clinical team will record that they have approached the patient in their electronic record, to ensure that they are not re-approached if they have elected not to participate.

It is only after the patient makes contact with the researcher that the researcher will have access to the personal details of the individual, with the exception that the patient has indicated to a member of the clinical team that they are happy for their details to be passed to the study co-ordinator or has provided those details themselves. The research team will not have access to the medical details (i.e. tumour type and treatment) of the patient until after they have consented to take part.

Recruitment of informal carers: phase 1

In terms of identifying informal carers, patients who have been interviewed will be asked to nominate someone who has been involved in helping care for/support them since diagnosis. The research team will provide the patient with a carer study pack (letter of invitation, information leaflet) and ask them to pass it on to the carer. Those carers who are interested will be asked to call or email the research team, using a dedicated study email address and phone number, provided on the information sheet. If an interviewed patient has nominated a carer, but the carer has not contacted the research team after 7-10 days, the research team will contact the patient by email or phone. They will ask whether the patient has asked the carer if they would be interested in participating in the study. If not, they will remind the patient to speak to the carer. If yes, and the carer has said they would be interested, the researcher will ask the patient to remind the carer to contact the research team.

Informal carers may also be identified in collaboration with healthcare professionals within the collaborating centres, as sometimes the healthcare professional know the carers from their attendance to support a patient at a clinic visit. Similarly, informal carers could be provided with an information sheet at a clinic visit. In these instances, recruitment will follow the processes set out above for the patients.

If required, we will also use other routes to recruit informal carers, including advertising through The Brain Tumour Charity's Research Involvement Network and on the Ways Ahead project website (see other methods of recruitment for phase 1 and 2). We will also post on relevant online forums and social media platforms, (i.e. Twitter and Facebook groups). These posts will provide a brief description of the study and contact details for the research team, as well as direct those interested to the project website, to find out more.

Recruitment of healthcare professionals & cancer support professionals: phase 1

We will identify all healthcare professionals who are members of the brain cancer MDT in collaborating centres. We will write inviting them to be interviewed, with an information sheet attached. Those interested will then be asked to call or email the research team. All professionals will be informed that we will call them by phone in a few days if we haven't heard from them.

If we do not recruit sufficient numbers by this route, we will promote the study through the Brain Tumour Charity healthcare professional network and invite potentially interested health professionals to contact the study co-ordinator by email

or telephone. Those who do so will be sent the study information sheet and contacted (by email or phone) to ask whether they would be willing to take part.

Cancer support professionals will be identified through patient support organisations or charities (i.e. Maggie's Centre Newcastle, Brain Tumour Support, and The Brain Tumour Charity). We will write inviting them to be interviewed, with an information sheet attached. We will also ask the organisation to circulate an invitation letter by email to relevant staff. We will also allow for snowball sampling here, whereby someone we interview suggests another potentially eligible cancer support professional.

Recruitment to phase 2

Recruitment for phase 2 co-production workshops will follow the same routes as phase 1. Participants from phase 1 will be invited to register their interest in taking part in phase 2, but we will also seek to include some patients, family-members/friends, healthcare professionals, and cancer support professionals who did not take part in phase 1.

Other methods of recruitment for phases 1 and 2

We also propose to have a study website, which will display the project contact details and provide access to all of the relevant study information, including participant information sheets, project team member profiles, and project partners (i.e. The Brain Tumour Charity). There will be facility for those interested in taking part to contact the study team for further information. Anyone who does so, and fulfils the eligibility criteria, will be provided with the relevant study information sheet. The study co-ordinator will contact them after a few days (by phone or email) to ask whether they have decided about participation.

We may also seek to invite members of the Brain Tumour Charity Research Involvement Network, and healthcare professional network, to take part.

Posters & flyers promoting the study will be placed in clinical waiting rooms, including contact details for the study co-ordinators and details of the project website.

We will use posters and leaflets to promote the study at any NHS organised events for people with low- and intermediate-grade gliomas. As for the website, those interested may contact the study team and recruitment will proceed as for those recruited via the website.

If necessary, we will seek to advertise for volunteers through the e-newsletter and website of the Brain Tumour Charity. We will also consider adopting snowball sampling (whereby participants are asked to recruit future participants through their own acquaintances/networks).

