

Understanding the Feasibility and Benefits of Exercise Programs in Individuals Living With a Brain Cancer Diagnosis: A Scoping Review Protocol

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Abstract

Objective: To describe a scoping review that aims to summarize the evidence of exercise interventions in individuals living with a primary brain cancer diagnosis. This work will map the implementation and characteristics of targeted exercise interventions designed to lower symptom burden and improve overall quality of life for those living with and beyond primary brain cancer.

Introduction: Individuals with primary brain cancer are often challenged by several highly debilitating physical, cognitive, and emotional side effects that can negatively impact overall quality of life. Exercise has the potential to aid in decreasing the burden of these symptoms; however, the use of exercise as a therapeutic intervention for individuals living with brain cancer has been limited and much is left to be explored. **Inclusion criteria:** Studies considered for this review will explore exercise-based interventions in individuals diagnosed with primary brain cancer. **Methods:** This scoping review will be conducted in accordance with Joanna Briggs Institute (JBI) methodology. Databases will be searched from inception to present and will include CINAHL, MEDLINE, Embase, SPORTDiscus, Scopus, and PsycInfo. A comprehensive search strategy was developed in accordance with JBI methodology to retrieve relevant sources. Two independent reviewers will screen titles, abstracts, and full texts of relevant sources. The results of the search and the study inclusion process will be reported in full in a PRISMA-ScR flow diagram. Data will be extracted by two independent reviewers and then mapped under the FITT (frequency, intensity, time, type) principles. The results will be presented narratively, using appropriate tables and figures. **Conclusion:** This review will provide a comprehensive summary of the feasibility and efficacy/effectiveness of exercise interventions for individuals living with primary brain cancer. This work will also describe the exercise protocols of the reviewed interventions and will highlight strategies to improve intervention design and implementation.

Keywords: cancer, physical activity, review protocol, brain cancer, GBM

Introduction and Background

Global incidence rates of central nervous system (CNS) cancers have shown a steady increase between 1999 and 2019. Brain tumours account for the vast majority of all primary CNS tumours (i.e., brain and spinal cord tumours; Mao et al., 1991; PDQ Adult Treatment Editorial Board, 2022; Smith et al., 2019), with the most common malignant brain cancer in adults being high grade gliomas (Hanif et al., 2017). Despite accounting for less than 2% of cancer diagnoses, with its high rate of morbidity and mortality brain cancer carries a disproportionate disease burden (Barnholtz-Sloan et al., 2018; Reynoso-Noverón et al., 2021). The symptom burden in patients with brain cancer is substantial. The combined effects of neurologic symptoms associated with tumour location, increased intracranial pressure (e.g., headaches), and treatment-related side effects lead to cognitive difficulties, emotional distress, fatigue, impaired functional status, and poor quality of life (Armstrong et al., 2016; Hanif et al., 2017). While disease symptoms and survival rates vary substantially with tumour type, size, location, and grade, as well as patient age at diagnosis, the five-year net survival rate for all primary malignant brain tumours remains low at 25% (Walker et al., 2021). Of note, survival from glioblastomas is considerably lower, at less than 5% at five years (Barnholtz-Sloan et al., 2018; Reynoso-Noverón et al., 2021).

In the face of a potentially devastating prognosis, the management of both the disease and treatment-related symptoms is essential for preserving and/or improving an individual's quality of life. Importantly, poor functional status has been linked to greater symptom burden and poorer prognosis (Liang et al., 2020; Sharma & Graber, 2021; Sizoo et al., 2010; Williams et al., 2021). Progressive muscle weakness resulting from fatigue, inactivity, or prolonged steroid use can lead to balance issues, risk of falls/fractures, loss of independence (i.e., inability to engage in activities of daily living), and reduced quality of life (Arvold et al., 2018; Dietrich et al., 2011; Ensign & Porter, 2022; Kim et al., 2023; Williams et al., 2021). Individuals who are diagnosed with brain cancer note that maintaining functional independence (i.e., maintaining their ability to work and perform physical tasks) is highly valued (Arvold et al., 2018).

Tailored exercise programs (i.e., adapted to disease, treatment, and individual characteristics) have been shown to be safe both during and post cancer treatment (Frikkel et al., 2021; Galvão et al., 2010; Rethorst et al., 2018; Sheill et al., 2019). However, primary brain cancer patients are a heterogeneous group with complex health care needs, and as a result exercise interventions are often assumed unfeasible or even contraindicated; as such, brain cancer patients are under-represented in the exercise oncology literature (Sandler et al., 2020). Thus, limited research is available on how to best implement supportive exercise programs for those living with a primary brain cancer diagnosis (Hurley et al., 2015; McNeely et al., 2019). Notwithstanding this, preliminary data suggests that exercise is safe, feasible, and likely beneficial, and positive changes have been noted in symptom severity, body composition, activity levels, aerobic capacity, neurocognitive functioning, headaches, mental health, and quality of life (Sandler et al., 2021; Travers & Litofsky, 2021).

