Interventions to enhance return-to-work for cancer patients (Review)

de Boer AGEM, Taskila T, Tamminga SJ, Frings-Dresen MHW, Feuerstein M, Verbeek JH

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[Intervention Review]

Interventions to enhance return-to-work for cancer patients

Angela GEM de Boer[1], Taina Taskila[2], Sietske J Tamminga[1], Monique HW Frings-Dresen[1], Michael Feuerstein[3], Jos H Verbeek[4]

[1]Coronel Institute of Occupational Health, Academic Medical Centre, Amsterdam, Netherlands. [2]Department of Primary Care and General Practice, University of Birmingham, Birmingham, UK. [3]Departments of Medical and Clinical Psychology and Preventive Medicine and Biometrics, Uniformed Services University of the Health Sciences, Bethesda, USA. [4]Occupational Safety and Health Review Group, Finnish Institute of Occupational Health, Kuopio, Finland

Contact address: Angela GEM de Boer, Coronel Institute of Occupational Health, Academic Medical Centre, Meibergdreef 9, Amsterdam, 1105 AZ, Netherlands. a.g.deboer@amc.uva.nl.

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ABSTRACT

Background

Cancer survivors are 1.4 times more likely to be unemployed than healthy people. It is therefore important to provide cancer patients with programmes to support the return-to-work process.

Objectives

To evaluate the effectiveness of interventions aimed at enhancing return-to-work in cancer patients.

Search strategy

We searched the Cochrane Central Register of Controlled Trials (CENTRAL, in *The Cochrane Library* Issue 2, 2010), MEDLINE, EMBASE, CINAHL, OSH-ROM, PsycINFO, DARE, ClinicalTrials.gov, Trialregister.nl and Controlled-trials.com to February 2010, reference lists of included articles and selected reviews, and contacted authors of relevant articles.

Selection criteria

Randomised controlled trials (RCTs) and controlled before-after studies (CBAs) of the effectiveness of psychological, vocational, physical, medical or multidisciplinary interventions enhancing return-to-work in cancer patients. The primary outcome was return-to-work measured as either return-to-work rate or sick leave duration. Secondary outcome was quality of life.

Data collection and analysis

Two authors independently selected trials, assessed the risk of bias and extracted data. We pooled studies with sufficient data, judged to be clinically homogeneous in different comparisons. We assessed the overall quality of the evidence for each comparison using the GRADE approach.

Main results

Fourteen articles reporting 14 RCTs and 4 CBAs were included. These studies involved a total of 1652 participants. Results indicated low quality evidence of similar return-to-work rates for psychological interventions compared to care as usual (odds ratio (OR) = 2.32, 95% confidence interval (CI) 0.94 to 5.71). No vocational interventions were retrieved. Very low evidence suggested that physical training was not more effective than care as usual on improving return-to-work (OR = 1.20, 95% CI 0.32 to 4.54). Eight RCTs on medical interventions showed low quality evidence that functioning conserving approaches had similar return-to-work rates as more radical treatments (OR = 1.53, 95% CI 0.95 to 2.45). Moderate quality evidence showed multidisciplinary interventions involving physical, psychological and vocational components led to higher return-to-work rates than care as usual (OR = 1.87, 95% CI 1.07 to 3.27). No differences in the effect of psychological, physical, medical or multidisciplinary interventions compared to care as usual were found on quality of life outcomes.

Authors' conclusions

Moderate quality evidence showed that employed patients with cancer experience return-to-work benefits from multidisciplinary interventions compared to care as usual. More high quality RCTs aimed at enhancing return-to-work in cancer patients are needed.

PLAIN LANGUAGE SUMMARY

Interventions to enhance return-to-work for cancer patients

Each year cancer survival rates are going up and the number of cancer survivors is rising sharply. Many survivors are doing well, although cancer survivors can continue to experience long-lasting problems such as fatigue, pain, and depression which may become chronic. These long-term effects can clearly cause problems with work participation of cancer survivors. Therefore, cancer is a significant cause of absence from work, unemployment and early retirement. Individuals, their families and society at large all carry part of the burden.

This review evaluated the effects of interventions aimed at enhancing return-to-work in cancer patients. It included 18 studies involving 1652 participants. Four types of interventions were found: psychological interventions, interventions aimed at physical functioning, medical interventions, and multidisciplinary interventions which incorporated physical, psychological and vocational components. No vocational interventions aimed at work-related issues were retrieved. Results suggest that multidisciplinary interventions involving physical, psychological and vocational components led to higher return-to-work rates of cancer patients than care as usual, while quality of life was similar.

BACKGROUND

With the sustained improvements in strategies to detect cancer early and treat it effectively, the number of cancer survivors is increasing (de Boer 2008; Hoffman 2005). Since the population is ageing in most countries and cancer survival is prolonged, the prevalence of cancer survivors is expected to rise further in the near future (Aziz 2007). In the absence of other competing causes of death, 66% of adults now diagnosed with cancer can expect to be alive five years post-diagnosis (American Cancer Society 2008).

Many survivors are doing well in general terms, although a significant proportion of survivors continue to experience physical, emotional and social problems such as fatigue, pain, cognitive deficits, anxiety and depression, which may become chronic or persistent (Smith 2007). These long-term medical and psychological effects of cancer or its treatment may cause impairments that diminish social functioning including obtaining or retaining employment (Spelten 2002; Taskila 2007a). Cancer diagnoses in working age individuals are becoming more common, with almost half of the adult cancer survivors being less than 65 years (Short 2005). Consequently, many are at an age at which the effects of cancer and its treatment could alter their employment position and their employment opportunities (Short 2005). Fortunately, many cancer patients are both willing and able to return to work following treatment (Taskila 2007a) without residual disabilities (Steiner 2010).

Returning to work is important for both cancer patients themselves and society. From the viewpoint of society, it is economically imperative to encourage patients to return to work whenever possible (Verbeek 2007). From an individual point of view,

prevention of work disability is essential because employment is an important component of quality of life (QoL). A UK study revealed that being able to work was viewed as the sixth most important aspect of QoL by healthy persons but for persons suffering from an illness, being able to work was judged to be the third most important aspect (Bowling 1995). This also applies to cancer patients who consider returning to work to be important (Verbeek 2007) because it is regarded as a marker of complete recovery (Spelten 2002) and regaining normality (Kennedy 2007). Moreover, returning to work can improve QoL of cancer patients, can have a positive effect on self-esteem and social or family roles (Verbeek 2007).

Since 1985, several studies have documented the impact of cancer on employment and they reported approximately 60% (ranging from 30% to 93%) of the cancer patients returning to work after one to two years (Spelten 2002; Taskila 2007a). However, cancer patients can experience problems getting back to work (Feuerstein 2007). Overall, cancer survivors are 1.4 times more likely to be unemployed than healthy controls and differs depending on diagnosis (de Boer 2009). Some studies have stated that cancer patients may experience impairments in mental and physical health as a result of their illness, and that these impairments sometimes lead to a decrease in their ability to work (Short 2005). On the other hand, work ability of cancer patients who work at the time of their diagnosis is severely impaired in the first months of treatment but does improve in the months afterwards (de Boer 2008). In a Finnish study, 26% of the cancer patients reported deteriorated physical work ability and 19% deteriorated mental work ability two to six years after diagnosis (Taskila 2007b).

