A systematic overview of reviews of the effectiveness and cost effectiveness of interventions to promote healthy lifestyle behaviours in people living with or beyond cancer.

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INTRODUCTION

Protocol registration

The protocol for this review was registered on the PROSPERO International Prospective Register of Systematic Reviews (Registration number 42016033777).

Background

An overview of systematic reviews synthesised evidence on the relationship between smoking, physical activity, dietary behaviours and alcohol consumption and important outcomes for people living with and beyond cancer. That review demonstrated that some lifestyle behaviours may be associated with important outcomes in people living with and beyond cancer (PLWBC). However it did not inform us of whether specifically delivering interventions aimed at modifying lifestyle behaviours effectively improve outcomes for PLWBC. How to promote and sustain healthy lifestyle behaviours in cancer populations is not well understood. A single, overarching summary of evidence from published systematic reviews of lifestyle interventions which compares and contrasts findings can provide policy and practice professionals with the evidence needed for more effective decision making. This overview of systematic reviews provides a synthesis of evidence on the effectiveness and cost-effectiveness of interventions aimed at altering lifestyle behaviours for improving outcomes for people living with and beyond cancer.

METHODS

Research Question

What is the effectiveness and cost effectiveness of interventions aimed at changing lifestyle behaviours for people living with and beyond cancer?

Criteria for considering reviews for inclusion

Types of studies

We included all systematic reviews of randomised controlled trials that assessed the effects of any intervention used to promote healthy lifestyle behaviours. To be included any review must have achieved a judgement of "Yes" on the third criterion on the AMSTAR tool for assessing the quality of systematic reviews (Shea 2007): "Was a comprehensive literature search performed?" as we deemed this a minimum requirement for a review to be considered systematic.

In our protocol our minimum criteria for considering a search "systematic" were that authors must have searched at least 2 electronic databases using a clear search strategy, and screened the reference lists of identified studies. We did not consider evidence from non-randomised studies in this review. Where reviews mixed randomised and non-randomised studies we considered, where possible, only the evidence from RCTs. We did not include reviews published prior to 2010. We included systematic reviews of health economic evaluations, or reviews that included health economic evaluations. We only included reviews published in the English language. Following initial screening of the searches it became apparent that there was a large volume of reviews with substantial overlap of primary studies but with mixed quality.

In light of this we made two post hoc amendments to our inclusion criteria. To be considered a systematic review we added the following minimum criteria to the existing one:

- The characteristics of the included studies must be summarised in tabulated format (AMSTAR Item 6)

- The scientific quality/ risk of bias of the included studies must be assessed and documented? (AMSTAR item 7).

We considered that this approach would only reduce the number of low quality reviews, which would have presented serious challenges to interpretation. We retained reviews that did not meet these further criteria if there were no other reviews identified on that topic area.

In addition we reviewed all eligible reviews for redundancy. We identified reviews that were essentially redundant on the basis that the review was superseded by a more up-to-date review that included the same participants, intervention type and outcomes. That is, where the earlier review did not offer additional relevant information provided by more recent reviews.

Types of interventions

Any intervention aimed at promoting healthier lifestyle behaviours was included in our review. This included physical activity/ exercise interventions, smoking cessation, and responsible drinking or healthy eating interventions. We excluded evidence relating to the use of dietary supplements. We also excluded reviews of psychological interventions that were not specifically focused on lifestyle behaviour change in relation to physical activity/ exercise, smoking, drinking or dietary behaviours, such as trials of counselling, or stress management.

Types of outcome measure

Included reviews were required to have measured one or more of the following outcomes:

- Mortality
- Recurrence
- Remission/ recovery
- Disease progression
- Co-morbidities
- Late effects and Consequences of Treatment (incidence or severity of any known consequence of cancer treatment)
- Behaviour Change, defined as the adoption of healthy lifestyle behaviours targeted by the intervention
- Measures of physical health or wellness which may include physical function, quality of life, wellbeing, fatigue, anxiety and depression.

For the health economic component, key outcomes were the outputs from cost, cost-utility, cost-effectiveness, cost-benefit and/or cost-consequence analyses.

Types of participants

Adults, 18 years or older living with or beyond cancer were included. This covered any group who had received a cancer diagnosis for any cancer type, at any stage in the treatment or recovery pathway.

Search methods for identification of reviews

Electronic searches

Electronic databases were searched to January 2016 using a combination of controlled vocabulary (MeSH) and free text terms. Search terms were developed to target cancer and systematic reviews. We incorporated the BMJ Clinical Evidence search filter for systematic reviews. The OVID MEDLINE search strategy can be found in Appendix A. All database searches were based on this strategy but

appropriately revised to suit each database. The following databases were searched from 2010 to the present:

- Cochrane Database of Systematic Reviews
- MEDLINE (on OVID)
- Scopus
- CINAHL (on OVID)
- Centre for Reviews and Dissemination (CRD) including:
    - Database of Abstracts of Reviews of Effects (DARE)
    - NHS EED (NHS Economic Evaluation Database)
    - HTA (Health Technology Assessment) database

Searching other sources

The reference lists of all eligible reviews were hand-searched to attempt to identify additional relevant reviews.

Identification of reviews

Search results were independently checked by two overview authors, and eligible reviews were included. Initially the titles and abstracts of identified studies were reviewed. If it was clear from the title and abstract that the study did not meet the inclusion criteria it was excluded. Where it was not clear from the title and abstract whether a study was relevant the full review was checked to confirm its eligibility. The selection criteria were independently applied to the full papers of identified reviews by two overview authors. Where 2 independent overview authors did not agree in their primary judgements they discussed the conflict and attempted to reach a consensus. If they could not agree then a third member of the overview team considered the title and a majority decision was made. Occasionally studies not fitting our inclusion passed this initial sift and were then excluded during the data extraction phase by agreement of two overview authors.

Data collection and analysis

Data extraction and management

Data were extracted independently by two overview authors using a standardised form. Discrepancies were resolved by consensus. Where agreement could not be reached a third overview author considered the paper and a majority decision was reached. The data extraction form included the following details:

- the assessment of methodological quality of the included review
- the objectives of the review
- the number and size of studies

- details of the included participants
- the interventions studied and control conditions used, including detail where available on the intervention content, dose and adherence
- the outcomes, and estimates of effectiveness, cost effectiveness and precision.
- the assessment of the methodological quality/ risk of bias of the included trials and judgements of the quality of the body of evidence (for example using the GRADE approach). The presence of possible conflicts of interest for authors of the included trials within a review, and for the authors of the review themselves.

We did not seek information from the included clinical trials that was not presented in the identified reviews.

Assessment of methodological quality of included reviews

We used the AMSTAR tool to assess the methodological quality of the included reviews (Shea 2007). AMSTAR assessments were made by two independent overview authors. Where the two independent overview authors did not agree in their primary judgements they discussed the conflict and attempted to reach a consensus. If this was not successful a third member of the overview team considered the title and a majority decision was made.

Assessment of the quality of the evidence in included reviews

Included reviews assessed the methodological quality/risk of bias of included studies in a variety of ways. We used the judgements made by the authors of original reviews regarding the quality of evidence/risk of bias but have reported it within the context of our assessment of the quality of the review itself.

Data synthesis

We tabulated summaries of the characteristics of the included reviews. The precise comparisons presented were determined by the content of the included reviews. We presented effect sizes using appropriate metrics including estimates of precision and cost-effectiveness where available. Data were grouped where possible according to diagnosis (cancer type), the type of intervention (exercise/ physical fitness, smoking cessation, drinking advice, healthy eating/ dietary interventions, general healthy lifestyle advice) the outcome and the stage of the cancer journey (during treatment, after treatment, advanced cancer). Important limitations within the evidence base have been presented and discussed. Where included reviews did not rate the quality of the body of evidence we applied the GRADE approach for all key comparisons (Guyatt et al. 2008).

In the GRADE approach, evidence from randomised studies is rated as of high quality. Ratings can be downgraded where there is concern over the limitations of the included studies, imprecision in observed effects, inconsistency, indirectness of the evidence to the population of interest or evidence of publication bias. Ratings can be upgraded where there is consistent evidence of large

effects, or other indicators that increase confidence in an estimate such as evidence of a dose-response relationship. Ratings can be high, moderate, low or very low quality. In terms of confidence in the findings the ratings can be defined as follows:

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

Many of the systematic reviews did not conduct meta-analyses and used a vote-counting approach to synthesis. For these reviews we summarised the synthesis presented for our overview. Where meta-analyses were conducted, these were reported in our overview.

FINDINGS – OVERVIEW OF SEARCH RESULTS

Results

Results of the searches

After removal of duplicates the electronic searches returned 6404 records for screening. Of these 167 records were retained after abstract and title screening and the full texts were assessed. 81 records were excluded at this stage and 8 further relevant reviews were identified through hand-searching of the reference lists of included reviews. A further 21 reviews were excluded on the basis of redundancy resulting in a total of 73 systematic reviews included in this overview. The search screening process is illustrated in Figure 1. See Appendix B for a list of excluded studies with reasons for exclusion.

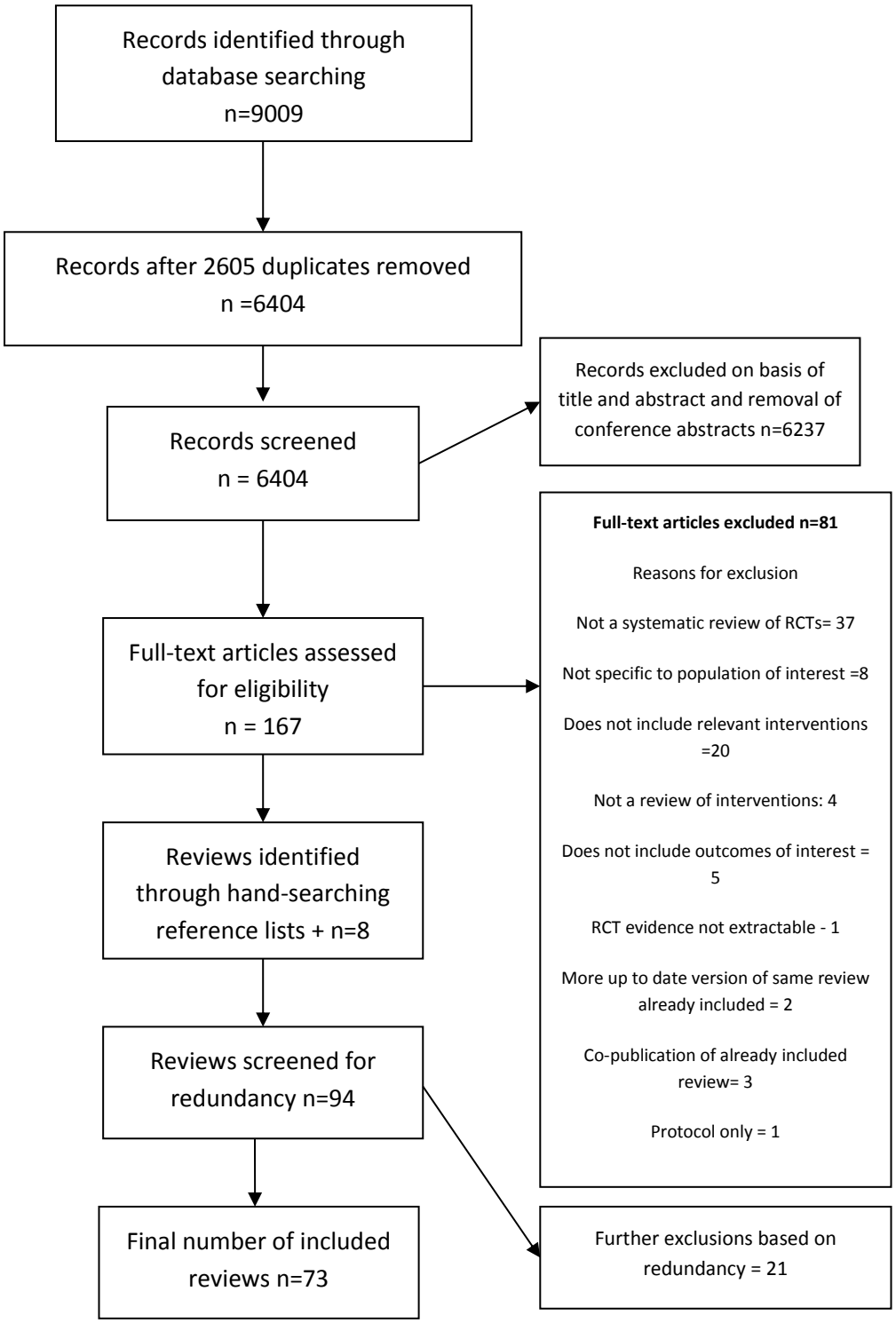
Characteristics of included reviews

The included reviews investigated a broad range of relevant interventions for a wide range of cancers. Included reviews variously investigated mixed "lifestyle interventions" that generally included a physical activity and or dietary advice component with behavioural change techniques and various levels of psychological and social support; a range of dietary interventions, some to facilitate weight loss and reduce obesity and some to facilitate healthy weight gain following cancer treatments that confer a risk of underweight and malnutrition; smoking cessation intervention and physical activity interventions varied and included aerobic exercise, resistance exercise, mixed content interventions, dance and movement therapy, range of motion exercise, yoga, tai chi and qigong. A wide range of outcomes were presented in the included review of relevance to our overview. For a tabulated summary of the characteristics of the included reviews see Appendix C. There was substantial overlap between many reviews in terms of the trials included. We identified no reviews of the evidence relating to interventions aimed at modifying alcohol related behaviours.

Quality of included reviews

The AMSTAR quality assessment scores for the included reviews ranged from 2 to 11 out of a maximum of 11 (median 6.5). The full results for the AMSTAR quality assessment are presented in Appendix D. Most common areas that review failed to achieve a positive judgement on the AMSTAR scale were the presentation of a list of excluded studies, the inclusion of grey literature and literature regardless of language, the consideration of the risk of publication bias and the reporting of conflicts of interest, particularly those relating to the authors of the included trials. Cochrane reviews tended to score more highly than non-Cochrane reviews. In part this is likely to reflect the better quality of those reviews but also the lack of restrictions on full reporting (for example word and table counts) when publishing in the Cochrane library and the shorter page count for journal articles. However, the use of online supplements means that most of these attributes could have been reported online even if they were not in the main paper.

Figure 1: PRISMA flow diagram of the search screening process



FINDINGS OF INCLUDED REVIEWS

Mixed "Lifestyle" interventions

MIXED CANCER POPULATIONS

Mixed cancer populations: Characteristics of reviews

Three reviews investigated the effectiveness of multicomponent interventions that included relevant lifestyle components in people with any cancer diagnosis. (De Boer et al. 2015, Scott et al. 2013, Sumamo et al. 2011)

One Cochrane review (De Boer et al. 2015) reviewed the effectiveness of interventions aimed at enhancing return to work (RTW) in cancer patients. This review was included in the current overview as some included studies delivered interventions that addressed relevant lifestyle behaviours. This review was given an AMSTAR score of 11/11.

The Cochrane review of Scott et al. (2013) examined the effect of multidimensional rehabilitation programmes for adult cancer survivors. Programmes had to incorporate a physical component (diet and/ or exercise) with a psychosocial component, compared to no treatment, standard care or an alternative intervention. Outcomes of interest were physical function, weight change, symptom control, quality of life, psychological measures, patient adherence, satisfaction with the rehabilitation programmes and adverse outcomes. This review had an AMSTAR score of 10/11.

Scott et al. (2013) identified 12 RCTs including 1669 participants. Study quality was assessed using the Cochrane risk of bias tool. No studies had a low risk. Four were classified as having a moderate risk of bias and eight a high risk of bias. Seven studies explicitly stated that the aim of the intervention was to promote physical and psychosocial wellbeing. Five studies focused specifically on improving physical wellbeing (predominantly physical function). Most studies delivered the interventions through face to face contact, with or without telephone follow-up. Two studies delivered the intervention through printed materials. Control groups varied from standard care or ales intensive interventions such a brief educational packages.

Similarly Sumamo et al. (2011) investigated the effectiveness of "lifestyle interventions" in people with breast and prostate cancer. To be included, interventions were required to include an exercise and/ or a dietary component and at least one of: behavioural change techniques, counselling, smoking cessation, stress reduction or group therapy. This review had and AMSTAR score of 10/11. Outcomes of interest were cancer recurrence, change in physical activity levels, diet, medication use and compliance with the intervention. The review by Sumamo et al.(2011) included three trials which were also included in the more up to date Cochrane review by Scott et al. (2013), one which included people with breast or prostate cancer, one specific to prostate cancer and one specific to breast cancer. Quality of the included trials was assessed with the Cochrane risk of bias tool. One trial was at high risk of bias and 2 at unclear risk of bias overall.

Interventions and comparisons in Sumamo et al (2011) included a telephone counselling programme to improve diet and physical activity levels, compared to a mailed workbook and telephone counselling on "other areas" (6 month intervention, n=182); a comprehensive lifestyle change intervention including a vegan diet, advice to do moderate aerobic exercise, stress management techniques with a weekly support group and nutritional education by a registered dietician physicians advice (1 year intervention, n=93) and a home-based programme based on social cognitive theory and trans theoretical models including personally tailored workbooks, a quarterly newsletter, telephone counselling and automated prompts compared to a waiting list control. The type of training was not reported in the original study (n=475, 1 year intervention).

Mixed cancer populations: Outcomes

Recurrence

Sumamo et al. (2011) included one study that reported serum Prostate Specific-Antigen (PSA) levels as a marker of recurrence and found reduced serum PSA in the intervention group (n=93, mean difference (MD) -0.63, 95%CI -1.41 to -0.12, scale not specified). As PSA is not only elevated in prostate cancer, but also in other prostate pathology, a small mean difference does not necessarily mean that cancer recurrence was lower in the intervention group compared to controls.

Weight change

Sumamo et al. (2011) included two studies that reported weight change in people with prostate cancer. Pooled results found greater weight loss (lbs) in the intervention groups (n= 309. mean difference -7.55 lbs 95%CI -13.05 to -2.05, p=0.007, I^2=44%, heterogeneity not significant).

In one study in breast cancer patients no statistically significant difference in weight loss (lbs) was seen (n=250, mean difference 3.90 95%CI -10.32 to +2.52, p=0.23).

Physical activity levels

Sumamo et al. (2011) reported that pooling of two studies produced a statistically significant increase in activity level in the intervention group (standardised mean difference (SMD) 0.43, 95%CI 0.13 to 0.72, number of participants for this comparison not reported, low heterogeneity, p value not reported). One study reported an increase in time minutes spent performing endurance or strength exercise. It was not clear whether this was minutes per day or per week (MD 15.04, 95%CI 0.09 to 29.99, p value not reported, n for comparison not reported). The same study looked at the number of sessions of exercise undertaken per week and found significant differences favouring the intervention in breast cancer for endurance exercise (MD 1.17 session 95%CI 0.38 to 1.96, n for comparison and p value not reported) and for strength exercise (MD 1.67 95%CI 1.18 to 2.16, n for comparison and p value not reported).

Dietary intake

Sumamo et al. (2011) reported inconsistent findings between studies on calories from fat consumption. Of 2 studies in prostate cancer one demonstrated a statistically significant decrease in calories from fat in the intervention group and one did not. The one study in breast cancer found a

statistically significant but very small (mean difference -1.76 calories, 95%CI -2.57 to -0.95) difference in favour of the intervention group.

In two studies that measured fruit and vegetable intake one found a statistically significant difference in favour of the intervention and one did not. One study reported a diet quality index and found a statistically significant difference in favour of the intervention at the end of the intervention that was not maintained at 6 month follow up.

Compliance with the intervention

Sumamo et al. (2011) reported "compliance" measured indirectly from withdrawals from the trials. It should be recognised that this is not a direct measure of adherence to the intervention. In two studies that reported withdrawal rates there was no statistically significant difference between the groups.

The authors of the review concluded that the strength of evidence regarding lifestyle interventions is low to insufficient across outcomes but that lifestyle interventions seem to have a positive effect on behavioural outcomes.

Quality of Life

Scott et al. (2013) were able to pool quality of life data (from the SF-36 scale) for 4 studies (with a mix of uni- and multi-dimensional focus interventions. They reported a statistically significant positive effect associated with the intervention on "physical function" (mean difference 2.22, 95%CI 0.12 to 4.31, p=0.04). However the only presented forest plot was for the SF-36 Physical Component Score and showed no statistically significant effect (mean difference 1.79, 95%CI -0.82 to 4.39, p=0.18, I^2=0%). The assessment time-point for this comparison ranged from 3 to 12 months across studies though there was no heterogeneity. No effect was seen on the mental health component scale.

Scott et al. (2013) conclude that their results "tentatively" indicate that interventions with a uni-dimensional focus may be more successful in generating a positive change in the target of their focus. There did not appear to be a difference between single cancer site and varied cancer-site programmes. Face to face interventions with telephone follow up appear to be more effectiveness and that positive effects plateau at 6 months.

Return to work

In the review by De Boer et al. (2015) analysis of multidisciplinary programmes demonstrated some improvement in return to work but no improvement in quality of life but this analysis also included studies that did not include clearly relevant lifestyle behaviours. As such no specific conclusions can be drawn about the benefit of interventions that included relevant lifestyle components.

Mixed cancer populations: GRADE summary

There is moderate quality evidence that lifestyle interventions may facilitate weight loss in people with prostate cancer (downgrade for limitations of studies) and low quality evidence (downgraded

for limitations of studies, inconsistency -single study) that they do not facilitate weight loss in people with breast cancer.

There is moderate quality evidence (downgraded for limitations of studies) that lifestyle interventions can increase physical activity levels. The evidence that lifestyle interventions can induce dietary change is conflicting and there is no direct evidence relating to intervention adherence.

There is low quality evidence (downgraded for limitations of studies and imprecision) that mixed lifestyle interventions do not offer consistent improvements in Quality of Life in survivors of various cancers. No specific conclusions can be drawn about the benefit of lifestyle interventions for return to work.

BREAST CANCER

Breast cancer: Characteristics of reviews

One review, Spark et al. (2013) specifically focused on the maintenance of behavioural change outcomes in trials of dietary and/or physical activity interventions in breast cancer survivors. They sought to identify the proportion of trials that reported maintenance of behavioural change, the proportion of trials that achieved successful change and any characteristics that might be common to ”successful” trials. This review had an AMSTAR score of 5/11.

Out of 63 trials they found 10 trials with 1536 participants in total that reported post-intervention maintenance of outcomes. Seven trials included women with breast cancer exclusively, and the other studies included both breast and prostate cancer survivors. 7 evaluated physical activity interventions, one evaluated a dietary intervention and one a combined physical activity and dietary intervention. The duration of interventions in the included trials ranged from one to 10 months, and the length of follow-up ranged from 3 to 12 months. To assess the quality of included studies that used a 10 point tool adapted from the CONSORT statement. The median quality score achieved was 6/10.

Breast cancer: Outcomes

Maintenance of behavioural change

Four of the ten trials reported successful maintenance of behaviour change for at least 50% of outcomes. Of these three were for physical activity interventions and one was for a combined physical and dietary intervention. In that trial only the dietary behaviour was successfully maintained.

Characteristics of “successful” behaviour change trials

Spark et al. (2013) report that maintenance of behaviour change appeared to be more common in trials that targeted participants who were undergoing treatment, rather than those after treatment and who were therefore closest to the point for diagnosis on entry to the trial.

Age, BMI of participants, the duration of the intervention or follow-up period and trial the quality score were not different between "successful" and "unsuccessful" trials. Only four trials described specific strategies for promoting maintenance of behaviour change of which 2 were successful and 2 were not. Successful trials were more likely to inadequately report the methods used for dealing with missing data. These characteristics should be treated with caution as they are based on a very small number of overall studies.

Breast cancer: GRADE summary

The authors concluded that there is very limited evidence to inform how best to sustain initial improvements in physical activity and dietary behaviours and recommend more research in this area. The nature of the question of this review does not lend itself to GRADE quality assessment.