Objective

The objective of this scoping review will be to explore, summarize, and map the existing evidence of exercise-based interventions to better understand the feasibility, intervention characteristics, and associated benefits of these programs for individuals living with primary brain cancer. A preliminary search of MEDLINE, the Cochrane Database of Systematic Reviews, and *JBI*

Evidence Synthesis was conducted and identified two recent systematic reviews: Sandler et al. (2021) focused primarily on current physical activity levels and health outcomes associated with physical activity, while the Khalequi-Sohi et al. (2022) review was limited to exercise studies with pediatric brain cancer. This scoping review will expand on these findings by comparing exercise intervention protocols (i.e., frequency, intensity, time, type; FITT) to better understand how to tailor future interventions for this population.

Review Questions

The review questions are as follows:

1. How feasible are available exercise interventions, including factors such as program adoption, safety, adherence, and attrition in individuals living with primary brain cancer?
2. What are the projected/reported benefits of exercise programs for those living with primary brain cancer? As part of this, what are the potential implications of treatment timelines on when exercise programs are deployed (i.e., concurrently with treatment, after treatment, etc.)?
3. What FITT principles and other intervention characteristics are used in exercise interventions for primary brain cancer patients?
4. What are the risks or potential determinants of exercise programs in patients with primary brain cancer?

Methodology

The proposed scoping review will be conducted in accordance with the Joanna Briggs Institute (JBI) methodology for scoping reviews (Peters et al., 2020). There was no patient or public involvement in the design, conduct, reporting, or dissemination plan of this research.

Search Strategy

The search strategy will aim to locate both published and unpublished studies in order to capture the most relevant and timely research. Only studies written in English will be considered, and no geographical or date limit will be employed in this review. The text words contained in titles and abstracts of relevant articles and the index terms used to describe the articles were used to develop a full search strategy (see Appendix A). The search strategy, including all identified keywords and index terms, will be adapted for each included database and/or information source. The reference list of all included sources of evidence will be screened for additional studies.

Participants

This review will consider literature that includes individuals of any age diagnosed and living with a primary brain tumour who are pre- or post-operative/treatment and who participated in a physical activity/exercise intervention.

Concept

This review will consider literature that explores exercise interventions for those living with primary brain cancer. Exercise interventions are defined as any exercise modality that includes purposeful movement. Elements of exercise program design (i.e., FITT principles, who delivered the program, and duration of the program) must be described in order to be included in this review. These intervention characteristics are important aspects when considering intervention design and delivery to enhance program feasibility and health outcomes.

Context

This review will consider studies located across all care settings (i.e., hospital, community, home-based, or combination of settings).

Types of Sources

This scoping review will consider both experimental and quasi-experimental study designs including randomized controlled trials, non-randomized controlled trials, pre-post studies, and interrupted time-series studies. In addition, analytical observational studies including prospective and retrospective cohort studies, case-control studies, and analytical cross-sectional studies will be considered for inclusion. This review will also consider descriptive observational study designs including case series, individual case reports, and descriptive cross-sectional studies. Qualitative studies will also be considered that focus on qualitative data including, but not limited to, designs such as phenomenology, grounded theory, ethnography, qualitative description, action research, and feminist research. In addition, systematic reviews that meet the inclusion criteria will also be considered, depending on the research question. Text and opinion papers will also be considered for inclusion.

Information Sources

The databases to be searched include MEDLINE, CINAHL, Embase, Scopus, and PsycInfo. Sources of unpublished studies and grey literature to be searched include ProQuest Dissertations & Theses Global and the first 10 pages of Google Scholar. We will also search for grey literature using the Canadian Agency for Drugs and Technologies in Health (2019) grey literature checklist *Grey Matters: A Practical Tool for Searching Health-Related Grey Literature*.

Study/Source of Evidence Selection

Following the search, all identified citations will be collated and uploaded into Mendeley V1.19.8 (<https://www.mendeley.com/>), and duplicates will be removed. Following a pilot test, titles and abstracts will be screened by two independent reviewers for assessment against the inclusion criteria. Potentially relevant sources will be retrieved in full and their citation details imported into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI; <https://sumari.jbi.global/>). The full text of selected citations will be assessed in detail against the inclusion criteria by two or more independent reviewers. Reasons for exclusion of sources of evidence at full text that do not meet the inclusion criteria will be recorded and reported in the scoping review. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved with an additional reviewer.