Therefore, it is important to provide employed cancer patients with programmes to support the return-to-work process. Such programmes exist, with programmes in America (Lepore 2003), the UK (Maguire 1983), the Netherlands (Nieuwenhuijsen 2006) and Germany (Hensel 2002) as examples. The programmes of Maguire et al. (Maguire 1983), Nieuwenhuijsen et al. (Nieuwenhuijsen 2006) and Hensel et al. (Hensel 2002) were executed within a clinical environment while the programme of Lepore et al. (Lepore 2003) was performed in an outpatient clinic. This last study included group education on topics such as control of physical side effects, stress and coping. The study of Maguire et al. (Maguire 1983) included physical exercises and follow-up on the progress on exercises, return-to-work and becoming socially active. The programme of Hensel et al. (Hensel 2002) was a general rehabilitation programme while in the study of Nieuwenhuijsen et al (Nieuwenhuijsen 2006) the medical specialist provided advice on return-to-work to the patients and sent medical information to the occupational physician.

Interventions focusing on a psychological, physical or medical therapy of cancer and its treatment effects could focus on enhancing return-to-work as well. It remains unknown whether any of these interventions are effective in enhancing return-to-work in workers with cancer.

Up until now, to our knowledge, no such systematic review has been published. Therefore, the aim of this review is to assess the effectiveness of interventions aimed at enhancing return-to-work in cancer patients.

OBJECTIVES

To evaluate the effectiveness of interventions aimed at enhancing return-to-work in cancer patients compared to alternative programmes including usual care or no intervention.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) were included in this review.

Since it is difficult to carry out RCTs in work organisations we also included quasi-RCTs, cluster-RCTs, and controlled before-after studies (CBAs). Quasi-RCTs are controlled clinical trials in which methods of allocation are subject to bias in assignment, such as: odd-even numbers, day of week or patient records. In a cluster-RCT, treatment is assigned randomly to groups of participants.

We planned to base our conclusions only on RCTs and see if quasi-RCTs, cluster-RCTs, and CBAs supported or contradicted these conclusions.

Types of participants

The population was limited to adults ($\geq$ 18 years old) who had been diagnosed with cancer and were in paid employment (employee or self-employed) at the time of diagnosis. The review aimed to include all types of cancer diagnosis.

Types of interventions

The review included any type of intervention with the aim to enhance return-to-work. Interventions might be carried out either with an individual or in a group and in a clinical setting or in the community. Interventions could primarily focus on different factors which influence return-to-work, e.g. on coping (in psychological interventions), on workplace adjustments (in vocational interventions), on physical exercises (in physical interventions) or on minimal surgery (in medical interventions). Interventions were thus divided into:

- Psychological - psychological interventions that included any type of psychological intervention such as counselling, education, training in coping skills, cognitive-behavioural interventions (CBT), and problem solving therapy (PST), undertaken by any qualified professional (e.g. psychologist, social worker or oncology nurse).
- Vocational - vocational interventions that included any type of intervention focused on employment. Vocational interventions might be person-directed or work-directed. Person-directed vocational interventions are aimed at the patient and incorporate programmes which aim to encourage return-to-work, vocational rehabilitation, or occupational rehabilitation. Work-directed vocational interventions are aimed at the workplace and include workplace adjustments such as modified work hours, modified work tasks, or modified workplace and improved communication with or between managers, colleagues and health professionals.
- Physical - interventions that included any type of physical training (such as walking), physical exercises (such as arm lifting) or training of bodily functions (such as vocal training).
- Medical or pharmacological - medical or pharmacological interventions that incorporated any type of medical intervention (e.g. surgical) or medication (such as hormone treatment).
- Multidisciplinary - a combination of psychological, vocational, physical and / or medical interventions.

Types of outcome measures

Data were taken from the follow-up measurement. When multiple follow-up measurements were given, the 12 month follow-up data were extracted.

Primary outcomes

Primary outcome was return-to-work. Return-to-work included return to either full- or part-time employment, to a reduced role or not and to either the previous job or any new employment. Two types of return-to-work data were considered:

- Return-to-work measured as event data such as return-to-work rates or (change in) disability pension rates.
- Return-to-work measured as time to event data such as number of days between reporting sick and any work resumption or the number of days on sick leave during the follow-up period.

Secondary outcomes

- Quality of life (QoL) included overall quality of life, physical quality of life and emotional quality of life.

Search methods for identification of studies

We considered articles of all languages.

Electronic searches

First, relevant trials were identified from the following sources:

- Cochrane Central Register of Controlled Trials (CENTRAL, in *The Cochrane Library* Issue 2, 2010)
- MEDLINE (1966 to February 2010)
- EMBASE (1947 to February 2010)
- CINAHL (1983 to February 2010)
- OSH-ROM (Occupational Safety and Health, 1960 to February 2010)
- PsycINFO (1806 to February 2010)
- Abstracts of Reviews of Effectiveness (DARE, 1995 to February 2010)
- ClinicalTrials.gov, accessed February 2010
- Trialregister.nl, accessed February 2010
- Controlled-trials.com, accessed February 2010

Cancer-related and work-related search terms were selected from an earlier meta-analysis on cancer and employment (de Boer 2006). The searches were based on the MEDLINE search strategy (Appendix 1) using the revised Cochrane randomised controlled trial filter (Robinson 2002) and the sensitive search of the Cochrane Occupational Safety and Health Group for retrieving studies of occupational health interventions. CENTRAL, EMBASE, CINAHL, OSH-ROM, PsycINFO and DARE searches were adapted as appropriate to the specifications for these databases. Searches on cancer and employment tended to result in many articles on occupational exposure, occupational diseases and biological research. Therefore, we used a set of search terms to exclude those articles.

Searching other resources

The second step was to check the reference lists of all articles that were retrieved as full papers and of all retrieved systematic and narrative reviews in order to identify potentially eligible studies. The third step was to write to the corresponding authors of all studies that fulfilled the inclusion criteria but provided insufficient data to inquire after any additional published or unpublished study that may be relevant to this review.

Data collection and analysis

Selection of studies

Two review authors (AdB, TT) independently screened all titles and abstracts of studies that were identified from the search strategy for inclusion and appropriateness based on the selection criteria. Review authors were not blind to the name(s), of the author(s), institution(s) or publication source at any level. If the title and abstract provided sufficient information to decide that it did not satisfy the criteria for selection, the study was excluded.

When there was a difference of opinion then a third review author (JV) arbitrated. The reasons for exclusion at this stage were documented. The full-text articles of the included studies were then independently examined by two review authors (AdB, TT) in order to decide which studies fulfilled all inclusion criteria. Where necessary, study authors were contacted for more detailed information. Again, a third review author (JV) arbitrated in case of a difference of opinion. The reasons for exclusion at this stage were also documented. All inclusion and exclusion reasons of the two independent review authors were discussed and reported in one final inclusion / exclusion database.

Data extraction and management

A data extraction form was constructed that enabled two review authors (AdB, TT) to independently extract the following data from the articles: study type, setting, country, recruitment, randomisation, blinding, funding, inclusion and exclusion criteria, number of patients, patient characteristics including diagnosis, medical treatment, sociodemographic data, and employment situation at baseline, intervention (content, duration, provider, discipline, context), co-interventions, follow-up time and follow-up measurements, number of patients lost to follow-up, return-to-work outcome measures used, statistical methods, and results for each return-to-work outcome measure at each follow-up measurement point for each group. The diagnoses were summarized in diagnostic groups: if at least 50% of the patients had a specific diagnosis, then the study was included in that specific cancer diagnostic group, otherwise it was designated mixed diagnoses. All results of the two independent review authors were discussed and reported in one final data extraction form for each study.
When an article reported more than one intervention and compared each intervention against a control group, each intervention was entered as a separate study. If two or more interventions were compared with the same control group, the number of patients in the control was divided equally over the intervention studies, i.e. the number of patients was halved if there were two intervention groups.

