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Exercise as a non-pharmacological intervention for the management of sleep disturbance in primary brain tumour survivors and their caregivers: A study protocol of a clinical trial

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ABSTRACT

Background: Sleep disturbance is a highly prevalent and impactful symptom experienced by those adversely affected by primary brain tumours. Despite this, there is a lack of literature exploring appropriate options for the management of sleep disturbance in these populations. As such, more holistic and patient-centred approaches to address sleep disturbance are needed. Exercise presents itself as a viable option for managing sleep disturbances given its numerous health benefits, minimal costs, and acceptability, though the feasibility of its use in the context of primary brain tumours is unknown.

Methods: Primary brain tumour survivors and their caregivers will enrol and participate in a supervised, eight-week exercise intervention delivered by telehealth. Feasibility will be assessed using predetermined study metrics, including eligibility, recruitment. and assessment completion rates. Acceptability will be assessed using retention to intervention rates, session attendance, and participant satisfaction. Sleep will be assessed both objectively, using ring sleep trackers, and subjectively, using questionnaires.

Conclusion: This study will be the first to explore the feasibility and acceptability of exercise for the management of sleep disturbance in primary brain tumour survivors and their caregivers. If successful, this protocol will contribute to the development and implementation of appropriate strategies to manage sleep disturbance in these populations.

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Key Points:

1. The exercise intervention described in this study protocol aims to improve sleep in primary brain tumour survivors and their caregivers. This intervention will be the first to explore the use of exercise for managing sleep disturbance in PBT's and their caregivers. Furthermore, it will contribute to the growing body of literature exploring the use of home-based, telehealth exercise in these populations.
2. Exercise has been shown to have positive influences on sleep regulating factors, such as melatonin production and thermoregulation, as well as improving regulation of stress and mood. While there is no PBT-specific evidence for the use of exercise for managing sleep disturbances, there is existing qualitative evidence in other cancer populations highlighting the positive effect of exercise on sleep.

1. Introduction

Primary brain tumours (PBT) are rare cancers of the central nervous system in adults, accounting for approximately 1.5% of all cancers diagnosed [1,2]. While advances in treatments have improved survival, treatment- and tumour-related complications impact numerous aspects of health-related quality of life (HRQoL), including physical, cognitive, and psychosocial function. These impact PBT survivors through all phases of survivorship [3–6]. Family caregivers, herein referred to as "caregivers", experience a unique level of burden due to their relationship with a PBT survivor due to their diagnosis with what many regard as a lifelong illness. The stress that occurs with caregiving negatively affects caregiver health, with studies indicating links to adverse psychological and physiological health consequences [7–9].

Sleep disturbance is one of the most common concerns experienced by both PBT survivors and caregivers, with our recent systematic review demonstrating that it is a pervasive and significant symptom that is poorly managed [10]. Sleep disturbance is a complex phenomenon in the context of PBTs given the involvement of a bi-directional interplay of heterogenous factors that extend across the biopsychosocial spectrum (e.g., biological – treatment- and tumour-specific impacts; psychological – worry, stress, depression, anxiety; social – altered behaviours), leading to its development and eventual chronicity [10–12]. Despite a growing awareness of the impact of sleep disturbances in the context of PBTs, our recent systematic review found no evidence of the development or utilization of any sleep-specific interventions [10].

While there are commonly used interventions to manage sleep disturbance, such as pharmacotherapy and cognitive behavioural therapy (CBT), there are a number of potential drawbacks that may outweigh their benefits in the context of PBTs. For example, pharmacotherapy use has a risk of dependency, impaired tolerance, and adverse effects (e.g., headaches, dizziness), particularly when used long term [13,14]. Furthermore, the utilization of clinician-led CBT interventions is constrained by the requirement of trained therapists and high treatment costs, limiting its accessibility at a community level [13]. As such, more holistic and patient-centred approach to address sleep disturbance involving non-pharmacological interventions may be more appropriate. Exercise presents as a viable option, with evidence from other populations highlighting several ways that exercise may positively influence sleep, such as increased melatonin production [15], improved thermoregulation [16], and improved regulation of stress and mood [17]. While there is limited literature on the benefits of exercise on sleep specifically for those adversely affected by PBTs, there is qualitative evidence highlighting a positive effect of exercise on sleep exists in cancer patients, with positive outcomes more frequently observed in survivors after treatment rather than those still undergoing treatment [18]. Despite the absence of sleep-focused interventions in the context of PBTs, our systematic review aligned with these qualitative outcomes, highlighting preliminary evidence supporting the use of physical activity as a non-pharmacological approach to manage sleep disturbances, drowsiness, and fatigue in PBT survivors specifically [10,18].