GYNAECOLOGICAL CANCERS

Gynaecological cancers: Characteristics of reviews

One reviews (Smits et al. 2015) evaluated the effectiveness of lifestyle interventions for quality of life. Smits et al. included endometrial or ovarian cancer survivors and had an AMSTAR score of 5/11.

Smits et al. (2015) included three RCTs (combined n= 153). Risk of bias was assessed using the Cochrane study methods group tool. Only one RCT blinded outcome assessors.

All three trials in the Smits et al. (2015) review delivered physical activity behavioural change programmes and 2 of those included a nutritional counselling component. The control group conditions were not clearly described. Intervention duration ranged from 12 weeks to 6 months and two of the interventions were described as home-based. Two of the trials include only overweight women and one only sedentary women with mild to severe fatigue.

Gynaecological cancers: Outcomes

Quality of Life

Smits et al. conducted a meta-analysis of 2 trials and did not find a statistically significant difference in global QoL scores at 3 months (p=0.76) or 6 months (p=0.49) (pooled n=153, p= no heterogeneity).

Physical functioning

One trial (n=45) did not demonstrate a statistically significant effect for physical functioning.

Fatigue

One trial (n=45) did not demonstrate a statistically significant effect for fatigue.

Weight Loss

Two studies (combined n=120) separately reported statistically significant weight loss in favour of the intervention though the effect sizes were not reported.

Physical activity

One trial (n=45) demonstrated a statistically significant difference in physical activity in favour of the intervention group though the effect sizes were not reported.

Depression

Two studies showed no significant difference in Beck Depression Inventory scores (effect sizes not reported).

Smits et al. (2015) concluded that lifestyle interventions have the potential to improve the QoL of gynaecological cancer survivors and may significantly reduce fatigue, but based this conclusion largely on non-RCTs not considered in this overview. The results of the clinical trials reported here do not concur with that conclusion. Both reviews concluded that more research was required in this area.

Gynaecological cancers: GRADE summary

Using GRADE there is low quality evidence (downgraded for limitations of studies and imprecision) that lifestyle interventions promoting physical activity with or without nutritional counselling do not improve quality of life in gynaecological cancer survivors. There is low quality evidence (downgraded for limitations of studies and imprecision) that these interventions do not improve fatigue or depression but that they might facilitate weight loss and physical activity, though the effect sizes were not reported.

PROSTATE CANCER

Prostate cancer: Characteristics of reviews

Three reviews reported on the effects of mixed lifestyle interventions in prostate cancer (Hackshaw-McGeagh et al. 2015, Mohamad et al. 2015, Larkin et al. 2014))

Hackshaw-McGeagh et al. 2015 reviewed the evidence of the effectiveness of dietary, nutritional and physical activity interventions for modifying disease progression and mortality in men with prostate cancer. This review had an AMSTAR score of 9/11.This review included 44 RCTs, of which most were not relevant to this overview as they specifically focused on dietary supplements. Eleven RCTs were relevant to this overview, 4 of which reported a physical intervention including resistance and/or aerobic training, 3 reported a complex nutritional intervention including an educational element and 4 reported a combined nutritional and physical activity element. The men in the included studies had undergone a variety of different cancer treatments or received the intervention prior to undergoing radical prostatectomy. Study quality was assessed using the Cochrane risk of bias tool. Overall most studies demonstrated a high or unclear risk of bias on the majority of criteria. No meta-analysis was conducted and results were synthesised narratively.

One review (Larkin et al. 2014) reviewed the effectiveness of non-pharmacological interventions employed specifically for managing cancer related fatigue in men with prostate cancer at any stage of disease who were undergoing current treatment for cancer or had received treatment within the previous 12 months. This review had an AMSTAR score of 5/11.They included 5 RCTs (combined n=408) of people with prostate cancer being treated with radiotherapy and or androgen deprivation therapy (ADT). The included interventions varied. All included an exercise component, of various types, one also included dietary advice. The dose and duration of the interventions varied from 8 to 24 weeks and variously included individualised and group exercise and self-directed home exercise component. All were compared to usual care or a waiting list control.

The quality of included studies was assessed using the Joanna Briggs Institute critical appraisal checklist. A score of more than 5/10 on this tool was considered by the reviewers the threshold for a high quality study. However this does mean that a study containing possibly substantial risks of bias might be classified as high quality. For example while all studies were randomised, concealed allocation was not reported in 3 of the 5 studies, outcome assessors were not blinded in two studies and one study did not account for attrition in the analysis.

One review (Mohamad et al. 2015) investigated the effect of dietary and physical activity interventions aimed at reducing body weight in men treated for prostate cancer at any stage of treatment. This review had an AMSTAR score of 7/11.This review included 20 RCTS with a combined n of 1298. This included 6 trials of dietary interventions, 8 of PA interventions and 6 of combined diet and exercise interventions. Study quality was assessed using the Cochrane risk of bias tool, and most studies were at unclear risk of bias on more than one criterion. Interventions were heterogeneous in terms of content, duration and the intensity of clinician contact. While behaviour change techniques appeared to be employed, none of the trials specifically named a behaviour change therapy underpinning their approach. No meta-analysis was conducted and the results were synthesised narratively.

Prostate cancer: Outcomes

Body weight

Mohamad et al. (2015) reported that studies of diet interventions that used low-fat or calorie restricted diets either alone or in combination with physical exercise tended to show more convincing changes in body weight and composition than other types of intervention and that less change in body weight or BMI was seen in exercise only interventions, though results were varied. They concluded that diet intervention, alone or in combination with exercise, can lead to weight loss in men treated for prostate cancer.

This review provides more up to date support than the review of Sumamo et al. (2011, see above) that there is moderate quality evidence that lifestyle interventions may facilitate weight change in people with prostate cancer (downgrade for limitations of studies).

Cancer-related fatigue

In the review by Larkin et al. (2014) no meta-analysis was conducted and the evidence was synthesised narratively. Four studies demonstrated statistically significant reductions in fatigue in favour of the intervention group, and one did not find a statistically significant difference. The study presented post intervention fatigue scores for each group in each study, but did not present between group differences.

Larkin et al. (2014) concluded that despite variation in the type of exercise, amount undertaken and duration of interventions, physical activity was shown to be beneficial in mitigating fatigue.

Disease progression

Hackshaw-McGeagh et al. (2015) included four RCTs (combined n=439) reported no consistent effect of physical activity interventions on PSA-based measures of disease progression. Three RCTs of low fat dietary interventions (combined n=256) reported no consistent effect PSA-based measures of disease progression. Four RCTs of combined dietary and PA based interventions (combined n=297) reported no "consistent" effect, though the outcome was not reported clearly for this comparison. Of note, this review included one trial that had been included in the review by Sumamo et al. (2011) which reported a positive effect of a vegan diet and aerobic exercise on PSA levels (see above) at 12 months follow up.

Mortality

No results were reported for mortality following interventions relevant to this overview.

Prostate cancer: GRADE summary

There is very low quality evidence (downgraded for limitations of studies, inconsistency and imprecision) that physical activity and dietary interventions do not positively impact on PSA-related measures of disease progression. There is low quality evidence (downgraded for limitations of studies and inconsistency) that lifestyle interventions with a physical activity component reduce cancer-related fatigue.

Patient education focused interventions

MIXED CANCER POPULATIONS

Mixed cancer patients: Characteristics of reviews

One review (Du et al. 2015) sought to evaluate the effectiveness of patient education programmes for cancer related fatigue in adults with cancer of any type, stage or clinical status. Relevant secondary outcomes included quality of life. This review scored 5/11 in the AMSTAR scale.

This review identified 10 RCTs of which 8 were relevant to this overview. Relevant trials focused on breast, lung or gastric cancers or did not specify the type of cancer. The review did not stratify studies by the type or stage of cancer. Two included advice on physical exercise (pooled n=382) and 6 included advice on nutrition and physical exercise (pooled n=665) compared to waiting lists or usual care controls. Interventions were delivered by a range of health professionals. The specific detail of the physical exercise or nutritional advice aspects of the interventions were not reported.

The quality of included studies was assessed using the Cochrane risk of bias tool. While none of the studies were able to blind participants, assessors were only blinded in 2 of the 8 relevant studies, 2 studies were at high risk of bias for allocation concealment and one was at unclear risk for adequate randomisation.

Mixed cancer patients: Outcomes

Cancer related fatigue

No meta-analysis was conducted. In a narrative synthesis, 5 trials, all of which included a nutritional and physical activity component, reported what was described by the reviewers as a "limited positive effect" and 2 trials found no effect. Only one trial, which included a physical activity component but no nutritional component, found a statistically significant positive effect. Following the convention of equating statistical significance with evidence of an effect would lead to the conclusion that of eight trials only one demonstrated a positive effect.

Quality of life

No meta-analysis was conducted. One trial (n=382) found that an intervention with a physical activity component demonstrated no effect.

Due et al. (2015) concluded that there was limited evidence for the use of patient education programmes to reduce cancer-related fatigue, but that they appear to play "some positive role". They cautiously recommend patient education programmes and call for more rigorous, and well characterised RCTs.

Mixed cancer patients: GRADE summary

There is low quality evidence (downgraded for imprecision and inconsistency) that patient education programmes that include a lifestyle behaviour component do not improve cancer related fatigue and quality of life. The lack of clear description of the content of the interventions makes interpretation of these data challenging.

Smoking cessation interventions

MIXED CANCER POPULATIONS

Mixed cancer populations: Characteristics of reviews

Only one review (Nayan et al. 2013) investigated the impact of tobacco cessation interventions. This review included RCTs and cohort studies that delivered smoking cessation programmes and compared them to standard usual care in adult smokers with a diagnosis of cancer. Studies had to report smoking cessation rates to be included. Analysis was conducted at short term (mean 5 weeks) and long term (≥ 6 month follow up). This review had an AMSTAR score of 7/11.

The review included 13 studies, 10 RCTs and 3 cohort studies with a total of 1301 participants. Risk of bias in the RCTs was assessed using a 7 point tool similar to the Cochrane risk of bias tool. The authors concluded that all studies were at low risk of bias. However none of the included studies reported allocation concealment, which is a known risk of bias associated with exaggerated effect sizes (Savovic et al. 2012, Wood et al. 2008). Risk of bias was not assessed for the included cohort studies. Interventions in the included studies were delivered by health care professionals and included pharmacological approaches (nicotine replacement therapy, bupropion or varenicline) and non-pharmacological approaches (CBT, counselling, self-help material, education modules, motivational interviewing).

Mixed cancer populations: Outcomes

Smoking cessation rates

Meta-analysis, which pooled RCTs with cohort studies, was conducted. Pooling all types of intervention together suggested no statistically significant effect of interventions on cessation rates in the short term (6 studies, n=433, Odds Ratio (OR) 1.54, 95%CI 0.909 to 2.64, p=0.108, I^2 = 8.7%) or the long term (8 studies, n=1214, OR 1.21, 95%CI 0.931 to 1.84, p=0.120, I^2 = 15%) with no significant heterogeneity.

Sensitivity analysis pooling only studies with purely non-pharmacological interventions demonstrated no statistically significant effect of the intervention (5 studies, n=not clearly reported, OR 1.35, 95%CI 0.62 to 0.97, p=0.120, I^2 = 0%). When studies of interventions that delivered combined pharmacological and non-pharmacological interventions were pooled, a statistically

significant increase of the odds of cessation was seen (8 studies, n= not clearly reported, OR 1.40, 95%CI 1.06 to 1.87, p value not reported, I^2=1.8%). Sensitivity analysis looking at interventions delivered in the perioperative period demonstrated a large statistically significant increase in cessation rates (5 studies, n not clearly reported, OR 2.31, 95% CI, 1.32 to 4.07; I^2 = 0%).

Considering these analyses it is arguable that pooling a range of different interventions into a single meta-analysis is inappropriate as we would not necessarily predict similar effect sizes from different approaches. Similarly pooling effect sizes from RCTs with those from cohort studies is controversial. However the low heterogeneity in effect sizes observed across the key analyses suggests that large differences in effect size between different approaches and study designs were not present. The results of sensitivity analyses should be treated with caution as it is not clear whether they were planned a priori or represent post hoc analysis.

The authors concluded that tobacco cessation interventions in the oncology population do not deliver statistically significant increases in cessation rates in cancer patients overall but that the perioperative period may be an important teachable moment.

Mixed cancer populations: GRADE summary

There is moderate quality evidence (downgraded once for imprecision as the numbers of patients for each analysis was not readily available) that tobacco cessation programmes do not improve cessation rates in people with cancer.

Nutritional/ Dietary Interventions

MIXED CANCER POPULATION AT RISK OF/ WITH MALNUTRITION

Mixed cancer population at risk of/ with malnutrition: Characteristics of reviews

One review (Baldwin et al. 2012) reviewed the evidence of effectiveness for oral dietary interventions in people with cancer who were malnourished or at risk of malnutrition. This review scored 7/11 on the AMSTAR tool.

Of 13 included RCTs 10 included a dietary advice component with or without oral nutritional supplements and were relevant to this overview. Trials included patients with gastrointestinal cancers, leukaemia, gynaecological cancers, lymphoma and cancer of the head and neck, breast, lung and bladder. The primary outcome for this review was mortality and a relevant secondary outcome was weight loss. Risk of bias in included trials was derived using an adapted version of the Cochrane risk of bias tool. All studies were judged to be at risk of bias from one or more characteristics.

Mixed cancer population at risk of/ with malnutrition: Outcomes

Mortality

In a meta-analysis of 9 studies (n=1240) no effect was seen compared to routine care (Relative Risk RR 1.06, 95%CI 0.92 to 1.22, p=0.43, I^2=0%) with no heterogeneity.

Quality of life

Baldwin et al. (2013) only included studies which measured QoL using the European Organization for Research and Treatment of Cancer (EORTC) scale in their meta-analysis, so excluded 2 of the 7 included RCTs that measured QoL.

Meta-analysis of global QoL (EORTC) scores demonstrated a statistically significant effect in favour of the intervention (4 studies, n=560 mean difference 24.02 (95%CI 14.22 to 33.72, p<0.00001) but with substantial heterogeneity (I^2=98%, p<0.00001). Length of follow-up period for these results ranged from 6 weeks to 6 months.

Sensitivity analysis removing the one study with results that appeared to be clear outliers substantially reduced heterogeneity and the effect size, though this remained statistically significant(3 studies, n= 374, mean difference 5.53 95%CI 0.73 to 10.33, p=0.02, I^2=27%). It is not clear whether this approach to exploring heterogeneity was planned a priori.

With regards to analysis of QoL subscales, statistically significant improvements were seen for emotional function and dyspnoea and loss of appetite on the symptoms scales.

Weight gain

In meta-analysis of weight gain (7 studies, n= 716) a statistically significant difference in weight gain in favour of the intervention was seen (mean difference1.86 kg, 95%CI 0.25 to 3.47, p=0.02) with high heterogeneity (I^2 76%, p<0.0001).

After removal of 2 studies accounting for heterogeneity no statistically significant increase was observed (5 studies, n=551 mean difference 0.31kg, 95%CI -0.60 to 1.21, p=0.5, I^2 0%) P=0.88.

The authors conclude that oral nutritional interventions have no effect on survival and that the effect on body weight and energy intake is inconsistent but that statistically significant improvements in some aspects of QOL may be achieved. They acknowledge the effect size for global QoL that it is not clear whether these are clinically meaningful changes in QoL to the patient.

Mixed cancer population at risk of/ with malnutrition: GRADE summary

There is moderate quality evidence that oral nutritional interventions have no effect on survival (downgraded for limitations of studies) in people with cancer who were malnourished or at risk of malnutrition.

There is low quality evidence (downgraded for limitations of studies and inconsistency) that oral nutritional interventions are not effective at promoting important weight gain in people with cancer who were malnourished or at risk of malnutrition.

There is low quality evidence (downgraded for limitations of studies and inconsistency) that oral nutritional interventions have a positive effect on quality of life in people with cancer who were malnourished or at risk of malnutrition, though the clinical importance of that difference is uncertain.

MIXED CANCER POPULATION AT ADVANCED STAGE OF CANCER WITH CACHEXIA

Mixed cancer population at advanced stage of cancer with cachexia: Characteristics of reviews

One review (Balstad et al. 2013) reviewed the evidence for the effectiveness of dietary counselling for treating weight loss in patients with advanced cancer with varying stages of cachexia. Secondary outcomes were physical function and quality of life. This review scored 6/11 on the AMSTAR scale.

The review identified three RCTs (combined n=561), one of patients with gastrointestinal and non-small cell lung cancer (NSCLC) patients, one with advanced colorectal and gastric cancer patients and one with metastatic NSCLC and colorectal cancer patients. Interventions included dietary advice to increase caloric intake with or without nutritional supplements. The quality of included studies was assessed using the Cochrane risk of bias tool. All 3 trials were rated at unclear or high risk of bias on at least criterion other than patient and clinician blinding. No meta-analysis was conducted for any outcome.

Mixed cancer population at advanced stage of cancer with cachexia: Outcomes

Quality of Life and Physical Function

One study (n=358) found no difference in QoL using 2 different scales. This study also found no difference in physical function.

One study (n=23) found a statistically improvement in a Linear Analog Scale Assessment (LASA) of leisure activity QoL and psychological QoL in favour of the intervention. The exact between group differences were not reported.

Weight

Of the three trials, 2 demonstrated no statistically significant difference weight gain (or reduced weight loss) during the intervention. Of these one trial reported no difference at 6 week follow up but a significant difference of 3.4kg at one year ($p<0.05$, confidence intervals not presented). At the end of one trial there was a statistically significant difference in weight loss of 3.4kg at the end of a 56 day intervention period.

The review authors concluded that dietary counselling can affect energy intake and body weight, but that there is insufficient evidence that dietary counselling given to patients with cancer is beneficial for improving weight or energy balance in the different cachexia stages.

Mixed cancer population at advanced stage of cancer with cachexia: GRADE summary

There is very low quality evidence (downgraded for limitations of studies, inconsistency and imprecision) that dietary counselling might help reduce weight loss in patients with advanced cancer and cachexia.

There is very low quality evidence that dietary counselling may have a limited positive influence aspects of Quality of life in this group (downgraded for limitations, inconsistency and imprecision). There is very low quality evidence (downgraded for limitations, inconsistency and imprecision) that dietary counselling does not improve physical function in this group.

HEAD AND NECK ADENOMA RECEIVING RADIOTHERAPY OR CHEMORADIOTHERAPY

Head and neck adenoma receiving radiotherapy or chemoradiotherapy: Characteristics of reviews

One review (Langius et al. 2013) reviewed the effectiveness of nutritional interventions in people with head and neck squamous cell cancers. Of these the most up to date (Langius et al. 2013) focused on people treated with radiotherapy or chemoradiotherapy. The AMSTAR score for this review was 8/11. Of 10 trials identified, 4 were relevant to this overview (combined n=192) as the delivered intervention was not just nutritional supplementation. Three of these trials were included in the mixed cancer population review of Baldwin et al. (2012) and one was included in the review of Balstad et al. (2014). The majority of participants had cancer of the pharynx or larynx. These 4 RCTs examined the effect of individualised dietary counselling, delivered by a dietician compared to no counselling or general nutritional advice by a nurse. To examine the quality of the included trials Langius et al. (2013) used the Cochrane risk of bias tool and found all included studies to have a high risk of bias. Lack of blinding was a common issue that is hard to avoid in these trials but all studies were at unclear or high risk of bias on other criteria. No meta-analysis was conducted.

Head and neck adenoma receiving radiotherapy or chemoradiotherapy: Outcomes

Mortality

No study reported mortality as an outcome.

Nutritional status

Langius et al. (2013) reported that all four studies found positive effects on nutritional status. Of these, three reported on bodyweight changes during and after radiotherapy and all found statistically significant positive effects of dietary counselling. Specific effect sizes with measures of precision were not reported although, from the raw data, differences in weight loss across the studies ranged from around 1 to 3 kg.

Three studies reported on malnutrition. All showed less malnourished patients in the intervention group but, of these, two studies only found this effect at 8 weeks after the start of radiotherapy and not at other points in time.

Quality of life

Two of the four studies reported statistically significant positive effects of dietary counselling, no effect sizes were reported.

The authors concluded that individualised dietary counselling by a dietician had some benefits for nutritional status and quality of life.

Head and neck adenoma receiving radiotherapy or chemoradiotherapy: GRADE summary

There is low quality evidence (downgraded for limitations of studies and imprecision) that individualised dietary counselling by a dietician offers some improvement in nutritional status and body weight, and very low quality evidence of a benefit for quality of life (downgraded for limitations of studies, imprecision and inconsistency) in patients with head and neck adenoma undergoing radio- or chemoradiotherapy.

LUNG CANCER

Lung cancer: Characteristics of reviews

Two further reviews (Kiss et al. 2014, Payne et al. 2013) investigated dietary/ nutritional interventions specifically in people with lung cancer. Kiss et al. 2014 focused on people undergoing chemotherapy and/ or radiotherapy and Payne et al. focused on people with advanced stage lung cancer. Kiss et al. (2014) scored 6/11 and Payne et al. (2013) scored 7/11on the AMSTAR scale. Payne et al. 2013 investigated the effects of nutritional interventions specifically for people with advanced stage NSCLC (stages IIIb or IV) regardless of whether they were receiving active treatment. They identified no RCTs relevant to this overview.

Kiss et al. identified 3 RCTs (combined n=399), two of which were included in the review by Balstad et al. (2014). Interventions included dietary counselling with or without nutritional supplements. Quality was assessed using the ADA tool and studies could be given a judgement of neutral positive or negative. Two studies were rated as neutral and one as negative. Outcomes of interest were dietary intake, weight, nutritional status, QoL, functional status, treatment response and survival. No meta-analysis was conducted. In all three studies patients were receiving chemotherapy. In no studies were patients receiving radiotherapy.

Lung cancer: Outcomes

Dietary intake

Two studies reported energy intake and both found a statistically significant increase in dietary intake. Effect sizes with precision estimates were not reported.

Nutritional status

One trial (n=105) reported assessed nutritional status using fat-free mass from triceps skinfold measurements. No differences were seen between the dietary counselling and control group.

Quality of life

Two trials (combined n=361) found no differences between the groups for QoL but, of those, one trial reported that the data were incomplete for this outcome due to incomplete questionnaires for some participants

Survival

Three trials found no difference in survival between the intervention and controls groups at 1 year.

Treatment Response

Two trials (combined n=285) reported no significant differences between groups in the number of people with a complete or partial response to their cancer treatment.

Weight

All three RCTs were reported to find no statistically significant differences in weight between the intervention and control groups during the intervention.

The authors concluded that dietary counselling improved energy and protein intake during chemotherapy in patients with lung cancer, and no benefit on other outcomes but that due to limitations in the evidence the results should be treated with caution. They found a lack of evidence relating to people receiving radiotherapy.

Lung cancer: GRADE summary

There is low quality evidence (downgraded for limitations of studies and imprecision (effect sizes with confidence intervals not reported) that dietary counselling improves energy intake in patients with lung cancer undergoing chemotherapy.

There is moderate quality evidence (downgraded for limitations of studies) that dietary counselling does not affect weight change, survival or response to chemotherapy in this group. There is low quality evidence that dietary counselling does not improve quality of life in this group.

There is no evidence relating to the effectiveness of dietary counselling for patients with lung cancer receiving radiotherapy.