Assessment of risk of bias in included studies

The quality of the included studies was independently assessed by two review authors (AdB, TT). The procedures described in the Cochrane Collaboration Handbook (Higgins 2009) were used to assess quality. The risk of bias was assessed with 10 criteria for the sources of risk of bias: adequate sequence generation, allocation concealment, blinding, incomplete data (drop-outs) addressed, use of ITT analysis, similarity of baseline characteristics, co-interventions avoided or similar, compliance acceptable, timing of outcome assessments similar, and being free of selective outcome reporting. The risk of bias was rated low when at least five or more of the criteria were met and there were no fatal flaws that put the validity in question while the risk of bias was scored high when fewer than five criteria were met with no fatal flaws (Furlan 2009). In addition, to assess the quality of non-RCTs we used the Downs and Black checklist (Downs 1998) for methodological quality assessment. The Downs and Black checklist is made up of scales for reporting, external validity and internal validity. We only used the scale for internal validity to assess the risk of bias and used both the scores on the scale and individual items and adapted the risk of bias table accordingly. The internal validity scale comprises seven items on bias and three on confounding. The methodological quality of non-RCTS was rated low if less than five items were met.
Where necessary, study authors were contacted for more detailed information. A sample of three articles was used to test whether the assessment criteria were applied consistently between two review authors (AdB, TT). Any disagreement about the criteria was followed by a discussion until consensus was reached. If the difference of opinion could not be resolved, a third review author (JV) was consulted. All results of the two independent review authors were discussed and reported in one final assessment of risk of bias form for each study.

Measures of treatment effect

For dichotomous data, such as return-to-work rates, the results of trials were plotted as odds ratios (ORs). For continuous variables such as the number of days on sick leave during the follow-up period, the mean difference (MD) was used. All estimates include a 95% confidence interval (CI).

Dealing with missing data

We contacted the authors of the following studies to obtain data missing in their report but needed for assessment of eligibility of the studies and/or input for the meta-analysis: Ackerstaff 2009; Jones 2005; Rogers 2009; Wiggins 2009. All these authors kindly provided the information requested. If statistics were missing such as standard deviations (SDs) we calculated them from other available statistics such as P values according to the methods described in of the Cochrane Handbook (Higgins 2009).

Assessment of heterogeneity

We first decided if studies were sufficiently homogeneous to be able to synthesize the results into one summary-measure. Homogeneous studies were defined as those with similar designs, similar interventions and similar outcomes measured at the same follow-up point. Interventions were classified as follows and considered as homogeneous categories: psychological, vocational, physical, medical and multidisciplinary interventions. Both return-to-work outcomes and sick leave duration outcomes were considered

return-to-work outcomes. General quality of life outcomes measured with different general quality of life instruments were considered similar indications of quality of life and were combined. Different diagnoses were combined within one analysis because we hypothesize that the mechanism of return-to work interventions is similar over the different cancer diagnoses.

We also tested for statistical heterogeneity with the I^2 measure. Studies were considered statistically heterogeneous if the I^2 measure was greater than 50%.

Assessment of reporting biases

Publication bias was assessed with a funnel plot if more than five studies were available.

Data synthesis

We pooled studies with sufficient data, judged to be clinically homogeneous, with RevMan 5.0 software in different comparisons. If the data allowed we made comparisons according to the interventions mentioned under the heading types of interventions. When studies were statistically heterogeneous, a random-effects model was used, otherwise a fixed-effect model was used.

For return-to-work outcomes we considered both the rate of return-to-work and time to return-to-work or the number of days on sick leave sufficiently similar to combine them as similar outcomes in the meta-analysis. Since the first is a dichotomous measure and the latter a continuous measure, we calculated effect sizes in order to enter them in the same comparison. For studies with continuous outcomes, we used the mean number of days off work with the standard deviation (SD) in both groups to calculate the standardised mean difference (SMD) using RevMan 5.0. Standardised mean differences were subsequently re-expressed as log odds ratios by multiplying them with 1.814 (Chinn 2000) as is the recommended method in the Cochrane Handbook (Higgins 2009). For studies with dichotomous return-to work rates, we recalculated the odds ratios into log odds ratios. Next, we calculated for both types of studies the standard errors (SE) of the log odds ratios from the 95% CI of the log odds ratios. We used the formula: SE = (upper limit log odds ratio - lower limit log odds ratio) / 3.92, as is the recommended method in the Cochrane Handbook (Higgins 2009). These log odds ratios and their standard errors were used as input into the meta-analysis using the generic inverse variance method as implemented in RevMan 5.0.

We assessed the overall quality of the evidence for each outcome. To accomplish this, we used an adopted GRADE approach, as recommended by the Cochrane Back Review Group (Furlan 2009). The quality of the evidence on a specific outcome was based on five main domains: limitations of the study design (risk of bias assessment), inconsistency (lack of similarity of estimates of treatment effects), indirectness (lack of ability to generalize) and imprecision (insufficient number of patients or wide confidence intervals) of results and publication bias (probability of selective publication of trials and outcomes) across all studies that measured that particular outcome. The overall quality of the evidence for each outcome is the result of a combination of the assessments in all domains. There are four levels of evidence:

- High quality evidence: at least 75% of the RCTs with no limitations of study design have consistent findings, direct and precise data and no known or suspected publication biases.
- Moderate quality of evidence: one of the domains is not met.
- Low quality evidence: two of the domains are not met.
- Very low quality evidence: three of the domains are not met.

Subgroup analysis and investigation of heterogeneity

Randomised controlled trials and CBAs were analysed separately. We intended to perform further subgroup analyses according to diagnosis and quality of the study when possible. However, the number of studies in the subgroups was too low to perform such subgroup analyses.

RESULTS

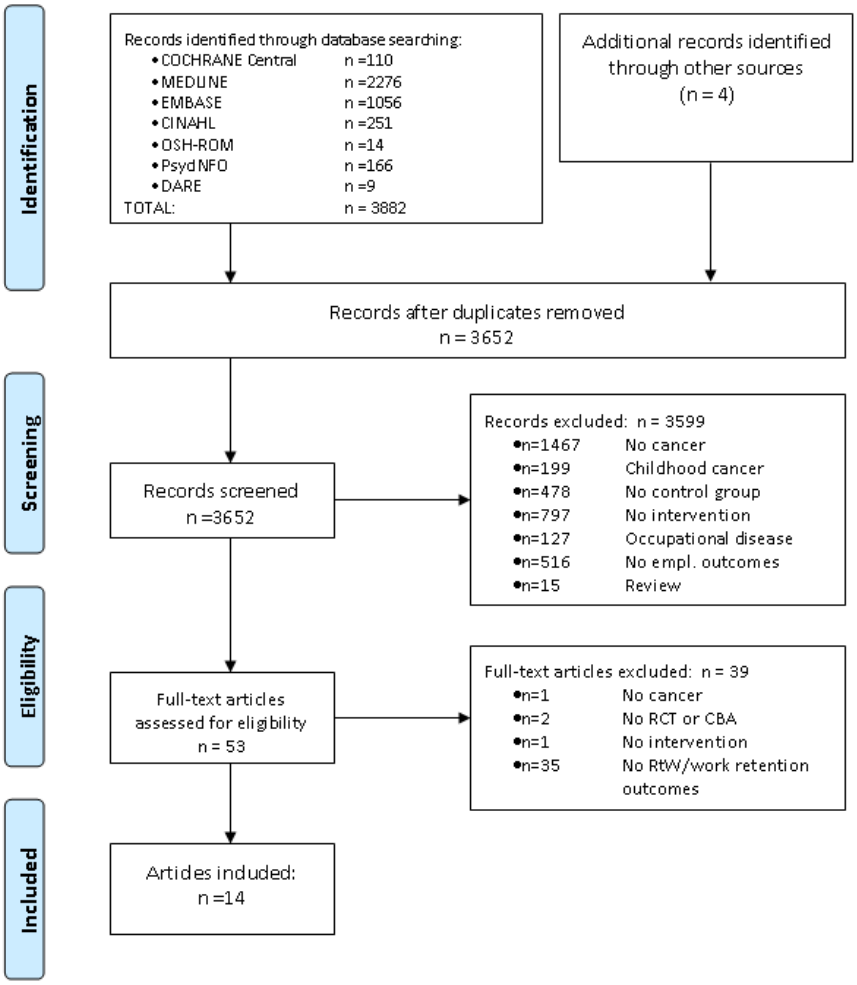
Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Results of the search

