



Effects of lifestyle modification on cancer recurrence, overall survival and quality of life in gynaecological cancer survivors: A systematic review and meta-analysis



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ABSTRACT

The benefits of lifestyle interventions for women who have survived gynaecological cancer (GC) remain unclear. This systematic review aimed to determine the effect of lifestyle interventions on cancer recurrence, overall survival and quality of life (QoL) in women with GC. We searched Medline, Embase, PsycINFO and EBM Reviews from June to July 2016 to identify relevant literature. We included randomized controlled trials in which a lifestyle intervention (diet, weight loss, physical activity and/or behavioural interventions) were compared with a control condition (usual care, placebo or other lifestyle interventions) in women who had survived endometrial or ovarian cancer. Primary outcomes included cancer recurrence and overall survival and the secondary outcome was QoL. Data extraction and risk-of-bias assessment were performed by two independent reviewers. A random-effects meta-analysis model was used to calculate mean differences (md) and 95% confidence intervals (CI). The literature search yielded 928 citations and three trials met the inclusion criteria. No randomized controlled trial assessed the effect of lifestyle interventions on cancer recurrence or survival. Meta-analysis of two randomized controlled trials on the effect of lifestyle interventions on total QoL at 3 or 6 months post-intervention showed no significant difference between intervention and control groups [(md; 1.60; 95% CI, -1.65 to 4.85) and (md; 2.07; 95% CI, -1.80 to 5.94), respectively]. That is, lifestyle intervention had no effect on overall QoL or individual QoL domains (physical, emotional, social wellbeing and fatigue) in GC survivors.

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1. Introduction

Gynaecological cancers (GCs) are amongst the most common malignancies affecting women with an estimated 61,000 and 22,000 new cases for endometrial and ovarian cancers in 2017, respectively [1]. Uterine cancer has a 5-year relative survival rate of 78%–83% in Australia, USA and UK [1–3]. However, despite significant improvements in survival rates over time, many ovarian cancers are still diagnosed at an advanced stage contributing to poor prognosis with overall 5-year survival rate of 44%–50% [1,4,5]. Therefore, research to identify factors that can improve survival after diagnosis of GC would be of great value.

The role of a healthy lifestyle on prevention of GC has been established over the past several decades [6,7]. In recent years, studies have focused on the impact of healthy behaviours on cancer survivorship. High body mass index (BMI) is associated with an adverse GC prognosis [8,9] and maintaining a healthy weight range via lifestyle modifications including diet and exercise could potentially reduce the risk of recurrence. Observational studies suggest that pre-diagnosis, healthy diet (fruits/vegetables based or a low fat diet) and regular physical activity may improve survival rates among ovarian cancer survivors [10–12]. However, a study by von Gruenigen et al. observed that most endometrial cancer survivors followed a poor and unhealthy lifestyle, as only 1% of participants adhered to all three American Cancer Society

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Guidelines on nutrition and physical activity and the majority had abdominal obesity [13]. Although the underlying mechanism by which a healthy lifestyle can modify endometrial and ovarian cancer risk or prognosis remains unclear, it is postulated that modulation of estrogen metabolism, inflammation biomarkers and oxidative DNA damage could play a role [14–16].

Approximately 25% of women diagnosed with GC are under 50 years of age and will develop menopause due to bilateral oophorectomy (BO) as part of their cancer treatment [17], which leads to significant morbidity and impaired quality of life (QoL) [18]. Early menopause (before 45 years), secondary to BO for benign conditions is associated with premature death including increased cardiovascular mortality [19]. Lifestyle factors including diet and exercise can reduce cardiovascular disease risk and non-cancer mortality in premenopausal and postmenopausal women [20,21].

Gynaecological cancers, particularly recurrent disease, are associated with emotional, psychological, physical and social challenges [22]. The positive role of diet, exercise and behavioural interventions on physical function, weight and overall QoL in women with GC has been previously demonstrated [23,24]. In a quasi-experimental study on ovarian cancer survivors, physical, emotional, social and functional wellbeing were significantly improved following an intensive health care intervention including group education, self-help support and 8 weeks home-based exercise/relaxation therapy (3 times/week) [25].