Specific dietary interventions

Low fat diet

BREAST CANCER

Breast cancer: Characteristics of reviews

One review (Xing et al. 2013) investigated the effectiveness of post-diagnosis low fat diet on recurrence and all-cause mortality in people with breast cancer. The review included RCTs and cohort studies and had an AMSTAR score of 3/11. Low fat diet was not clearly defined. No formal assessment of the quality of the included studies was presented. Of the 2 RCTs included both were health promotion interventions. The Women's Intervention Nutrition Study (WINS) compared

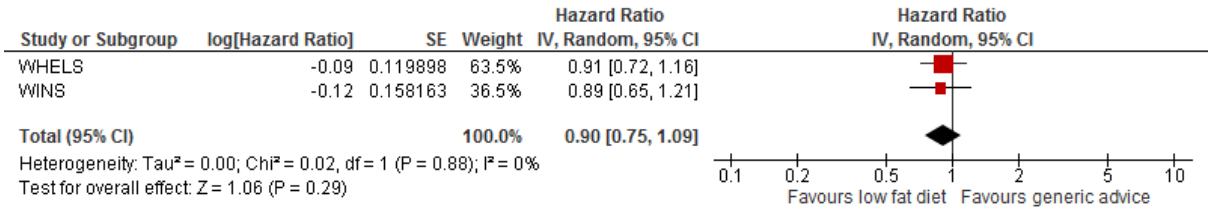
promoting the reduction of fat intake to 15% of total intake while maintaining nutritional adequacy, supported by monthly telephone support with dieticians and annual workshops for a median follow up time of 60 months to general dietary / nutritional guidelines with 3 monthly telephone support from a dietician. The Womens Healthy Eating and Living (WHEL) study compared a diet very high in fruit, vegetables and fibre, but low in fat (15-20% of total intake) supported by cooking classes and telephone counselling in the early phase to self-monitoring and newsletters in the later phase for 4 years to printed nutritional information describing a more generic healthy diet supplemented by a smaller number of cooking classes and newsletters.

Breast cancer: Outcomes

All-cause mortality

Evidence from 2 RCTs pooled with one multi-centre cohort study (combined n=9996) demonstrated a non-significant 17% decrease in the relative risks of mortality (HR 0.83, 95%CI 0.69 to 1.00, p=0.05, I^2=17%). However there were similar discrepancies between the effect sizes from the original RCTs in this meta-analysis and those reported in the original papers. We conducted our own meta-analysis of the hazard ratios presented in the original papers, using the generic inverse variance method and a random effects model as recommended in the Cochrane Handbook (Higgins et al. 2011). This new analysis, which only included the RCTs, found no statistically significant effect of low fat diet on overall mortality, without heterogeneity (2 studies, n=5526, HR 0.90, 95%CI 0.75 to 1.09, p=0.29, I^2 0%, figure 2).

Figure 2: Meta-analysis of low fat diet vs generic healthy diet advice. Outcome: Mortality

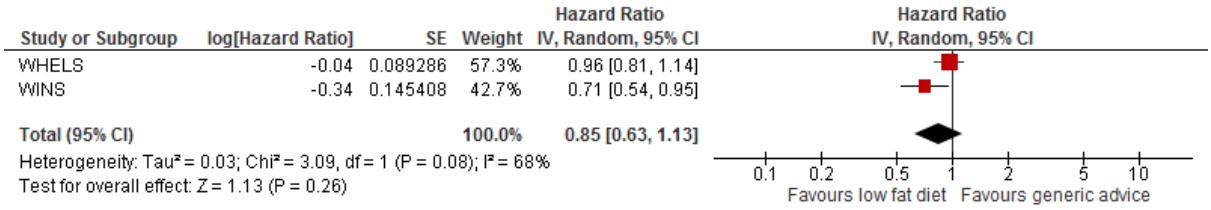


Xing et al. (2013) concluded that post-diagnostic low fat diet may improve breast cancer survival by reducing risk of recurrence. Our re-analysis of the data does not support their conclusions.

Recurrence

Xing et al. (2013) presented a meta-analysis of two large RCTs (n=5525) and reported a statistically significant 33% reduction in the relative risk of recurrence (HR 0.77, 95%CI 0.63 to 0.94, p=0.009, I^2 0%). However there were discrepancies between the effect sizes from the original studies in this meta-analysis and those reported in the original papers, raising concerns about its accuracy. As a result we took the step of conducting our own meta-analysis of the hazard ratios presented in the original papers, using the generic inverse variance method and a random effects model as recommended in the Cochrane Handbook (Higgins et al. 2011). This new analysis found no statistically significant effect of low fat diet on recurrence, with heterogeneity (2 studies, n= 5526, HR 0.85, 95%CI 0.63 to 1.13, p=0.26, I^2 68%, figure 3).

Figure 3: Meta-analysis of low fat diet vs generic healthy diet advice. Outcome: Recurrence



Breast cancer: GRADE summary

Using GRADE we found low quality evidence (downgraded due to unknown limitations of studies and inconsistency) that low fat diet does not reduce the risk of recurrence in people following a diagnosis of breast cancer, and moderate quality evidence (downgraded for limitations of studies) that a low fat diet does not reduce all-cause mortality in this group.

Low Bacterial Diet

MIXED CANCER POPULATION RECEIVING CHEMOTHERAPY

Mixed cancer population receiving chemotherapy: Characteristics of reviews

One Cochrane review (van Dalen et al. 2012) investigated the efficacy of a low bacterial diet (LBD) for preventing the occurrence of infection and infection-related mortality in adults and paediatric cancer patients receiving chemotherapy that was causing episodes of neutropenia. Secondary outcomes of interest were the need for antibiotic therapy and quality of life. This review had an AMSTAR score of 10/11. This review included three RCTs comparing LBD to a control diet, of which 2 were in adults and relevant to this overview. Included patients had various types of haematological malignancies or solid tumours. For all three studies the description of the intervention regimens was described as "scant". One trial (n=153) compared a cooked diet to a raw diet and one study (n=20) compared a LBD to a normal hospital diet. Risk of bias was assessed using the Cochrane risk of bias tool and all studies were at high or unclear risk of bias on a number of criteria.

Mixed cancer population receiving chemotherapy: Outcomes

Mortality

In one study that reported mortality (not specifically infection-related) no difference between cooked and raw food diet was observed (n=153, p=0.36).

The authors concluded that there was insufficient evidence and noted that no evidence for an effect does not necessarily equate to evidence of no effect.

Rate of infection

One study n=153 compared a cooked to a raw diet and found no significant difference in the risk of infection between groups (RR 1.15, 95%CI 0.98 to 1.34, p=0.08).One study compared LBD to a

normal hospital diet (n=20) but did not report infection rates in a useable format. However the study reported no statistically significant difference (p=0.48).

Mixed cancer population receiving chemotherapy: GRADE summary

Using GRADE there is low quality evidence (downgraded for limitations of studies and imprecision) that low bacterial diets do not reduce infection rates and mortality in people with cancer undergoing chemotherapy.

Green tea

LUNG CANCER

Lung cancer: Characteristics of reviews

One review (Fritz et al. 2013) reviewed the evidence for the safety and efficacy of green tea or the treatment and prevention of lung cancer, considering potential interactions with chemotherapy or radiotherapy. This review had an AMSTAR score of 5/11. They identified no RCTs relevant to this overview.

Lung cancer: GRADE summary

There is insufficient (no) evidence relating to the effectiveness or safety of green tea for the treatment of lung cancer.

Soy

BREAST CANCER

Breast cancer: Characteristics of reviews

One review (Fritz et al. 2013) investigated the effectiveness of soy and red clover for reducing the risk of recurrence of breast cancer. Secondary outcomes of interest to this overview were adverse events and hot flushes. This review had an AMSTAR score of 5/11.

This review found 40 RCTs, though many did not investigate outcomes of relevant to this overview or investigated the delivery of specific supplements, rather than manipulation of normal dietary intake. The evidence pertaining to red clover all came from studies of supplements and so was not considered in this overview. The quality of the included studies was assessed using the Newcastle-Ottawa scale. The reporting of this was difficult to interpret for specific studies but overall a number of studies did not clearly use appropriate randomisation and allocation concealment. No RCTs were reported that provided evidence on cancer recurrence. They rated these studies as " moderate" risk of bias".

Breast cancer: Outcomes

Hot flushes

Five trials (combined n not reported) evaluated the use of soy for reducing hot flushes. The comparison groups and number of participants were not clearly reported. All trials found no significant differences.

Adverse events

The most common adverse event was mild to moderate gastro-intestinal (GI) discomfort, though rates were equal between the soy and control groups in all but one study. In that study 47% in the soy group reported GI discomfort compared to 22% in the control group.

The authors concluded that while there is no clear evidence of harm better evidence of safety is required for both soy and red clover and that there is a lack of evidence to support an effect on hot flashes.

Breast cancer: GRADE summary

There is low quality evidence (downgraded for limitations and imprecision) that soy does not reduce hot flashes in women with breast cancer.

Physical Activity/ Exercise Interventions

Mixed exercise intervention reviews

MIXED CANCER POPULATIONS

Mixed Cancer Populations: Characteristics of reviews

15 reviews examined the effectiveness of exercise interventions for people with mixed cancer diagnoses (Bourke et al. 2013, Brown et al. 2012, Chan et al. 2015, Craft et al. 2012, Cramp et al. 2012, Ferrer et al. 2011, Fong et al. 2012, Knols et al. 2010, Loughney et al. 2015, Menses-Echavez et al. 2015a, Mewes et al. 2012, Mishra et al. 2012, Singh et al. 2013, Stene et al. 2013, van Haren et al. 2013). These reviews had varied focus in terms of participants and outcomes and the quality of these reviews varied. Of these review 3 were Cochrane reviews (Bourke et al. 2013, Cramp et al. 2012, Mishra et al. 2012) and scored highly on the AMSTAR scale (10/11, 10/11 and 11/11 respectively).

Bourke et al. (2013) investigated the effectiveness of interventions to promote exercise behaviour in sedentary people living with and beyond cancer and specifically included studies that recruited people regardless of cancer site and stage who were sedentary at baseline. Outcomes of interest were exercise behaviours and adherence, markers of fitness and adverse events.

Bourke et al. (2013) included 14 RCTs with a total of 648 participants. Eight studies prescribed aerobic exercise, and 6 studies prescribed a mix of aerobic and resistance training. 12 of the trials were in people with a diagnosis of breast cancer. Trials variously delivered supervised exercise, home based exercise or a combination of the 2 and contact with exercise professionals or researches ranged from 20 times over 12 weeks to weekly calls after an initial one to one consultation. There was variation in the theoretical model used on the intervention, the level of goal setting and the use of specific behavioural change strategies. Study quality was measured using the Cochrane risk of bias tool. On the 14 RCTs only 3 were considered not to include a high risk of bias and the risks extended beyond the difficulties of blinding patients and therapists.

Chan et al. (2015) reviewed the evidence of interventions to manage the cognitive effects of chemotherapy. This review had an AMSTAR score 8/11 and included 2 trials relevant to this overview, one of yoga (n=20) and one of Speed-feedback therapy with a bicycle ergometer (n=78). Using the Cochrane risk of bias tool, bot trials were at high or unclear risk of bias on more than one criterion.

Cramp et al. (2012) also evaluated the effectiveness of exercise interventions for cancer-related fatigue. Other outcomes included exercise maintenance, time spent exercising, aerobic capacity QoL, anxiety and depression, though meta-analysis was only reported for fatigue. This review included 56 studies with 4068 participants. The risk of bias of the included studies was assessed using the Cochrane risk of bias tool. Included studies were all rated at unclear or high risk of bias across multiple criteria and the risks extended beyond the difficulties of blinding patients and therapists. There was substantial overlap in the scope of these three Cochrane reviews and they shared a large number of the same included trials. A review by Ferrer et al. (2011) (AMSTAR score 7/11) used moderator analysis explored possible predictors of intervention success of HR-QoL.

Fong et al. (2012) investigated the effectiveness of physical activity interventions on a range of outcomes. This review included 36 studies (total number of participants not reported) and had an AMSTAR score of 7/11.

Knols et al.(2010) reviewed whether physical activity interventions increased daily walking activity in cancer survivors. This review had an AMSTAR score of 6/11 and included 5 RCTs with a very heterogeneous range of interventions that included endurance training, individual exercise at a health club, walking programmes, supervised and home exercise, telephone counselling, pedometers and leaflets promoting physical activity. Five studies were included with 660 participants. Study quality was assessed using the PEDro scale and studies score between 7 and 9 out of a possible 11.

Menese-Echavez et al. (2015a) reviewed the evidence for supervised exercise for cancer related fatigue. This review included people with any cancer diagnosis at any stage. This review had an AMSTAR score of 9/11 and included 11 trials with 1530participants and included many of the same trials. This review similarly found statistically significant benefits of exercise on fatigue, though in their subgroup analysis the effect was statistically significant for interventions that combined aerobic and resistance training but not for resistance training only or aerobic training only. However the aerobic training subgroup demonstrated very high heterogeneity (I^2=100%).

Mewes et al. (2012) reviewed the effectiveness of multidimensional cancer survivor rehabilitation. The AMSTAR score for this review was 4/11. They included 5 RCTs relevant to this overview with 647 participants, in which at least one intervention arm included an exercise component. Interventions also commonly included some form of psychological therapy or self-help education and some were delivered in an in-patient setting. The quality of the included studies was assessed using the Cochrane risk of bias tool and all relevant studies were rated at unclear or high risk of bias on multiple domains.

Mishra et al. (2012) evaluated the effectiveness of exercise interventions on HRQoL, and symptoms among adult cancer survivors after -cancer treatment (any type of cancer of cancer treatment). They included 40 studies of which 38 were RCTs and 2 were quasi-randomised trials. These studies included a total of 1764 participants and compared exercise with usual care or other non-exercise interventions. Exercise modalities include aerobic exercise, resistance exercise, mixed aerobic and resistance interventions, yoga, qigong and tai chi. Interventions ranged from 3 weeks to 1 year in duration, with variations in setting, frequency of contact with the exercise professional, number of sessions and the type of professional delivering the intervention. The risk of bias of the included studies was assessed using the Cochrane risk of bias tool. All trials were rated at unclear or high risk of bias across multiple criteria and the risks extended beyond the difficulties of blinding patients and therapists.

2 reviews (Craft et al. 2012, Brown et al. 2012) also reviewed the evidence for the effectiveness of that exercise for reducing depressive symptoms on people with cancer. Both reviews had an AMSTAR score of 7/11. Both review used the PEDro quality scale to assess study quality and concluded that quality was good overall. Brown et al. included 37 RCTs including 2929 participants, Craft et al. included 15 studies due to more stringent inclusion criteria. Both review identified small, statistically significant improvements in depression scores post-intervention in the exercise group with heterogeneity.

Stene et al. (2013) investigated the effectiveness of exercise interventions for improving muscle strength in people with cancer who were about to commence or currently undergoing active cancer treatment. This review had an AMSTAR score of 7/11. Quality assessment of the included studies was done using a tool similar to the Cochrane risk of bias tool. The review included 16 studies (number of participants 1377). A substantial number of these either did not describe the method of randomisation, report allocation concealment or blinding of the outcome assessors, and other biases were also common.

Mixed Cancer Populations: Outcomes

Adherence and exercise behaviour

In the review by Bourke et al. (2013) none of the included trials reported that ≥75% of participants in the intervention group met guideline levels of aerobic exercise at any given follow up and only three trials reported adherence of 75% or more to the prescribed exercise. These three studies were noted to share the following features: programming of a set goal, prompting generalisation of a target behaviour, prompting self-monitoring of behaviour, prompting practice. It should be noted that from

these data one cannot conclude with confidence that these features were responsible for the higher rates of adherence in these studies as there were no trials comparing different features of behaviour change interventions.

In the review by Cramp et al. (2012) exercise maintenance at follow up and time spent exercising were rarely reported and what data were available came from a small number of participants. No summary results were reported in this review.

For daily walking, 2 out of 5 studies found statistically significant increases in step counts. Meta-analysis of 3 studies (all in participants with breast cancer diagnoses) demonstrated a SMD of 0.4 (95%CI: 0.0 to 0.7, I = 79%). Heterogeneity was substantial and the lower confidence interval met the line of no effect suggesting imprecision. The mean change in daily step activity was 1099 steps daily, with a range from 1087 to 3182 steps. Knols et al. (2010) concluded that combined physical activity improved daily step count and that included studies were of good quality.

Anxiety

Mishra et al.(2012) reported small statistically significant improvements in anxiety in the short term (4 studies, 455 participants, SMD 0.26, 95% CI -0.44 to -0.07, I^2 0%) but not at medium or long term follow up.

Body Weight and composition

Fong et al. (2012) found that physical activity resulted in small reductions in BMI score compared to control conditions (no. of studies and participants not reported, mean difference -0.4, 95%CI -0.6 to -0.2) and in body weight (no. of studies and participants not reported, mean difference -1.1kg, 95%CI -1.6 to -0.6), though heterogeneity for these comparisons was not reported.

Cognitive effects of chemotherapy

Chan et al. (2015) reported that a trial of speed feedback therapy found a statistically significant improvement in executive and motor function in favour of the intervention (frontal assessment battery, mean difference -2.50, 95%CI -4.56 to -0.44). In the study of yoga a reduction of cognitive disorganisation (as measured by the Profile of Mood State [POMS] Concentration subscale) was found in favour of the yoga group (mean difference=-2.50, 95% CI, -4.56 to-0.44). Chan et al. (2015) concluded that physical activity interventions appear promising, but additional studies were required to establish their efficacy.

Depression

Mishra et al. (2012) reported statistically significant improvements in depression scores in the short term (12 studies, 707 participants, SMD -0.41, 95%CI -0.65 to -0.17, I^2 53%) but not at later follow-up time points.

In subgroup analyses Craft et al. (2012) reported larger effects in supervised exercise interventions and no benefit of unsupervised exercise. They also reported that longer duration exercise bouts (>30 mins) had larger effects than shorter bouts (<30 mins). In their subgroup analyses Brown et al. (2012) reported that the weekly volume of aerobic exercise reduced depression in a dose dependent fashion and that supervised sessions were more effective.

Exercise Tolerance

In the review by Bourke et al. (2013), meta-analysis demonstrated statistically significant increases in exercise tolerance (7 studies, 330 participants, SMD 0.73, 95%CI 0.51 to 0.95, I^2 0%) at short term follow-up. This finding was robust to a sensitivity analysis where studies at high risk of bias were removed. Significant increases in exercise tolerance were also found at 6 month follow-up (5 studies, 271 participants, SMD 0.70, 95%ci 0.45 to 0.94, I^2 0%). Bourke et al. (2013) concluded that interventions to promote exercise in cancer survivors who report better levels of adherence share some common behaviour change techniques.

Fong et al. (2012) found that physical activity was associated with significantly increased peak oxygen consumption (2.2 mL/kg/min, 95% 1.0 to 3.4, P<0.01), peak power output (21.0 W, 95%CI 13.0 to 29.1; p<0.01), and the distance walked in six minutes (29 m, 95%CI 4 to 55; p=0.03). They concluded that physical activity interventions are associated with improvements in these "physical functions".

Fatigue

Mishra et al. (2012) reported statistically significant improvements in fatigue scores in the short term (18 studies, 994 participants, SMD -0.30, 95%CI -0.46 to -0.14, I^2 33%) but not at later follow-up time points.

Cramp et al. (2012) also reported statistically significant improvements in fatigue. At the end of the intervention period exercise was statistically more effective than the control (32 studies, 2646 participants (SMD -0.27, 95%CI -0.37 to -0.17, I^2 33%). This effect was observed in participants during cancer treatment and following cancer treatment. No meta-analysis was conducted for long term outcomes in this review but a narrative synthesis reported that the majority of studies that reported longer term outcomes did not report significant benefits. Pre-planned subgroup analysis by exercise type found statistically significant effects with aerobic exercise but not with resistance or mind-body (Yoga, Tai Chi, Qigong) forms of exercise. Subgroup analysis by cancer type found statistically significant effects in breast cancer populations and prostate cancer populations but not in those with haematological malignancies.

Quality of life

Mishra et al.(2012) found statistically significant benefits in QoL in the short term ≤3 months (16 studies, 760 participants SMD 0.49, 95% CI 0.24 to 0.74, with heterogeneity I^2 62%); not in the medium term (between 3 and 6 months) (5 studies, 353 participants SMD 0.11, 95% CI -0.10 to 0.43, I^2=0%) or longer term follow up >6 months (2 studies, 115 participants, SMD 0.25, 95%CI -0.12 to 0.62, I^2= 0%). Subgroup analysis found that the short term effect was present in studies where the exercise was reported as moderate to vigorous but not when the exercise was mild or moderate.

Fong et al (2012) also found statistically significant positive effects on quality of life in the short term. In their moderation analysis, Ferrer et al. (2014) found that exercise intensity and the length of the intervention were positively correlated to effect size. Smaller studies were also associated with larger effects.

Mewes et al. (2012) did not conduct a meta-analysis but reported that effect of QoL varied substantially between studies with 3 out of 5 demonstrating statistically significant improvements. They report that short term effects were often not sustained at longer term follow up.

Muscle strength

No meta-analysis was presented by Stene et al. (2013) for this outcome but narrative synthesis of trials reported that aerobic exercise, resistance exercise and combined resistance and aerobic exercise interventions led to statistically significant improvements in muscle strength compared to usual care, with some indication that resistance exercise was superior to aerobic exercise.

Physical function

Mishra et al. (2012) reported statistically significant improvements in physical function the short term with heterogeneity (15 studies, 878 participants SMD 0.42, 95% CI 0.20 to 0.64, I^2 70%).

Cramp et al. (2012) concluded that aerobic exercise can be regarded as beneficial for individuals with cancer-related fatigue during and post-cancer therapy, specifically those with solid tumours.

Mixed Cancer Populations: GRADE summary

There is moderate quality evidence (downgraded for imprecision) that combined physical activity interventions may improve daily step count.

There is moderate quality evidence (downgraded for limitations) that interventions to promote exercise interventions improve aerobic capacity in people living with and beyond cancer. Adherence appears to be problematic and there is very low quality evidence that specific goal setting and monitoring strategies may facilitate better adherence (non-randomised data, downgraded for limitations).

There is moderate quality evidence (downgraded for limitations) that that exercise interventions improve anxiety and fatigue in people following cancer treatment in the short term, but that these effects are not sustained in the longer term. The evidence relating to fatigue is stronger for aerobic exercise than other forms of exercise. There is very low quality evidence (downgraded for limitations of studies, inconsistency and imprecision, as single study, that yoga or speed feedback training using a cycle ergometer may have a positive influence on the cognitive effects of chemotherapy.

There is low quality evidence (downgraded for limitations and inconsistency) that exercise interventions improve quality of life, depression, exercise tolerance, and physical function, in the short term in people with any cancer diagnosis, but that these effects may not be sustained in the longer term.

There is low quality evidence (downgraded for limitations and inconsistency) that that exercise interventions improve muscle strength and result in small reductions in body weight and BMI in people following cancer treatment.

PRE-SURGICAL CANCER PATIENTS

Pre-surgical cancer patients: Characteristics of reviews

Singh et al. (2013) reviewed the evidence for pre-surgical exercise for cancer patients about to undergo surgery for their cancer treatment. Outcomes of interest were walking capacity and cardiorespiratory fitness, quality of life, rate of return to continence and length of hospital stay. This review had an AMSTAR score of 5/11 included 9 RCTs with 710 participants. Quality assessment was measured using a modified Delphi list and all studies failed to report or did not meet a number of the quality criteria. No meta-analysis was conducted. Interventions include d-pelvic floor training for prostate surgery candidates, aerobic exercise interventions, resistance exercise interventions, breathing exercises prior to lung cancer surgery.

However results from RCTs were not presented separately from other study designs and it was not clear where results were reported that they were based on between group comparisons so no results relevant to this review were extractable.

CANCER PATIENTS CURRENTLY UNDERGOING TREATMENT FOLLOWING SURGERY

Cancer patients currently undergoing treatment following surgery: Characteristics of reviews

Loughney et al. (2015) reviewed the evidence relating to exercise interventions in people currently undergoing adjuvant treatment following surgery and included a broad range of intervention types and outcomes from randomised and non-randomised studies. The AMSTAR score for this review was 4/11. Methodological Quality was measured using the Downs and Black Scale. Of 11 included RCTs with 1092 participants, quality scores ranged from 20 to 24 out of 28.