Figure 1 shows a flow diagram of included and excluded studies. Through a comprehensive literature search, 3882 potentially relevant records were identified through database searching with the majority (59%) retrieved by MEDLINE. After removing duplicates, a total of 3652 potentially relevant references were identified and screened for retrieval. A total of 3599 references were excluded based on the title and abstract with the most frequent reasons for reference exclusion being 1) study not aimed at cancer patients (41%); 2) study does not involve an intervention (22%); or 3) no return-to-work outcomes reported (14%). Other reasons were: no control group (13%), study involves survivors of childhood cancer (6%), study is aimed at cancer as an occupational disease (4%) or study is a review (N = 15, 0.4%).

Figure 1. Flow diagram of included studies.



Our search of the websites of ClinicalTrials.gov, Trialregister.nl and Controlled-trials.com identified an additional four ongoing studies (Bunnell 2010; Saarto 2010; Tamminga 2010; Velthuis 2010) which are listed in the Characteristics of ongoing studies table.

The reference lists of 15 retrieved systematic and narrative reviews (Beck 2003; de Backer 2009; Haaf 2005; Harvey 1982; Hersch 2009; Hoving 2009; Irwin 2004; Kirshbaum 2006; Kirshblum 2001; Liu 2009; McNeely 2006; Oldervoll 2004; Stanton 2006; Steiner 2010; van der Molen 2009) were checked to identify potentially eligible additional studies. Four additional potentially eligible studies were found. We contacted the corresponding authors of four studies that fulfilled the inclusion criteria but provided insufficient data, to inquire after any additional published or unpublished study data that may be relevant. Based on the information kindly provided by the authors, two studies were included (Ackerstaff 2009; Rogers 2009) and two studies were excluded (Gordon 2005; Wiggins 2009). The reference lists of all articles that were retrieved as full papers were checked in order to identify potentially eligible studies but no additional studies were identified.

Included studies

Characteristics of studies and participants

Fourteen articles describing altogether 14 RCTs and 4 CBAs were included. These studies involved a total of 1652 participants. Table 1 gives an overview of the main characteristics of the 14 articles which described a total of 18 studies. All of the studies were conducted in high income countries, with the majority of articles describing research from the United States (N = 7) while another seven articles reported studies in Europe (UK N = 2; Sweden N = 2; the Netherlands N = 1; France N = 1; Germany N = 1). Interventions in eight studies were aimed at breast cancer patients (Berglund 1994; Gordon (breast) 1980; Johnsson (goserelin) 2007; Johnsson (tamo+gose) 2007; Johnsson (tamoxifen) 2007; Lee 1992; Maguire 1983; Rogers 2009). Three studies involved prostate cancer patients (Burgio 2006; Lepore (PE) 2003; Lepore (PE+discus) 2003), two studies thyroid cancer patients (Borget 2007; Emmanouilidis 2009), two gynaecological patients (Capone 1980; Kornblith 2009), and one study each showed results for melanoma patients (Gordon (melanoma) 1980), head and neck cancer patients (Ackerstaff 2009), and laryngeal cancer patients (Hillman 1998). For further details regarding the study populations and settings see 'Characteristics of included studies'.

Table 1. Characteristics of included studies

Author	Year	Country	Diagnosis	Design	Number	Intervention	Control	Type
Ackerstaff	2009	Netherlands	Head, neck	RCT	34 vs 28	Intra-arterial chemoradiation	Intravenous chemoradiation	Medical
Berglund	1994	Sweden	Breast	RCT	81 vs 73	Physical training, patient education and training of coping skills re RTW	Care as usual	Multidisciplinary
Borget	2007	France	Thyroid	CBA	173 vs 119	Thyroid stimulating hormone after surgery	Later provision of TSH	Medical
Burgio	2006	USA	Prostate	RCT	28 vs 29	Biofeedback behavioral training	Care as usual	Multidisciplinary
Capone	1980	USA	Gynaecologic	CBA	20 vs 14	Individual counselling	Care as usual	Psychological

Table 1. Characteristics of included studies (*Continued*)

Emmanouilidis	2009	Germany	Thyroid	RCT	7 vs 6	L-thyroxine after surgery	Later provision of L-thyroxine	Medical
Gordon	1980	USA	Breast Melanoma	CBA	16 vs 19 43 vs 28	Patient education and individual counselling	Care as usual	Psychological
Hillman	1998	USA	Laryngeal	RCT	80 vs 63	Chemotherapy	Laryngectomy	Medical
Johnsson	2007	Sweden	Breast	RCT	53 vs 17 55 vs 17 64 vs 17	1) Tamoxifen 2) Goserelin 3) Tamoxifen+Goserelin	No endocrine therapy	Medical
Kornblith	2008	USA	Endometrial	RCT	164 vs 73	Laparoscopy	Laparotomy	Medical
Lee	1992	UK	Breast	RCT	44 vs 47	Breast conservation	Mastectomy	Medical
Lepore	2003	USA	Prostate	RCT	41 vs 20 43 vs 20	1) Patient education 2) Patient education + group discussion	Care as usual	Psychological
Maguire	1983	UK	Breast	RCT	42 vs 46	Physical training, individual counselling and encouragement of RTW	Care as usual	Multidisciplinary
Rogers	2009	USA	Breast	RCT	14 vs 14	Physical activity training	Care as usual	Physical

Type of return-to-work interventions

This review reports on the results of five psychological interventions, one physical intervention, nine medical interventions and three multidisciplinary interventions which were a combination of psychological, vocational and physical interventions. No vocational interventions were found nor multidisciplinary interventions which included a medical intervention.

Of the five psychological interventions, one included patient education alone (Lepore (PE) 2003), one included individual counselling alone (Capone 1980), two were a combination of patient education and individual counselling (Gordon (breast) 1980; Gordon (melanoma) 1980) and one was a combination of patient education and group discussion (Lepore (PE+discus) 2003). Patient education involved providing information about medical system and patient's own condition while counselling was mostly aimed at coping. In both cases, the intervention was usually provided by an oncology nurse or psychologist. In the study of Lepore et al. (Lepore (PE) 2003) an intervention which only included patient education involving lectures delivered by an expert on e.g. physical side effects, stress and coping was compared with care as usual. In a second intervention group, group discussions to improve coping were added to the patient education and also compared to care as usual. With regard to the CBAs, in the studies of

Gordon et al. (Gordon (breast) 1980; Gordon (melanoma) 1980) the interventions focused on educating the patient about how to live with the disease effectively and on patient counselling, focused on the patient's reactions and feeling toward disease. The intervention was executed separately in two studies for breast cancer patients (Gordon (breast) 1980) and melanoma patients (Gordon (melanoma) 1980), each with their own control group. Capone et al. (Capone 1980) evaluated an individual counselling programme modelled on crisis intervention including encouraging return to social roles.

