

BMJ Open Non-pharmacological approaches to procedural anxiety reduction for patients undergoing radiotherapy for cancer: systematic review protocol

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ABSTRACT

Introduction Procedural anxiety relates to an affective state of anxiety or fear in relation to a medical procedure. Various treatment-related factors may elicit anxiety among oncology patients, including fear of diagnostic imaging (such as MRI scans) and impending treatment and medical procedures (such as chemotherapy and radiotherapy). It is common in oncology settings to manage acute anxiety relating to medical procedures with anxiolytic medication. However, pharmacological approaches are not suitable for many patients. Despite this, non-pharmacological interventions are infrequently used. The aim of this systematic review is to determine whether non-pharmacological interventions delivered prior to, or during, radiotherapy are effective in reducing procedural anxiety.

Methods and analysis Data sources will include the bibliographic databases CINAHL, MEDLINE, EMBASE, PsycINFO and Cochrane Central Register of Controlled trials (CENTRAL) (from inception onward). Eligible studies will include adult patients with cancer undergoing radiotherapy treatment. Included studies will be those which employ a non-pharmacological intervention, delivered within existing radiotherapy appointments, with the aim of reducing procedural anxiety related to radiotherapy. All research designs with a control or other comparison group will be included. The primary outcome will be change in levels of self-reported procedural anxiety. Secondary outcomes will be changes in scores on physiological measures of anxiety and/or changes in treatment completion and/or changes in psychological distress. Two investigators will independently complete title and abstract screening, full-text screening, data extraction and assessment of methodological quality. If appropriate, a meta-analysis will be performed. Any important amendments to this protocol will be updated in the PROSPERO registration and documented in the resulting review publication.

Ethics and dissemination No ethical issues are anticipated from this review. The findings will be disseminated through peer-reviewed publication and at conferences by presentation.

Systematic review registration CRD42019112941.

Strengths and limitations of this study

- This systematic review will summarise evidence for non-pharmacological approaches to reducing procedural anxiety among patients undergoing, or about to undergo, radiotherapy.
- Publication of the protocol for this review, together with PROSPERO registration, will limit the possibility of duplication of this review and will increase transparency of the methodology.
- Inclusion of articles published in languages other than English will ensure that important findings are not excluded.
- As the number of randomised controlled trials in this field is likely to be limited, studies of lower methodological quality will be included in order to provide a comprehensive overview of the literature.

BACKGROUND

In 2014, 127 887 people were diagnosed with cancer in Australia,¹ with numbers rising every year. Approximately half of those diagnosed with cancer are expected to receive radiotherapy (48%), with almost 67 800 courses of radiotherapy delivered in Australia in 2017–2018.^{2,3} Although some level of anxiety or apprehension in response to a cancer diagnosis is to be expected, 10%–20% of patients with cancer undergoing radiotherapy experience significant symptoms of anxiety.⁴ There are many factors that may elicit anxiety in oncology patients, for example, fear and worry about disease progression, symptoms, treatment side effects and death. In addition, patients may also feel anxious and fearful of impending treatment and during treatment and medical procedures, such as MRI scans, chemotherapy and radiotherapy.⁵

As opposed to the broader concept of psychological distress in the oncology literature, the term procedural anxiety relates to an affective state of anxiety or fear in relation

to a medical procedure.⁶ The fear or anxiety is specifically about a medical procedure, can occur during or in anticipation of the procedure, and is generally transient.⁶ Procedural anxiety is not a DSM-V diagnosis, although severe cases could potentially meet criteria for specific phobia.⁷ Procedural anxiety is associated with acute distress and may result in behavioural disruption such as avoiding or terminating medical procedures.⁶ Procedural anxiety differs from other forms of anxiety in terms of the specific focus on the procedure (vs the broader range of concerns in generalised anxiety disorder) and its possible discomforts and implications.⁸

There are several factors that may increase a patient's susceptibility to procedural anxiety prior to radiotherapy. For example, patients who are parents with dependent children, and are undergoing treatment for advanced cancer, are more likely to experience procedural anxiety.⁹ Patients with a history of anxiety or trauma, and patients with claustrophobia are also at increased risk.⁵ Other research suggests that a patient's level of pain or receiving concurrent chemotherapy can increase anxiety.¹⁰ Procedural anxiety can also differ across cancer groups, depending on the treatment procedures for that cancer. For example, most patients will be fitted with an immobilisation device to ensure the patient remains in the same position for treatment each time.¹¹ For patients with head and neck cancer, an immobilisation mask is specifically moulded to each patient.¹¹ The mask is placed over the head, neck and sometimes the shoulders and secured to the treatment couch during treatment.¹² The mask moulding is standard care to ensure safe and accurate delivery of radiotherapy dose, limiting patient movement to a range of 2 mm.¹³ Because of the restrictive nature of the mask, it can heighten anxiety for many patients.^{14 15}