No meta-analysis was conducted and the narrative reporting of the results in this review was unclear. It was not clear whether the description of results was referring to within-group or between-group comparisons, which makes the results difficult to interpret accurately.

Loughney et al. (2015) concluded that exercise training was safe and feasible in people undergoing adjuvant cancer treatment post–surgery and that it may improve physical fitness, quality of life and fatigue, though not all findings were statistically significant.

Cancer patient currently undergoing treatment following surgery: GRADE summary

The lack of clarity in the reporting of results in this review precluded GRADE assessment.

CANCER PATIENTS UNDERGOING HAEMATOPOIETIC STEM CELL TRANSPLANTATION

Cancer patients undergoing haematopoietic stem cell transplantation: Characteristics of reviews

Van Haren et al. (2013) reviewed the effectiveness of exercise interventions administered before, during and after haematopoietic stem cell transplantation (HSCT) for QoL, psychological well-being, fatigue and physical function. The AMSTAR score for this review was 6/11.

They included 11 RCTs with 734 participants in total and included any intervention where physical exercise was the main component. Six studies implemented the exercise programme during hospital admission, 3 implemented it prior to admission and 3 implemented after hospital discharge. Interventions included combined endurance and resistance exercise (6 studies), endurance training only (1 study), endurance training with activities of daily living training (1 study), endurance training with range of movement training, dynamic exercises and psychological education (1 study) resistance training only (1 study), and one study of bed exercises with relaxation techniques and breathing exercises. Interventions ranged from 4 weeks to 6 months in duration. Control groups included usual care, no exercise, range of movement exercise or being instructed to exercise at home. The Cochrane risk of bias tool was used and all but one of the included studies was rated at high or unclear risk of bias on more than one criteria.

Cancer patients undergoing haematopoietic stem cell transplantation: Outcomes

Fatigue

Meta-analysis of two studies found a statistically significant improvement in fatigue at discharge in the intervention group (n=115, SMD 0.53, 95%CI 0.16 to 0.91, p=0.005, I^2 0%). Of four studies not included in the meta-analysis two found a statistically significant effect on fatigue in favour of the intervention group and 2 did not.

Physical functioning

Physical function was variously measured as muscle strength or aerobic fitness. Due to heterogeneity in outcomes and intervention characteristics no meta-analysis was conducted. Of eight studies measuring strength, 5 showed statistically significant improvements in favour of the intervention group. Of 9 studies measuring aerobic fitness, 5 showed statistically significant improvements in favour of the intervention group.

Psychological well-being and distress

Two studies measured anxiety and depression using the 0-21 Hospital Anxiety and Depression scale (HADS) and included aerobic and resistance training during hospitalisation. Meta-analysis of these studies demonstrated no significant difference in anxiety, but with substantial heterogeneity (n=113, mean difference -1.05, 95%CI -3.67 TO 1.56, p=0.43, I^2 80%) and no significant difference in depression with less heterogeneity (n=115, mean difference -1.11, 95%CI -2.37 to 0.14, p=0.06, I^2 38%).

Of 2 studies not included in the meta-analysis one study found no difference in measures of psychological well-being and one found a statistically significant improvement in favour of the intervention group at both discharge and follow up.

Quality of Life

Meta-analysis of 3 studies that delivered their intervention during or immediately after hospitalisation (n=148) found that at the point of discharge from hospital, QoL was statistically significantly higher in the intervention group (EORTC QLQ-C30 0-100 scale, mean difference 8.73, 95%CI 3.13 to 14.31, p=0.02) with no heterogeneity.

In 2 of these studies that followed participants up at 3 and 6 months post-intervention one showed no difference in quality of life between groups and one found a statistically significant improvement in favour of the intervention group. No effect sizes were reported for these comparisons.

Of the 2 studies that were not entered into the meta-analysis one found no difference in quality of life between groups and one found a statistically significant improvement in favour of the intervention group at the post-intervention follow up.

Van Halen et al. (2013) concluded that physical exercise in aerobic or resistance training was feasible and beneficial in patients undergoing an HSCT.

Cancer patients undergoing haematopoietic stem cell transplantation: GRADE summary

There is low quality evidence (downgraded for limitations and inconsistency) that exercise interventions may have short –term positive effects on quality of life, fatigue and aspects of physical function. It is not clear whether these benefits are sustained in the longer term.

There is very low quality evidence (downgraded for limitations, inconsistency and imprecision) that exercise interventions do not affect psychological well-being.

BREAST CANCER

Ten reviews (Bluethmann et al. 2015, Carayol et al. 2015, Chung et al. 2013, McNeely et al. 2010, Meneses-Echavez et al. 2015b, Short et al. 2013, Spark et al. 2013, Stuiver et al. 2015, Tatham et al. 2013, Zeng et al. 2014) specifically evaluated the evidence for exercise programmes in people with breast cancer.

BREAST CANCER PATIENTS: ANY STAGE

Breast cancer patients - any stage: Characteristics of reviews

Meneses-Echavez (2015b) reviewed supervised exercise interventions for cancer-related fatigue in breast cancer survivors at any stage of the disease. This review had an AMSTAR score of 9/11 and included 8 RCTs with 1156 participants. All interventions included aerobic exercise and 6 also included resistance training and stretching exercises. The average (mean) duration of the

intervention was 21.4 weeks (SD15.8) and intensity varied considerable, from 50 to 80% maximal heart rate. The methodological quality of the included studies was measured using the PEDro scale. The mean score was 6.33, which Meneses-Echavez et al. (2015b) interpreted as implying consistent quality and low risk of most biases. However 5 studies did not report concealed allocation, 4 studies did blind outcome assessors and 4 studies did not report intention to treat analyses. As such there were multiple risks of bias present. Analyses were based on post intervention outcomes.

Breast cancer patients - any stage: Outcomes

Adverse events

No major adverse effects were reported among studies and minor adverse events were not consistently higher in the exercise intervention groups.

BMI

Meta-analysis (number of trials and participants not reported) found no statistically significant effect on BMI without heterogeneity (SMD -0.14, 95%CI -0.38 to 0.11, p=0.28, I^2 0%).

Depression

Meta-analysis (number of trials and participants not reported) found no statistically significant effect of exercise interventions on depression with heterogeneity (SMD -0.23, 95%CI -0.55 to 0.09, p=0.16 I2 stat).

Fatigue

Meta-analysis of 9 trials (n=1156) found that exercise was statistically significantly more effective than conventional care in improving cancer related fatigue among breast cancer survivors, with heterogeneity (SMD= −0.51, 95%CI −0.81 to −0.21, I^2 75%). Subgroup analysis of studies that included a resistance component remained statistically significant but the effect of this on heterogeneity was not reported masking it difficult to interpret. There was some evidence of publication bias.

Physical Activity levels

Meta-analysis (number of trials and participants not reported) found no statistically significant effect on physical activity levels, with heterogeneity (SMD 1.10, 95%CI -0.41 to 2.62, p=0.15, I^2 85%)

Quality of Life

Meta-analysis (number of trials and participants not reported) found statistically significant effects in favour of exercise interventions on physical wellbeing (SMD 0.63, 95%CI 0.08 to 1.18, p=0.02, I^2 89%) and functional wellbeing subscales (SMD 0.60, 95%CI 0.08 to 1.11, p=0.02, I^2 89%) with heterogeneity, but not on social or emotional wellbeing subscales.

Menseses-Echavez et al. (2015b) concluded that high volume exercises were safe and effective in improving cancer related fatigue.

Breast cancer patients - any stage: GRADE summary

There is low quality evidence (downgraded for limitations of studies and possible publication bias) that exercise interventions improve cancer related fatigue and components of QoL. There is low quality evidence (downgraded for limitations of studies and inconsistency) that exercise interventions do not lower BMI or improve physical activity levels or improve depression in the broader breast cancer population.

BREAST CANCER PATIENTS UNDERGOING ADJUVANT TREATMENT

Breast cancer patients undergoing adjuvant treatment: Characteristics of reviews

Carayol et al. (2015) specifically reviewed the evidence for exercise interventions delivered during adjuvant therapy (chemotherapy or radiotherapy) for breast cancer compared to usual care or attention controls. This review had an AMSTAR score of 6/11 and included 36 RCTs with a total of 2723 participants with non-metastatic breast cancer. Intervention duration ranged from 5 to 34 weeks but no further details were reported. Study quality was assessed using the PEDro scale. The median quality score was 7/10 with a minority of studies blinding outcome assessors and less than half reporting concealed allocation or intention to treat analysis.

Breast cancer patients undergoing adjuvant treatment: Outcomes

Anxiety

Meta-analysis of 21 studies (number of participants not reported) demonstrated a statistically significant benefit of exercise on anxiety with heterogeneity (SMD 0.16, 95%CI 0.04 to 0.28, I^2 87%) (Carayol et al. 2015)

Depression

Meta-analysis of 21 studies (number of participants not reported) demonstrated a statistically significant benefit of exercise on depression with heterogeneity (SMD 0.12, 95%CI 0.08 to 0.33, I^2 58%) (Carayol et al. 2015)

Fatigue

Meta-analysis of 21 studies (number of participants not reported) demonstrated a statistically significant benefit of exercise on fatigue with heterogeneity (SMD 0.17 (0.08 to 0.25, I^2 50%) (Carayol et al. 2015).

Quality of life

Meta-analysis of 21 studies (number of participants not reported) demonstrated a statistically significant benefit of exercise on QoL with heterogeneity (SMD 0.16, 95%CI 0.05 to 0.28, I^2 76%) (Carayol et al. 2015)

Moderators of effect

Meta-regression models were used to examine a number of potential moderators of effect size. The effect of exercise on fatigue was negatively associated with the number of patients receiving chemotherapy. Shorter exercise interventions or lower dose exercises were associated with greater improvements in fatigue, anxiety and depression. Yoga, Tai Chi and Qigong interventions delivered larger effect sizes for anxiety and fatigue than aerobic and/or resistance interventions. However, importantly, studies that reported intention to treat analyses and low attrition rates showed no effect of exercise on anxiety or depression. There was some evidence of publication bias.

Carayol et al. (2015) concluded that exercise interventions may improve fatigue, QoL, anxiety and depression but that the evidence relied largely on studies prone to methodological biases.

Breast cancer patients undergoing adjuvant treatment: GRADE summary

There is low quality evidence (downgraded for limitations of studies, inconsistency and possible publication bias) that exercise interventions may improve fatigue, QoL, anxiety and depression in people undergoing chemotherapy or radiotherapy for breast cancer.

BREAST CANCER PATIENTS POST-TREATMENT

Breast cancer patients post-treatment: Characteristics of reviews

Bluethmann et al. (2015) and Short et al. (2013) reviewed the evidence that physical activity and behaviour change interventions increase physical activity behaviour in people with breast cancer in the post-treatment period. Bluethmann et al. (2015) included 14 RCTs with 2140 participants and a broad range of interventions. This review had an AMSTAR score of 7/11. Short et al. (2013) included 10 trials of 1299 participants, again with a broad range of exercise interventions. Bluethmann et al. (2015) used a CONSORT checklist to assess study quality and Short et al. (2013) used the McMaster quality assessment tool. Bluethmann et al. (2015) reported that most studies achieved 80% or more of the quality criteria but there was variation in the transparency of reporting for a number of features. Short et al. (2013) rated only 2 studies as providing strong evidence, 5 studies as “moderate” and three studies as providing ”weak” evidence.

Three reviews (Chung et al. 2013, McNeely et al. 2010, Stuiver et al.2015) investigated the effectiveness and safety of exercise interventions for upper limb lymphoedema following breast cancer treatment. Stuiver et al. (2015 conducted a Cochrane review of conservative interventions for preventing clinically detectable upper limb lymphoedema. This review had an AMSTAR score of 10/11 and included 5 studies of exercise interventions. Of these two evaluated the safety of progressive resistance exercise and 3 compared early versus late commencement of shoulder mobility exercise after breast cancer surgery. Risk of bias in the included studies was assessed using the Cochrane risk of bias tool and all studies were at high or unclear risk of bias across multiple criteria.

McNeely et al. (2010) conducted a Cochrane review (AMSTAR score 10/11) of exercise interventions to prevent, minimise or improve upper limb dysfunction due to breast cancer treatment. They included 24 studies with 2132 participants in total. Interventions included range of motion and stretching exercises, yoga, tai chi and resistance exercises. Risk of bias was assessed using a 6 point scale and the majority of studies were at risk of bias on multiple criteria. They also found no statistically significant effect of early vs delayed exercise, or exercise compared to no exercise on lymphoedema, though these comparisons were based on a small number of trials.

Chung et al. (2013) also reviewed the evidence of the effect of exercise on upper limb lymphoedema following breast cancer treatment. This review had an AMSTAR score of 6/11 and included 8 RCTs with 603 participants. Study quality was assessed using the SIGN checklist. Chung et al. (2013) concluded that most studies "tried well to minimise bias". Narrative synthesis of the included studies found no impact of exercise in lymphoedema.

Tatham et al. (2013) reviewed the efficacy of exercise therapy for reducing shoulder pain related to breast cancer treatment. This review had an AMSTAR score of 7/11 and included 4 RCTs with 377 patients/ Study quality was assessed using the PEDro scale. Interventions included range of motion/ stretching exercises with or without resistance exercise and / or manual therapy. All but one study was at risk of bias for multiple criteria

Zeng et al. (2014a) reviewed the effectiveness of exercise interventions for improving quality of life in people who had completed active treatment for breast cancer. This review had an AMSTAR score of 7/11 and identified 25 trials that included a total of 2926 participants. Study quality was assessed using the Cochrane risk of bias tool and most studies had a high risk of bias with limitations common across multiple criteria. Interventions include aerobic, combined aerobic and resistance, combined aerobic and anaerobic, resistance training, resistance training and stretching, yoga and tai chi. Duration of the interventions ranged from 4 to 52 weeks and frequency varied from 1 to 5 times per week.

Breast cancer patients post-treatment: Outcomes

Quality of Life

Zeng et al conducted a number of meta-analysis of QoL. Meta-analysis of global quality of life found statistically significant positive effects with heterogeneity (6 studies, n=373, SMD 0.70, 95%ci 0.21 to 1.19, p=0.005, I^2 78%)

Meta-analysis of cancer specific QoL scale also found statistically significant positive effects with heterogeneity (10 studies, n=1037 participants, SMD 0.38, 95%CI 0.03 to 0.74, p=0.04, I^2 84%).

Meta-analysis of the FACT-B breast cancer-specific QoL scale also found statistically significant positive effects with heterogeneity (6 studies, 388, mean difference 5.72, 95%CI 1.98 to 9.46, p=0.003, I^2 89%). Zeng et al. (2015) concluded that exercise interventions had positive effects on quality of life.

Physical activity behaviour

Bluethmann et al. (2015) conducted a meta-analysis pooling post intervention mean minutes of moderate to vigorous physical activity (MVPA) with mean MET hours per week and found a statistically significant effect in favour of the interventions with heterogeneity (14 studies, n for comparison not reported, SMD 0.46, 95%ci 0.25 to 0.67, I^2 76%).

Short et al. (2013) conducted a narrative synthesis of included studies. They found significant effects of self-reported physical activity in eight out of 10 studies post intervention. Of 5 studies that reported in the longer term three reported maintenance of this effect.

Bluethmann et al. (2015) concluded that most interventions were effective at producing short term increases in physical activity behaviours. Short et al. (2013) concluded that behavioural physical activity interventions hold promise in effectively changing physical activity behaviour.

Upper limb lymphoedema

Meta-analysis of early versus late onset of shoulder mobility exercises on the occurrence of lymphoedema (Stuiver et al. 2015, 3 studies, n=278) found no statistically significant difference (RR 1.69, 95%ci 0.94 to 3.01), P=0.08, I^2 19%).

Meta-analysis of resistance exercise compared to no exercise found no statistically significant difference in lymphoedema occurrence (Stuiver et al. 2015,2 studies, n=351, RR 0.58, 95%CI 0.30 to 1.13, I^2 0%).

Stuiver et al. (2015) and McNeely et al. (2010) concluded that early exercise and progressive resistance exercise did not seem to present a higher risk of lymphoedema following breast cancer treatment but that the results should be interpreted with caution.

Upper limb pain

No meta-analysis was conducted. In a narrative summary all of the trials found statistically significant benefits on pain in favour of the exercise intervention. Effect sizes with precision estimates were not reported.

Tatham et al. (2013) concluded that exercise targeting shoulder pain related to breast cancer treatment may be effective but that definitive conclusions could not be drawn due to the lack of methodological quality and homogeneity of the studies included.

Breast cancer patients post-treatment: GRADE summary

There is low quality evidence (downgraded for limitations of studies and inconsistency) that physical activity and behaviour change interventions can improve physical activity behaviour in people with breast cancer after active cancer treatment.

There is low quality evidence (downgraded for limitations of studies and inconsistency) that exercise interventions may improve quality of life in people with breast cancer after active cancer treatment.

There is low quality evidence (downgraded for limitations and imprecision) that exercise interventions do not affect the occurrence of lymphoedema in breast cancer patients following treatment.

There is low quality evidence (downgraded for limitations of studies and imprecision) that exercise interventions may improve shoulder pain after breast cancer treatment.

COLORECTAL CANCER

Colorectal cancer: Characteristics of reviews

One review (Cramer et al. 2014) reviewed the evidence for the effectiveness of exercise interventions in colorectal cancer patients at any stage of the disease. Outcomes of interest were QoL, fatigue and physical fitness. This review had an AMSTAR score of 5/11.The review included 5 RCTs with a total of 238 participants. All had completed cancer treatment prior to the start of the study.

Two RCTS compared 14 day supervised exercise programmes including moderate intensity cycling to low intensity cycling. Two RCTs compared home-based mixed exercise programmes to usual care and one RCT compared aerobic exercise and dietary advice to usual nurse-led care. The quality of included studies was assessed using the Cochrane risk of bias tool. Three were rated as having a low risk of bias and 2 as having a high risk of bias. However inspection of the risk of bias assessment revealed that all studies were at unclear risk of bias across multiple criteria.

Colorectal cancer: Outcomes

Fatigue

Meta-analysis of 3 studies (n=157) found no statistically significant difference between the intervention and control groups for fatigue (SMD 0.18, 95%CI-0.22 to 0.59, p=0.38, I^2 27%).

Physical fitness

Meta-analysis of 3 studies (n=157) found a statistically significant difference in physical fitness (measured using different treadmill protocols across studies) in favour of the intervention group (SMD 0.59, 95%CI 0.25 to 0.93, p=0.0006, I^2 0%).

Quality of life

Meta-analysis of 3 RCTs (n=157) found no statistically significant difference between the intervention and control groups, with heterogeneity (SMD 0.18, 95%CI -0.39 to 0.76, p=0.53, I^2 59%).

Cramer et al. (2014) concluded that exercise interventions were effective for improving physical fitness but that there was no evidence of effectiveness on quality of life or fatigue.

Colorectal cancer: GRADE summary

There is moderate quality evidence (downgraded for limitations of studies) that exercise interventions post-cancer treatment improve physical fitness in people with colorectal cancer.

There is low quality evidence (downgraded for limitations of studies and inconsistency) that exercise interventions do not produce positive effects on quality of life or fatigue in people with colorectal cancer, following cancer treatment.

HAEMATOLOGICAL CANCERS

MIXED HAEMATOLOGICAL CANCERS

Mixed haematological cancers: Characteristics of reviews

Three reviews (Persoon et al. 2013, Smith-Turchyn et al. 2015, Wolin et al. 2010) specifically reviewed the evidence for the effectiveness of exercise interventions for people with haematological cancers. Wolin et al (2010) reviewed the evidence with any haematological diagnosis at any stage. This review had an AMSTAR score of 2/11. They included 10 RCTs in adults (number of participants not reported). Study quality was measured using an 8 point scale. The quality score ranged from 1 to 7 out of 8, with a median of 4/8.

Mixed haematological cancers: Outcomes

Mixed

Wolin et al. (2010 did not conduct a meta-analysis and the results of individual trials were reported descriptively with details of only selected studies given and no effect sizes reported. The authors concluded that there was strong evidence for a benefit of exercise on body composition and weak but promising evidence for fitness, fatigue, muscle strength, physical function and QoL. However these conclusions were based on both randomised and non-randomised studies.

Mixed haematological cancers: GRADE summary

Due the approach taken to the reporting of this review it is difficult to apply GRADE to these findings.

ACUTE MYELOID LEUKAEMIA

Acute myeloid leukaemia: Characteristics of reviews

Smith-Turchyn et al. 2015 reviewed the evidence for the effectiveness of exercise interventions for individuals with acute myeloid leukaemia. This review had an AMSTAR score of 5/11. Two RCTs were included, with a total of 62 participants all with acute myeloid leukaemia. Risk of bias in these studies was assessed using the Cochrane risk of bias tool. Both studies were rated at high risk of bias

across multiple criteria. One RCT (n=38) compared a 12 week programme of aerobic, strength and flexibility training delivered face to face with a concurrent home exercise programme to usual care in people who had completed intensive chemotherapy or stem cell transplantation and were in complete remission. One RCT (n=24) compared a 3 week aerobic exercise walking programme to routine care in in-patients currently undergoing chemotherapy.

Acute myeloid leukaemia: Outcomes

Fatigue

One study (n=28) found statistically significant improvements in measures of fatigue in favour of exercise at the end of the intervention (effect size not reported). The other study (n=38) did not find statistically significant differences between exercise and routine care.

Physical functioning

One study (n=28) found statistically significant improvements in the 12 minute walk test in favour of exercise at the end of the intervention (effect size not reported). The other study (n=38) did not find statistically significant differences between exercise and routine care.

Psychological distress

Both trials found no statistically significant difference in measures of psychological wellbeing at the end of the intervention.

Quality of life

One study (n=38) found no significant difference in quality of life (effect size not reported).

Smith-Turchyn et al. (2015) concluded that exercise appeared safe and feasible in acute myeloid leukaemia but that the evidence for its effectiveness was inconclusive.

Acute myeloid leukaemia: GRADE summary

Using GRADE there is low quality evidence (downgraded for limitations of studies and imprecision) that exercise interventions do not improve measures of psychological wellbeing or quality of life in people with myeloid leulkaemia. The evidence for an effect on physical functioning is limited and conflicting.

HAEMATOLOGICAL CANCER FOLLOWING STEM CELL TRANSPLANTATION

Haematological cancer following stem cell transplantation: Characteristics of reviews

Persoon et al. (2013) reviewed the evidence in people treated with stem-cell transplantation for haematological malignancy. This review had an AMSTAR score of 6/11. They included 8 RCTs with a total of 472 participants. Risk of bias was assessed using the Cochrane risk of bias tool. All studies were at high or unclear risk of bias across multiple criteria.

Interventions were predominantly supervised, six studies delivered a mix of aerobic and resistance training or aerobic and ADL training, one delivered resistance training alone and one delivered aerobic training alone. The duration of interventions ranged from 4 weeks to 6 months with the number of sessions varying from 2 to 10 per week. The control groups were usual care, with some of those being given some advice to remain active.

Haematological cancer following stem cell transplantation: Outcomes

Cardiorespiratory fitness

Meta-analysis of 6 studies using various measures of cardiorespiratory fitness (n=237) found a statistically significant increase in physical fitness with heterogeneity in favour of the exercise intervention (SMD 0.53, 95%ci 0.13 to 0.94, p=0,009, I^2 64%).

Fatigue

Meta-analysis of 4 studies (n=238) found a statistically significant effect in favour of the intervention group (SMD 0.53, 95%CI 0.27 to 0.79, P<0.0001 I^2 0%).

Muscle strength

Meta-analysis of 6 studies (n=312), using various measures of lower limb muscle strength found a statistically significant increase in muscle strength favouring the exercise group, with heterogeneity (SMD 0.56, 95%CI 0.18 to 0.94, p=0.004, I^2 57%). Meta-analysis of 5 studies (n=263) using various measures of upper limb muscle strength found a statistically significant increase in muscle strength favouring the exercise group (SMD 0.32, 95%CI 0.08 to 0.57, p=0.01 I^2 0%).