The physical intervention included a moderate walking programme (Rogers 2009). This training programme included an individually supervised exercise session, face to face counselling sessions with an exercise specialist, and home-based exercises.

The nine medical interventions were diverse and were aimed at intra-arterial chemoradiation (Ackerstaff 2009), thyroid stimulating hormones after surgery (Borget 2007; Emmanouilidis 2009), chemotherapy (Hillman 1998), endocrine therapy (Johnsson (goserelin) 2007; Johnsson (tamo+gose) 2007; Johnsson (tamoxifen) 2007), laparoscopy (Kornblith 2009) and breast conservation (Lee 1992). Ackerstaff 2009 et al. compared a group of head and neck patients receiving intra-arterial cisplatin infusion versus a group receiving the standard intravenous chemoradiation. Another RCT evaluated the effect of the use of recombinant human TSH directly after thyroidectomy, hence avoiding hypothyroidism compared to the use of recombinant human TSH after a period of withholding thyroid hormones (Emmanouilidis 2009). Borget 2007 evaluated the effect of early provision of thyroid hormones in patients with thyroid cancer in an earlier CBA study. Three RCTs studied the effect of an intervention using more minimal surgery compared to more radical surgery with return-to-work as one of the outcomes: two studies on chemotherapy versus surgery and laparoscopy versus laparotomy (Hillman 1998; Kornblith 2009) and another study in breast cancer patients comparing conservation surgery compared to mastectomy (Lee 1992). The effect of a minimal adjuvant treatment (no medication) compared to the administration of three different types of adjuvant endocrine therapy compared on return-to-work in breast cancer patients was studied by Johnsson et al. (Johnsson (goserelin) 2007; Johnsson (tamo+gose) 2007; Johnsson (tamoxifen) 2007).

The three multidisciplinary interventions involved physical training, in combination with patient education (Berglund 1994; Burgio 2006), or counselling (Maguire 1983). Two of these studies incorporated vocational counselling training aimed at encouragement of return-to-work (Maguire 1983) and training of coping skills regarding return-to-work (Berglund 1994) while the third study included behavioural biofeedback (Burgio 2006).

Setting, design and outcomes

Sixteen studies were conducted in a hospital, one study was set in the community (Rogers 2009) and in one study the setting was not reported (Berglund 1994). Fourteen studies employed a randomised controlled study design (RCT) (Ackerstaff 2009; Berglund 1994; Burgio 2006; Emmanouilidis 2009; Hillman 1998; Johnsson (goserelin) 2007; Johnsson (tamo+gose) 2007; Johnsson (tamoxifen) 2007; Kornblith 2009; Lee 1992; Lepore (PE) 2003; Lepore (PE+discus) 2003; Maguire 1983; Rogers 2009) and four studies used a controlled before-after design (CBA) (Borget 2007; Capone 1980; Gordon (breast) 1980; Gordon (melanoma) 1980).

Return-to-work measured as event rates such as return-to-work rates was measured in 15 studies of which 11 were RCTs (Ackerstaff 2009; Berglund 1994; Burgio 2006; Hillman 1998; Johnsson (goserelin) 2007; Johnsson (tamo+gose) 2007; Johnsson (tamoxifen) 2007; Lee 1992; Lepore (PE) 2003; Lepore (PE+discus) 2003; Maguire 1983) and 4 were CBAs (Borget 2007; Capone 1980; Gordon (breast) 1980; Gordon (melanoma) 1980). Return-to-work measured as time to event data such as number of days between reporting sick and any work resumption or the number of days on sick leave during the follow-up period was reported in three RCT studies (Emmanouilidis 2009; Kornblith 2009; Rogers 2009). Quality of life was measured as a secondary outcome in seven RCTs (Ackerstaff 2009; Berglund 1994; Burgio 2006; Kornblith 2009; Lepore (PE) 2003; Lepore (PE+discus) 2003; Rogers 2009).

Excluded studies

Of the 3882 potentially relevant records, 53 articles were retrieved for a more detailed evaluation. Of these 53 full-text articles 39 were excluded because the intervention was not aimed at cancer patients (N = 1), the study design was not RCT or CBA (N = 2) or the article did not describe an intervention (N = 1). Most articles (N = 35) were excluded because no return-to-work outcomes were reported. Of these 35 articles, four trials used the vocational environment scale instead of return-to-work and in three articles the outcome was return to normal activity including household tasks, social and family roles. For a detailed description of the reasons for exclusion see the table of 'Characteristics of excluded studies'.

Risk of bias in included studies

For results of risk of bias assessment of RCTs, see 'Characteristics of included studies'. The results are summarised in the risk of bias graph which is an overview of the review authors' judgements about each risk of bias item presented as percentages across all included studies (Figure 2). Figure 3 shows the risk of bias summary of each risk of bias item for each included study. Overall, twelve RCTs (Ackerstaff 2009; Burgio 2006; Hillman 1998; Johnsson (goserelin) 2007; Johnsson (tamo+gose) 2007; Johnsson (tamoxifen) 2007; Kornblith 2009; Lee 1992; Lepore (PE) 2003; Lepore (PE+discus) 2003; Maguire 1983; Rogers 2009) were considered to have low risk of bias for the relevant outcomes (Table 2) whereas the remaining two studies were assessed to have high risk of bias (Berglund 1994; Emmanouilidis 2009).

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies. Please note that the blank space corresponds to the study(ies) having a CBA design.

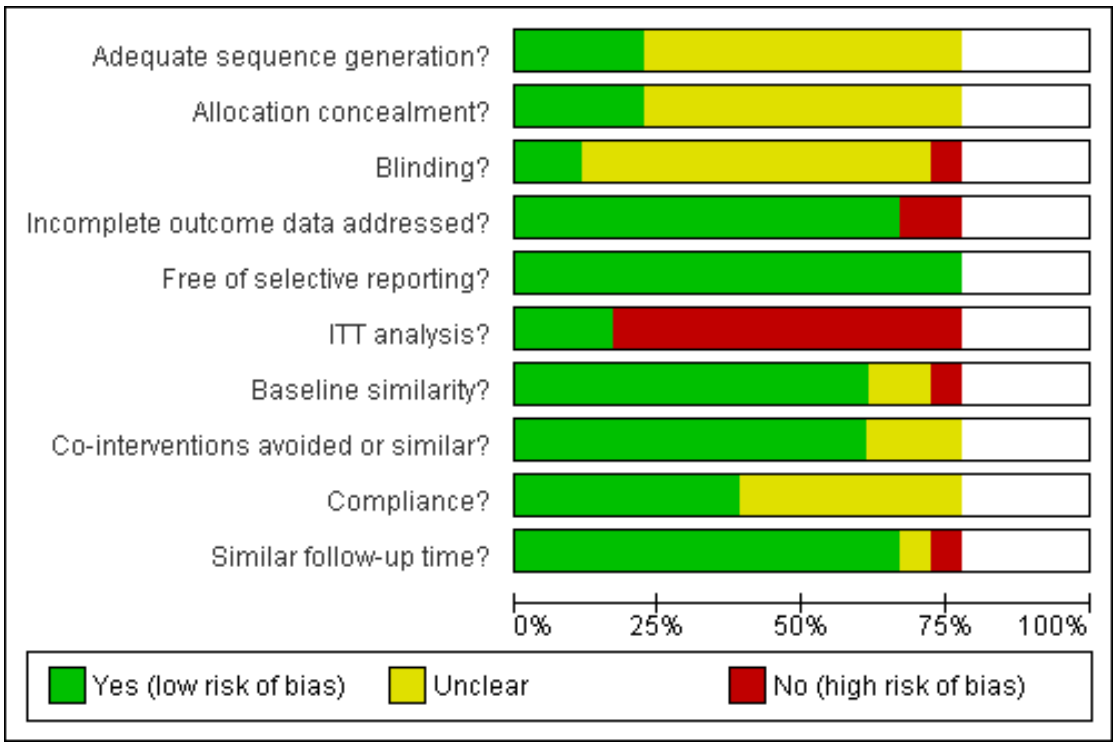


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study. Please note that the blank space corresponds to the study(ies) having a CBA design.