6.3.1 Participant remuneration

Patients and family-members/friends who participate in the phase 1 interviews will be offered a £20 voucher for taking part as well as reimbursement of any travel expenses. The voucher is intended as a thank-you to participants for their time, and

is not intended to coerce individuals into taking part when they would rather not. Participants will be offered the voucher at the beginning of the interview to express that the voucher is a reward for their participation/attendance and not for what they say.

Patients and family-members/friends who participate in the phase 2 co-production workshops will be offered a £40 voucher (in addition to any travel expenses, where applicable). This is in-line with INVOLVE guidance and recognises that participants should be reimbursed and rewarded for their time and contribution, particularly those who may have to come during their working hours.

The time of healthcare professionals to participate in the interviews and workshops has been costed and will be made available to clinical sites.

6.4 CONSENT

All potential participants will be presented with a relevant information booklet (participant information sheet), detailing the study objectives and what is involved in taking part. They will also be provided the opportunity to ask any questions they may have. This will give potential participants sufficient information and length of time to make an informed decision about participation.

Prior to the interview, participants will be informed that participation is voluntary and that they can withdraw from the study at any point, without affecting their medical care or legal rights (see 6.4.1). They will also be asked to agree to the interview being audio-recorded. Should they agree, they will be informed that the audio-recording will be transcribed and that their personal/identifying details will be removed from the transcription. It will be made clear to participants that any information arising from the study will be anonymised so they cannot be identified in any publications or report. They will also be asked to indicate their understanding that this anonymous information may be used in future related research, or may be shared with other researchers, including students.

Written informed consent will be obtained from those being interviewed in person. For interviews over the phone or Skype/video conference, verbal informed consent will be audio recorded. The researcher will read each step of the consent document to the participant and ask them to confirm whether they understand and agree to this part of the process. The participant will be asked to state verbally that they understand each step of the document and the researcher will initial on their behalf. The stand-alone audio file recording of the consent process will be transferred as soon as is practical to Newcastle upon Tyne NHS Hospitals Trust (NuTH) secure drives. A paper copy record of the consent form will be held securely in the local site file.

As part of the consent process for patients, participants will be asked to consent to the researcher clarifying the details of their brain tumour diagnosis and treatment with their clinical team. Patients may not always know the precise details of, for example, their tumour site or the treatment(s) they have had; such information is important to be able to document participants' characteristics. Therefore, it will be sought in a

standardised way for each participant from their medical records. The medical record abstraction will be done by a member of the clinical team.

Finally, participants will be asked whether they would like to receive a summary of the findings of the research once the study is over (see 6.4.2). Those who would like to receive this information will be asked how they would like to receive the information. Their preferred means of contact will be retained separately from the consent forms and solely for the purposes of sharing the study results.

The same consent procedures apply to the phase 2 co-production workshops, except separate participant information sheets will apply, and due to group participation, participants will be informed that workshops will be audio-recorded. Patient medical records will not be confirmed following phase 2 participation.

6.4.1 Study withdrawal

The rights of individuals to change their mind about participation in the study and/or withdraw without giving a reason will be respected. Participants may withdraw their consent at any time. If the participant withdraws during the interview, the partial recording will be discarded. If a participant decides to withdraw after the interview has been completed, their personal data will be destroyed but their anonymised interview transcript will be retained (consistent with the current advice from the HRA). Consent forms will be retained but will be marked as a withdrawn participant.

In terms of the co-production workshops, or any group interviews/focus groups with cancer support professionals (phase 1), individuals may withdraw at any time but any recordings they are part of will not be destroyed; this is made clear on the relevant participant information sheets.

6.4.2 Feedback of study results

Participants will be asked at the time of interview and workshop whether they wish to receive a summary of the study findings. If so, their personal details will be retained for this purpose; only the Chief Investigator (Professor Sharp), and named members of the research team who require such access for legitimate purposes (e.g. study co-ordinators) will have access to these personal details. The individual's preferred means of contact will be stored separately from consent forms and from electronic or paper copies of the transcripts. If the participant does not want a copy of the summary of findings, their personal details will be destroyed once the details of their brain tumour diagnosis and treatment have been abstracted from their medical records and any relevant papers from the study have been published.