While the evidence for *why* exercise improves sleep is lacking, there is a plethora of research devoted to exploring the beneficial effects of exercise throughout the disease trajectory of cancer, with research highlighting positive outcomes in both physical and psychological domains [19–24]. For example, regular exercise has been associated with improvements in cognition, mood, reductions in anxiety and depression, enhanced quality of life, as well as improved physical outcomes such as cardiovascular fitness, muscular strength, balance, and flexibility [23,24]. However, a recent systematic review conducted by Sandler et al. highlights low levels of physical activity among brain cancer survivors, with most individuals unable to meet recommended physical activity guidelines for cancer survivors [21]. This may be due to the unique challenges experienced by those adversely affected by PBTs, such as treatment- and disease-related side effects, which make engaging in exercise difficult. Despite these unique challenges, exercise interventions have been shown to be safe and PBT survivors, eliciting beneficial outcomes in several physical and psychological domains [21,25,26]. Thus, identifying the most appropriate format for the delivery of exercise with those adversely affected by PBTs is crucial to ensuring increased physical activity levels in an effort to maximise these beneficial outcomes.

Home-based exercise may provide an appropriate solution, with previous literature among PBT survivors, highlighting a preference and high rate of acceptability for these types of interventions [27,28]. Furthermore, telehealth emerges as a promising alternative to face-to-face supervision, further improving the practicality of home-based interventions. Supportive care via telehealth platforms provides a unique level of accessibility to personalised care away from a clinical setting that results in reduced disruption to the day to day lives of those involved while still provided a safety net through ongoing connection with health professionals [29]. Accordingly, we have designed a feasibility study exploring the use of telehealth supervised, home-based exercise as an intervention for the management of sleep disturbance with those adversely affected by PBTs. Herein, we present the study protocol, including design, methodology, data analytic plan, and rationale for this research.

2. Aims

This clinical trial explores the preliminary efficacy, safety, and acceptability of an 8-week, telehealth, home-based exercise intervention for the management of sleep disturbance in PBT survivors and their caregivers.

3. Methods

3.1. Study design

This intervention will employ a quasi-experimental design through an exercise intervention with adults with primary brain tumours and their caregivers. They will perform 8-weeks of supervised telehealth exercise comprised of combined resistance and aerobic training overseen by an accredited exercise physiologist (AEP; Exercise and Sports Science Australia). A sub-group of participants will be given a sleep tracking device, the Oura Ring (Oulu, Finland) [30], to be worn during a controlled observation period of 4 weeks to establish baseline sleep patterns prior to the 8-week intervention. This study has received ethical approval from necessary institutional review boards and was prospectively registered on the Australian and New Zealand Clinical Trials Registry (ACTRN12623001099617).

3.2. Eligibility criteria

Eligibility criteria include: 1) Adults ≥18 years of age; 2a) Histologically confirmed PBT and completed planned initial treatment ≥8 weeks prior to recruitment; 2b) self-endorsing or identified by PBT survivor as a relative or loved one who assists with medical care and/or activities of daily living on a regular basis who is not paid for their help; 3) Subjectively reported sleep concerns and/or disturbance/disruption within the previous month discussed during standard care clinical routines and/or outpatient consultations with medical or allied health professional; 4) Medical clearance for exercise, if required (e.g., from treating oncologist or GP); 5) The ability to give written consent and undertake study measures in English. PBT survivors and caregivers may be recruited together or separately; they are not inter-dependent for recruitment (e.g., if a PBT survivor would like to participate, but caregiver does not, the PBT survivor is still eligible for participation).