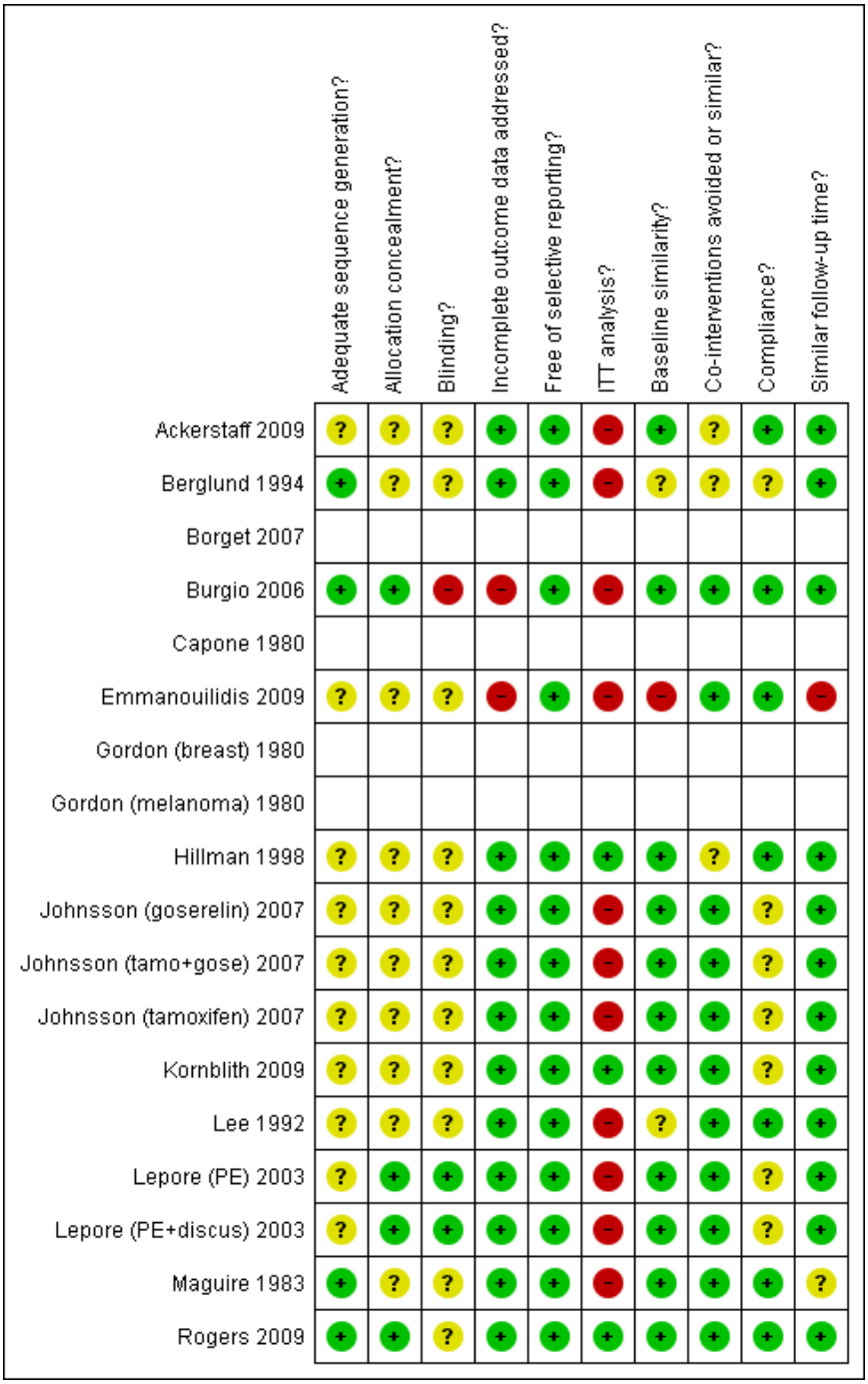


Table 2. Quality of the evidence (GRADE)

Comparison / outcome	Study design	Risk of bias in studies	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence
Psychological versus Care as usual / return-to-work	2 RCTs	Low	Low	High	High	Low	Low quality
Psychological versus Care as usual / return-to-work	3 CBA	Low	Low	High	High	Low	Low quality
Physical versus Care as usual / return-to-work	1 RCT	Low	-	High	High	Low	Very low quality
Medical function conserving versus Medical more radical / return-to-work	8 RCTs	Low	High	Low	High	Low	Low quality
Medical function conserving versus Medical more radical / return-to-work	1 CBA	High	-	High	High	Low	Very low quality
Multidisciplinary physical, psychological and vocational interventions versus Care as usual / return-to-work	3 RCTs	Low	Low	High	Low	Low	Moderate quality

Column headings (with explanations in parentheses): Study design (RCT = randomised controlled trial, CBA = controlled before-after study), Risk of bias in studies (likelihood of reported results not being an accurate estimate of the truth), Inconsistency (lack of similarity of estimates of treatment effects), Indirectness (lack of ability to generalize) and Imprecision (insufficient number of patients or wide confidence intervals) of results and Publication bias (probability of selective publication of trials and outcomes) across all studies that measured that particular outcome.

An overview of the risk of bias in non-RCTs (Borget 2007; Capone 1980; Gordon (breast) 1980; Gordon (melanoma) 1980) was assessed using the Downs and Black checklist (Downs 1998) for methodological quality assessment and the results are reported in Table 3. Three CBA studies were considered to have low risk of bias (Capone 1980; Gordon (breast) 1980; Gordon (melanoma) 1980) and one study was assessed to have high risk of bias (Borget 2007)

Table 3. Methodological quality (risk of bias) in non-randomised studies

Study	Gordon (breast) 1980	Gordon (melanoma) 1980	Capone 1980	Borget 2007
Blinding subjects	0	0	0	0
Blinding assessors	0	0	0	0
No unplanned subgroup analyses	1	1	1	1
Follow-up similar	0	0	1	0
Appropriate statistical tests	1	1	1	1
Compliance reliable	1	1	0	0
Measurements valid and reliable	1	1	1	0
Recruitment same population	1	1	1	0
Recruitment same time	1	1	1	0
Loss to follow-up small	1	1	0	0
Overall risk of bias	Low	Low	Low	High

Allocation

Of the 11 articles describing a randomised controlled trial, only four articles reported adequate sequence generation and adequate allocation concealment (Berglund 1994; Burgio 2006; Maguire 1983; Rogers 2009). Random numbers generated by a computer or random number tables were used. Allocation was concealed be-

cause randomisation was performed by a research nurse or independent interviewer.

Blinding

The majority of randomised trials did not report any information on blinding of either the patients, the persons performing the intervention or the assessors of the outcomes. The studies of Lepore et al. (Lepore (PE) 2003; Lepore (PE+discus) 2003) reported blinding the interviewer assessing the outcomes and blinding the patients for the hypothesis. One study (Burgio 2006) explicitly reported that patients and interventionists were not blinded. Also, the four studies reporting a controlled before-after study did not blind either the patients or assessors (Borget 2007; Capone 1980; Gordon (breast) 1980; Gordon (melanoma) 1980).