Quality of Life

Meta-analysis of global quality of life scores found a statistically significant effect in favour of the intervention (5 studies, 294 participants, SMD 0.41, 95%CI 0.18 to 0.64, p=0.0005, I^2 0%). These effects were seen across all QoL subscales except role functioning and social functioning.

Persoon et al. (2013) concluded that exercise had benefits for people with haematological cancers treated with stem cell transplantation.

Haematological cancer following stem cell transplantation: GRADE summary

There is moderate quality evidence (downgraded for limitations of studies) that exercise interventions can lead to improvements in upper limb muscle strength, QoL and fatigue in people treated with stem-cell transplantation for haematological malignancy. There is low quality evidence (downgraded for limitations of studies and inconsistency) that exercise interventions can improve lower limb muscle strength and cardiorespiratory fitness.

HEAD AND NECK CANCERS

Head and neck cancers: Characteristics of reviews

One Cochrane review (Carvalho et al. 2012) evaluated the effectiveness of exercise interventions for reducing shoulder dysfunction in patients with head and neck cancer. This review had an AMSTAR score of 9/11 and included 3 RCTs with 104 participants with a clinical and histological diagnosis of head and neck cancer who had received surgery. 2 RCTs compared progressive resistance training to standard physiotherapy consisting of range of motion and stretching exercises. One RCT compared combination of free active exercises, stretching, postural care, re-education of scapula-thoracic postural muscles and strengthening of shoulder muscles with routine postoperative physiotherapy care in the hospital (respiratory care and verbal advice on early active movement of the neck and affected shoulder). Risk of bias was assessed using the Cochrane risk of bias tool. One study was at low risk of bias, and 2 were at high or unclear risk of bias for criteria other than blinding.

Head and neck cancers: Outcomes

Adverse events

Two studies (n=69) described adverse events. Of these there was one reported case of nausea and one of increased pain.

Quality of Life

Meta-analysis of two studies of resistance training (n=69) found no statistically significant benefit of the intervention on QoL (5.05, 95%CI -3.01 to 13.12, p=0.22, I^2 0%). The study of mixed exercise also found no statistically significant difference.

Shoulder function

Meta-analysis of two studies of resistance training (n=69) found a statistically significant reduction in shoulder pain and disability measured using the Shoulder Pain and Disability Index (SPADI) disability subscale, in favour or progressive resistance exercise (mean difference - 8.48, 95%CI -15.07 to -1.88, p=0.012, I^2 0%), but not for the SPADI total score. Using the Constant Shoulder Assessment, the study of mixed exercise showed no difference in favour of the exercise group.

Carvalho et al. (2012) concluded that there was limited evidence that progressive resistance exercise improved pain, disability and range of motion of the shoulder joint compared to standard physiotherapy, but did not improve quality of life. They commented that measured benefits of the intervention may be small.

Head and neck cancers: GRADE summary

Using GRADE there is low quality evidence (downgraded for limitations of studies and inconsistency (between the SPADI subscale and total score) that progressive resistance exercise may lead to small

additional benefits compared to a standardised physiotherapy programme for shoulder and arm disability in people following surgery for head and neck cancer.

There is moderate quality evidence (downgraded for limitation of studies) that exercise interventions do not improve quality of life. There is very low quality (downgraded for limitations, imprecision and inconsistency, as a single study) evidence that a mixed exercise intervention consisting of free active exercises, stretching, postural care, re-education of scapula-thoracic postural muscles and strengthening of shoulder muscles is not better than routine post-operative physiotherapy in this group.

LUNG CANCER

Four reviews (Cavalheri et al. 2013, Crandall et al. 2013, Granger et al. 2011, Payne et al. 2013, Paramanandam et al. 2015) specifically investigated the effectiveness of exercise interventions in people with lung cancers. Of these reviews, three (Cavalheri et al. 2013, Crandall et al. 2014, Granger et al. 2011) included only studies of people with Non small cell lung cancer (NSCLC) and one (Payne et al. 2013) included only those with advanced NSCLC.

NSCLC FOLLOWING LUNG RESECTION SURGERY

NSCLC following lung resection surgery: Characteristics of reviews

Cavalheri et al. (2013) conducted a Cochrane review of exercise training undertaken by people within 12 months of lung resection surgery for NSCLC. This review had an AMSTAR score of 10/11. They included 3 RCTs with 178 participants in total. The primary outcome was exercise capacity and other outcomes of interest included QoL, dyspnoea, fatigue, anxiety and depression mortality and the development of post-operative complications. The included interventions consisted of strength and mobility training, aerobic and resistance exercise, and aerobic and resistance exercise with dyspnoea management strategies. Interventions varied from twice-daily inpatient exercise for five days plus 12 weeks of home-based exercises to out-patient programmes that commenced four weeks after hospital discharge and were conducted twice a week for 12 weeks. Risk of bias was assessed using the Cochrane risk of bias tool. Other than blinding of participants and personnel all studies were at unclear or high risk of bias on more than one other criterion.

Crandall et al. (2014) similarly reviewed studies of exercise interventions in people with NSCLC who had undergone surgery, but did not limit studies to those that delivered the intervention within one year of surgery. This review had an AMSTAR score of 8/11. They included 8 RCTs with 341 participants. Interventions varied in content but all included aerobic activity with resistance training included in 5 studies, and most included breathing exercises. Duration, frequency and intensity of training all varied across studies, but most studies reported their programme as moderate intensity. In the majority of studies the control condition was usual care. In the reporting of results Crandall et al. (2014) largely appeared to focus on change from baseline in the intervention group, which is not the comparison of interest for this overview as it does not reflect the effect specifically attributable

to the intervention. Study quality was assessed using the Downs and Black tool and none of the RCTs were free from risk of bias.

Granger et al. (2011) reviewed the evidence for exercise interventions to improve exercise tolerance and quality of life in people with NSCLC at any cancer stage. This review had an AMSTAR score of 7/11. They include 2 RCTs with 79 participants in total. These studies were also included by either Crandall et al. (2014) or Cavalheri et al. (2013). One of these was in a pre-operative group and one in a post-operative group. Exercise interventions consisted of an inpatient exercise programme with a home exercise programme, or a home exercise programme alone. Using the PEDro scale to assess study quality both studies score 6/11 with a lack of assessor blinding in both studies.

NSCLC following lung resection surgery Outcomes

Exercise capacity

Cavalheri et al. (2013) reported a meta-analysis of all three studies, which demonstrated a statistically significant increase in the six-minute walking distance (6MWD) in favour of the intervention (139 participants, mean difference 60m, 95%CI 15 to 85m, p=0.005, I^2 0%).

In their narrative synthesis Crandall et al. (2014) reported that all but one study showed improvement in 6MWD scores.

Fatigue

One review (Paramanandam et al. 2015, AMSTAR score 4/11) specifically investigated the effectiveness of exercise to improve cancer-related fatigue in people with lung cancer and identified no RCTs. Cavalheri et al. (2013) also found no data on fatigue. Crandall et al. (2014) did not clearly report between-group comparisons for this outcome.

Hospital length of stay

Crandall et al. (2014) reported that 3 out of 4 RCTs demonstrated significantly fewer days in hospital for patients in the exercise arm than in the control arm. The effect size specifically from RCTs was not reported.

Muscle strength

Cavalheri et al. (2013) summarised one study (n=67) which measured quadriceps force and found no statistically significant difference between the intervention and control groups. Based on 3 studies Crandall et al. (2014) found that 2 studies showed a significant improvement and one did not. It was not clear whether this was based on within- or between-group comparisons.

Quality of life

Cavalheri et al. (2013) reported a meta-analysis of 3 studies (n= 147) which demonstrated no statistically significant difference in quality of life between the exercise intervention group and the control group (SMD 0.17, 95%ci -0.16 to 0.49, p=0.32, I^2 24%).

Crandall et al. (2014) reported conflicting results with some studies showing improvements and some no change. It was not clear whether this was based on within- or between-group comparisons.

Post-operative complications

One study (n=67) commenced the intervention during the immediate post-operative period and reported complications. There were 2 complications in the intervention group and three in the control group, the nature of which were not specified.

NSCLC following lung resection surgery: GRADE summary

Cavalheri et al (2013) concluded that exercise training resulted in statistically significant improvements in exercise capacity but that there was no evidence that it benefitted quality of life and muscle strength. Crandall et al. (2014) concluded that there is insufficient evidence regarding the optimal exercise intervention for this group. Granger concluded that exercise interventions are associated with positive benefits on exercise capacity, symptoms and some subdomains of HR-QoL but these conclusion regarding HR-QoL and symptoms were not based on RCT-level evidence.

There is moderate quality evidence (downgraded for limitations of studies) that exercise training can improve exercise tolerance in people following lung resection surgery.

There is moderate quality evidence (downgraded for limitations of studies) that exercise interventions do not improve quality of life in people following lung resection surgery.

There is very low quality evidence (downgraded for limitations of studies, imprecision and inconsistency) that a strength and mobility intervention may not improve quadriceps strength in people following lung resection surgery.

There is low quality evidence (downgraded for limitations of studies and imprecision) that exercise interventions may reduce length of hospital stay in people following lung resection surgery.

PROSTATE CANCER

PATIENTS DURING AND AFTER PROSTATE CANCER TREATMENT

Patients during and after prostate cancer treatment: Characteristics of reviews

Five reviews investigated the effectiveness of physical activity interventions in prostate cancer (Baumann et al. 2012, Chipperfield et al. 2014, Gardner et al. 2013, Hackshaw-McGeagh et al. 2015, Mohamad et al. 2015). Some details and results of 2 of these reviews (Hackshaw-McGeagh et al. 2015, Mohamad et al. 2015) have been reported above (see “Mixed lifestyle interventions/ prostate cancer”).

Baumann et al. (2012) reviewed the evidence for the effectiveness of exercise interventions in people with a prostate cancer diagnosis, with no stated limitations on the stage of disease. This review had an AMSTAR score of 4/11.

Chipper field et al. (2014) reviewed the evidence for the efficacy of physical activity to improve psychological outcomes in men receiving androgen deprivation therapy for prostate cancer. This review had an AMSTAR score of 4/11.

Gardner et al. (2013) reviewed the effects of exercise on treatment-related adverse events outcomes in men receiving androgen deprivation therapy for prostate cancer. This review had an AMSTAR score of 4/11.

Baumann et al. (2012) included 25 RCTs. In 21 of these the exercise intervention was commenced during cancer treatment and in 4 it was commenced during aftercare. The interventions included endurance training, resistance training and pelvic floor/ sphincter training and outcomes included fitness (aerobic and strength), incontinence, quality of life, fatigue, psychological parameters and side effects. Assessment of individual study quality was not directly reported but the quality of the evidence base was summarised using the evaluation system of the Oxford Centre for Evidence Based Medicine (OCEBM).

Patients during and after prostate cancer treatment: Outcomes

Body Weight

In a narrative synthesis of 8 trials of exercise interventions, variously including aerobic exercise, resistance exercise and circuit based exercise Mohamad et al. (2015) concluded that the data were conflicting and there appeared to be less change in body weight with exercise only interventions than in combined exercise and dietary interventions.

Disease progression

Hackshaw-McGeagh et al. (2015) identified 4 RCTs (combined n=439) that reported a physical intervention including resistance and/or aerobic training. They reported that these trials found no consistent effects of physical activity interventions on prostate specific antigen (PSA)-based measures of disease progression (as measured by PSA level). One of these trials was considered to have a low risk of bias.

Multiple outcomes

In a narrative synthesis of results Baumann et al. (2012) reported that resistance training and aerobic exercise during irradiation treatment showed significant improvement in quality of life, fatigue, aerobic fitness and muscle strength. They reported that pelvic floor and sphincter training programmes significantly reduced incontinence and increased quality life, and the interventions appeared to be more effective when commenced earlier, including prior to surgery.

Incontinence

Baumann et al. (2012) reported that pelvic floor and sphincter training programmes during aftercare significantly reduced incontinence. Baumann et al. (2012) judged that the level of evidence ranged from level 1b (due to lack of reporting of precision around effect estimates) to level 2b (due to weaker methodological quality).

Patients during and after prostate cancer treatment: GRADE summary

Due the approach taken to the reporting of this review it is difficult to apply GRADE to these findings, though given the likely limitations of studies and imprecision it is likely to represent moderate to low quality evidence.

PATIENTS RECEIVING ANDROGEN DEPRIVATION THERAPY FOR PROSTATE CANCER

Patients receiving androgen deprivation therapy for prostate cancer: Characteristics of reviews

Chipper field et al. (2013) investigated the effect of exercise specifically on psychological outcomes. They included 4 RCTs with 362 participants and interventions consisted of resistance training, mixed aerobic, resistance and flexibility training and mixed aerobic and resistance training with programmes lasting between 12 and 16 weeks. This review did not assess the risk of bias of included studies but was retained in this overview as it was the sole review specific to this group that considered depression.

Gardner et al. (2014) specifically reviewed the effects of exercise on treatment related consequences in people with prostate cancer receiving ADT. They included 5 RCTs including 336 participants. Interventions consisted of aerobic training, resistance training or a combination of both. Study quality was assessed using the Downs and Black checklist. Score ranged from 29 to 30 out of a possible 30 points.

Patients receiving androgen deprivation therapy for prostate cancer: Outcomes

Aerobic fitness

Gardner et al. (2014) reported conflicting results, with 1 RCT reporting a statistically significant improvement in aerobic fitness and 3 studies reporting non-significant differences. No meta-analysis was conducted.

Body composition

Gardner et al. (2014) reported that 2 trials demonstrated that exercise successfully prevented loss of lean body mass, though estimates of effect or measures of significance were not reported. The evidence that exercise is effective in preventing increases in body fat was conflicting.

Depression

Chipperfield et al. (2013) reported that one study n=100 that delivered an unsupervised 16 week programme of mixed aerobic, resistance and flexibility training found no statistically significant effect on depression scores.

Fatigue

Gardner et al. (2014) reported that 2 RCTs found statistically and clinically significant improvements in fatigue in favour of the exercise group and two found no statistically significant improvement.

Muscle strength

Gardner et al. (2014) reported that 4 RCTs consistently demonstrated statistically significant improvements in muscle strength following resistance, aerobic or combined exercise interventions. Effect sizes were not reported.

Quality of life

In a narrative synthesis of results Chipperfield et al. (2013) the RCT results were not summarised separately from non-randomised studies. However from the description of 3 RCTs, 2 demonstrated statistically significant improvements compared to the control condition and one did not. Effect sizes and the follow-up time-points for these comparisons were not reported. Gardner et al. (2014) similarly reported inconsistent results across trials on QoL.

Chipperfield et al. (2014) concluded that preliminary findings supported the use of exercise for improving quality of life. Gardner et al. (2014) concluded that exercise was safe and may ameliorate a range of treatment-induced adverse effects.

Patients receiving androgen deprivation therapy for prostate cancer: GRADE summary

There is moderate quality evidence (downgraded for limitations of studies) that exercise interventions may improve cancer-related fatigue and muscle strength in prostate cancer patients undergoing ADT.

There is very low quality evidence (downgraded for limitations of studies, inconsistency and imprecision) that exercise interventions may improve quality of life and aerobic fitness in prostate cancer patients undergoing ADT.

There is very low quality evidence (downgraded for unknown limitations of studies, inconsistency and imprecision) that exercise does not improve depression scores in this group.

Aerobic Exercise intervention

MIXED CANCER POPULATIONS

Mixed Cancer Populations: Characteristics of reviews

Tian et al. (2016) reviewed the evidence for the effects of aerobic exercise only on cancer related fatigue. This review had an AMSTAR score of 6/11 and included 26 RCTs with a total of 2830 participants. The majority of trials (13) were in breast cancer patients, but a range of other cancer diagnoses were included. Trials compared aerobic exercise interventions to usual care or no exercise and the include interventions varied in content, were a mixture of supervised or home based and took place two–five times per week for 6–24 weeks. The risk of bias was assessed using the 12 point scale of the Cochrane Back review group. The authors used a threshold of ≥6/12 points to denote a study at low risk of bias and found that 24 or 26 studies had a low risk of bias. It should be noted that many studies were unclear or failed to meet a number of these criteria and might still be considered at risk of bias.

Mixed Cancer Populations: Outcomes

Fatigue

Meta-analysis of 24 studies (reported number of participants 2830) found a statistically significant small effect of exercise on fatigue in favour of the exercise intervention, with substantial heterogeneity (SMD -0.22, 95%CI -0.39 to -0.04, p=0.01, $I^2$78%). However inspection of the analysis suggests a unit of analysis error. Nine trials that included more than one treatment arm were entered into the analysis more than once, with no correction for the number of participants in the usual care group. This led to a number of participants in the control arms being double-counted in the analysis. As such the analysis should be interpreted with caution.

Subgroup analysis by treatment status suggested statistically significant effect only in people off-treatment. Subgroup analysis by malignancy type suggested statistically significant effects only in those with nasopharyngeal cancer. Subgroup analysis by supervision status suggested statistically significant effects only in supervised exercise programmes. It is not clear whether heterogeneity was reduced in these subgroups. Given the issues with the overall analysis these subgroup analyses should be interpreted with extreme caution. Inspection of a funnel plot suggested a degree of possible publication bias.

Tian et al. (2015) concluded that aerobic exercise was effective for the management of cancer-related fatigue.

Mixed Cancer Populations: GRADE summary

There is very low quality evidence (downgraded for limitations of studies, inconsistency, imprecision due to errors in the analysis and signs of publication bias) that aerobic exercise might have a small beneficial effect on cancer-related fatigue.

HAEMATOLOGICAL CANCER

Haematological cancer: Characteristics of reviews

One Cochrane review (Bergenthal et al. 2014) evaluated the evidence sfor aerobic exercise specifically in people with haematological malignancies. This review had an AMSTAR score 9/11 and included 9 trials with 818 participants with acute myeloid leukaemia, multiple myeloma, and lymphoma. Interventions were compared to standard care and included cycle ergometer exercise, walking programmes and aerobic programmes with resistance work. Risk of bias was assessed using the Cochrane risk of bias tool and all studies were at unclear or high risk of bias across multiple criteria.

Haematological cancer: Outcomes

Aerobic capacity

In a narrative synthesis of measures of aerobic capacity and cardiovascular fitness Bergenthal et al. (2014) reported that of 8 trials, 7 had a "tendency" or statistically significant effects in favour of the intervention group.

Body composition

Meta-analysis of two studies (n= 253) found no statistically significant difference between the groups for body weight (MD 0.30 kg; 95% CI -4.08 kg to 4.68 kg p=0.89, I^2 28%) or lean body mass (MD1.34 kg, 95% CI -1.34 kg to 4.02 kg, p=0.33, I^2 0%)

Fatigue

Meta-analysis of fatigue scores demonstrated a statistically significant effect in favour of the intervention (7 studies, n=692, SMD 0.24, 95%ci 0.08 to 0.40, p=0.003, I^2 0%).

Mortality

Meta-analysis of 3 studies (n=269) found no statistically significant effect on mortality rates (RR 0.93, 95%CI 0.59 to 1.47, p=0.75, I^2 0%).

Quality of Life

Meta-analysis of 4 studies (n=352) found no statistically significant effect on QoL (SMD 0.15, 95%CI -0.15 to 0.45, p=0.32 I^2 49%). Sensitivity analysis removing one trial that demonstrated a baseline imbalance on QoL scores in favour of the intervention group resulted in a statistically significant small effect in favour of the intervention (SMD 0.26, 95%CI 0.03 to 0.49, p=0.03, I^2 0%).

Serious adverse events

There was no statistically significant difference in serious adverse events in a meta-analysis of 3 trials that reported on this outcome (n=266, RR 1.44; 95% CI 0.96 to 2.18, p = 0.06, I^2 = 0%).

Haematological cancer: GRADE summary

Bergenthal et al. (2014) used GRADE and concluded that aerobic exercise interventions had no effect on mortality (moderate quality evidence) but could improve quality of life (low quality evidence), aerobic capacity (no grade rating given), and fatigue (moderate quality evidence).For aerobic capacity our GRADE rating is one of low quality evidence (downgraded for limitations and imprecision). No GRADE rating was reported for body composition. Our own rating is one of moderate quality evidence (downgraded for limitations of studies) of no effect of exercise interventions on body weight or lean body mass in people with haematological cancers.

Walking programmes

MIXED CANCER POPULATIONS

Mixed cancer populations: Characteristics of reviews

One review (Chiu et al. 2015) evaluated the effectiveness of walking exercise programmes for improving sleep in people with cancer. This review had a score of 7/11 on the AMSTAR scale and included 9 RCTs with a total of 599 participants. All interventions included a walking exercise component, 5 in combination with other exercises. The average length of the intervention was 9.5 weeks, with an average of 4.5 sessions. Most interventions used moderate intensity exercise. Study quality was assessed using 6 risk of bias domains. All of the nine studies were at unclear or high risk of bias on at least one criterion (other than blinding or participants and providers).

Mixed cancer populations: Outcomes

Sleep

Sleep quality was measured using a variety of different scales. Meta-analysis of nine studies (599 participants) demonstrated a statistically significant difference in favour of the intervention group (SMD -0.52, 95%ci -0.79 to -0.25, p value not reported, I^2 61%). Subgroup analyses were conducted but the resulting heterogeneity in subgroups was not reported. Effects remained significant in studies of walking alone, or walking combined with other interventions and regardless of cancer stage. Meta-regression identified no significant moderators of effects.

Chiu et al. (2015) concluded that moderate intensity walking was effective in improving sleep in individuals with cancer.

Mixed cancer populations: GRADE summary

Using GRADE there is low quality evidence (downgraded for limitations of studies and inconsistency (heterogeneity)) that walking interventions improve sleep quality in people with cancer.

Resistance exercise

MIXED CANCER POPULATIONS

Mixed cancer populations: Characteristics of reviews

Three reviews (Cramp et al. 2010, Lonbro et al. 2014, Strasser et al. 2013) reviewed the effectiveness of resistance exercise in people with varied cancer diagnoses.

Cramp et al. (2010) focused on quality of life as their primary outcome. This review had an AMSTAR score of 6/11 and included 6 RCTs with 666 participants with a variety of cancer diagnoses. All studies included supervised interventions ranging from 12 to 26 weeks in duration, with 2-3 sessions per week. Quality of the included studies was assessed using the CASP tool and the quality of included studies was described as variable.

Strasser et al. (2013) reviewed the effects of resistance training on muscle function, body composition and fatigue during and after cancer treatment. This review had an AMSTAR score of 8/11 and included 11 RCTs with 1167 participants. 6 studies delivered the intervention during treatment and 5after the completion of treatment. Study quality was assessed using the JADAD scale. The median score was 4/5 points.

Lonbro et al. (2014) reviewed the effects of resistance exercise on lean body mass. This review had an AMSTAR score of 4/11 and included 6 RCTs with 443 participants. The PEDro scale was used to assess study quality and the median score from RCTs was 6/10.

Mixed cancer populations: Outcomes

Adverse events

Cramp et al. (2010) reported that no serious adverse events were reported due to resistance training.

Aerobic capacity

Strasser et al. (2013) reported no statistically significant difference in VO_{2MAX} between the exercise and control groups but a statistically significant increase in the 12 minute walk test (number of studies not reported, n=111 mean difference (metres 143.65, 95%CI 70.46 to 216.83, p=0.0001, I^2 0%).

Body composition

Lonbro et al. (2014) reported that 4 of 6 trials found statistically significant increases in lean body mass in favour of the intervention group but did not report effect sizes. Strasser et al. (2013) reported on meta-analyses and found statistically significant increases in lean body mass (number of studies not reported, (n=565, mean difference 1.07kg, 95%CI 0.676 to 1.37, p=<0.001, I^2 0%) and decreases in % of body fat (n=713, mean difference -2.08%, 95%CI -3.46 to -0.70, p=0.003, I^2 74%).