All participants will also need to: 1) be able and willing to attend pre- and post-intervention exercise testing at Queensland University of Technology (QUT) Health Clinics at Kelvin Grove (Brisbane, QLD); 2) have access to a device with a forward-facing camera and microphone; 3) have a smartphone with Bluetooth connectivity if allocated an Oura Ring (participants allocated an Oura Ring will be required to download the Oura Ring app for data collection); 4) have stable and secure internet connection to support telehealth component of the intervention, determined by asking participants if they can watch videos without buffering or interruptions; 5) have access to an appropriate space at or near home to set up their device to perform the exercise intervention.

3.3. Participant recruitment

PBT survivors and their caregivers will be recruited from the Princess Alexandra Hospital (PAH), Brisbane, QLD, Australia. Screening will be performed by clinical staff during standard of care clinical activities and outpatient consultations. Following identification of eligible participants, consent to share contact details (e.g., phone call, text message, and/or email) with the study team will be sought, for the purposes of independently discussing the project. The research team will contact eligible participants to discuss the study, as well as provide participant information sheets as appropriate.

3.4. Data collection

Data collection will occur at several timepoints throughout the intervention, including baseline and post-intervention assessments and interviews, as well as continuously throughout the intervention (Table 1).

Functional outcome measures will be recorded during baseline and post-intervention testing session which will be completed at the QUT's Exercise Physiology Clinic. These sessions will be scheduled for 1-h, including both subjective questioning (e.g., background and

Table 1
Assessment schedule from screening through to post-intervention.

Assessments	Registration	Baseline	Post-intervention	Throughout intervention
Eligibility Screening	X			
Medical Clearance	X			
Informed Consent	X			
Demographic and Clinicopathologic Data	X			
Feasibility				
Eligibility rate	X			
Recruitment rate	X			
Assessment completion rate		X	X	
Acceptability				
Attrition rate				X
Session attendance				X
Participant satisfaction			X	X
Sleep Outcome Measures				
Pittsburgh Sleep Quality Index [32]		X	X	
Insomnia Severity Index [33]		X	X	
Oura Ring [34]				X
Consensus Sleep Diary [31]				X
Health Related Quality of Life				
EORTC QLQ - C30 [35]		X	X	
EORTC QLQ - BN20 [36]		X	X	
CQOLC [37]		X	X	
Mental Health				
DASS-21 [38]		X	X	
Anthropometry				
Height (cm)		X	X	
Weight (kg)		X	X	
Body Mass Index (kg/m^2)		X	X	
Functional Outcome Measures				
Romberg Test [39]		X	X	
Timed Up and Go [40]		X	X	
6-Minute Walk Test [41]		X	X	
5RM Leg Press [42]		X	X	
5RM Chest Press [42]		X	X	
Safety and Adverse Events				
Edmonton Symptom Assessment [43]				X
CTCAE [44]				X
Semi-Structured Qualitative Interviews		X	X	

Abbreviations: EORTC QLQ - European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; CQOLC – Caregiver Quality of Life – Cancer; DASS – Depression Anxiety Stress Scale; 5RM – 5 Repetition Max; CTCAE – Common Terminology Criteria for Adverse Events.

demographic/clinicopathologic questions) and objective functional assessments, including anthropometry, dynamic and static balance, cardiorespiratory fitness, and muscular strength. One week prior to both (i.e., baseline and post-intervention) scheduled assessments, electronic questionnaires assessing sleep quality (along with instructions on how to complete) will be sent to participants. Physical copies will be available prior to exercise testing sessions in the event that they are unable to do so prior.

Measures of feasibility and acceptability will be recorded appropriately from screening through to post-intervention. All participants will be provided with physical copies of the Consensus Sleep Diary – Core [31] to be completed on a daily basis. Additionally, alternating participants (i.e., every second recruited) will be provided with a multi-sensor, wearable device that is already commercially available in Australia – the Gen II Oura Ring (Oulu, Finland) [30]. Participants allocated an Oura Ring will receive this 4-weeks prior to their scheduled baseline assessment to allow for a "normalising" period where continuous data will be collected to record an accurate and individualised baseline of the participants sleep patterns to feed into the Oura data algorithm. Participants allocated a ring will be instructed to wear the ring at all times throughout the 4-weeks prior to their baseline assessment as well as 8-week exercise intervention, with an emphasis on ensuring that it is worn at night to accurately track sleep. Finally, safety and adverse events will be monitored throughout the intervention using subjective questioning at the beginning of each exercise session, the Edmonton Symptom Assessment, and the Common Terminology Criteria for Adverse Events.