Incomplete outcome data

Most studies reported reasons for drop-out of the patients and had the incomplete outcome data addressed. In two studies no information was provided for patients with missing data (Burgio 2006) or no drop-outs were reported (Emmanouilidis 2009). There was no adequate adjustment for confounding in the analyses because in most studies no intention-to-treat analyses were performed. Intention-to-treat (ITT) analyses were reported in the three studies of Hillman and Rogers in which ITT-analyses were performed between the two randomised groups even if the procedure was converted to the other randomisation (Hillman 1998; Rogers 2009), and the study of Kornblith in which 21% converted to control group but ITT analyses were performed (Rogers 2009). Of the four non-RCT studies, only the studies of Gordon reported a small loss to follow-up (Gordon (breast) 1980; Gordon (melanoma) 1980).

Selective reporting

All RCT studies were judged to be free of selective reporting of the outcomes because all outcomes described in the methods were reported. No non-RCT studies performed any unplanned subgroup analyses.

Other potential sources of bias

Baseline characteristics of the patients were similar in most studies. However, some studies included a heterogeneous group of patients but obviously could only perform the analyses on employment outcomes in patients employed at baseline. Separate data on the similarity of baseline characteristics on these groups of employed patients were not given (Burgio 2006; Hillman 1998; Kornblith 2009; Lepore (PE) 2003; Lepore (PE+discus) 2003; Rogers 2009). In two studies it was stated that baseline characteristics were similar but the actual data were not given (Lee 1992; Maguire 1983), in one study no baseline characteristics were provided (Berglund 1994) and in one study the baseline characteristics were different (Emmanouilidis 2009).

Co-interventions were avoided or similar in both groups. Compliance with the intervention was not always reported but was satisfactory in those studies that did report it (Ackerstaff 2009; Burgio 2006; Emmanouilidis 2009; Gordon (breast) 1980; Gordon (melanoma) 1980; Hillman 1998; Lee 1992; Rogers 2009). Follow-up time was similar in all studies except for Emmanouilidis (Emmanouilidis 2009) and unclear in the studies of Maguire (Maguire 1983), Gordon (Gordon (breast) 1980; Gordon (melanoma) 1980) and Borget (Borget 2007). In the non-RCT studies, Gordon (Gordon (breast) 1980; Gordon (melanoma) 1980) and Capone (Capone 1980) patients for both groups were recruited from the same population and in the same time period.

One study was funded by the pharmaceutical company supplying the medication in the study (Borget 2007).

Effects of interventions

The 18 included studies evaluated the effects of four types of interventions in cancer patients: psychological interventions, physical intervention, medical interventions and interventions which are a combination of psychological, vocational and physical interventions.

Psychological interventions

Two RCTs reported in the same article (Lepore (PE) 2003; Lepore (PE+discus) 2003) compared the effect of a psychological intervention to care as usual. The results of these two studies indicated that there is low quality evidence (Table 2) of no difference in the effect of psychological interventions compared to care as usual on return-to-work (OR = 2.32, 95% CI 0.94 to 5.71).

Results of the CBAs (Capone 1980; Gordon (breast) 1980; Gordon (melanoma) 1980) showed that there is low quality evidence (Table 3) that psychological interventions improve the return-to-work in cancer patients more than alternative care as usual (OR = 4.67, 95% CI 2.04 to 10.70).

The results for the RCTs for the secondary outcome quality of life for physical functioning and mental functioning showed that there is no difference in the effect of psychological interventions compared to care as usual in physical functioning or mental functioning quality of life (MD = 1.43, 95% CI -0.71 to 3.57 and MD = 0.14, 95% CI -1.62 to 1.91).

Vocational interventions

No vocational interventions were retrieved.

Physical interventions

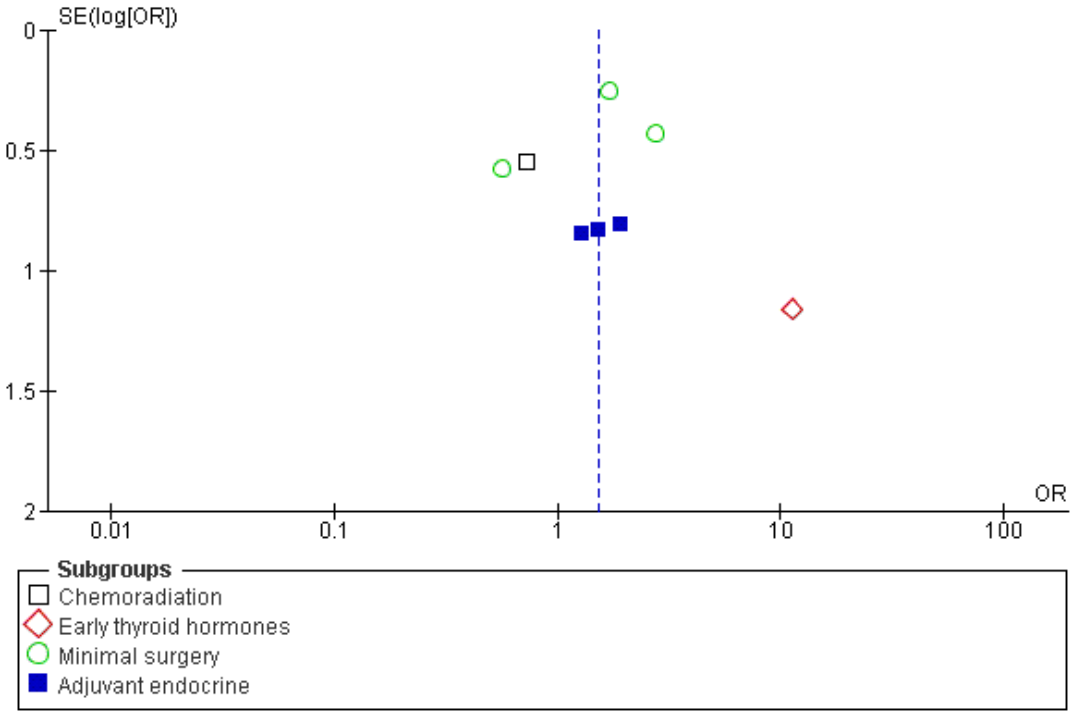
Rogers et al. (Rogers 2009) reported an RCT in which breast cancer patients were offered a physical training programme. Results showed that there is very low quality evidence (Table 2) that the physical training programme was not more effective than care as usual on improving return-to-work (OR = 1.20, 95% CI 0.32 to 4.54) or quality of life (MD = -4.60, 95% CI -11.99 to 2.79) .

Medical interventions

Nine studies, that included eight RCTs and one CBA, assessed the effects of a medical intervention on return-to-work. In all studies a less radical or function conserving medical intervention was compared with a more radical treatment, with the hypothesis that a function conserving medical treatment would improve return-to-work in cancer patients.

Results of the meta-analysis of the eight RCTs showed that there was low quality evidence (Table 2) that function conserving approaches had similar return-to-work rates as more radical treatments (OR = 1.53, 95% CI 0.95 to 2.45). Possible publication bias was assessed for the eight RCT studies assessing the effect of a less radical medical treatment on return-to-work. The funnel plot (Figure 4) showed that there might be a publication bias for studies reporting non-significant outcomes but results are unclear.

Figure 4. Funnel plot of comparison: 4 Medical function conserving versus Medical more radical-RCTs, outcome: 4.1 return-to-work.



Results of the one CBA study showed very low quality evidence (Table 3) that a medical, function conserving approach has similar return-to-work rates as a more radical treatment.

