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Mind-body therapies adjuvant to chemotherapy improve quality of life and fatigue in top cancers: a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - Loughborough University.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 September 2023 and was last updated on 11 September 2023.

INTRODUCTION

Review question / Objective Population: breast, lung and colorectal cancer survivors. Intervention: the mind-body therapies, yoga, Tai chi and Qigong. Comparator: control group receiving standard care only. Outcome measures: quality of life (QoL), fatigue and the 6-minute walk test (6MWT). This metanalysis evaluates the effects of yoga, Tai chi and Qigong in alleviating the adverse effects of chemotherapy.

Rationale Breast, lung and colorectal cancers are 3 of the top 4 most common cancers worldwide. Their treatment with chemotherapy often results in adverse effects on quality of life, fatigue and functional exercise capacity amongst patients. Mind-body therapies, including yoga, Tai chi and Qigong, are commonly used as complementary and alternative therapies in cancer. This meta-analysis evaluates the effects of yoga, Tai chi and Qigong in alleviating the adverse effects of

chemotherapy by measuring the impact of these interventions on quality of life, cancer-related fatigue and performance in the 6-minute walk test.

Condition being studied Breast cancer, lung cancer and colorectal cancer are 3 of the top 4 most diagnosed cancers worldwide, accounting for approximately 32% of all global cancer cases. Lung cancer contributes the most to cancer deaths with 18.45 million occurring annually, followed by colorectal cancer (940,000 annual deaths), and breast cancer (685,000 annual deaths). Chemotherapy is the most common adjuvant treatment option given before or after surgical resection and serves to reduce recurrence risk and improve disease-free survival. Despite clinical successes and mainstream use of chemotherapy, side effects include exacerbation of fatigue and worsening of functional exercise capacity (FEC) which can decrease psychological health and overall quality of life (QoL). Maintaining good QoL in patients should be a priority alongside effective cancer treatment, and reports from clinical trials can inform therapeutic decisions to achieve this. The condition being studied is cancer, specifically breast, lung and colorectal cancers.

METHODS

Search strategy This systematic review and metaanalysis follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) quidelines. A comprehensive literature review was conducted on the following platforms: PubMed, Science Direct, Cochrane Reviews, EBSCO, Web of Science and SportDiscus. Final searches were conducted in March 2022. Specific search terms to achieve the aims and Boolean operators 'AND', 'OR' and 'NOT' were used. All identified publications were imported into the screening tool, Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at http://www.covidence.org.), duplicates were automatically removed. Publications were systematically evaluated for eligibility, first by abstract and then by full text review, in Covidence according to the following inclusion criteria: 1) published after 2016; 2) randomised controlled trial; 3) participants were adults (over 18); 4) included breast, lung or colorectal cancer patients; 5) article was written in English; 6) research measures at least one of yoga, Tai chi and/or Qigong; 7) included a complete dataset. Included publications were subsequently moved to the extraction tool in Covidence for further analysis.

Participant or population "breast cancer" OR "lung cancer" OR "colorectal cancer".

Intervention "mind-body therapy" OR "mind body therapy" OR "Tai chi" OR "Tai chi Chuan" OR "Qigong" OR "yoga".

Comparator Non-active controls included: standard care, waitlist control, psychosocial support, standard health education program, cognitive behavioural therapy, standard support therapy; Active controls included: stretching, strength training, or physical exercise.

Study designs to be included Randomised controlled trials.

Eligibility criteria published >2016; participants >18 years; article written in English; included complete dataset.

Information sources A comprehensive literature review was conducted on the following platforms: PubMed, Science Direct, Cochrane Reviews, EBSCO, Web of Science and SportDiscus.

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Main outcome(s) Criteria outcome measures identified from screened publications were QoL, fatigue and the Six-Minute Walk Test (6MWT). All these outcomes are continuous measures and different measurement scales were included if the direction of impact was comparable.