Previous research indicates that patient anxiety is associated with disruptions during the early treatment sessions of radiotherapy.¹⁵ It is common in oncology settings to manage anxiety, particularly acute anxiety relating to medical procedures, with benzodiazepines or other non-benzodiazepine anxiolytics.⁵ However, there are many disadvantages to pharmacological approaches to anxiety management. Benzodiazepines present a risk of dependence and should not be considered an option for continued use over a course of radiotherapy.^{5 9} They can also become problematic for certain patient groups. For example, given the shared properties of benzodiazepines and alcohol, leading to drowsiness, slowed breathing and reduced coordination, patients with alcohol use disorder may be at increased risk of injury or overdose.¹⁶ Benzodiazepines sometimes have a paradoxical effect on elderly patients, due to the increased likelihood of delirium following benzodiazepine use,¹⁷ and can worsen fatigue among patients undergoing concurrent chemotherapy.⁵ Anxiolytic medications can also be troublesome for patients attending appointments without a support person as driving is not permitted after use and patients then need to arrange alternative transport home. For oncology departments, managing anxiety with medication

can also be time consuming. This is especially true if patient anxiety is not identified prior to the appointment as radiation therapy staff need to wait for a radiation oncologist to attend and prescribe medication, and then wait for the medication to take effect. Given the problems that anxiolytic medication can present, researchers are attempting to identify non-pharmacological strategies to reduce anxiety which are suitable for cancer treatment settings.^{18–20}

A previous systematic review of interventions to reduce anxiety among patients undergoing radiotherapy was conducted by Elsner and colleagues in 2017.²¹ The review included 12 studies with sample sizes ranging between 12 and 568.^{15 22–32} All types of study designs were included. One third of studies were rated as 'low' on a measure of methodological quality,^{24 25 27 29} seven were rated as 'moderate',^{15 22 23 26 28 31 32} and only one study was rated as 'high'.³⁰ The interventions included patient information and education (five studies),^{26–30} radiation therapist support (patient perspectives), including effective communication, being treated as an individual and empathy (three studies),^{22 24 25} and screening and needs assessment to initiate appropriate psychosocial care (four studies).^{15 23 31 32} The authors reported that comprehensive information and education prior to treatment, positive relationships with radiation therapists and continuity of staff during the course of treatment were associated with reduced patient anxiety. Despite these noteworthy findings, the review was limited to strategies delivered by radiation therapists.²¹ Indeed, radiation therapists are ideally placed to deliver psychosocial support, as they are the only healthcare provider that has daily contact with patients during the course of radiotherapy treatment. Existing interventions that have been delivered by other healthcare providers (such as oncology nurses) to reduce procedural anxiety may be appropriate to be delivered by radiation therapists. Consequently, this review will include interventions to reduce procedural anxiety delivered by any healthcare provider within the radiotherapy department.

Clearly, the development of non-pharmacological interventions for procedural anxiety, particularly in adult cancer populations, is a priority. In 2018, a systematic review and meta-analysis summarised the literature for non-pharmacological interventions (including music therapy, hypnosis and distraction) to reduce procedural anxiety in paediatric patients undergoing treatment for cancer.³³ However, the evidence for adult populations has not been comprehensively reviewed. The present review fills this gap in the literature and proposed possible directions for future research.

OBJECTIVES

This review will aim to determine whether non-pharmacological interventions delivered to adult patients with cancer prior to, or during radiotherapy, are effective relative to a comparison group in:

Primary objective

1. Reducing levels of self-reported procedural anxiety;

Secondary objectives

1. Reducing physiological symptoms of procedural anxiety;
2. Reducing anxiety-related treatment disruptions; and
3. Reducing psychological distress.

METHODS

The present protocol has been registered within the PROSPERO database and is being reported in accordance with guidance provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) statement.³⁴ The proposed systematic review and meta-analysis will be reported in accordance with guidance provided in the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement.³⁵ Any important changes to the protocol will be updated in the PROSPERO registration and will be clearly documented and reported in the final review.

Participants

Inclusion criteria

Participants will include adult patients with cancer currently undergoing, or about to undergo, radiotherapy treatment, with or without concurrent chemotherapy.

Exclusion criteria

Studies solely involving paediatric participants (under 18 years) and carers will be excluded.

Interventions

Inclusion criteria

Types of interventions to be included will be non-pharmacological interventions delivered within the radiotherapy department either at an existing appointment (eg, at the new patient clinic or in the waiting room prior to treatment), or at the time of radiotherapy. Included interventions will aim to reduce procedural anxiety related to the radiotherapy procedure. Interventions may include (but are not limited to) music therapy, additional information, distraction, relaxation or mindfulness-based stress reduction. Interventions to be included can be delivered by any healthcare provider within the radiotherapy department (eg, radiation therapists, nurses, social workers, dietitians, psychologists, speech pathologists or administrative staff).

