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Evaluation of a telehealth psychological support intervention for people with primary brain tumour and their family members: Study protocol for a randomised controlled trial

Short title: A telehealth intervention for brain tumour

Abstract

Objective: There is a lack of research on interventions that address the specific psychosocial needs of people with brain tumour and their families. This paper describes the protocol for a pragmatic randomised control trial (RCT) evaluating the clinical efficacy and cost-effectiveness of the Making Sense of Brain Tumour program delivered via telehealth (Tele-MAST) relative to standard care.

Methods: 148 adults with primary brain tumour will be randomly allocated to the 10-session Tele-MAST videoconferencing program or standard care from a cancer counselling service. The primary outcome is level of depression and secondary outcomes are quality of life, mental health and incremental cost per quality-adjusted life year. The mental health and quality of life of family members will also be assessed. Assessments will be conducted at pre-intervention, post-intervention (primary endpoint), 6-weeks post-intervention and 6-months post-intervention. The main analysis will determine whether the Tele-MAST intervention is more effective than standard care at post-intervention, and whether these effects are sustained at follow-up.

Conclusion: Results will indicate whether the Tele-MAST program is associated with better clinical outcomes and is more cost-effective than existing cancer support services. Such outcomes will contribute to effective and accessible psychosocial care for the brain tumour population.

Trial registration: Australian New Zealand Clinical Trials Registry (ANZCTR)): ACTRN12618001737224. Registered on October 22, 2018 (updated October 31, 2018).

Key Words: Brain tumour, cancer, telehealth, psychological support, mental health, quality of life

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Introduction

Although relatively uncommon (2.6-6.6 per 100,000), malignant brain tumour has an average five-year survival rate of only 35% (Leece et al., 2017; Ostrom et al., 2017). Primary brain tumours in general are associated with more neurocognitive impairments than any other cancer (Lidstone et al., 2003). These symptoms restrict the ability to drive, work, and live independently, and reduce people's social role functioning and quality of life (QoL) (Cubis, Ownsworth, Pinkham, & Chambers, 2018). The stress associated with the diagnosis, an uncertain prognosis, and complex neurological and functional impairments has a major impact on the mental health and QoL of people with brain tumour and their family caregivers (Bergo et al., 2015; Ownsworth, Henderson & Chambers, 2010).

High rates of depression and anxiety (40-50%) have been reported for people with brain tumour (Arnold et al., 2008) and their family caregivers (31-59%; Pawl, Lee, Clark, & Sherwood, 2013). Psychological distress has been found to persist beyond the primary treatment phase, as individuals face an ongoing threat of recurrence and functional decline (Trad et al., 2015). Despite the significant psychosocial burden of brain tumour, there is a lack of evidence-based interventions for improving mental health and QoL of people with brain tumour and their family caregivers (Piil, Juhler, Jakobsen & Jarden, 2016; Pill, Jarden & Pii, 2017).

To help address this gap, Ownsworth et al. (2015) developed the Making Sense of Brain Tumour (MAST) program, a 10-session (1 session per week) psychological support intervention delivered face-to-face in people's homes. A randomised controlled trial (RCT) of the MAST program (n = 50) indicated significant improvements in mental health and QoL for people with brain tumour relative to standard care (wait list controls). Such improvements were evident for people with benign, low-grade and high-grade tumours. Mean pre-post-intervention change scores for depression were over half a *SD* (-.60) for the MAST group

which represented a moderate size reduction in depression. In contrast, change scores for the wait list controls were +.23 of a *SD*, which indicated a slight increase in depression.

In recent international palliative care guidelines for adults with glioma (Pace et al., 2017) the MAST program was endorsed as showing clinically significant benefits for managing depression, with the quality of evidence rated higher than for pharmacological interventions. Further, in a systematic review of 10 RCTs of interventions for adults with brain tumour (Pan-Weisz et al., 2018), MAST was the only psychosocial program associated with significant improvements in QoL relative to control conditions.