Fatigue

Cramp et al. (2010) reported that, of 4 trials that measured fatigue, 2 showed no significant effects of exercise and 2 showed a statistically significant effect. No meta-analysis was conducted and no effect sizes were presented. Strasser et al. (2013) et al. found no statistically significant effect on fatigue with no heterogeneity in a meta-analysis of 437 participants (MD 1.86, 95%CI -0.03 to 3.75,p=0.05, I^2 0%).

Muscle strength

Cramp et al. (2010) reported that of 3 trials that measured muscle strength, all showed a statistically significant effect of exercise. No meta-analysis was conducted and no effect sizes were presented.

Quality of life

Cramp et al. (2010) reported a meta-analysis of post intervention quality of life scores that found a small, positive effect in favour of the intervention that came close to statistical significance (6 studies, n= 548, SMD -0.17,95%CI -0.34 to 0.00, p=0.05, I^2 0%). Strasser et al. (2013) reported conflicting results on quality of life outcomes though effects observed in positive trials were described as "slight".

Strasser et al. (2013) conducted meta-analyses of upper and lower limb muscle strength and found statistically significant increases in strength, with heterogeneity, in favour of the exercise group for upper limb strength (9 studies, n=752, mean difference 6.9kg, 95%CI 4.78 to 9.03, p<0.001, I^2 79%) and lower limb strength (number of studies not reported, n=719, mean difference 14.57 kg,95%CI 6.34 to 22.80 kg, p=0.005, I^2 91%).

Strasser et al. (2013) and Lonbro et al. (2014) concluded that resistance training led to improvement in muscle strength and body composition.

Mixed cancer populations: GRADE summary

There is low quality evidence (downgraded for limitations of studies and imprecision) that resistance exercise does not led to important improvements in quality of life. There is low quality evidence (downgraded for limitations of studies and imprecision) that resistance exercise can improve muscle strength in people with cancer. There is moderate quality evidence (downgraded for limitations of studies) that resistance exercise improves lean body mass.

BREAST CANCER

Breast cancer: Characteristics of reviews

Two reviews (Cheema et al. 2014, Paramanandam et al. 2014) reviewed the evidence for resistance exercise specifically in people with breast cancer. Cheema at al. (2014) included 15 RCTs with 1652 participants. The AMSTAR score for this review was 8/11. All interventions include progressive resistance training, most studies were in people who had complete active cancer treatment. Duration of the interventions varied across studies. Study quality was assessed using a checklist based on the CONSORT statement and reported quality scores ranged from 5 to 9.5/10.

Paramanandam et al. (2014) had an AMSTAR score of 5/11 and included 8 RCTs with 1091 participants of people specifically at risk of lymphoedema after breast cancer treatment. Study quality was assessed using the PEDro scale and quality scores ranged from 4-8/10.

Breast cancer: Outcomes

Adverse effects

Cheema et al. (2014) found few reported adverse effects with some incidences of muscle soreness, muscle injury and joint pains.

Breast cancer related lymphoedema

Cheema et al. (2014) reported a meta-analysis of the incidence/ exacerbation of breast cancer related lymphoedema (BCRL) and found a statistically significant reduction in the odds of BCRL in favour of resistance exercise (5 studies, number of participants not reported, OR 0.53, 95%CI 0.31 to 0.90, I^2 0%). However no significant differences were seen in arm volume between the exercise and control groups.

Paramanandam et al. (2014) included 6studies and found no statistically significant effect on lymphoedema severity or lymphoedema incidence (6 studies, number of participants not reported, RR 0.77, 95%CI 0.52 to 1.15, $I^2$0%).

Muscle strength

Paramanandam et al. (2014) reported a meta-analysis of upper limb strength and found statistically significant increases in favour of the exercise group (4 trials, number of participants not reported, SMD 0.93, 95%ci 0.73 to 1.12, I^2 0%). Similar effects were seen for lower limb muscle strength with heterogeneity (4studies, SMD 0.75, 95%CI 0.47 to 1.04, I^2 51%).

Quality of life

Paramandaram (date) reported a meta-analysis of global QoL scores from 3 studies (number of participants not reported) and found no statistically significant differences between the exercise and control groups, though statistically significant improvements were seen on the physical health subdomain.

Cheema et al. (2014) concluded that progressive resistance training improved physical functioning and reduced the risk of BCRL. Paramanandam et al. (2014) concluded that weight training appeared to be safe and beneficial in improving limb strength and physical components of quality of life in women with or at risk of lymphoedema.

Breast cancer: GRADE summary

Using GRADE there is low quality evidence (downgraded for limitations and imprecision) that resistance training does not affect the severity or incidence of treatment related lymphoedema in people following breast cancer treatment.

There is moderate quality evidence (downgraded for limitations of studies that resistance training improves muscle strength in this group.

There is low quality evidence (downgraded for limitations of studies and imprecision) that resistance training does not impact global QoL but that it may improve physical components of quality of life in this group.

PROSTATE CANCER

Prostate cancer: Characteristics of reviews

One review (Hasenoerhl et al. (2015) reviewed the effects of resistance exercise on physical performance and health related quality of life in people with prostate cancer specifically. This review had an AMSTAR score of 4/11 and included 13 RCTs with 879 participants. Study quality was assessed using the Downs and Black scale and scores ranged between 23 and 30 out of 30.Interventions varied in terms of dose and duration but all included resistance training as a core component. No meta-analysis was conducted and no effect sizes were presented.

Prostate cancer: Outcomes

Cardiorespiratory fitness

Narrative synthesis of results found that 4 of 9 studies were able to demonstrate a statistically significant increase in cardiorespiratory performance in favour of the exercise group on at least one time point.

Fatigue and Quality of life

Seven of nine studies reported statistically significant improvements in fatigue in the exercise group after the intervention. It was not clearly reported which studies reported on QoL and which reported on fatigue.

Muscle strength

11 studies assessed muscle strength. 4 studies were reported to demonstrate statistically significant increases in muscle strength and endurance capacity in favour of the exercise group.

Hasenoerhl et al. (2015) concluded that resistance exercise was safe and with beneficial effects on physical performance capacity.

Prostate cancer: GRADE summary

Using GRADE this review provides very low quality evidence (downgraded for limitations of studies, imprecision and inconsistency) that resistance exercise might improve muscle strength, cardiorespiratory fitness, fatigue and quality of life.

Mind-body exercise (Yoga/ TaiChi/ Qigong)

Four reviews (Buffart et al. 2012, Chan et al. 2012, Cramer et al. 2012, Shneerson et al. 2013, Zeng et al. 2014b) reviewed the evidence for the effectiveness of mind-body type exercise interventions (yoga, tai chi, qigong) in people living with and beyond cancer.

Yoga

BREAST CANCER

Breast cancer: Characteristics of reviews

Three reviews included studies of yoga (Buffart et al. 2012, Cramer et al. 2013 Shneerson et al. 2013) and the presented results were based solely on breast cancer populations.

Buffart et al. (2012) investigated the possible physical and psychosocial benefits of yoga in people with any type of cancer either during or after treatment. This review has an AMSTAR score of 6/11 and included 13 RCTs with 783 participants. Twelve of these studies were in breast cancer and so 766 of the included participants were female. All trials delivered a supervised yoga programme with physical poses, breathing techniques and relaxation or meditation, and were reported to be led by experienced yoga instructors, and compared yoga to either usual care, patient education, counselling or coping preparation. The median duration of programmes was 7 weeks and they ranged from 6 weeks to 6 months. Study quality was assessed using the Verhagen 9 point tool. Included studies met a median of 67% (range 22 to 89%) of quality criteria.

Cramer et al. (2012) also reviewed the effectiveness of yoga, specifically in breast cancer patients. This review had an AMSTAR score of 6/11 and included 12RCTs with 742 patients. Using the Cochrane risk of bias tool they found that most studies were at unclear or high risk of bias on multiple domains.

In a broader review of complementary and alternative therapies, Shneerson et al. (2013) also reviewed the effectiveness of yoga in cancer survivors. This review had an AMSTAR score of 9/11 and focused on quality of life outcomes and identified 5 studies. Using the Cochrane risk of bias tool they found that all studies were at unclear or high risk of bias on multiple domains.

Breast cancer: Outcomes

Anxiety

Meta-analysis of post-intervention anxiety scores resulted in a statistically significant effect in favour of yoga with heterogeneity (Buffart et al. 2012, 6 studies, number of participants not reported, SMD -1.08, 95%CI -1.93 to -0.46, $p<0.001$, I^2 58%).

Depression

Meta-analysis of post-intervention depression scores resulted in a statistically significant effect in favour of yoga (Buffart et al. 2012, 6 studies, number of participants not reported, SMD -0.69, 95%CI -1.02 to -0.37, p<0.001, I^2 44%).

Distress

Meta-analysis of post-intervention distress scores resulted in a statistically significant effect in favour of yoga with heterogeneity (Buffart et al. 2012, 6 studies, number of participants not reported, SMD -0.75, 95%CI -1.09 to -0.42, p<0.001, I^2 59%).

Fatigue

Meta-analysis of post-intervention fatigue scores resulted in a statistically significant effect in favour of yoga (Buffart et al. 2012, 7 studies, number of participants not reported, SMD -0.51, 95%CI -0.79 to -0.22, p=0.001, I^2 44%)() .

Functional wellbeing

Buffart et al. (2012) reported a meta-analysis of post-intervention functional wellbeing scores, which resulted in a small, statistically significant effect in favour of yoga (4 studies, number of participants not reported, SMD 0.31, 95%CI 0.04 to 0.58, p=0.03, I^2 0%).

Physical function

Buffart et al. (2012) reported a meta-analysis of post-intervention self-reported physical function scales and found a small and statistically non-significant effect of yoga (6 studies, number of participants not reported, SMD 0.17, 95%CI -0.06 to 0.40, p=0.14, I^2 0%). Inclusion of one "outlier" trial to this analysis increased heterogeneity but still did not result in a statistically significant effect.

Quality of life

Meta-analysis of post-intervention global quality of life scores found a statistically significant effect in favour of yoga with heterogeneity (Buffart et al. 2012, 6 studies, number of participants not reported, SMD 0.61, 95%CI 0.16 to 1.06, P=0.008, I^2 69%).

Shneerson et al. (2013) and Cramer et al. (2012) similarly found statistically significant effects on overall QoL in favour of yoga at the end of the intervention. Shneerson et al. (2013) reported that in the one study with a longer follow up (6 months) no significant effect was observed. Meta-analysis of mental quality of life domains demonstrated a statistically significant effect but that this was not found for physical quality of life domains. Cramer et al. (2012) reported that the effects on QoL were only present in studies rated at high or unclear risk of bias. Like Buffart et al. (2012), Cramer et al. (2012) also found that yoga resulted in short term effects on various indices of psychological health. In a subgroup analysis they found these effects were present in studies that delivered yoga during activity cancer treatment but not after completion of active cancer treatment. It is unclear whether this was a pre-planned subgroup analysis. As such is should be considered with caution. Cramer found no long term statistically significant effects in meta-analysis of depression, stress or distress scores.

Buffart et al. (2012) concluded that Yoga appeared to be a feasible intervention and that beneficial short term effects on several physical and psychosocial symptoms were reported. Shneerson et al. (2013) concluded that Yoga appeared to improve overall and mental QOL, but not physical QOL.

Breast cancer: GRADE summary

There is moderate quality evidence (downgraded for limitations of studies) yoga can improve short term functional wellbeing, depression and fatigue scores in people with breast cancer.

There is low quality evidence (downgraded for limitations of studies and inconsistency) that yoga does not improve physical function but does improve quality of life, anxiety and distress in people with breast cancer in the short term.

HAEMATOLOGICAL CANCERS

Haematological cancers: Characteristics of reviews

One Cochrane review (Felbel et al. 2014) investigated the effectiveness of yoga in addition to standard care in patients with haematological malignancies. This review had an AMSTAR score of 10/11 and one RCT of 39 patients. This RCT was at high or unclear risk of bias across multiple criteria.

Haematological cancers: Outcomes

Mixed

The study did not find statistically significant differences in favour of yoga for distress, fatigue anxiety, depression or quality of sleep.

Haematological cancers: GRADE summary

Felbel et al. (2014) rated the quality of evidence as very low using GRADE and concluded that no reliable conclusions can be drawn about the effectiveness of yoga for people with haematological malignancies.

Qigong

MIXED CANCER POPULATIONS

Mixed cancer populations: Characteristics of reviews

Two reviews (Chan et al. 2012, Zeng et al. 2014) investigated the effectiveness of Qigong exercise in people with cancer. Chan et al. (2012) included 8 RCTs with 558 participants. This review had an AMSTAR score of 8/11 and included studies with a range of cancer diagnoses. Study quality was

assessed using a number of tools. Most studies were at unclear or high risk of bias on more than one criterion. Zeng et al. (2014) had an AMSTAR score of 6/11 included 5 RCTs of Qigong with 413 participants. Using the Cochrane risk of bias tool all were at high risk of bias for multiple domains.

Mixed cancer populations: Outcomes

Depression and anxiety

Zeng et al. (2014) presented meta-analyses of depression scores (3 studies 314 participants) and anxiety scores (2 studies 219 participants) and found no statistically significant effect in favour of Qigong therapy.

Fatigue

Chan et al. (2012) reported that one RCT found that fatigue was significantly better in the Qigong group at the end of the intervention. Zeng et al. (20140 reported a meta-analysis of 2 studies and found a statistically significant effect on fatigue score as 12 week follow up with substantial heterogeneity (SMD -0.93, 95%ci -1.80 to -0.06, p=0.001, I^2 0%).

Quality of life

Of four RCTs that measured QoL, Chan et al. (2012) reported that 2 found statistically significant effects in favour or Qigong and 2 did not. Zeng et al. (2014) reported a meta-analysis of cancer-specific quality of life scores, measured in the FACT-G scale and found a statistically significant benefit with substantial heterogeneity (4 studies 395 participants, mean difference 6.57, 95%CI 2.32 to 10.83, p=0.002, I^2 96%).

Chan et al. (2012) concluded that it was difficult to draws firm conclusions due to the limitations in the evidence base but that there was some evidence in favour of a benefit on QoL and fatigue. Zeng et al. (2014) concluded that positive effects of Qigong were seen for QoL but that the results should be interpreted with caution.

Mixed cancer populations: GRADE summary

There is low quality evidence (downgraded for limitations of studies and inconsistency) that Qigong may have positive effects on quality of life and fatigue and that it is not effective for depression and anxiety.

Tai Chi

MIXED CANCER POPULATIONS

Mixed cancer populations: Characteristics of reviews

One review Zeng et al. (2014) reviewed the evidence for Tai Chi in people with cancer of any diagnosis and one review (Lee et al. 2014) specifically reviewed the evidence for tai chi as part of supportive care in breast cancer patients.

Lee et al. (2010) identified 3 RCTs with a total of 107 patients with breast cancer. This review had an AMSTAR score of 5/11. Zeng et al. (2014) included 7 trials of tai chi with 160 patients. Both reviews found that the majority of included trials had a high risk of bias.

Mixed cancer populations: Outcomes

Body composition

Zeng et al. (2014) reported meta-analyses of 2 studies (n=40) that showed no statistically significant changes in BMI (with heterogeneity) or % body fat.

Quality of Life

Zeng et al. (2014) presented a meta-analysis of 2 studies (73 participants) that used the SF-36 quality of life tool. No statistically significant difference was seen on any of the subscales of this tool except "mental health" (mean difference 2.38, 95%CI 1.75 to 3.01, p=<0.001, I^2 0%).

Lee et al. (2010 reported a meta-analysis of global QoL that included 2 studies (38 participants) and found no statistically significant effect (SMD 0.45, 95%CI -0.25 to 1.14, p=0.21, I^2 0%).

Zeng et al. (2014) concluded that Tai Chi may have positive effects on QoL but that these findings should be interpreted with caution. Lee et al. (2010) concluded that the existing trial evidence for tai chi in supportive cancer care is not convincing.

Mixed cancer populations: GRADE summary

Using GRADE there is low quality evidence (downgraded for limitations of studies and inconsistency) that tai chi does not improve global QoL or measures of body composition.

Dance and movement therapy

MIXED CANCER POPULATIONS

Mixed cancer populations: Characteristics of reviews

One Cochrane review (Bradt et al. 2015) reviewed the effectiveness of dance and/or movement therapy compared to standard care on psychological and physical outcomes in people with cancer. This review had an AMSTAR score of 11/11 and included 3 RCTs with a total of 207 participants. All 3 trials were in people with breast cancer who had had active cancer treatment within 5 years of the onset of the trial. The interventions various included "authentic movement", the Lebed method or a combination of dance and movement approaches. The risk of bias of the included studies was assessed using the Cochrane risk of bias tool and 2 of the 3 studies were at unclear or high risk of boas for criteria other than participants and therapist blinding.

Mixed cancer populations: Outcomes

Anxiety

Meta-analysis of 2 studies (pooled n=170) found no significant effect (SMD 0.21, 95%CI -0.09 to 0.51, p=0.18, I^2 0%).

Depression

Meta-analysis of 2 studies (pooled n=170) found no significant effect (SMD 0.02, 95%CI -0.28 to 0.32, p=0.89, $I^2$0%).

Fatigue

Meta-analysis of 2 studies (pooled n=170) found no significant effect (SMD -0.36, 95%CI -1.26 to 0.55, p=0.44, I^2 0%).

Quality of Life

Only one study (n=37) reported results for QoL and found a statistically significant effect on QoL in favour of the intervention (SMD 0.89, 95%CI 0.21to 1.57).

Mixed cancer populations: GRADE summary

Bradt et al. (2015) rated the quality of the evidence as very low for all comparisons and concluded that the limited number of studies prevented them from drawing conclusions regarding the effectiveness of dance/ movement therapy in people with cancer.

Health Economic Evidence

MIXED CANCER POPULATION

Mixed cancer population: Characteristics of the reviews

One review (Mewes et al. 2012) considered the cost effectiveness of multidimensional cancer survivor programmes. This review had an AMSTAR score of 5/11 included 6 health economic evaluations (total number of participants not reported) or quasi-randomised trials of exercise interventions combined with inpatient rehabilitation programs, CBT, psychological education, psychological education and information, self-help education, information support, and information support plus CBT. The Drummond tool was used to assess the quality of the economic evaluations.

The 2 studies relevant to this overview were conducted in Australia in people with breast cancer diagnoses. One study (n=275) compared 3 consecutively selected groups of patients who received either a home-based physiotherapy programme (n=36), a group-based physiotherapy programme and psychosocial intervention (n=31) or no intervention (n=208). No further details were reported in the review regarding the characteristics of the interventions. The outcomes measured up to 12 months post intervention were the number of rehabilitated cases and quality adjusted life years (QALYs). Mewes et al. (2012) judged that the non-randomised nature of this study raised uncertainty over the effectiveness of the intervention. They also raised queries regarding the valuation process employed. The study did not compare its results to other studies or adequately consider issues relevant to all users. This study found that, compared with no intervention, the incremental cost effectiveness ratio (ICER) for home based physiotherapy was AUS$ 1,344 and for group based exercise with psychosocial intervention it was AUS$ 14,478.

The other study within the systematic review was an RCT (n=73) that compared a multi-media home based programme consisting of strength, balance, shoulder mobility and cardiovascular endurance exercise with a control group who received an active intervention of flexibility and relaxation exercises and followed participants up for 6 months. Mewes et al. (2012) judged that this study conducted a reasonable health economic analysis. Improvements in QoL in the short term were not consistent across different QoL scales and no improvements were seen at 6 month follow up. The total mean costs for the multimedia activity programme were AUS$3,864 and for the control condition they were AUS$3,594. The intervention was not cost-effective. The willingness to pay per QALY threshold would need to be AUS$484,884 for the intervention to be considered cost-effective, or AUS$340,391 if health care cost outliers were excluded. This is highly unlikely to be considered cost-effective.

While Mewes et al. (2012) concluded that included reviews showed acceptable cost-effectiveness ratios, their conclusion does not accurately summarise the results of the studies relevant to this overview. The first study offers very low quality evidence (from a single non-randomised study) that a home-based physiotherapy programme or a group-based physiotherapy programme and psychosocial intervention may be cost-effective when compared with no intervention. The second

study offers low quality evidence (downgraded for limitations and imprecision) that a multi-media home based programme consisting of strength, balance, shoulder mobility and cardiovascular endurance exercise is not cost effective when compared to an active intervention of flexibility and relaxation exercises. On the basis of this limited evidence no firm conclusions can be drawn regarding the cost-effectiveness of lifestyle interventions in people with cancer.

DISCUSSION

Summary of main findings

Tables 1, 2 and 3 (overleaf) summarise the findings and quality of evidence by intervention and cancer type. Overall while multimodal lifestyle interventions that include physical activity and a dietary component do appear to be effective at increasing levels of physical activity, at least in the short term, there is little compelling evidence that this impacts meaningfully on quality of life or psychological variables. The exception to this is the low quality evidence that these interventions may improve cancer-related fatigue.

There is little evidence from RCTs that dietary interventions meaningfully impact on cancer recurrence or mortality. In those at risk of underweight and malnutrition following head and neck cancer dietary counselling may improve nutritional status and successfully increase body weight. The effects of dietary interventions on quality of life seem inconsistent.

Interventions designed to increase physical activity levels, usually delivered through specific exercise programmes do seem overall to increase physical fitness in terms of aerobic capacity, muscle strength and in some cases impact on measures of body composition. There is also some evidence for short term positive effects on psychological variables, quality of life, sleep, and cancer- related symptoms such as fatigue but these findings are not consistent across interventions or cancer types and the size of effects varies considerably. There is again little evidence for an effect of physical activity interventions on cancer recurrence or survival.

Our findings are in broad agreement with those of another recent overview of reviews (Payne et al. 2012). This overview investigated the efficacy of interventions used specifically in the management of fatigue and/or unintentional weight loss in adults with advanced progressive illness by reviewing the evidence in the Cochrane library. They concluded that there is a lack of robust evidence for interventions to manage fatigue and/or unintentional weight loss in the advanced stage of progressive illnesses such as cancer, though exercise and self-management interventions may provide some benefit.

We identified little useful information relating to the health economic aspects of lifestyle interventions. We identified one moderate quality review (Mewes et al. 2012) with limited relevant evidence from which no firm conclusions can be drawn regarding the cost-effectiveness of lifestyle interventions in people with cancer. The cost-effectiveness of these interventions remains uncertain. Given the inconsistency in positive findings relating to quality of life outcomes found in this overview we might predict a mixed picture regarding the cost-effectiveness of lifestyle interventions. It should be noted that complex lifestyle interventions can be resource-intensive and represent an opportunity cost. Better information on the health economic properties of services with existing evidence of effectiveness should be a priority.