3.5. Intervention

The intervention will involve 8-weeks of individually prescribed, moderate intensity, mixed-modality exercise supported by an AEP (see Fig. 1). In an effort to maintain the fidelity and rigour of the study, the AEP will be independent to the research team and has experience in delivery of exercise interventions with cancer survivors. The exercise programs will be informed based on guidelines stipulated by Exercise and Sports Science Australia [19], Clinical Oncology Society of Australia [45] and American College of Sports Medicine [46] position statements for exercise and cancer. The weekly exercise target dosage will be 150 min of moderate intensity exercise, with intensity measured using a rating of perceived exertion (RPE) scale [47]. This will be prescribed over 2 × supervised, telehealth sessions on non-consecutive days (e.g., Monday & Wednesday) to allow for adequate recovery following each session, and 2 × unsupervised, prescribed exercise sessions per week. The supervised telehealth sessions will be between 45 and 60 min incorporating both resistance (1–4 sets of 6–12 repetitions per set of 5–8 exercise) and aerobic training at an RPE of 12–14/20, and the unsupervised sessions between 15 and 30 min incorporating aerobic training at an RPE of 12–14/20. Individualisation will be based on functional outcome measures including aerobic capacity, muscular strength, and balance scores which will be recorded during baseline intervention testing sessions. Furthermore, individual limitations such as treatment related side effects, clinical characteristics, safety, and personal goals will also be taken into consideration when developing the exercise programs. All sessions will be organised and timetabled prior to commencing the exercise intervention, in consultation with participants at mutually agreeable times.

Telehealth sessions will be conducted individually, though in circumstances where participants are recruited together (e.g., spouses), the sessions may be conducted at the same time. Participants will be provided with an equipment pack containing resistance bands of varying tension (e.g., easy, medium, hard, very hard), fabric loop bands of varying tension (e.g., easy, medium, hard), a 28 kg Kettlebell set (1 × 4 kg, 6 kg, 8 kg, 10 kg), and an exercise/yoga mat. Additionally, pieces of furniture (e.g., chairs, benches, tables, steps, etc.) may also be utilised to complete these sessions where necessary.

4. Outcome measures

4.1. Demographic & clinicopathologic information

Prior to baseline evaluations, participants will undergo a short subjective consultation (approximately 10–15 min) where demographic and clinicopathologic information will be recorded (Table 2).

4.2. Feasibility

Eligibility rate and reasons for ineligibility, recruitment rate, and assessment completion (baseline & post-intervention) rates will be recorded. Adequate feasibility metrics, adapted from previous neuro-oncology-specific literature, include recruitment accrual of ≥50% of eligible participants and baseline assessment completion >80%, post-intervention assessment completion >70% [26,48].

4.3. Acceptability

Participant retention rates, session attendance rates, participant satisfaction, and whether participants would recommend the study to others will recorded. Study intervention and procedures will be deemed