Despite the recognised clinical efficacy, face-to-face delivery of MAST in the home is not feasible for broader translation into service delivery due to therapist travel requirements. Yet, people with brain tumour face many barriers to accessing clinic-based counselling, such as inability to drive or use public transport due to poor physical health, cognitive impairments and financial strain. Those living in rural and remote areas face further barriers to accessing specialist psychological support. Telehealth platforms may therefore offer a potentially more accessible and cost-effective option for delivering the MAST program.

Telehealth interventions reduce the need for travel and can improve access to specialist services, and hence decrease disparities in healthcare access (World Health Organization, 2016). Videoconferencing interventions have been found to be beneficial and convenient for the broader cancer population (Cox et al., 2016), but these have not been systematically evaluated for use with the brain tumour population. The feasibility of remote delivery is supported by pilot research on telephone-based delivery of MAST (Jones, Ownsworth & Shum, 2015). In 2017, Zoom videoconferencing calls were trialed with 10 people with brain tumour and family members. All “strongly agreed” that they felt comfortable using the Zoom platform and expressed that they would be keen to access support remotely via the Internet. Unlike standard telephone, videoconferencing allows health professionals to see people as

they interact with them in their own homes. Due to the visual aspect, the quality of communication is enhanced and screen-sharing of materials can support people with sensory-perceptual, language and cognitive impairments to process, learn and retain new information (Ownsworth, Arnautovska, Beadle, Shum & Moyle, 2017).

Objectives and Hypotheses

The primary aim of this RCT is to evaluate the effectiveness of the Tele-MAST videoconferencing intervention for improving mental health and QoL of adults with primary brain tumour and their family caregivers relative to standard care. We also aim to evaluate the cost-effectiveness of the Tele-MAST intervention relative to standard care. The hypotheses are:

1. At post-intervention (primary endpoint) and 6-weeks follow-up, participants receiving the Tele-MAST intervention will report significantly lower levels of depression than those receiving standard care after controlling for baseline functioning.
2. At post-intervention and 6-weeks follow-up participants receiving the Tele-MAST intervention will report significantly lower levels of anxiety and higher levels of existential well-being and QoL than those receiving standard care after controlling for baseline functioning.
3. Compared with standard care the Tele-MAST intervention will be cost-effective, defined as being below AU$50,000 per quality-adjusted life year (QALY), the acceptable incremental cost-effectiveness ratio threshold in Australia.
4. Relative to pre-intervention levels, participants will report significantly better mental health and QoL at 6-month follow-up after the Tele-MAST intervention.

The project will also examine the impact of the Tele-MAST program on participating family caregivers' mood and QoL, and investigate the factors influencing intervention outcomes.

This will help to determine individual characteristics likely to influence the efficacy of the Tele-MAST intervention in clinical practice.

Method

Design

In this two-arm pragmatic RCT, the effectiveness of the Tele-MAST intervention will be evaluated relative to standard care or existing cancer support services. Mental health and QoL will be assessed at baseline (T1), post-intervention (T2), 6 weeks post-intervention (T3), and 6-months (T4) follow-up. Participants in the standard care condition will be offered the Tele-MAST intervention after the 6-week follow-up (T3). The study was guided by the CONSORT statement for social and psychological intervention trials (Grant et al., 2018).

Participants

Recruitment

Over a 3-year period (November 2018-2021), 148 participants with primary brain tumour will be recruited from a community-based cancer support service and a major metropolitan hospital in Brisbane, Australia. Participants will be screened for eligibility by doctors and care coordinators (hospital) and cancer information and support staff (community). They will provide potential participants with a brief overview of the study and obtain verbal consent for their contact details to be provided to the project coordinator via a secure online project-specific form. Details of the project and the project coordinator's contact details will also be disseminated at community forums for health professionals and people with brain tumour and their families. The project coordinator will post or email the Participant Information Sheet and Consent Form to potential participants and then contact them via telephone to obtain informed consent. Family caregivers will also be asked to provide informed consent.

Eligibility criteria

Participants will be eligible if they: 1) are aged ≥18 years; 2) have been diagnosed with a benign or malignant primary brain tumour at any stage of disease or time post-onset; 3) report psychological distress on screening (i.e., Distress Thermometer [DT] score ≥4; Keir, Calhoun-Eagan, Swartz, Saleh & Freidman, 2008); 4) have adequate cognitive capacity and receptive and expressive English language skills as assessed by a telephone-based cognitive assessment; and 5) have reliable access to the Internet and a suitable electronic device, which they can operate independently or with support from their family.