7 ETHICAL AND REGULATORY CONSIDERATIONS

7.1 ASSESSMENT AND MANAGEMENT OF RISK

It is recognised that participating in qualitative research may have emotional consequences for the interviewee and may involve them considering and discussing potentially upsetting issues related to their own, or their loved one's, cancer. The researchers are experienced in interviewing cancer survivors and other potentially

vulnerable patient groups. If an interviewee does not wish to answer any question during the interview, this will be respected. If the interviewee becomes upset, the researcher will ask them if they wish to stop the interview, either temporarily or permanently. Moreover, if an interviewee becomes very distressed, the researcher will ask whether they would like them to contact someone (e.g. a family member, friend, GP, or consultant) on their behalf.

Patients and informal carers will be provided with a post-interview sheet (draft attached) which will contain information about who they might contact if they feel they want to discuss any issues arising from taking part in the study. For example, this will suggest that they contact their GP, or their clinical team in the hospital (patients), and direct interviewees to information and helplines such as those offered by The Brain Tumour Charity, Samaritans, and Mind.

7.2 RESEARCH ETHICS COMMITTEE (REC) REPORTING

Before the start of the study, a favourable opinion will be sought from a UK Health Departments Research Ethics Service NHS REC for the study protocol, informed consent forms, letters of invitation, information sheets and topic guides.

Substantial amendments that require review by NHS REC will not be implemented until that review is in place and other mechanisms are in place to implement at site. All correspondence with the REC will be retained. The chief investigator will organise the production of research reports as required and notify the REC of the end of the study. An annual progress report (APR) will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the study is declared ended. If the study is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination. Within one year after the end of the study, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the REC.

7.3 REGULATORY REVIEW AND COMPLIANCE

Before any site can enrol patients into the study, the Chief Investigator or a designee will ensure that appropriate approvals from participating organisations are in place.

For any amendment to the study, the Chief Investigator or designee, in agreement with the sponsor, will submit information to the appropriate body in order for them to issue approval for the amendment. The Chief Investigator or designee will work with sites (R&D departments at NHS sites as well as the study delivery team) so they can put the necessary arrangements in place to implement the amendment and to confirm their support for the study as amended.

7.4 AMENDMENTS

If a substantial amendment to the REC application or the supporting documents is required, the sponsor will submit a valid notice of amendment to the REC for consideration. The national coordinating function of the UK country where the lead NHS R&D office is based will be informed. The CAG will also be notified of any substantial amendments in case the amendment affects their opinion of the study.

Substantial and non-substantial amendments will be communicated to the participating organisations (R&D office and local research team) departments of participating sites to assess whether the amendment affects the NHS permission for that site. Note that some amendments that may be considered to be non-substantial for the purposes of REC still need to be notified to NHS R&D (e.g. a change to the funding arrangements).

The Chief Investigator will be responsible for the decision to amend the protocol and any supporting documents. They will be responsible for deciding whether an amendment is substantial or non-substantial. The amendment history will be logged in the site-files. The protocol and all supporting documents will be version tracked, so that the most recent versions can be identified easily.

7.5 PEER REVIEW

The project has been funded by 'The Brain Tumour Charity'. The funding application for this project was independently peer reviewed by three independent experts and by The Brain Tumour Charity funding panel.

7.6 PATIENT AND PUBLIC INVOLVEMENT

A PPI Panel comprising adult LIGG patients and family-members/friends who support a LIGG patient has been established. We have also consulted with members of The Brain Tumour Charity's Research Involvement Network (RIN). The Panel and the RIN have been consulted about the protocol, study information sheets (and language used on these), topic guides, and the project website.

The PPI Panel will be actively involved throughout the project, providing advice to the research team on design, conduct, interpretation and dissemination. Where required we will obtain additional input through the RIN. The Panel will be invited to: comment/reflect on findings from the qualitative interviews; identify what they see as the key messages that need to be disseminated to patients, family members and the public; co-design the lay summary of findings; and advise on other dissemination activities. They will be actively involved in designing the supported self-management programme (via the co-production workshops). The study co-ordinator will be the designated PPI contact point and have responsibility for liaison between the Panel and research team.

7.7 DATA PROTECTION AND PATIENT CONFIDENTIALITY

If the patients are identified through clinical centres, their consultants will act as 'gate keepers' and the patients will be initially informed of the study via their healthcare professionals. The research team will not have access to contact details for any patients or informal carers, until they themselves give their permission or indicate to the relevant member of the clinical team that they are happy for them to be passed onto the researcher.