Exclusion criteria

Interventions delivered outside of the radiotherapy department and/or requiring additional appointments (eg, yoga classes, massage therapy, psychology) will be excluded.

Comparisons

Inclusion criteria

Trials to be included will be comparing standard care plus a non-pharmacological intervention for procedural anxiety, with:

1. Standard care alone; and/or
2. Standard care plus an alternative non-pharmacological intervention; and/or
3. Standard care plus placebo.

Exclusion criteria

Studies without a comparison group will be excluded.

Outcomes

Studies employing any of the following primary or secondary outcome measures will be included in this review:

Primary outcome

1. Validated self-report measures of anxiety, such as the State-Trait Anxiety Inventory (STAI),³⁶ Hospital Anxiety and Depression Scale (HADS)³⁷ and/or visual analogue scales (VAS); and/or

Secondary outcomes

1. Physiological symptoms of anxiety (including measures of heart rate (HR), respiratory rate (RR), blood pressure (BP), heart rate variability (HRV), electroencephalogram (EEG), skin conductance, stress hormones (cortisol)); and/or
2. Treatment completion (including anxiety-related treatment disruptions, inability to complete treatment due to significant anxiety); and/or
3. Treatment duration (duration of each radiotherapy treatment appointment); and/or
4. Psychological distress using validated measures such as the Symptom Checklist-90-Revised³⁸ and Beck Anxiety Inventory.³⁹

Types of studies

Inclusion criteria

The following study designs will be included in the review:

- Randomised controlled trials, including cluster randomised controlled trials and stepped wedge trials;
- Quasi-experimental designs with comparison or control groups—including pre/post trials; and
- Natural experimental studies with a comparison or control group.

Exclusion criteria

- Observational studies.
- Qualitative studies.

Publication characteristics

There will be no restriction on year of publication or language. Abstracts of publications in languages other than English will be translated using Google Translate to determine eligibility. Publications deemed eligible for full-text review will be professionally translated.

Information sources

Electronic databases

The following electronic databases will be searched for potentially eligible articles: CINAHL, MEDLINE, EMBASE, PsycINFO and Cochrane Central Register of

Controlled trials (CENTRAL) (from inception onwards). Details of the search strategy as used in MEDLINE are detailed in online supplemental appendix 1.

Other sources

Other sources will be searched, including:

- ▶ Reference lists of all full-text articles included in the review.
- ▶ A hand search of four relevant journals, issues from the previous 5 years: *Complementary Therapies in Medicine*, *Supportive Care in Cancer*, *PsychoOncology* and *Clinical Journal of Oncology Nursing*.
- ▶ Hand search of conference abstracts published in the previous 2 years from the International PsychoOncology Society conference (IPOS).
- ▶ A grey literature search using Google Scholar (the first 200 citations published in the last 2 years).

Data collection and analysis

Titles and abstracts of the identified articles retrieved from electronic databases and other searches will be exported to systematic review management software, *Covidence* (standard production platform for Cochrane reviews), and duplicates will be removed. Two reviewers (authors EF and ES) will independently screen all titles and abstracts according to the eligibility criteria. A pre-piloted standardised screening tool will be developed detailing the eligibility criteria to ensure consistency between reviewers. Papers that do not meet the eligibility criteria will be excluded from further screening. The full text of all potentially eligible articles will be further reviewed by the two reviewers against the eligibility criteria. If insufficient information is reported to determine eligibility (including intervention methods and intervention characteristics), the authors will contact the authors of that study no more than three times to gain further information. Articles deemed ineligible will be recorded, together with the reason for ineligibility, and this information will be reported in the excluded studies table in the published review manuscript. Any discrepancies between the two reviewers during abstract screening or full-text screening will be discussed until a consensus is reached. A third reviewer will be consulted if necessary.

Data extraction

Data extraction will be performed by two reviewers, authors EF and ES. A data extraction form will be developed based on the recommendations by the *Cochrane Handbook for Systematic Reviews of Interventions*.⁴⁰ The Template for Intervention Description and Replication (TIDieR checklist) items⁴¹ will also be incorporated into the data extraction form to ensure all important characteristics of the intervention are extracted. Prior to use, the extraction form will be piloted on several papers and amended as needed. The data extraction form will be used by reviewers to independently extract data from all articles deemed eligible after full-text

screening. Discrepancies between the two reviewers will be discussed until a consensus is reached. A third reviewer will be consulted if necessary. Reviewers will not be blinded to study information including administering institution, author names or journal. Extracted data will be exported to statistical software for statistical analysis.