Ethical clearance and registration

The research protocol has been approved by the Human Research Ethics Committees (HREC) of Metro South Health (HREC/18/QPAH/95) and Griffith University (GU Ref No: 2018/808). The trial is prospectively registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12618001737224).

Procedure

Randomisation

Following the baseline assessment, participants will be randomised to the Tele-MAST intervention or standard care. The random allocation will be conducted by a research assistant independent of the assessment and intervention using a predetermined computer-generated random sequence. Randomisation will be stratified according to baseline distress (DT scores of mild-to-moderate [4-7] vs. severe [≥8]) and family involvement in therapy (yes vs. no). Allocation will be concealed using sequentially numbered and sealed opaque envelopes.

Measures

The Brief Test of Adult Cognition by Telephone (BTACT; Tun & Lachman, 2006) will be administered at the baseline assessment to assess participants' global cognitive status and receptive and expressive language. Sociodemographic data and details of family members'

involvement in therapy will be obtained via interview. Clinical data (e.g., tumour type, grade, location, disease status and treatment) will be accessed from medical records. Outcome measures will be administered via telephone by a blind assessor. All measures have been validated for use in the brain tumour or other cancer populations. Table 1 summarises the clinical and health economic outcome measures and time point/s of administration.

The primary outcome of depression will be assessed using the semi-structured interview format of the Montgomery-Asberg Depression Rating Scale (MADRS; Williams & Kobak, 2008). The 10 items are clinician-rated from 0 (no or minimal symptoms) to 6 (maximum symptoms), with total scores of 0 to 60. Scores $\geq$ 12 signify clinical levels of depression. In the previous MAST trial (Ownsworth et al., 2015), the MADRS demonstrated good test-retest reliability (r = .85) and sensitivity to change, as administered by telephone. A reliable change index of 5.67 was derived from wait list control re-assessment data which is consistent with 10% of the instrument's range, as recommended as a general benchmark for interpreting the minimal clinically important difference (MCID). Inter-rater reliability will be examined on 20% of audiotaped interviews.

Secondary outcomes measures for participants with brain tumour include the DT, Functional Assessment of Cancer Therapy-Brain (Webster, Cella & Yost, 2003), Depression subscale of the Depression Anxiety and Stress Scales-21 (DASS-21; Lovibond & Lovibond, 1995), Generalized Anxiety Disorder-7 (Spitzer, Kroenke, Williams & Löwe, 2006); and McGill Quality of Life Questionnaire (Cohen, Mount, Tomas & Mount, 1996). Family caregivers' mental health and QoL will be assessed using the DASS-21 and WHOQOL-BREF (World Health Organization, 1996).

For the cost-effectiveness analysis, the EuroQoL-5D (EQ-5D-5L; Herdman et al., 2011) will be used to calculate QALYs and incremental cost per QALY gained for the Tele-MAST intervention relative to standard care. EQ-5D scores (0 = worse possible health to 1 = perfect

health) will be used to weight survival time to generate QALYs according to an Australian algorithm (Viney et al., 2011).

All health system costs or resources required to conduct the Tele-MAST intervention (e.g., therapist training, computer and Internet costs) will be monitored. Health care costs will include those incurred by the government and individual out-of-pocket expenses. Medicare records will be extracted for health care consultations, services, medication and procedures (approval obtained October 31, 2018). Participants' out-of-pocket expenses relate to receiving psychological support and the financial impact of brain tumour will be assessed at the 6-week follow-up (see Table 1).