Table 1: Mixed Lifestyle Interventions: outcomes and evidence quality

INTERVENTION	In which CANCER TYPE?	Leads to which OUTCOMES?	What is the EVIDENCE QUALITY (GRADE)?
Lifestyle (mixed)	Mixed	Increased physical activity	Moderate
		No consistent improvement in QoL	Low
		No improvement in QoL	Low
		Inconclusive on RTW	
		Decreased fatigue with physical activity component	Low
	Breast	No facilitation of weight loss	Low
	Gynaecological	No improvement in QoL	Low
		No improvement in fatigue or depression	Low
		Facilitation of weight loss and increased physical activity	Low
	Prostate	Facilitation of weight loss	Low
		No positive impact on PSA measures of disease progression	Very low

Table 2: Smoking Cessation Interventions: outcomes and evidence quality

INTERVENTION	In which CANCER TYPE?	Leads to which OUTCOMES?	What is the EVIDENCE QUALITY (GRADE)?
Smoking Cessation	Mixed	No improvement in smoking cessation rates	Moderate

Table 3: Patient Education Interventions: outcomes and evidence quality

INTERVENTION	In which CANCER TYPE?	Leads to which OUTCOMES?	What is the EVIDENCE QUALITY (GRADE)?
Patient Education	Mixed	No improvement in fatigue or QoL lifestyle	Low

Table 4: Diet and Nutrition Interventions: outcomes and evidence quality

INTERVENTION		In which CANCER TYPE?	Leads to which OUTCOMES?	What is the EVIDENCE QUALITY (GRADE)?
Diet and nutrition	Mixed dietary counselling interventions	Mixed	No effect on survival if malnourished	Moderate
			No effect on weight gain if malnourished	Low
			Positive effect on QoL if malnourished	Low
			No reduction in infection rate or mortality during chemotherapy (low bacterial diet)	Low
			Reduced weight loss in advanced cancer/cachexia	Very low
			No improvement in physical function in advanced cancer/cachexia	Very low
			Uncertain clinically important effect in QoL in advanced cancer/cachexia	Very low
		Head and Neck	Improvement in nutritional status and body weight during treatment	Low
			Improvement in QoL during chemotherapy treatment	Very low
		Lung	No effect on weight change, survival or response to chemotherapy	Moderate
			Improvement in energy intake during chemotherapy	Low
			No improvement in QoL during chemotherapy	Low
	Soy	Breast cancer	No reduced hot flushes (high soy intake)	Low
	Low bacterial diet		No reduction in infection rate or mortality during chemotherapy	Low
	Low fat diet		No reduced risk of mortality	Moderate
			No reduced recurrence	Low

Table 5: Physical Activity Interventions: outcomes and evidence quality

INTERVENTION		In which CANCER TYPE?	Leads to which OUTCOMES?	What is the EVIDENCE QUALITY (Grade)?
Physical Activity	Mixed Exercise	Mixed	Improvement in daily step count	Moderate
			Improvement in aerobic capacity	Moderate
			Improvement in anxiety and fatigue (short term)	Moderate
			Improvement in quality of life, depression, exercise tolerance, and physical function (short term)	Low
			Improvement in muscle strength and small reductions in body weight & BMI (post cancer treatment)	Low
		Breast Cancer	No effect on BMI , Physical activity levels and depression	Low
			Improvement in cancer related fatigue and physical/ functional wellbeing any stage)	Low
			Improvement in QoL (post-treatment)	Low
			Improvement in physical activity (post treatment)	Low
			No effect on occurrence of lymphoedema (post treatment)	Low
			Improvement in shoulder pain	Low
			Improvement in fatigue, QoL, anxiety and depression (during chemotherapy or radiotherapy treatment)	Very low
		Colorectal	Improve physical fitness after treatment	Moderate
			Do not improve QoL or fatigue after treatment	Low
		Haematological	Improvement in upper limb muscle strength, QoL and fatigue (stem-cell transplantation for haematological malignancy)	Moderate
			No effect on psychological wellbeing or quality of life (acute myeloid leukaemia)	Low
			Improvement in lower limb muscle strength and cardiorespiratory fitness	Low
			Improvement in wellbeing or QoL (myeloid leukaemia)	Very low
		Head and Neck	No improvement in QoL (post-surgery)	Moderate
			No better than post-operative physiotherapy (post-surgery mixed exercise)	Very low

		Lung	Improvement in exercise tolerance (post-surgery)	Moderate
			No improvement in QoL (post-surgery)	Moderate
			Reduced length of hospital stay (post-surgery)	Low
			Strength and mobility: No improvement in quadriceps strength (post-surgery strength and mobility)	Very low
		Prostate	Improvement in fatigue and muscle strength (during ADT treatment)	Moderate
			Improvement in quality of life and aerobic fitness (undergoing ADT treatment)	Very low
			No improvement in depression scores (post treatment)	Very low
	Aerobic	Mixed	Small beneficial effect on cancer related fatigue	Very low
		Haematological	Improvement in cancer related fatigue	Moderate
			No effect on mortality	Moderate
			No effect on body weight or lean body mass	Moderate
			Improvement in QoL	Low
	Resistance	Mixed	Improvement in lean body mass	Moderate
			Improvement in muscle strength	Low
			No improvement in QoL	Low
		Breast	Improvement in muscle strength (post cancer treatment)	Moderate
			No effect on severity or incidence of treatment related lymphoedema	Low
			Improvement in physical components of QoL	Low
		Head/ Neck	Improvement in shoulder / arm disability (post-surgery resistance training)	Low
		Prostate	Improvement in cardiorespiratory fitness, fatigue & QoL	Very low
	Qigong	Mixed	Positive effect on QoL and fatigue	Low
			No effect on depression and anxiety	Low
	Tai Chi	Mixed	No improvement in QoL or body composition	Low
	Walking	Mixed	Improvement in sleep quality	Low
	Yoga	Mixed	Positive influence on cognitive effects of chemotherapy (yoga or speed feedback training)	Very low
		Breast	Improved functional wellbeing depression and fatigue (yoga)	Moderate
			No improvement in physical function; improvement in QoL, anxiety and distress (yoga)	Low

Completeness of the included evidence

In terms of the volume of systematic reviews, more reviews have been published relating to breast cancer than for other forms of cancer, particularly in relation to dietary and physical activity related behaviours. There have been substantially more systematic reviews of physical activity interventions than for any other lifestyle behaviour. The lack of review evidence identified for other cancers and behaviours is not a direct measure of the amount of available evidence on those topics, although the lack of reviews conducted may in part reflect a tacit knowledge in the research community of the paucity of primary literature. Additionally it may also reflect the relative rarity of those cancers with low coverage in this overview, or difficulty accessing funding for research into those cancer types.

We took a deliberately broad and inclusive approach to our definition of a "lifestyle intervention". As a result some of the interventions tested in the included reviews might arguably be better considered to be part of post-operative or post cancer treatment care rather than a genuine "lifestyle intervention". A clear example of this is the evidence relating to physiotherapy and exercise programmes for people following breast cancer and lymph node surgery in terms of managing post-operative lymphoedema and upper limb pain and disability. We recognise this limitation but agreed with our key stakeholders to take an inclusive approach in this regard.

There is very little evidence related to the effect of lifestyle interventions on recurrence and survival. This likely reflects the challenges and costs of conducting trials of adequate size and follow up to decisively answer this question, but perhaps also a recognition that any impact on these outcomes might be predicted to be small. We also found no reviews focused on the evidence for interventions aimed at modifying alcohol related behaviours.

The included reviews overlapped substantially in terms of the trials included as there were numerous reviews that focused on similar topics but varied on at least one aspect of their PICO inclusion criteria. As such it should be noted that reviews specific to cancer types are likely to have drawn their conclusions from at least some of the trials included in reviews of the same intervention for mixed cancer types. Due to the way most reviews were conducted and reported it was often not possible to clearly stratify the results by the stage in the cancer journey of various populations. Many reviews took a broad approach, including people post-diagnosis or post-cancer treatment. Where reviews did focus specifically on a distinct group in this regard we have presented their findings separately.

We took a deliberately broad and inclusive approach to our definition of a "lifestyle intervention". As a result some of the interventions tested in the included reviews might arguably be better considered to be part of post-operative or post cancer treatment care rather than a genuine "lifestyle intervention". A clear example of this is the evidence relating to physiotherapy and exercise programmes for people following breast cancer and lymph node surgery in terms of managing post-operative lymphoedema and upper limb pain and disability. We recognise this limitation but agreed with our key stakeholders to take an inclusive approach in this regard.

Quality of the included evidence

We only included reviews of RCTs and wherever possible only considered evidence from RCTs. In some reviews making clear distinctions between the evidence arising from trials and that arising from non-randomised studies was challenging. In addition some reviews were not clear in terms of whether the reported effects were based on the between group difference, and therefore reflected the effectiveness of the interventions, or on within-group differences, which do not provide specific estimates of treatment effect. We have reflected that uncertainty in our reporting of the results.

Despite focusing on RCTs our GRADE summaries of the quality of the available evidence range from "moderate" to "very low" and we could not rate the quality of the evidence as "high" for any comparison. This was largely due to limitations in the included studies. While reviews varied in the approach that they took to assessing study quality it was common for a substantial proportion of the included trials to be rated at unclear or high risk of bias (or fail to score on a quality criterion) on more than one domain. Importantly, while it is clearly challenging or not possible to blind participants or providers to most of these interventions, many trials did not blind outcome assessors or were at risk of bias for other core aspects such as allocation concealment or dealing appropriately with attrition. Further, inconsistency was frequently found across included studies in terms of whether statistically significant improvements were seen for specific outcomes or reflected in substantial statistical heterogeneity in the outputs of many meta-analyses.

The evidence base for many of the comparisons considered is dominated by small trials. While many reviews did not consider the influence of publication biases, for others there was insufficient data to investigate this formally. However it is likely that small study effects, wherein there is a propensity for negative studies to not reach full publication, might lead to an overly positive picture for some interventions, particularly in a field with such a limited evidence base (Dechartres et al. 2013; Nüesch et al. 2010)

The quality of the included systematic reviews (measured using the AMSTAR tool) varied considerably. Many of the included reviews omitted aspects of good practice in systematic review methods, raising the risk that important evidence may have been missed. Cochrane reviews generally scored more highly on the AMSTAR tool than non-Cochrane reviews. It should be noted that the AMSTAR assessment effectively assesses the quality of reporting rather than directly measuring the quality of review conduct. The fact that most non-Cochrane reviews did not publish protocols puts them at a disadvantage on the first criterion of the AMSTAR tool ("Was an 'a priori' design provided?") and in some cases non-Cochrane reviews may be disadvantaged by the limitations on full and thorough reporting imposed by a journal's publishing requirements such as limitations on word counts or the number of tables permitted. Accepting this, the varied quality of reviews and the common lack of pre-registration of review protocols on PROSPERO introduces a further risk of bias.

Conducting clinical trials and synthesising the findings of clinical trials of complex interventions is challenging. These types of interventions vary in myriad ways and in this overview the included interventions commonly varied in terms of content, underpinning theory, setting, the health professionals involved, targeted outcomes, duration and dose. In addition to this there is likely

substantial heterogeneity in the fidelity of the interventions in terms of quality of delivery and the engagement and adherence of participants. These multiple sources of clinical heterogeneity mean that the summary estimates of effectiveness derived from meta-analyses should be treated cautiously and overarching summary statements regarding effectiveness are unavoidably broad. As such, where we have not found compelling evidence that interventions are effective for any given outcome it should be noted that it remains possible, if less likely, that a specific intervention, delivered in an optimal way might still deliver benefits. Meta-analyses were often unable to include data from all identified trials, most commonly due to inadequate reporting of outcomes in the trials themselves. However where the included reviews reported the outcomes of studies outside of their meta-analyses we have reported these.

It is difficult from the evidence reviewed to make confident statements regarding the characteristics that might increase the effectiveness of interventions. We were reliant on the level of detail reported in the included reviews regarding intervention characteristics, and those reviews were dependent largely on the detail in the original trial reports. This further degree of separation from the original evidence represents a limitation of overview of reviews. It has been recognised that the standard of reporting of interventions and controls in published reports of clinical trials of complex interventions is commonly insufficient (Hoffman et al. 2013) and there have been recent attempts to address this issue by developing reporting standards (see the TIDieR checklist, Hoffman et al. 2014) though most of the included trials preceded that initiative.

Few reviews formally considered possible mediators of better outcomes. Spark et al. (2013) observed that it was difficult to identify characteristics common among trials achieving successful maintenance of outcomes, compared to those that did not. Though Carayol et al. (2013) reported that yoga and tai chi interventions appeared to deliver larger effects than other forms of exercise, they also found that failure to meet certain risk of bias criteria were also associated with larger effects. The lack of head to head comparisons between different types of intervention in clinical trials means that we cannot confidently identify specific intervention characteristics as causal agents in the positive outcomes observed.

Strengths and Limitations of the overview process

The comprehensive search strategy ensures that this overview represents a comprehensive summary of all existing eligible systematic reviews in the English language published prior to the search dates and the pre-publication of our protocol on PROSPERO ensures methodological transparency and militates against potential post-hoc decision making which can introduce bias to the process. Dual screening of searches and data extraction and independent quality assessment of included reviews ensured a rigorous process.

Taking published systematic reviews as the sole evidence increases the potential risk of publication lag, wherein possible important new evidence that has not yet been included in published systematic reviews is not identified and included. The included reviews used a range of different methodological quality and risk of bias assessment tools. Given that we relied primarily on the quality and bias judgements of the included reviews, and did not systematically apply a standard risk

of bias tool to each original study, it is possible that important sources of potential bias may have been missed or that judgements in the included reviews were too lenient or punitive.

The use of the GRADE criteria introduces an element of subjective judgement. It was also found to be more difficult when we were primarily assessing the included reviews rather than the original studies, all of which assessed and reported study quality in different ways. A consistent approach to judgements across the different interventions has been applied but it should be recognised that these judgements are open to interpretation.

Changes between the review protocol and the final review.

As noted in the methods we made two post hoc amendments to our inclusion criteria: we increased the stringency of the criteria for considering a review to be adequately systematic and we further excluded studies for redundancy. Both of these changes were driven by the large volume of overlapping reviews identified in the initial search screening. The first ensured that we were able to draw an assessment of the quality of the evidence identified and the second was to enable us to efficiently synthesise such a large group of overlapping reviews.

Implications for practice

Note: for discussion with MacMillan

Implications for research

Overall the included reviews presented evidence from a relatively large number of RCTs and yet substantial uncertainty remains. It might be argued that this speaks to a broader issue of research waste (see McLeod et al. 2014). This overview highlights the need for any future trials of interventions to be large enough to offer a reliable answer, designed to reduce risk of bias as far as possible, based on sound theoretical foundations, delivered with adequate fidelity, and importantly, reported to standards of best practice and transparency. For the broad majority of interventions considered in this overview, further small exploratory trials are unlikely to increase certainty. For both trials and reviews we would strongly encourage a focus on effect sizes and precision rather than using p values as a surrogate for effectiveness.

Future reviews

There have been a large number of reviews across this area, and for many intervention types and cancers it is arguably unlikely that further reviews will substantially reduce the remaining uncertainty. Exceptions include reviews of interventions to affect alcohol related behaviours, though it should be noted that in the companion review to this overview there was no compelling evidence that alcohol consumptions was related to important outcomes in PLWBC. In addition there were very few reviews focused on non-dietary interventions for gynaecological cancers, non-physical

activity interventions for haematological cancers or any interventions for colorectal or upper aero-digestive and gastric and cancers. We would recommend that future reviews have a specific focus in terms of intervention type and cancer type and stage in order to reduce clinical sources of heterogeneity and facilitate meaningful data synthesis. Such reviews should include pre-registered protocols and comply with the PRISMA and MOOSE reporting guidelines (see http://www.equator-network.org/). Given the complex nature of these interventions there is a case for conducting realist synthesis incorporating both traditional effectiveness evidence with information from process evaluations and qualitative enquiry (Rycroft-Malone et al. 2012) to better understand the complex interaction of contextual factors in these interventions.

Future primary intervention research

Since an absence of reviews for a given intervention in a specific cancer group does not necessarily reflect an absence of trials it is challenging to offer a clear direction to which type of interventions should be prioritised for future research. In future trials of lifestyle interventions we would recommend compliance with the MRC guidance on the development and testing of complex interventions (Moore et al. 2015), with interventions being strongly driven by theory and identified need, developed in close collaboration with service users and caregivers to optimise the relevance and acceptability of the intervention. Outcomes of importance to service users should have primacy, measured with validated tools for the target population and over the long term. We would suggest that long term behaviour change should be the key focus. After feasibility testing definitive trials should endeavour to include diverse and representative samples and carefully consider mechanisms for optimising treatment fidelity in terms of dose, quality and adherence. There would be value in embedding a mixed methods approach to careful process evaluation. Where trials demonstrate significant benefits, there is a need for further implementation studies to better understand how successful these interventions are under “real-world conditions” and the factors that influence that success (Peters et al. 2013). Finally we have identified a dearth of economic evaluation evidence on lifestyle interventions. We recommend that future primary intervention research includes appropriate economic evaluation and that those interventions with existing evidence of effectiveness are appraised for their cost-effectiveness.

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SUPPLEMENTARY MATERIAL

Appendices

Appendix A: Search Strategy (OVID MEDLINE)

1. MeSH descriptor: [neoplasms] explode all trees)
2. Lifestyle OR healthy OR exercis* OR fit* OR active*OR diet* OR eating* OR smok* OR sedentar* OR tobacco OR drink* OR alcohol* OR nutrit*.ab.ti
3. meta-analysis.pt.
4. meta-analysis.sh.
5. (meta-analys* or meta analys* or metaanalys*).ab.ti.
6. (systematic* adj5 review*).ab.ti.
7. (systematic* adj5 overview*).ab.ti.
8. (quantitativ* adj5 review*).ab.ti.
9. (quantitativ* adj5 overview*).ab.ti.
10. (quantitativ* adj5 synthesis*).ab.ti.
11. (methodologic* adj5 review*).ab.ti.
12. (methodologic* adj5 overview*).ab.ti.
13. (integrative research review* or research integration).ab.ti.
14. OR/ 3-13
15. 1 AND 2 AND 14

Appendix B: Reasons for study Exclusions

Review	Reason for exclusion
Albrecht 2012	Redundancy
Arnold 2010	Redundancy
Alshadwi 2013	Not a systematic review
Billson 2013	Does not include relevant interventions
Boehm 2012	Redundancy
Brown 2011	Redundancy
Bourke 2014a	Not a systematic review
Bourke 2015	Not a systematic review
Bradt 2011	Does not include relevant interventions
Broderick 2014	Not a systematic review
Carayol 2013	Redundancy
Cavalheri 2014	Co-publication of included review
Cavanaugh 2011	Not a systematic review
Cemal 2013	Does not include relevant interventions
Cheifetz 2010	Not a systematic review
Cramer 2012	Does not include relevant interventions
Cramer 2014	Does not include outcomes of interest
Culos-Reed 2012	Redundancy
Dale et al. 2010	Redundancy
Deng 2013	Not a systematic review
Dieng 2016	Does not include relevant interventions
Duijts 2011	Not a systematic review
Dy 2010	Not a systematic review

Egan 2013	Not a systematic review
Falavigna 2014	Not a systematic review
Focht 2013	Not a systematic review
Freedland 2014	Not a systematic review
Fritz 2010	Not a review of interventions
Galway 2012	Does not include relevant interventions
Garg 2010	Redundancy
Glanville 2015	Not specific to the population of interest
Grande 2014	Does not include outcomes of interest
Green 2015	Not a systematic review
Guinan 2013	Does not include outcomes of interest
Hammer 2015	Not a systematic review
Hopkinson 2011	Redundancy
Hu 2011	Not a systematic review
Huang 2011	Not specific to the population of interest
Husebo 2013	Not a review of interventions
Hutton 2015	Review protocol only
Inoue 2012	Not a systematic review
Isner-Horobeti 2013	Not a systematic review
Jin 2013	Does not include relevant interventions
Jones 2010	More up to data version included
Jones 2011a	Not a systematic review
Jones 2011b	Does not include outcomes of interest
Jun 2012	Redundancy
Kampshoff 2014	Not a review of interventions
Koutoukidis 2015	Redundancy
Kruijsen-Jaarsma 2013	Does not include outcomes of interest
Kuijpers 2013	Not specific to the population of interest
Kwan 2011	Redundancy
Langford 2012	Not a systematic review
Lee 2013	Not a systematic review
Ling 2012	Does not include relevant interventions
Liu 2013	Does not include relevant interventions
Loh 2012	Not a systematic review
Lowe 2013	Not a systematic review
Luckett 2011	Does not include relevant interventions
Martin 2013	Not a systematic review
Mazzarino 2015	Not specific to the population of interest
McCahon 2015	Not specific to the population of interest
McLoone 2013	Does not include relevant interventions
McMillan 2011	Not a systematic review
McNeely 2011	Redundancy
Midtgaard 2015	Not a review of interventions
Minton 2015	Not a systematic review
Mishra 2014	Co-publication of included review
Mishra 2015	Co-publication of included review
Moreland 2010	Not a systematic review
Murthy 2012	Not a systematic review

Nayan 2011	More up to data version included
Ostermann 2012	Does not include relevant interventions
Pappalardo 2015	Does not include relevant interventions
Parsons 2014	Not a systematic review
Pastakia 2011	Redundancy
Payne 2012	Not a systematic review of RCTs
Puetz 2012	Redundancy
Rabin 2010	Not specific to the population of interest
Rodriguez-Larrad 2014	Does not include relevant interventions
Sadja 2013	Redundancy
Sawyer 2014	Not a systematic review
Scherpenhuizen 2015	Does not include relevant interventions
Sharma 2013	Not a systematic review
Silver 2015	Not a systematic review
Slatore 2014	Does not include relevant interventions
Speck 2010	Not a systematic review
Spence 2010	Redundancy
Steel 2014	Does not include relevant interventions
Storic 2013	Redundancy
Sturgeon 2014	Not a systematic review
Velthuis 2010	Redundancy
Wanchai 2010	Does not include relevant interventions
Wanchai 2011	Not a systematic review
Wang 2014	Does not include relevant interventions
Warburton 2010	Not specific to the population of interest
Wheelwright 2013	Does not include relevant interventions
Winters-Stone 2014	Not a systematic review
Yang 2015	Not specific to the population of interest

Appendix C: Characteristics of included reviews

Review	Search dates (to)	Participants or cancer type*	Interventions included*	Outcomes*	N of studies/ participants*	Study quality tool used.
Baldwin 2012	Feb 2010	All cancer types and stages	Oral nutritional interventions	Mortality QoL Energy intake Weight loss	13 RCTs n=1414	Criteria derived from Cochrane and Schulz
Balstad 2014	April 2013	patients with advanced cancer and different stages of cachexia	Dietary counselling	Weight Energy intake Physical functioning QoL	3 RCTs n=258	Modified Cochrane ROB tool
Baumann 2012	December 2011	patients with prostate cancer	Endurance training, resistance training, combined endurance and resistance training, and pelvic floor/sphincter training	Improving physical fitness (strength, endurance), incontinence quality of life fatigue psychological parameters, medical side effects.	25 RCTs n=2473	The evaluation system of the Oxford Centre for Evidence-Based Medicine (OCEBM).
Bergenthal 2014	January 2014	Participants with acute myeloid leukaemia, multiple myeloma, lymphomas, or mixed haematological malignancies	Physical exercise in addition to standard care.	Overall survival, Mortality quality of life physical performance, serious adverse events wellbeing at discharge	9 RCTs n=818	Cochrane ROB tool
Bluethmann 2015	October 2013	Post treatment breast cancer survivors	PA interventions	PA behaviour change	14 RCTs n=2140	CONSORT checklist
Bourke 2013	August	Adults with any	Any exercise intervention	Aerobic exercise behaviour	14 RCTs	Cochrane ROB