Data items

The following information will be extracted:

- ▶ Publication information (author, year, journal).
- ▶ Intervention methods (participant inclusion criteria, study design, healthcare setting, eg, radiation oncology department, country, sample size).
- ▶ Participant demographics and characteristics (age, sex, ethnicity, cancer site, cancer stage, number of treatment fractions, concurrent chemotherapy or other treatment, eg, surgery).
- ▶ Characteristics of the intervention (intervention components, duration and delivery methods).
- ▶ Comparison group (eg, standard care alone, standard care plus alternative intervention).
- ▶ Self-report outcome measure (eg, validated measures such as the STAI,³⁶ HADS³⁷).
- ▶ Physiological outcome measures (HR, RR, BP, HRV, EEG, skin conductance, stress hormones, ie, cortisol levels).
- ▶ Treatment information (treatment time (duration of each radiotherapy treatment appointment); treatment completion (including anxiety-related treatment disruptions, inability to complete treatment due to significant anxiety)).

There are no pre-planned data assumptions or simplifications.

Methodological quality assessment

The Effective Public Health Practice Project Quality Assessment Tool (EPHPP) will be used to assess the methodological quality and risk of bias of included studies.⁴² The EPHPP is a suitable tool for evaluating randomised and non-randomised designs (eg, pre-post, case-control⁴³) and has been reported to have both content and construct validity, and acceptable inter-rater reliability.^{42 44} Reviewers EF and ES will independently review selected studies and judge risk of bias by assessing the adequacy of six domains: selection bias, study design, confounders, blinding, data collection method, withdrawals/dropouts, intervention integrity and analyses. Discrepancies between the two reviewers will be discussed until a consensus is reached, and a third reviewer will be consulted if necessary.

DATA ANALYSIS

Measures

There are a number of commonly used self-report and physiological measures of anxiety used within cancer settings.^{36 37 45 46} The authors anticipate that a number

of these outcome measures, and combinations of these measures, will be used across different studies.

Data synthesis and analysis

The findings will be reported narratively and supplemented with a summary of findings table, if a meta-analysis of the included studies is not suitable. The narrative synthesis will include the type of intervention used, the method of delivery (including setting and who delivered the intervention), the sample size, sample demographics, comparison group(s) and outcomes. The characteristics of the included studies will be examined to identify differences and similarities between the studies. Given the nature of this review, we anticipate substantial differences between studies (eg, type of intervention delivered, who the intervention is delivered by, when and how the intervention is delivered); therefore, interventions will be grouped accordingly for analysis and clarity of reporting. Studies may be further grouped into subgroups if necessary. A relative risk ratio (studies with dichotomous outcomes) and effect size using Cohen's formula (studies with continuous outcomes) will be calculated for all primary outcomes. A meta-analysis will be performed using an inverse variance random-effects model if more than five studies are identified and deemed appropriate. The Hartung-Knapp-Sidik-Jonkman method⁴⁷ will be used to estimate the variance of the pooled effect. Data will not be pooled for studies using different research designs (eg, randomised vs non-randomised). A sensitivity analysis will be performed to identify studies at high risk of bias, and these studies will be removed from secondary analysis, as well as removing any outliers contributing to study heterogeneity.

Assessment of study heterogeneity

A visual examination of forest plots will be performed together with the I^2 statistic to determine study heterogeneity. As recommended by the *Cochrane Handbook for Systematic Reviews of Interventions*, where heterogeneity exceeds 75% I^2 (75% to 100%=considerable heterogeneity), subgroups will be further explored.⁴⁰

Grading the strength of evidence

As recommended by the *Cochrane Handbook for Systematic Reviews of Interventions*,⁴⁰ the quality of the evidence for each study outcome (self-reported symptoms of anxiety, physiological symptoms of anxiety, treatment completion and duration) will be assessed using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach. The GRADE approach involves consideration of within-study risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias. In accordance with the GRADE definitions,⁴⁸ the quality of evidence will be reported as high, moderate, low or very low quality.

Ethics and dissemination

Ethics Committee approval will not be sought for this review as no primary data will be collected. The findings

will be disseminated through peer-reviewed publication and also at conferences by presentation.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

DISCUSSION

A comprehensive review of the available evidence for non-pharmacological approaches to reducing procedural anxiety among patients undergoing, or about to undergo, radiotherapy is planned. The review will benefit policy-makers and oncology departments by highlighting safe, easy-to-deliver and (potentially) inexpensive strategies to manage anxiety as an alternative to pharmacological approaches. This would result in an improved experience for patients and potentially improved performance within departments.

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Contributors EF drafted the manuscript of the protocol and is the guarantor of this review. ALB, KC, BB and KM were involved in the design of the search strategy and made significant contributions to the conception and design of the protocol. SO made significant contributions to the conception of the review and has contributed to revisions of the manuscript. ES was involved in the design of the review methodology and has made significant contributions to the manuscript. ES is also the second reviewer for the review. CO has made significant contributions to the statistical plan for the review and contributed to manuscript revisions.

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