Data Extraction

Data will be extracted from papers included in the scoping review by a minimum of two independent reviewers using a data extraction tool developed by the reviewers. The data extracted will include specific details about the study (e.g., concept, context, participants), intervention methods, and key findings relevant to the review question(s). Before data extraction begins, two independent reviewers will pilot the data extraction tool with five articles, and they will discuss any additional information that needs to be extracted.

A draft extraction form is provided (see Appendix B). The draft data extraction tool will be modified and revised as necessary during the process of extracting data from each included evidence source. Modifications will be detailed in the final scoping review. Any disagreements that arise between the reviewers will be resolved through discussion between the two reviewers or a third

party. If appropriate, authors of papers will be contacted to request missing or additional data where required.

Data Analysis and Presentation

Data on available programs will be compiled in tabular format. We will then analyze these programs using the FITT principles and other narrative analyses to better understand how feasible and effective they are. Given the focus of this scoping review on mapping the existing literature, we will not be explicitly performing a risk of bias assessment.

The results of the search and the study inclusion process will be reported in full in the final scoping review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) flow diagram (Page et al., 2021). The extracted data will be presented in tabular form that aligns with the study's objective. A narrative summary will accompany these presentations and will describe how the findings relate to the review's objectives and questions. Results will be classified under main conceptual categories: study characteristics (including country or origin, study population, study setting, design), outcomes measures, intervention characteristics, reported key findings, and implications.

Potential Implications

The information gained from this scoping review may provide insight into the use of exercise as an important supportive care resource for individuals living with primary brain cancer. This scoping review will map available interventions and compare implementation and feasibility outcomes to see what is currently being used to improve/maintain functional well-being and other health outcomes in this population. This review will not directly inform care, but will aid in the development of a more robust understanding of exercise and whether it is safe and effective for this population. This review may inform future work in developing evidence-based, tailored programs for those living with and beyond primary brain cancer.

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Conflicts of Interest

There is no conflict of interest in this project.

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Appendix A

Search Strategy

Search Terms	
1	exp Brain Neoplasm/
2	(cancer* or neoplas* or tumour* or tumours*) adj3 (brain or glioblastoma* or GBM* or glioma* or meningioma* or adenoma* or meduloblastoma*)
3	exercise or "resistance training" or aerobic* or "motor activity" or "exercise therapy" or "physical activity"
4	1 or 2
5	3 and 4

Note. Search conducted on October 15, 2021, and February 16, 2023.

Appendix B

Data Extraction Codebook

General study information	
Title	Full title of the study
Authors	Authors' last name and initials
Year of publication	What year was the manuscript or report published? Make a note if there are multiple papers on the same study
Country of origin	Where is the primary author based? For example, author may be based in Australia (country of origin) and conducting the study in Vietnam (study setting)
Methods	
Study aim/purpose	What is the aim/purpose of the papers?
Study setting	Where did the study take place? (e.g., hospital, community, school) Also indicate country if different from where the author is based
Study design	What was the study design? Reported and/or assessed by reading the paper
Intervention dates	Dates and/or duration of the study
Population description	Description of the common characteristics of the group being analyzed
Inclusion criteria	Which characteristics were necessary for participants to be included in the study?
Exclusion criteria	Which characteristics excluded participants from the study?
Method of recruitment	How were potential participants informed about the study and invited to join it?
Participant details	
Number of participants	Total number of participants included in the study

Age demographic	Does the study focus on pediatric, adolescent, or adult participants? Specific age range provided
Tumour status	What is the grade of the tumour (range)?
Performance status	What is the performance measure and the performance status of the group?
Treatment	The intention (curative, non-curative) and type (chemotherapy, radiation) of treatment
Surgery details	Type(s) of surgery undergone and planned (biopsy, debulking, complete resection)
Chemotherapy details	The dosage, type, and location of the chemotherapy received
Control group	If the study had a control group, who was included and what were they required to do?
Intervention details (exercise details)	What was the exercise prescribed based on the FITT principles (frequency, intensity, time, type)? What was the length of time participants were engaged in the exercise intervention? What time of day was the exercise intervention delivered at (morning, afternoon, evening)? What setting was the exercise performed in (home, community, hospital settings)? Who was the exercise program delivered by (title or qualifications)?
Age	What is the average age or age range of the participants participating in the intervention (all participants or for the different groups)?
Results	
Main outcome measurement	What was the result collected or effect observed regarding the main outcome of the study?
Direction of effect	Was the effect positive, negative, or were there no effects observed?
Discussion	
Key findings	Based on the results, what key findings or conclusions can be drawn?
Implications	What are the implications associated with the findings?
Limitations	What were the limitations of the study?