	2012	cancer diagnosis and a sedentary lifestyle		Resistance exercise behaviour Aerobic fitness Muscle strength Adverse events	n=648	tool
Bradt 2015	July 2014	People diagnosed with any type of cancer in active treatment or in recovery	standard treatment combined with dance/movement therapy	Psychological outcomes Symptom relief Physical outcomes Secondary outcomes Relationship and social support QoL Body image	3 RCTs n=207	Cochrane ROB tool
Brown 2012	November 2010	Adults with any type of cancer regardless of stage of diagnosis or type or stage of treatment.	Exercise interventions, (resistance or aerobic), occurring in any setting, with or without supervision	Depressive symptoms	37 RCTs n=2929	PEDro scale
Buffart 2012	November 2011	Adults with any cancer diagnosis either during or after treatment	Yoga including physical postures	Psychosocial outcomes Physical Outcomes Physical function Functional wellbeing Physical symptoms	11 RCTs n=783	Verhagen Delphi quality assessment tool,
Carayol 2015	June 2014	Adult women with non-metastatic breast cancer	Any exercise intervention to improve or maintain one or more components of physical fitness	cancer related fatigue HR QoL anxiety depression	33 RCTs n=2723	12-point scale derived from PEDro and Cochrane ROB tool
Carvalho 2012	July 2011	head and neck cancer, at any	Progressive resistance training	Shoulder disability Function	3 RCTs n=104	Cochran eROB tool

		stage, with dysfunction of the shoulder due to having received any type of cancer treatment of the head and neck region		range of movement pain		
Cavalheri 2013	February 2013	Participants with NSCLC who had recently undergone lung resection	Exercise training of any type (started within 12 months of lung resection	exercise capacity physical capacities Psychosocial outcomes QoL Fatigue Anxiety and deptression mortality	3 RCTs n=178	Cochrane ROB tool
Chan 2012	November 2010	cancer patients who received qigong intervention alone or combined with other treatments	qigong intervention alone or combined with other treatments,	Physical and psychosocial QoL Distress Survival rate Fatigue Physical functioning Body weight Tumour size Biomedical	8 RCTs n=613	Cochrane ROB tool
Chan 2015	May 2014	Breast cancer patients during or after chemotherapy or multimodal therapy incl. chemotherapy	Non-pharmacologic interventions for cognitive alterations Incl. yoga / aerobic exercise	Cognitive function	2 RCTs n=98	Cochrane ROB tool
Cheema 2014	Nov 2013	Breast cancer patients and	Progressive resistance training interventions including any	Breast cancer-related lymphedema (BCRL)	15 RCTs n=1,652	CONSORT 2010 statement

		survivors (with diagnosis; in treatment; completed treatment).	form of resistive type exercise	incidence/exacerbation, arm volume symptom severity Physical functioning (upper and lower body muscular strength); HRQoL		
Chipperfield 2013	March 2013	Participants of any age who had received ADT for prostate cancer of any disease stage	Physical activity interventions; Exercise interventions;	Depression Anxiety QoL Cognitive function	4 RCTs n=362	Not reported
Chiu 2015	15th July 2014	Any type of cancer and aged 18 or over	Walking interventions (walking only or walking combined with e.g. other exercise activities, a discussion group	Self-reported sleep outcome	9 RCTs n=599	6 domains too similar to Cochrane ROB tool
Chung 2013	2012 (no month)	Women with breast cancer who had undergone any type of surgical procedure	Exercise interventions including physiotherapy	physical, psychological, physiological, or behavioural	8 RCTs n=503	SIGN methodology Checklist, Scottish Intercollegiate Guideline Network (2008)
Craft 2012	Not specified	Adults with cancer	Exercise intervention at least 4/52 in duration	Depressive symptoms	14 RCTs n= 1287	PEDro
Cramer 2012	February 2012	Breast cancer patients and survivors	Yoga, any active treatment such as mindfulness-based stress reduction	Health related quality of life or well-being (global health-related quality of life, mental, physical, functioning, social and/or spiritual well-being) and/or psychological health (depression, anxiety,	12 RCTs n = 742	Cochrane ROB tool

				perceived stress, and/or psychological distress). Safety data where available served as secondary outcome measures.		
Cramer 2014	December 2012	Adult patients with a history of colorectal cancer	Exercise – 2x aerobic for 14 days, supervised and home based mixed aerobic and resistance for 12 weeks, home based aerobic for 16 weeks, home based aerobic for 12 weeks	Quality of life, fatigue, physical fitness	5 RCTs n=238	Cochrane ROB tool
Cramp 2010	October 2009	Adults, any cancer any stage	Resistance training	QoL. fatigue anxiety and depression self-efficacy to exercise body composition muscle function tumor-specific outcomes	6 RCTs n=548	Critical Appraisal Skills Programme (CASP)
Cramp 2012	March 2011	Adults. Any gender, tumour type, tumour stage and type of cancer treatment.	Exercise interventions: including aerobic exercise, strength training and flexibility exercises.	Fatigue aerobic capacity/cardiovascular function QoL body composition physical activity levels general mood depression anxiety	56 RCTs n= 4068	Oxford Quality score Cochrane ROB tool
Crandall 2014	May 2013	patients surgically treated for non-small cell lung cancer	Exercise interventions	Exercise capacity pulmonary function quality of life safety/adverse events	8 RCTs n=341	Downs and Black scale

				feasibility/acceptability; length of hospital stay and post-op complications; fatigue; muscle strength		
De Boer 2015	March 2014	Adults with cancer and were in paid employment at the time of diagnosis.	Interventions aiming to enhance RTW (including a physical activity component)	RTW QoL	3 RCTs n=176	Cochrane ROB tool
Du 2015	April 2014	Adults with cancer regardless of their cancer categories, or their clinical status	Patient education programs	Cancer-related fatigue QoL	8 RCTs n=1047	Cochrane ROB tool
Felbel 2014	February 2014	Adult with all stages of Hodgkin and non-Hodgkin's lymphoma, with and without current cancer treatment	Tibetan yoga	Anxiety depression quality of sleep distress fatigue	1 RCT n=39	Cochrane ROB tool
Ferrer 2011	Not stated	Adult cancer survivors	Interventions designed to affect exercise behaviour	Quality of Life	43 RCTs n=2,432 in RCTs)	PEDro Scale (10 item)
Finnegan-John 2013	June 2012	over 18 years having/having had treatment for cancer	Complementary and alternative medicine (CAM)	Measures of fatigue	15 RCTs n=1313	Oxford Quality Score/Jadad scale
Fong 2012	September 2011	Patients with a diagnosis of cancer who had	Exercise interventions including aerobic, resistance and strength training	Physical functions Body composition Psychosocial outcomes	34 RCTs n= 4113	Scottish Intercollegiate Guidelines

		completed their main treatment for cancer but who still may be undergoing hormonal treatment.		QoL		Network (SIGN)
Fritz 2013a	Nov 2011	People with lung cancer	Green tea	Treatment related side effects Mortality	0 RCTs	CONSORT checklist
Fritz 2013b	March 2013	People with breast cancer	Soy, Red Clover, and Isoflavones	Hot flashes Adverse events	5 RCTs, n not reported	CONSORT checklist
Gardner 2014	July 2013	Men receiving any form of ADT for clinically diagnosed PCa	Aerobic and/or resistance exercise program	Physical, physiological, psychological, or functional consequences of ADT	5 RCTs n=336	Downs and Black checklist
Granger 2011	Sept 2010	NSCLC diagnosis, any stage	Pre-operative and posttreatment Physical Activity/Exercise Intervention	Exercise capacity, HRQoL physical activity levels cancer symptoms mortality safety or feasibility	2 RCTs n=79	NHMRC Hierarchy of evidence and PEDro
HacksHaw-McGeagh 2015	July 2014	Prostate cancer	Nutritional, physical activity or combined interventions.	Disease progression Mortality	11 RCTs n=992	Cochrane ROB tool
Hasenoehrl 2015	September 2014	Prostate cancer patients	Supervised or unsupervised resistance training	Quality of life, fatigue, physical performance	13 RCTs	Unclear criteria
Kiss 2014	March 2012	Lung cancer, during chemotherapy or radiotherapy	Dietary counselling	Dietary intake Nutritional status Survival Treatment response QoL	3 RCTs n=541	quality rating)using the ADA tool
Knols 2010	November	Cancer survivors,	physical activity (walking,	Change in daily walking	5 RCTs	PEDro scale (2

	2009	excluding hospitalized patients.	physical exercise, counseling, yoga, relaxation or a combination of these).	activity	n=660	of the 11 points were excluded due to blinding not being possible)
Langius 2013	January 2012	HNSCC patients with RT or CRT as primary therapy or as post-operative therapy	Individualized dietary counselling (with or without supplementation)	Nutritional status, QoL Mortality	4 RCTs n=192	Cochrane ROB tool
Larkin 2014	March 2012	Prostate cancer any stage of disease and treated for prostate cancer currently or within the previous 12 months	Non-pharmacological interventions employed specifically for the management of cancer-related fatigue. including exercise; exercise with diet and lifestyle modification; education;	Fatigue	5 RCTs n=408	Joanna Briggs Institute (JBI) Critical Appraisal Checklist
Lee 2010	December 2009	Patients with breast cancer	The use of Tai Chai alone or combined with other treatments	Fatigue) QoL BMI aerobic capacity Mood Depression	3 RCTs; n=61	Modified Cochrane ROB tool
Lonbro 2014	March 2013	Previously diagnosed with malignancy and treated with curative intent (i.e. radiotherapy, chemotherapy, surgery and more) and now free from cancer.	Progressive resistance training interventions	Lean body mass increase (%)	6 RCTs (n=443), 3	PEDro scale
Loughney 2015	April 2015	adults with cancer	exercise training in people with cancer undergoing adjuvant	Safety Physical fitness	11 RCTs n=1092	Downs and Black checklist

			cancer treatment following surgery	HRQoL Clinical outcomes Other clinically relevant outcomes such as fatigue		
McNeely 2010	August 2008	Adults with a cancer diagnosis and post cancer surgery	Exercise interventions including rehabilitative exercises for alleviating ROM, upper-limb strength and function, pain and lymphedema.	Upper-extremity ROM, muscular strength, lymphedema and pain Upper-extremity/shoulder function QoL	24 RCTs n=2132	modified version of the validated Jadad 5-point scale
Meneses-Echavez 2015a	September 2013	People diagnosed with any type of cancer, any stage	Supervised physical activity interventions	Cancer-related fatigue. Physical wellbeing Functional wellbeing	11 RCTs n=1530	PEDro Scale
Meneses-Echavez 2015b	Not stated	People diagnosed with any type of cancer any stage	multi-modal exercise including aerobic, resistance, and stretching exercise.	Cancer related fatigue	9 RCTs n=772	PEDro scale
Mewes 2012 (effectiveness data)	June 2012	Cancer survivors	Exercise interventions	Quality of life (physical, mental, global), general health appraisal	10 RCTs n=797	Cochrane ROB tool
Mewes 2012 (health economic data)	Dec 2011	Breast cancer	Home-based physiotherapy group-based exercise Psychosocial intervention; Multimedia physical activity program (home based strength, balance, shoulder mobility and cardiovascular endurance program.	Number of rehabilitated cases and/or QALYs	Before/after study with a total of 275 participants. 1 RCT with 73 patients	10-point Drummond checklist
Mishra 2012	September 2011	Adult cancer survivors, any cancer any stage	Exercise interventions initiated after completion of active cancer treatment	HRQoL	38 RCTs N=	Cochrane ROB rool
Mohamad 2015	August	Prostate cancer regardless of age,	Diet and exercise interventions	Body weight,	20 RCTs	Cochrane ROB

	2013	stage of cancer or treatment.		Body composition	n=1298	tool
Nayan 2013	October 2012	Any cancer population	Smoking cessation interventions	Cessation rates	10 RCTs n=1150	8 point tool similar to Cochrane ROB tool.
Paramanandam 2014	August 2012	Women at risk of developing lymphoedema during or following breast cancer treatment.	Low or moderate intensity weight training or resistance exercises	BCR Lymphoedema, incidence or severity measured by volume QoL Muscle strength Body Mass index	8 RCTs n=1091	PEDro
Paramanandam 2015	April 2012	adults with lung cancer with or at risk of developing cancer-related fatigue	Any exercise intervention	Cancer related fatigue	0 RCTs	Levels of Evidence developed by The Oxford Centre for Evidence Based Medicine
Payne 2012	October 2012	adults (≥18 years of age) with stage iiib or iv NSCLC	physical activity as main intervention or with independently extractable data within wider intervention	Patient reported outcomes and clinical measures Fatigue Appetite Weight loss Physical performance QoL Adverse events Survival	3 RCTs n=106	Cochrane ROB tool
Persoon 2013	November 2011	Patients treated with stem cell transplantation for a	Exercise	Fatigue, HRQoL (also cardiorespiratory fitness, muscle strength)	8 RCTs n=472	Cochrane ROB tool

		haematological malignancy				
Scott 2013	February 2012	Any type or stage of cancer and who have completed their primary active treatment	"Multidimensional rehab programmes" must incorporate a physical component (diet , exercise) with a psychosocial component.	Physical or functional status symptom control QoL Anxiety Depression. Patient adherence and satisfaction with rehabilitation programmes Adverse outcomes	12 RCTs n=1669	Cochrane ROB tool
Shneerson 2013	February 2013	Cancer patients who had previously received anti-cancer treatment with surgery, chemotherapy and/or radiotherapy	Complementary therapies; yoga; meditation/mindfulness; yoga and meditation; homeopathy; energy healing; medical qigong; mistletoe therapy:	QoL – overall; physical; mental Adverse outcomes	13 RCTs n=1228	Cochrane ROB tool
Short 2013	July 2012	Breast cancer survivors – stages ranged 0-IIIa	Promotion of physical activity – behaviour change approaches	Aerobic PA levels (objective and self-report)	10 RCTs n=1299	The Effective Public Health Practice Project (EPHPP) adapted current SR methods to questions related to public health nursing.
Singh 2013	May 2012	Adult patients with lung, prostate or abdomen cancer	Interventions consisting of pre-surgical exercise	Physiological performance Functional performance QOL	10 RCTs, n= 710	Modified Delphi list
Smith-Turchyn 2015	August 2014	acute myeloid leukaemia and 1	Mixture of Walking, cycling, strength training, muscle	Fatigue, quality of life, physical functioning,	5 RCTs n=132	Cochrane ROB tool

		had chronic myeloid leukaemia	stretches	psychological distress, safety, adherence		
Smits 2015	July 2015	Endometrial and ovarian cancer survivors	"Lifestyle interventions" (not further defined)	QoL Function Fatigue	3 RCTS n=153	Cochrane Studies Methods Group tool
Spark 2013	March 2012	Breast and prostate cancer patients (survivors post treatment and survivors undergoing treatment)	Physical activity and diet (separate or mixed)	Primary outcomes included physical activity and/or diet behavioral outcomes, and clinical outcomes (i.e., functional status, cancer-related fatigue, and quality of life).	10 RCTs n=1536	Based on CONSORT statement
Stene 2013	January 2012	Adults with a confirmed cancer diagnosis who were about to start or undergoing active cancer treatment at trial entry	Exercise intervention; Aerobic, resistance or a combination of aerobic and resistance	Muscle mass Strength	16 RCTs n=1497	The assessment was based on the criteria for "risk of bias" within the GRADE system for rating quality of evidence
Strasser 2013	December 2012	Adult patients with cancer either actively receiving treatment or be in long-term follow-up.	Resistance training interventions	lower- imb and upper-limb muscle strength (kg). lean body mass (kg), fat mass (kg) percentage of body fat aerobic capacity fatigue	11 RCTs n= 993	Jadad scale (5-point scale)
Stuiver 2015	May 2013	People at risk of developing upper	Exercise therapy	lymphoedema Infection	5 RCTs n=736	Cochrane ROB tool

		limb lymphoedema after treatment for breast cancer		HRQoL Psychosocial morbidity Level of functioning in ADL		
Sumamo 2011	March 2010	Breast or prostate cancer survivors	"Lifestyle interventions" incl. exercise and/ or diet component and at least one more of the following - behavioural change, counselling, smoking cessation, stress reduction or group therapy)	Recurrence Weight change Physical activity Change in diet Change in meds use, Compliance with intervention	3 RCTs n= 750	Cochrane ROB tool
Tatham 2013	April 2011	Breast cancer patients, adults	Physiotherapy, such as exercise and manual therapy	Pain	4 RCTs n=377	PEDro
Tian 2016	December 2014	Adult patients (≥18 years) diagnosed with any type of cancer, regardless of gender, tumor stage, and type of cancer treatment	aerobic exercise excluding those focused only on improvements in range of motion	Fatigue	26 RCTs n= 2830	Cochrane Back Review Group (12 criteria list)
van Dalen 2012	October 2011	Cancer patients who received chemotherapy causing episodes of neutropenia	Low bacterial diet	Infection rate Infection-related mortality QoL	3 RCTs n=192	Cochrane ROB tool
Van Haren 2013	October 2011	Adults diagnosed with cancer and undergoing hematopoietic stem cell transplantation	Exercise interventions	QOL Psychological well-being and distress Fatigue Physical functioning.	11 RCTs n=734	Cochrane ROB tool
Wolin 2010	September	Adults and	Aerobic exercise and resistance	Results not categorised. Wide	10 RCTs,	Quality

	2009	children with haematological cancer	training or combined; walking, cycling and yoga.	variety of physical and condition-related outcomes reported.	n=unclear	assessment process unclear
Xing 2014	August 2013	People with breast cancer	Low fat diet interventions	Breast cancer survival All cause survival	2 RCTs n=5525	Not reported
Zeng 2014a	July 2013	Breast cancer survivors, 18+ years old, , had completed active cancer treatment	Exercise intervention - aerobic, anaerobic or combined.	All QOL outcomes measured by generic, cancer-specific, or cancer site-specific QOL scales	19 RCTs n=2926	Cochrane ROB tool
Zeng 2014b	June 2013	Adults 18 and over, any cancer any stage	Any type of qigong or tai chi for cancer patients.	General and cancer-specific QoL Psychological symptoms Physical health effects Adverse events	13 RCTs n=592	Cochrane ROB tool
Zou 2014	July 1, 2013	Breast cancer patients receiving chemotherapy	Aerobic exercise	Cancer-related fatigue	12 clinical comparative studies n=1,014	Newcastle-Ottawa Scale (NOS) criteria

Appendix D: Amstar quality assessment for included reviews

REVIEW	1. a priori design?	2. duplicate selection & extraction?	3. comprehensive search?	4. Incl. grey lit and language?	5. List of studies incl/ excl	6. characteristics of studies presented?	7. quality assessed and reported?	8. Quality used appropriately	9. pooling appropriate?	10. publication bias assessed?	11. CoI stated?	Overall SCORE /11
Baldwin 2012	CA	Y	Y	N	N	Y	Y	Y	Y	Y	N	7
Balstad 2014	CA	N	Y	N	Y	Y	Y	Y	NA	N	N	6
Baumann 2012	CA	N	Y	N	N	Y	Y	CA	NA	N	N	4
Bergenthal 2014	Y	Y	Y	N	Y	Y	Y	Y	Y	N	Y	9
Bluethmann 2015	CA	Y	Y	N	N	Y	Y	Y	Y	Y	N	7
Bourke 2013	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	10
Bradt 2011	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	11
Brown 2012	Y	N	Y	N	N	Y	Y	Y	Y	Y	N	7
Buffart 2012	CA	Y	Y	N	N	Y	Y	Y	Y	N	N	6
Carayol 2015	CA	y	y	CA	N	N	Y	Y	Y	Y	N	6
Carvalho 2012	Y	Y	Y	N	Y	Y	Y	Y	Y	N	Y	9
Cavalheri 2013	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	10
Chan 2012	CA	Y	Y	Y	N	Y	Y	Y	NA	Y	N	8
Chan 2015	CA	Y	Y	N	Y	Y	Y	Y	NA	Y	N	8
Cheema 2014	CA	Y	Y	N	Y	Y	Y	Y	Y	Y	N	8
Chipperfield 2013	Y	N	Y	N	N	Y	N	N	NA	N	N	4
Chiu 2015	CA	Y	N	N	Y	Y	Y	Y	Y	Y	N	7
Chung 2013	CA	Y	Y	N	N	Y	Y	CA	NA	Y	N	6
Craft 2012	CA	Y	Y	N	Y	Y	Y	N	Y	Y	N	7
Cramer 2012	CA	Y	Y	N	N	Y	Y	Y	Y	N	N	6

Cramer 2014	CA	N	Y	N	N	Y	Y	Y	Y	N	N	5
Cramp 2010	CA	Y	Y	N	N	Y	Y	Y	Y	N	N	6
Cramp 2012	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	10
Crandall 2014	Y	Y	Y	N	N	Y	Y	Y	NA	Y	N	8
De Boer 2015	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	11
Du 2015	CA	Y	N	N	N	Y	Y	Y	NA	N	N	5
Felbel 2014	Y	Y	Y	N	Y	Y	Y	Y	NA	NA	Y	10
Ferrer 2011	CA	N	Y	Y	N	Y	Y	Y	Y	Y	N	7
Fong 2012	CA	Y	Y	N	N	Y	Y	Y	Y	Y	N	7
Fritz 2013a	CA	Y	N	N	N	Y	Y	Y	NA	N	N	5
Fritz 2013b	CA	CA	Y	N	N	Y	Y	Y	NA	N	N	5
Gardner 2014	CA	CA	Y	N	N	Y	Y	N	NA	N	N	4
Garg 2010	CA	Y	Y	CA	N	Y	Y	Y	Y	N	N	6
Granger 2011	N	Y	Y	N	N	Y	Y	Y	NA	Y	N	7
Hacksaw-McGeagh 2015	Y	Y	Y	Y	N	Y	Y	Y	NA	Y	N	9
Hasenoehrl 2015	CA	N	Y	N	N	Y	Y	CA	NA	N	N	4
Hopkinson 2011	Y	N	Y	N	N	Y	N	N	NA	N	N	4
Kiss 2014	CA	Y	Y	N	N	Y	Y	Y	NA	N	N	6
Knols 2010	CA	N	Y	N	N	Y	Y	Y	Y	Y	N	6
Koutoukidis 2015	CA	Y	Y	Y	N	Y	Y	N	NA	N	N	6
Langius 2013	Y	Y	Y	N	Y	Y	Y	Y	NA	N	N	8
Larkin 2014a	Y	N	Y	N	N	Y	Y	N	NA	N	N	5
Larkin 2014b	CA	N	Y	N	N	Y	Y	N	NA	N	N	4
Lee 2010	CA	CA	Y	N	N	Y	Y	Y	Y	N	N	5
Lonbro 2014	CA	N	N	CA	N	Y	Y	Y	NA	N	N	4
Loughney 2015	CA	N	Y	N	N	Y	Y	N	NA	N	N	4
McNeely 2010	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	10

Meneses-Echavez 2015a	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	N	9
Meneses-Echavez 2015b	CA	Y	Y	Y	N	Y	Y	Y	Y	Y	N	8
Mewes 2012	CA	N	Y	N	N	Y	Y	Y	NA	N	N	5
Mishra 2012	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	11
Mohamad 2015	CA	Y	Y	N	Y	Y	Y	Y	NA	N	N	7
Nayan 2013	Y	Y	Y	N	Y	Y	Y	N	Y	N	N	7
Paramanandam 2014	Y	N	Y	N	N	Y	Y	Y	Y	Y	N	7
Paramanandam 2015	CA	N	Y	N	N	Y	Y	N	NA	N	N	4
Payne 2013	CA	CA	Y	Y	N	Y	Y	Y	NA	Y	N	7
Persoon 2013	CA	Y	Y	N	N	Y	Y	Y	Y	N	N	6
Scott 2013	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	9
Shneerson 2013	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	N	9
Short 2013	CA	N	Y	N	N	Y	Y	Y	NA	Y	N	6
Singh 2013	CA	N	Y	N	N	Y	Y	Y	NA	N	N	5
Smith-Turchyn 2015	CA	Y	Y	N	N	Y	Y	N	NA	N	N	5
Smits 2015	CA	N	Y	N	N	Y	Y	Y	Y	N	N	5
Spark 2013	CA	Y	N	N	N	Y	Y	Y	NA	N	N	5
Stene 2013	CA	Y	Y	N	N	Y	Y	Y	Y	Y	N	7
Storic 2013	CA	N	N	N	N	Y	Y	N	NA	N	N	2
Strasser 2013	CA	Y	Y	N	Y	Y	Y	Y	Y	Y	N	8
Stuiver 2015	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	10
Sumamo 2011	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	10
Tatham 2013	CA	Y	Y	Y	N	Y	Y	Y	NA	N	N	7
Tian 2016	CA	Y	Y	N	N	Y	Y	N	Y	Y	N	6
van Dalen 2012	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	10
Van Haren 2013	CA	N	Y	N	N	Y	Y	Y	Y	Y	N	6

Wolin 2010	CA	CA	Y	N	N	N	Y	N	N	N	N	2
Xing 2014	CA	CA	Y	N	N	Y	N	N	Y	N	N	3
Zeng 2014a	CA	Y	N	Y	N	Y	Y	Y	Y	Y	N	7
Zeng 2014b	CA	Y	N	N	N	Y	Y	Y	Y	Y	N	6
Zou 2014	CA	Y	Y	N	N	Y	Y	N	Y	Y	N	6