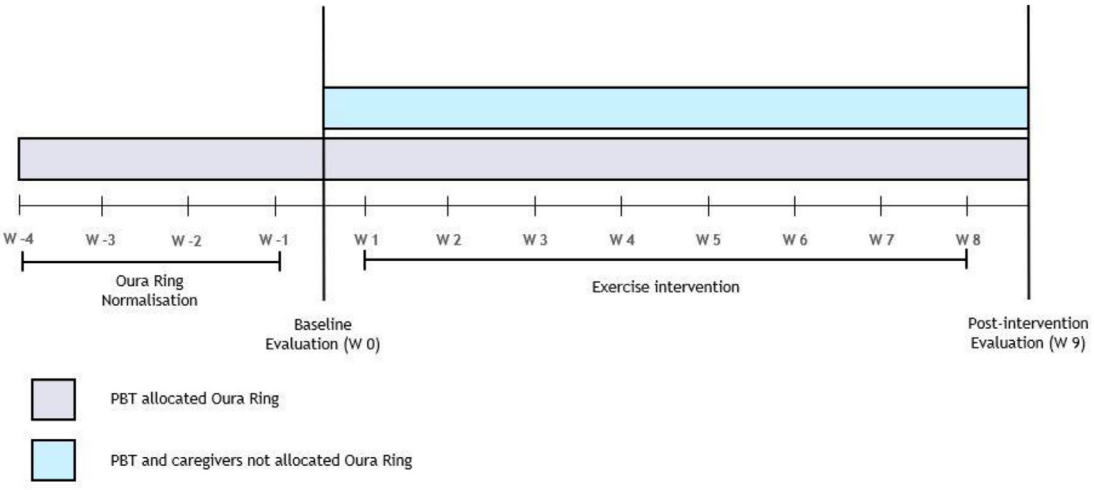

Fig. 1. Intervention timeline.

Table 2
Demographic and clinicopathologic information.

PBT & Caregiver	PBT	Caregiver
Age	ECOG Performance Status	Relationship as caregiver (e.g., spouse)
Sex	Tumour Diagnosis	Duration of care (time frame)
	WHO Grade	
Marital Status	Tumour Location (e.g., lobe, laterality)	Other care duties (e.g., dependent children)
Smoking/Alcohol Consumption	Treatment/medical history • Time since diagnosis • Surgery, Radiation, Chemotherapy	
	Recurrences	
Occupation/Employment status/Change in employment since diagnosis	Treatment side effects (e.g., neurological deficits, neutropenia, thrombocytopaenia, seizures)	
Comorbidities (e.g., cardiovascular issues, psychological disorders, sleep disorders etc.)		
Current physical activity levels		
Medication use		
Type (e.g., prescription/over the counter, indication for use)		

acceptable as evidenced by attrition rate (<20%), session attendance rate (>80%), and if they would recommend the intervention to others (>75%). Additionally, semi-structured interviews will be performed where participants will be afforded the opportunity to discuss their satisfaction with the intervention and provide both positive and negative feedback.

4.4. Safety and adverse events

Safety and recording of adverse events will be monitored and recorded throughout the telehealth exercise sessions. A holistic clinical assessment will be performed at the start of each exercise session, including appropriate subjective questioning (e.g., general health and well-being, follow-up on previous sessions) and, for PBT survivors specifically, the Edmonton Symptom Assessment System (ESAS). Given the complexity of PBT diagnoses and their associated symptoms, the ESAS will be used to systematically monitor and address potential adverse effects or changes in symptomology with PBT survivors. This will allow for timely adjustments to the intervention on an individualised level to ensure safety during the exercise intervention. The ESAS consists of a numerical rating scale from 0 to 10, with 0 indicating the absence of a symptom and 10 indicating the most severe symptom. The ESAS evaluates nine common symptoms, including pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, well-being, and shortness of breath [43]. Adverse events will be defined by using the revised National Cancer Institute's CTCAE V5 Grading Criteria [44]. This will include appropriate attribution (e.g., exercise intervention, medication side effects, etc), as well as timing (e.g., during supervised exercise session vs post session). An adverse event will be defined as any unfavourable or unintended sign, symptom or injury including abnormalities in physiological testing/examination that may require further clinical investigation beyond completing a repeat of the abnormal testing.

4.5. Clinical outcome measures

A range of outcomes will be recorded and assessed throughout the intervention to evaluate the efficacy and impact of the intervention. This will be achieved using validated self-report measures and clinical assessments outlined in Table 3 Please refer to the Supplementary Material for descriptions of these outcome measures.

4.6. Semi-structured qualitative interviews

This semi-structured interview, performed with patients and caregivers, will occur both pre- and post-intervention to gain deeper insight into their sleep experiences prior to cancer diagnosis and their perceptions of impact and causal factors of sleep disturbance. It will also explore participant perceptions of the home-based exercise intervention and its potential role as a tool to manage sleep disturbance.