Intervention procedures

Participants allocated to the Tele-MAST intervention will receive 10 x 1 hour weekly sessions delivered by a psychologist using Zoom videoconferencing. Participants will receive an initial training session to set up a Zoom account and practice receiving a call and navigating the audio-visual features on their device. Guided by the MAST therapist manual (Stewart & Ownsworth, 2014), the psychologist will deliver a combination of core sessions (1, 2 & 10) and module-based sessions (3-9) selected in accordance with an individual's goals and family member's involvement (individual and couple sessions), as follows:

- Session 1: describing the symptom onset, diagnosis, treatment and the everyday impact of the tumour (i.e., "telling my story").
- Session 2: exploring functional changes, issues of concern and life values to guide goal setting and selection of relevant therapy modules.
- Sessions 3-9: module-based sessions selected according to goals, for example, understanding the effects of brain tumour, managing emotional, cognitive and behavioural difficulties, improving relationship functioning, and addressing fears/concerns regarding end-of-life.

- Session 10: reviewing goals and therapy progress and plans for maintaining skills and strategies (e.g., coping with future stressors).

Therapy sessions will be audio-recorded using Zoom Cloud Recording with 15% reviewed (random selection) to examine adherence to the MAST therapy protocol.

Standard care for people with cancer in the Queensland context is based on a stepped care model (Hutchison, Steginga & Dunn, 2006) and clinical practice guidelines (Holland, Watson & Dunn, 2011) which advocate the need for routine screening of distress and referral for psychosocial intervention. People presenting to community-based cancer support services with low-to-moderate distress typically receive guided self-help from a nurse counsellor in a single session. Those with high levels of distress will bypass this service and receive up to 5 sessions of psychological support. In the current study, participants allocated to standard care will receive up to 5 sessions of individual and/or couples therapy from a psychologist that focuses on stressors or concerns related to their illness. The number, duration, focus of support and delivery mode (i.e., face-to-face, telephone or videoconferencing) of sessions will be systematically recorded.

As used in the telephone MAST pilot (Jones et al., 2015) and routinely used in clinical practice, the Session Rating Scale (Duncan et al., 2003) will be used by psychologists in both conditions to assess therapeutic alliance in each session.

Sample size

The previous RCT (Ownsworth et al., 2015) found moderate-to-large effect sizes for between-group differences in mental health and QoL (η_p^2 =.12-.17) for the MAST intervention, relative to wait list controls. Due to the need for caution in using effect sizes derived from pilot studies (Leone, Davis & Kraemer, 2010), an estimated moderate effect size (η_p^2 =.08) was used in a power analysis through G*Power (Faul, Erdfelder, Lang & Buchner, 2007). With alpha set at .05, and power of .90, this analysis indicated that a sample

size of n = 123 (62 per group) would be required to detect a moderate-sized difference in level of depression between the Tele-MAST and standard care groups at the post-intervention assessment (primary endpoint) controlling for baseline depression. Based on an estimated participant attrition rate of 20% at 6-weeks post-intervention, the recruitment goal is n = 148.

Statistical Analysis

Clinical outcome evaluation

A mixed-model approach with group allocation as the between-subjects factor, time (post-intervention, 6-weeks follow-up) as the repeated factor and baseline functioning (T1) as the covariate will be used to evaluate whether the Tele-MAST intervention is more effective than standard care for the primary and secondary outcome measures at post-intervention (T2), and whether these effects are sustained at 6-weeks follow-up (T3). Any demographic or clinical variables (e.g., tumour type, global cognitive status) that are significantly associated with the outcome variables will be included as covariates. The same approach will be used to examine the impact of the Tele-MAST intervention on family caregivers' mood and QoL. Longer-term outcomes of the Tele-MAST intervention will be examined using the 6-month follow-up data (T4), relative to baseline functioning (T1). For all analyses missing data will be estimated using multiple imputation (Lane, 2008). To investigate factors influencing the Tele-MAST intervention outcomes, participants meeting the MCID on the MADRS ('improvers') will be identified. Demographic and clinical outcome predictors of improvement will be determined using logistic regression.