This systematic review aimed to determine whether lifestyle interventions can prevent cancer recurrence and improve overall survival and QoL in endometrial and ovarian cancer survivors.

2. Methods

2.1. Search strategy

This review adheres to the principles of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. The systematic search was based on the selection criteria and combining MeSH terms and text words using the OVID platform. Electronic databases including Medline, Embase, PsycINFO and all EBM Reviews incorporating Cochrane Database of Systematic Reviews were searched to identify the relevant published literature. We also searched the bibliographies of the retrieved studies to identify any additional papers. The search strategy was limited to English language articles and there was no restrictions on date of publication. The keywords for searches are detailed in Appendix A. The review protocol is according to PRISMA statement and is available from http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016043719.

2.2. Criteria for study inclusion

2.2.1. Types of studies

We included randomized controlled trials and randomized parallel group trials including pilot studies.

2.2.2. Participants

Endometrial and ovarian cancer survivors aged over 18 years with no evidence of recurrence were included.

2.2.3. Interventions

Studies with a lifestyle intervention including those comprising dietary modification, nutritional supplementation, and/or increased physical activity with or without behavioural interventions such as cognitive therapy, relaxation therapy, meditation and psychotherapy were considered for inclusion in this review. There were no restrictions on frequency, duration and intensity of interventions. There was also no limitation on intervention setting (e.g. hospital based, home based, individual/group counselling, face to face, telephone or computer based counselling).

2.2.4. Controls

We included studies comparing lifestyle intervention to usual care, placebo or any other lifestyle intervention.

2.2.5. Outcome measures

The primary outcomes of interest were cancer recurrence and overall survival. The secondary outcome was QoL.

2.3. Data collection

A preliminary screening was performed through titles and abstracts of all articles retrieved by the first reviewer (LY). Duplicate articles and those not meeting the inclusion criteria were excluded from further review.

2.4. Data extraction and risk of bias assessment

Two reviewers (LY and CH) independently extracted data and assessed risk of bias. Any disagreement was resolved by discussion to reach a consensus. Data was extracted from included studies according to the selection criteria. Information was collected on general characteristics of the trials (authors, year of publication, country of origin and study design), intervention (duration, intervention components and setting), participants (age, selection criteria, sample size, randomized and analysed, withdrawals/losses to follow-up) and results (mean and standard deviation for continuous variables, within and between group p-values). Where required, the corresponding author was contacted for additional data.

Articles were also assessed for risk of bias using a standard template for critical appraisal of a randomized controlled trial [26]. Quality appraisal components consisted of specified selection criteria, method of randomization, allocation concealment, blindness of patients/investigators/health care providers, outcome assessment, statistical analysis, controlling the confounders, study power and authors conflict of interest. The articles were assessed as high, low, or unclear risk using recommendations for judging risk of bias of the “Cochrane Handbook for Systematic Reviews of Interventions” [27].

2.5. Data synthesis

Review Manager Software (RevMan 5.3-2014) was used for the meta-analysis. The homogeneity of studies tested with an I^2 (> 50% indicating heterogeneity). A random-effects model was used for the meta-analysis, using mean difference/95% CI.

3. Results

3.1. Results of the search

A detailed diagram of the review process is shown in Fig. 1. The initial literature search was conducted from June to July 2016, yielded 928 citations. We repeated the search strategy in July 2017 to update the review prior to publication and no further articles were identified. Following the screening of titles and abstracts, 16 potentially eligible studies were identified for full text review and finally three studies met the inclusion criteria and were included for review.

925 out of 928 studies were excluded for the following reasons: duplicate references, non-randomised controlled trial, single arm studies, no lifestyle intervention, participants did not meet our criteria, women diagnosed with other types of cancers and studies focus on primary cancer prevention or risk reduction.

3.2. Included studies

Of the 928 studies included for review, no study was found to evaluate the effect of lifestyle modification on cancer recurrence and

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