Participants will be interviewed privately in a one-on-one format, following a semi-structured interview schedule (see Tables 4 and 5), in the same week as their post-intervention evaluation by a member of the research team (JM). Organisation of day and time will be based on preference of the participant, with the option to do this over the phone or via telehealth. To prevent cognitive overload, it will be preferred that patients do not complete with qualitative interview on the same day as their evaluation. All qualitative interviews will be audio recorded and transcribed for thematic analysis. Interviews will be informed by the following interview schedules:

Table 3
Clinical outcome measures.

Clinical Outcome Measures	Specific Measurements	Estimated Completion Time	Metric and method of aggregation
Sleep	Pittsburgh Sleep Quality Index [32]	5–10 min	Effect of time on mean scores between baseline and post intervention
	Insomnia Severity Index [33]	5–10 min	
	Consensus Sleep Diary [31]	5–10 min daily	
Health Related Quality of Life & Mental Health	EORTC QLQ - C30 [35]	12 min	Effect of time on mean scores between baseline and post intervention
	EORTC QLQ - BN20 [36]	5–10 min	
	CQOLC [37]	5–10 min	
	DASS-21 [38]	5–10 min	
Functional Outcome Measures	Romberg Test [39]	5 min	Effect of time on mean scores between baseline and post intervention
	Timed Up and Go [40]	5 min	
	6-Minute Walk Test [41]	15 min	
	5RM Leg Press [42]	15–20 min	
	5RM Chest Press [42]	15–20 min	

Table 4
Baseline semi structured interview schedule.

1. Exploring current sleep experiences
Q. Could you describe to me how your sleep is currently?
Probes/prompts:
• Trouble falling/staying asleep.
• Inquire about how much sleep they are getting.
• Any concerns about sleep habits.
2. Comparison to previous sleep experiences - pre-diagnosis
Q. Can you tell me what your sleep was like before to your diagnosis?
Probes/prompts:
• Any changes since diagnosis.
• If yes – slow/gradual vs sudden.
3. Exploring perception of causative factors/aetiology[a]
Q. What do you think contributes to your current sleep experiences?
Probes/prompts:
• Sleep hygiene (e.g., technology before bed); mental health; routine, etc.
• Physical/psychological impacts of diagnosis?
4. Impact of current sleep experiences – functioning/activities of daily living/quality of life[a]
Q. How does your sleep affect/impact you on a daily basis?
Probes/prompts:
• How does it affect concentration/focus/memory/mood/physical functioning/ performing day to day tasks.
• If still working – impact on work.
5. Management strategies for impaired sleep
Q. Is there anything that you do to manage your current sleep experiences?
Probes/prompts:
• Discussed options with GP?
• Sleep medications? Other sleep focused interventions?
• Attitudes/beliefs around management options – are they necessary?
6. Exercise/physical activity history
Q. How physically active are you? (or how much do you move around during the day?)
If yes: How often do you exercise? Intensity of exercise (easy/hard)?
If no: What stops you from being physically active?
Q. Prior to the diagnosis, were you physically active?
Probes/prompts:
• Previously participation in any sports.
• Preferences – Likes/dislikes

[a] - denotes themes/questions that have an interchangeable order dependent on flow of interview.

Table 5
Post-intervention semi structured interview schedule.

1. Exploring current sleep experiences
Q. Could you describe to me how your sleep has been over the past 8-weeks?
Probes/prompts:
• Trouble falling/staying asleep.
• Inquire about how much sleep they are getting.
• Any concerns about sleep habits.
2. Comparison to previous sleep experiences – pre-intervention
Q. How would you compare you sleep over the past 8-weeks to before the start of the intervention?
Probes/prompts:
• Any changes since diagnosis.
• If yes – slow/gradual vs sudden.
3. Exploring perception of causative factors/aetiology[a]
Q. In the last 8-weeks, what do you think has contributed most to your overall sleep experiences?
Probes/prompts:
• Sleep hygiene (e.g., technology before bed); mental health; routine, etc.
• Changes in routine/habits.
4. Impact of current sleep experiences – functioning/activities of daily living/quality of life[a]
Q. Has there been any change in how your sleep has affected/impacted you on a day to day basis in the past 8-weeks?
Probes/prompts:
• How does it affect concentration/focus/memory/mood/physical functioning/ performing day to day tasks
• If still working – impact on work.
5. Management strategies for impaired sleep
Q. Reflecting on the past 8-weeks, have you noticed any changes in your approach to managing your sleep compared to before the intervention?
Probes/prompts:
• Daily habits, routine before bed, etc.
Q. Is there anything new that you are doing now to manage your sleep that?
• Inquire about any new medications or advice that they may have received.
6. Acceptability of the intervention
Q. Were you satisfied with the exercise program that was given to you?
• What did you like about the exercise program?
• What would you change about the exercise program?
Q. How was working with an exercise physiologist over the past 8-weeks?
Probes/prompts:
• Did you feel like the supervision helped your adherence with sessions?
• Enquire about exercising with caregiver/PBT and if this was helpful
Q. Based on your experience in participating in the intervention, do you feel like doing more physical activity/exercise is a suitable strategy to help with improving sleep?
Q. Would you recommend to others to try performing more physical activity/exercise to improve sleep?