The Newcastle upon Tyne Hospitals NHS Foundation Trust is the sponsor for this study and will act as the data controller. Any identifiable data, including audio recordings of consent will be stored securely on REDCap software, as required by

the sponsor. Electronic and paper records of consent from participants, which contain names only, will be kept for five years in order to allow for audit of the research process. This is a Trust requirement. No other personal data such as contact details will be kept longer than is necessary and any identifying information will be anonymised in the data for analysis.

Audio-files of the recorded interviews will be stored securely on Newcastle University systems in 7Zip encrypted folders with unique password protection as soon as possible after interview and will not be saved using filenames containing any personal data. Access will be restricted to named members of the research team. After download, audio files will be immediately deleted from the voice recorders. Transcription of interviews will be done by a university approved service (www.typeitwritetranscription.co.uk) who have signed a confidentiality agreement. Audio files will be encrypted during transfer to the transcription service with the password for decryption provided separately via email or phone.

Transcripts from the interviews will be anonymised (e.g. removing places, names) and stored on the secure Newcastle University systems. Each transcript will be saved with a unique study identification number. Co-investigators on the study will only have access to anonymized transcripts. Any potential visual output from the co-design workshops (i.e. Jamboard) will be securely stored in the same manner as the transcripts.

Newcastle University IT systems enable access to files to be restricted to members of the project team holding secure log-on credentials, and IT administrators. The original audio recordings will be kept during the analysis period to allow researchers to return to the data if needed, e.g., to check how intonation might have contributed to meaning or to listen again to impaired speech. Following analysis the audio files will be permanently deleted from Newcastle University systems.

A site file will be compiled for the study. This will be held by the Principal Investigator for each site in a lockable office. This folder will contain important information about the study (protocol, participant information, ethical approvals etc.) and recruitment logs for the study site (who has been approached/written to about the study) and who has agreed to take part. These folders will also contain the study IDs assigned to each participating patient. This ensures that this information is not stored with the patient transcriptions.

All investigators and study site staff will comply with the requirements of the Data Protection Act 2018, with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles and General Data Protection Regulation (GDPR). After the study has ended, anonymised data will be archived in line with Newcastle University policy once the final report and publication are complete. Research data will remain available for 5 years following any publication, after which retention will be reviewed.

The consent procedures include informing participants about the sharing of data. It will be made clear to them that only their fully anonymised information will be used in future relevant research or shared with other researchers. It will be verbally explained

to participants that co-investigators on the study will only see the anonymized transcripts.

7.8 ACCESS TO THE FINAL STUDY DATASET

The final anonymised data set will be accessible by the study team (BR, LD, LS, JL, SW, VAS, TF, RB and PG) as well as any researchers who join the study team. This may also be accessible to students for secondary analysis, under the supervision of members of the study team, enabling the data to be used to its full potential. Participants will be informed of this on the study consent form.

7.9 DISSEMINATION POLICY

We will establish a project website, hosted by Newcastle University. The study co-ordinator will have the responsibility of maintaining and updating the website. The website will contain information for both scientific and lay audiences, including the study protocol and a final study report.

For scientific dissemination, the research findings will be presented at relevant national and international meetings (e.g. National Cancer Research Institute conference, European Association of Neuro-oncology, UK Society of Behavioural Medicine conference). Papers will be submitted to journals in neuro-oncology (e.g. Neuro-oncol; Neuro-oncol Pract; CNS oncol), cancer survivorship (e.g. J Cancer Survivorship, Support Cancer Cancer), and psycho-oncology/behavioural science (e.g. Psycho-Oncol, Implement Sci, Patient Educ & Counselling). Papers and conference presentations will be publicised on the project website. When we present at conferences and publish papers, we will liaise with the Brain Tumour Charity to press release the research.

For lay dissemination, research participants will be given the option of receiving a lay summary of the results once the final study report has been compiled. To reach patient and general populations, updates will be posted on the project website, with key messages (crafted together with the PPI Panel) highlighted. We will embed pod-casts within the website, with members of the project team (and, potentially, the PPI Panel) talking about the research, what it means and what patients can do to self-manage. Where appropriate, these will also be posted on YouTube. We will hold a dissemination event for brain tumour patients and healthcare professionals. If there is sufficient interest, we will live stream this event to other locations (e.g. collaborating centres). We will also record parts of the event and post on the website.

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