Combined QoL: A pooled Mean Difference (MD) of 5.30 (95% Cl: -11.41 to 22.01; p=0.45), although not statistically significant, shows a favorable effect of these interventions. For yoga, a positive effect of 6.45 (95% Cl: -26.31 to 39.21; p=0.58) was observed. For Tai chi and Qigong, favourable effects were shown with a pooled MD of 3.88 (95% Cl: -1.99 – 9.75; p=0.5).

Combined fatigue: an overall decrease in fatigue was observed in intervention groups by 0.54 (95% CI: -2.46 to 1.37; p = 0.43). For colorectal cancer patients, the common effects model was interpreted as only 2 studies were combined. A mean difference of -1.40 (95% CI: -2.24 to -0.56; p = 0.001) was observed.

Six-Minute Walking Test: Unfavourable effects were shown in the pooled MD of -36.05 (95% Cl -441.67 to 369.58; p=0.4) suggesting MBT interventions decrease FEC assessed by the 6MWT compared to controls.

Data management Full data sets are reported in the appendices. Once published, this will be made available through the Loughborough University research repos.

Quality assessment / Risk of bias analysis Risk of bias (RoB) assessment was completed to evaluate how the selected publications minimise potential bias which could compromise the validity of the results. Two independent researchers assessed RoB using the National Toxicology Program's Office of Health Assessment and Translation (OHAT) Risk of Bias rating tool, and the Covidence data extraction quality assessment template builder. Discrepancies were resolved through a consensus meeting. RoB assessment of included publications determined five as 'definitely low' risk of bias and the 4 remaining publications were rated 'probably low'. The individual RoB assessments for each included publication were used to inform the interpretation of meta-analysis results.

Strategy of data synthesis Data were extracted using the Covidence data extraction tool and results were grouped to compare effect sizes of outcome measures across studies. RStudio statistical software was used to generate effect

sizes and complete all statistical analysis (RStudio: Integrated Development Environment for R [Internet]. Boston, MA; 2015. Available from: http://www.rstudio.com/). Computed mean difference (MD) with Hedges g bias correction were the primary summary measures. Functions of the 'meta' package including 'metacont' and 'forest.meta' were applied to conduct the analysis and visualise the data in forest plots. RStudio was used to calculate the 95% confidence interval (CI) and prediction intervals (PI). Statistical significance for the p value was set at 0.05. Pls were only calculated for meta-analyses with greater than 2 publications.

The inverse variance method was applied and automatic calculation of variance of distribution of true effect size and between study variance was generated using RStudio. I2 describes percentage variability within effect estimates resulting from heterogeneity rather than sampling error. The Sidik-Johnson estimator for $\tau 2$ was used to accommodate for the small number of studies within each analysis. Observed heterogeneity of the studies meant that results from the random-effects model were interpreted. A funnel plot to assess publication bias was computed using functions from the 'dmetr' package.

Subgroup analysis Subgroup analyses were performed for yoga, Tai chi and Qigong combined, and colorectal cancer only due to limited numbers of studies for inclusion. Where random-effects models were reported, heterogeneity levels (I2) for usage in the power calculations were defined using the following categories: 25: = low; 50% = moderate and 75% = high.

Sensitivity analysis Sensitivity analysis for transformed data sets, using the QoL model as an example, showed differences in outcome values were less than 5% after exclusion of the data, so it can be assumed that overall MD and Cl values are not as a result of the imputed SD and the study can be included in the analysis.

Language restriction Only articles written in English will be included.

Country(ies) involved United Kingdom.

Keywords Cancer; Fatigue; Functional exercise capacity; Mind-Body Therapy; Quality of life.

Dissemination plans Results will be published in a peer-reviewed journal (e.g., Complementary Therapies in Clinical Practice).

Contributions of each author

Author 1 - Mhairi Morris - Conceptualisation: MAM & LEB; Methodology: MAM & LEB; Software: LEB; Validation: MAM & LEB; Formal analysis: LEB; Investigation: LEB; Resources: Loughborough University; Data curation: LEB; Writing - Original Draft: LEB; Writing - Reviewing & Editing: MAM; Visualisation: LEB; Supervision: MAM; Project administration: MAM.

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