[a] - denotes themes/questions that have an interchangeable order dependent on flow of interview.

5. Statistical analysis

5.1. Sample size

The project will aim to recruit 30 to 50 people (15–25 PBT survivors and a matched number of caregivers). As this study is feasibility in nature, no formal sample size calculation has been performed. However, this sample size is based on a realistic estimation of potential participants for screening based on PBT admission to the Princess Alexandra Hospital in a calendar year (40-70 adults with PBT eligible for screening), as well as comparisons to similar study designs [21,25,49].

5.2. Data analysis plan

5.2.1. Quantitative analysis

To assess feasibility, detailed records of the number of individuals screened, eligible, enrolled, complete assessment measures, attend telehealth exercise sessions will be kept. Individuals who do not attend sessions will be contacted to assess continued interest in participation, with each attempt to contact the participant recorded. Reasons for attrition will be documented. To explore feasibility outcomes, we will analyse frequencies and proportions. To assess acceptability outcomes, we will analyse means and standard deviations.

Descriptive statistics (mean, standard deviation) will be computed for participant characteristics along with scores of study measures. The objective sleep parameters from the Oura Ring will be derived from CSV files downloaded from online data storage and exported into Excel spreadsheets for analysis using SPSS statistical software package (version 20.0, SPSS, Inc., Chicago, IL). Data from the functional assessments and the questionnaires will be transcribed into Excel for subsequent SPSS analysis. Scores from the self-report sleep assessments will be determined and the prevalence of sleep disturbance computed using the validated cut-off scores (e.g., PSQI global >5, ISI ≥ 15).

Normality of data will be assessed using the Shapiro–Wilk test along with visual assessment of scatter plots, histograms and box and whisker plots. Pre- and post-intervention differences will be assessed using a paired samples t-test if the data is normally distributed, otherwise Wilcoxon matched-pairs signed rank test will be used. Where missing data may occur, Little's missing completely at random test will be used to determine the pattern of the missing data. If non-systemic, listwise deletion will be implemented; if systemic, multiple imputation will be implemented. To explore potential risk factors for sleep disturbance (e.g., PBT survivors – depression, anxiety, fatigue, pain, neurocognitive disturbance, quality of life; caregivers – depression, anxiety, health, quality of life, patient dependence), univariate binary logistic regression models will be computed for individual variables, and forward stepwise binary logistic regression models for multi-variable analysis. Finally, Bland and Altman limits of agreement test will be performed to assess the agreement between the sleep assessment tools used in the study. This will be performed on the quantitative parameters assessed by all tools (Oura Ring, questionnaires)

that are similar, including total sleep time, sleep latency measures and sleep efficiency. Effect sizes will be determined using Cohen's d, and statistical significance will be accepted at an alpha of $p < 0.05$.

5.2.2. Qualitative analysis

All interviews will be digitally recorded and transcribed verbatim. Interview transcripts and field notes that may capture participants non-verbal responses will be imported into NVivo qualitative data analysis software (QSR International v2, 2019). A hybrid approach to thematic analysis, consisting of both inductive and deductive analyses, will allow the research team to comprehensively analyse the data produced [50]. The inductive approach forms the foundation of the analysis, allowing for the emergence of themes directly from the data obtained from the semi-structured interviews. An inductive approach will develop a deeper understanding of the data through identifying concepts that will be constructed allowing for data to be arranged semantically. Groups of codes with similar meanings will then be created, before finally being arranged into tables, labelled by groups and themes. Simultaneously, a deductive approach, involving a pre-defined grouping of questions, will be applied in alignment with existing theoretical frameworks.