Health economic evaluation

The goal of the cost-effectiveness analysis is to compare the costs and health benefits of Tele-MAST with standard care from a health system perspective. The health benefits will be: 1) QALYs; and 2) % of improvers, based on the MCID on the EQ-5D-5L. Generalised

estimating equations will assess both time and treatment effects and allow for non-parametric and missing data. Using the area-under-the-curve method and EQ-5D scores at each time point, a single QALY for each person will be calculated at the last time point (Drummond, Stoddard & Torrance, 2005). Costs will be aggregated across the groups and means generated. The difference in mean costs divided by the difference in mean QALYs or % improvers generates the incremental cost per QALY or % improver ratios. Analyses will be performed using TreeAge Pro 2017 (TreeAge Software Inc) and one-way and probabilistic sensitivity analyses will be undertaken to address uncertainty.

Discussion

Primary brain tumour is a complex and potentially life-threatening illness associated with distressing functional impairments. There is a need for effective and accessible interventions to support individuals and their families to adjust to the diagnosis and ongoing stressors throughout the illness. The previous RCT of the face-to-face MAST program (Ownsworth et al., 2015) supported the conceptual approach to psychosocial intervention for people with brain tumour and pilot research supports the feasibility of remote delivery (Jones et al., 2015). This RCT will determine the clinical efficacy and cost-effectiveness of the MAST intervention delivered via videoconferencing relative to standard care.

As a pragmatic trial, it is not possible to match the dosage of therapy between the Tele-MAST intervention and standard care. Instead, the aim is to determine whether an extended brain-tumour specific intervention yields better clinical outcomes than the current standard of care in the cancer context. If the Tele-MAST intervention is associated with better mental health and QoL outcomes than existing cancer support services and is found to be cost-effective, the findings would support the uptake of the Tele-MAST intervention into clinical practice. Conversely, if the Tele-MAST program does not yield better clinical

outcomes than standard care, this would suggest it is not beneficial to change the nature and intensity of psychological support provided to people with brain tumour. The findings may reveal that a subgroup of people with brain tumour with particular characteristics benefits more from the Tele-MAST program than standard care. In line with the principles of stepped care, identification of these individual characteristics may guide the allocation of resources to deliver best care. It is also possible that the findings will indicate clinical efficacy, but suggest that the Tele-MAST intervention is not cost-effective from the health system perspective. The findings will identify the characteristics of individuals most likely to benefit from telehealth psychosocial interventions to support the targeting of treatment and maximise healthcare effects within available resources.

By determining the health outcomes, resource consumption and cost-effectiveness of the Tele-MAST intervention, this research has significant potential to improve both the quality and sustainability of psychosocial care for this population. In particular, the research findings are expected to inform implementation of a feasible and effective psychosocial care program that can be translated to community cancer support services.

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Table 1

Summary of Clinical Outcome and Health Economics Measures and Time Point of Administration

Measures	Items and construct assessed	Baseline	Post-intervention	6-week follow-up	6-month follow-up
Primary outcome					
Montgomery-Asberg Depression Rating Scale	10 clinician-rated items assess the presence and severity of depression	X	X	X	X
Secondary outcomes					
Distress Thermometer	Single item rating of psychological distress (0-10); ≥4 will be used to indicate distress warranting psychological support.	X	X	X	X
Functional Assessment of Cancer Therapy-Brain	27 items assess global QoL and physical, social, emotional, and functional well-being; 23 items assess brain tumour specific symptoms	X	X	X	X
Depression scale, DASS-21	7 items assess low mood (cognitive and affective symptoms of depression)	X	X	X	X
Generalized Anxiety Disorder-7	7 items assess cognitive and affective components of anxiety	X	X	X	X
McGill Quality of Life Questionnaire	12 items assess psychological and existential well-being (e.g., sense of control, purpose, meaning in existence & self-worth)	X	X	X	X
EuroQoL-5D-5L	5 items used to calculate quality-adjusted life years (QALYs) and incremental cost per QALY	X	X	X	X

Patients Costs Questionnaire	6 item study-specific measure to assess out-of-pocket expenses over the past 3 months related to receiving psychological support			X	
COST-Functional Assessment of Chronic Illness Therapy	12 items assess the financial impact of the brain tumour			X	
Family caregivers					
DASS-21	21 items assess symptoms of depression, anxiety and stress	X	X	X	X
WHOQOL-BREF	26 items assess physical, psychological, social and environmental health and wellbeing	X	X	X	X