Initially, the individual interview transcripts will be split into the pre-determined question groups, then read to obtain a sense of the outcomes and to become familiar with the data. After this initial reading and familiarization with the data by organizing it into pre-determined question groups, repeated readings will be performed where the researcher team will engage in the process of initial coding by systematically assigning short descriptive labels or codes to segments of the data that capture key concepts, ideas, or patterns. Two researchers involved in the qualitative analysis will independently code the transcripts, allowing for multiple perspectives and interpretations; a third researcher will be used after the generation of themes to consolidate data and to manage any conflicts that may arise. Regular team meetings will be held to discuss and compare codes, fostering consensus and addressing any discrepancies in coding. This iterative process of reading, coding, and team discussion will continue until a comprehensive set of initial codes is established. Following the initial coding phase, the researchers will collaboratively identify broader patterns and themes by grouping related codes together. This inductive process allows for the emergence of themes directly from the data. These themes will be refined and defined through ongoing team discussions, ensuring a thorough and nuanced representation of the participants' experiences.

6. Discussion

Herein we have detailed the protocol of a feasibility trial exploring the use of exercise for the management of sleep disturbance in PBT survivors and their caregivers. Sleep disturbance is one of the most common and impactful symptoms reported by PBT survivors and their caregivers, yet there is a distinct lack of representation of these populations in sleep-focused intervention studies. While there has been a recent increase in the attention afforded to managing sleep disturbances in these populations, this feasibility study will be the first to explore the use of exercise as a holistic, non-pharmacological intervention for sleep disturbance specifically. We hypothesize that the protocol will be deemed safe, feasible, and acceptable for PBT survivors and their caregivers recruited to the intervention. We have included exploratory outcomes that will allow us to assess the clinical significance of the intervention both quantitatively and qualitatively. By triangulating these quantitative and qualitative findings, we aim to gain a holistic understanding of the preliminary efficacy, feasibility, and acceptability of the intervention to guide future developments and interventions for the management of sleep disturbance in the context of PBTs.

There are several strengths to this study. Firstly, it not only contributes to a significant gap in the sleep-focused literature, but also contributes to the growing body of exercised-focused literature within neuro-oncology. The systematic review conducted by Sandler et al. shows that levels of physical activity are low among brain cancer survivors, likely due to the unique challenges experienced by those adversely affected by PBTs (e.g., treatment- and disease-related side effects) [21]. Identifying the most appropriate and accessible formats for the delivery of exercise with those adversely affected by PBTs is crucial to ensuring increased physical activity levels in these populations. Secondly, PBT survivors and their caregivers are susceptible to a range of physical and psychological concerns that occur throughout all points of disease trajectory. Exercise has been shown to elicit beneficial outcomes in a plethora of these physical and psychological concerns, with improvements in these areas likely to be a contributing factor to the improvement of sleep disturbance in these populations. As such, we are likely to see a number of improvements, not just sleep disturbance itself, as a result of this intervention. Thirdly, this trial has been designed to maximise accessibility by being available through telehealth while still being delivered by AEPs. This combination ensures safety for participants through supervision and guidance from experienced health professionals while having the ability to engage with intervention from the comfort of their own homes in an effort to promote adherence and engagement through the entirety of the intervention. Finally, the inclusion of caregivers in our study is important as there is a significant lack of research inclusion on their part within PBT-focused literature. Caregivers play an indispensable role in the ongoing care and support of PBT survivors but often face unique challenges themselves because of the complex and intimate nature of their relationship with who they are caring for - typically a family member of someone diagnosed with a PBT. By exploring interventions that may positively influence the sleep and overall health of caregivers, we contribute to a more comprehensive and holistic approach to care that acknowledges and supports the well-being of both survivors and caregivers.

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Credit author statement

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Declaration of competing interest

The authors declare that there are no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jsampl.2024.100059.

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