No differences in the effect of function conserving medical interventions compared to more radical treatment were found on quality of life outcomes (MD = 1.37, 95% CI -0.62 to 3.36).

Multidisciplinary interventions

Meta-analysis showed that there is moderate quality evidence (Table 2) that multidisciplinary interventions which combined

physical exercises with patient education, patient counselling, biofeedback assisted behavioral training and / or vocational counselling led to higher return-to-work rates than care as usual (OR = 1.87, 95% CI 1.07 to 3.27). No differences in the effect of multidisciplinary interventions compared to care as usual were found on quality of life outcomes (MD = -0.07, 95% CI -0.33 to 0.19).

DISCUSSION

Summary of main results

Eighteen studies described in fourteen articles met the inclusion criteria of this review. The 18 studies included a total of 1652 participants comprising 14 RCTs and 4 CBAs. There was moderate quality evidence from two RCTs that psychological interventions do not result in an improved return-to-work (Lepore (PE) 2003; Lepore (PE+discus) 2003) while the low quality evidence results of the CBA studies did find an improved return-to-work for psychological interventions (Capone 1980; Gordon (breast) 1980; Gordon (melanoma) 1980). No vocational interventions were retrieved. One trial compared physical training with care as usual and showed very low evidence for no significant differences on return-to-work compared to care as usual (Rogers 2009). Low quality evidence from eight RCTs indicated no differences between the execution of either function conserving versus more radical medical interventions for return-to-work outcomes and this was confirmed with very low evidence from a CBA study (Ackerstaff 2009; Borget 2007; Emmanouilidis 2009; Hillman 1998; Kornblith 2009; Lee 1992; Johnsson (goserelin) 2007; Johnsson (tamo+gose) 2007; Johnsson (tamoxifen) 2007). There was moderate evidence that multidisciplinary interventions of physical exercises combined with patient education, counselling, biofeedback assisted behavioural training and / or vocational counselling are effective in enhancing return-to- work (Berglund 1994; Burgio 2006; Maguire 1983).

Overall completeness and applicability of evidence

The studies described in this review were conducted over a large time span of almost forty years. While some studies were executed in the 1970s and reported in the 1980s (Capone 1980; Gordon (breast) 1980; Gordon (melanoma) 1980; Maguire 1983), no studies were carried out in the 1980s, few studies were accomplished in the 1990s (Berglund 1994; Hillman 1998; Lee 1992) and most studies of this review have been performed in the last decade (Ackerstaff 2009; Borget 2007; Burgio 2006; Emmanouilidis 2009; Johnsson (goserelin) 2007; Johnsson (tamo+gose) 2007; Johnsson (tamoxifen) 2007; Kornblith 2009; Lepore (PE) 2003; Lepore (PE+discus) 2003; Rogers 2009). In these forty years, medical treatment for cancer has changed enormously. For this reason, older medical studies (Hillman 1998; Lee 1992) might describe medical treatments which are not employed anymore. With regard to the psychological and multidisciplinary interventions described in the older studies it has to be noted that they have changed as well because they are more evidence-based, more cognitive behavioural therapy-oriented, briefer, more targeted and more effective than 20 to 30 years ago. Thus, it can be assumed they are at least as relevant today as they were in the 1970s because of these theoretical and practical improvements underneath these interventions.

The present review considers patients from both the USA and Europe. Social security systems and labour markets differ widely between countries and thus the effects of cancer survivorship on employment vary. However, in all studies the effect of the interventions were compared in the same country and usually in a RCT and, therefore, the influence of a social security system was equal within studies. When generalising the results from one country to another, the potential effect of a country's social security sytem should still be considered. For the generalisation of the results of this review to countries outside Europe or the USA, cultural differences regarding employment and cancer disclosure should be taken into account.

Patients with breast cancer were the most studied diagnosis group (Berglund 1994; Gordon (breast) 1980; Johnsson (goserelin) 2007; Johnsson (tamo+gose) 2007; Johnsson (tamoxifen) 2007; Lee 1992; Maguire 1983; Rogers 2009) while other studies were aimed at patients with prostate cancer (Burgio 2006; Lepore (PE) 2003; Lepore (PE+discus) 2003), thyroid cancer (Borget 2007; Emmanouilidis 2009), gynaecological cancer (Capone 1980; Kornblith 2009), melanoma (Gordon (melanoma) 1980), head and neck cancer (Ackerstaff 2009), and laryngeal cancer (Hillman 1998). Breast cancer is the most prevalent cancer diagnosis within the working population followed by blood and lymph cancers, prostate cancer, thyroid cancer, and colorectal cancer (Short 2005). No studies were aimed at patients with colorectal, blood or lymph cancer (despite them being common in cancer survivors of working age) nor aimed at less prevalent cancer diagnoses including brain cancer, bone cancer and other gastro-intestinal cancers. We think that the mechanisms of the return-to-work interventions will perform similarly over cancer diagnoses and thus patients with colorectal, blood or lymph cancer will experience the same benefits from any interventions aimed at improving return-to-work. However, long-term and late effects of specific treatments for specific cancers may differ and play a role in the return-to-work process. Ultimately, we do not know this because of the lack of evidence. Furthermore, only multidisciplinary interventions of physical exercise with or without vocational counselling plus either patient education, counselling or behavioural biofeedback were proven to be effective in improving return-to-work. These studies were conducted in patients with breast cancer (Berglund 1994; Maguire 1983) or prostate cancer (Burgio 2006) so it is not proven that patients with any other diagnoses will benefit from multidisciplinary interventions.

Although most multidisciplinary interventions did have a vocational component, no vocational interventions focusing on employment issues were found. This is remarkable because one would expect interventions aimed at return-to-work to consist of work-related components such as work adjustments or involvement of the supervisor. Earlier research in young cancer survivors concluded that vocational rehabilitation interventions such as vocational training, job search assistance, job placement services, on-the job support and maintenance services were all associated with an increased odds for employment (Strauser 2010). Since multidisciplinary interventions containing vocational counselling or coping with employment issues proved to be effective, more specific or more targeted vocational interventions should be developed and evaluated.

Quality of the evidence

In general, in the majority of the studies it was not reported and thus remains unclear if intention-to-treat analyses were performed. Moreover, the included studies did in general not implement blinding of providers, patients or outcome assessors or the blinding was unclear. It can be argued that blinding is not feasible in this kind of study and that lack of blinding should not be considered a weakness, but the absence of blinding can be associated with bias even though blinding is not feasible. However, blinding of the outcome assessors and blinding of the patients to the hypothesis of the study are possible. The possibility for bias should, therefore, be taken into account but unfortunately it was not discussed in most of the reports. Further selection bias might have been induced in the majority of the studies because adequate sequence generation and allocation concealment were scored 'unclear' in most RCTs.

In this review a total of 18 studies involving 1652 participants were analysed which is a considerable number of patients. However, the number of patients analysed in the studies was generally low with 11 studies providing less than 50 patients in each group thus limiting the power of the studies. In addition, four different types of interventions were considered and each type of intervention contained several subtypes of interventions. As a result most subtypes of interventions only described one study and meta-analyses for the subtypes of interventions were not possible. Therefore, it was not possible to perform subgroup analyses according to diagnosis or quality of the study.

For multidisciplinary, physical, psychological and vocational interventions compared to care as usual, we included three studies with 299 patients, and concluded that there is moderate quality evidence as assessed with the GRADE approach that multidisciplinary physical, psychological and vocational interventions are more effective than care as usual in return-to-work. However, for most other comparisons and outcomes, the quality of the evidence was downgraded due to few available studies, non-RCT design, risk of bias, indirect results and imprecise effect estimates. GRADE assessments are partly based on subjective judgements and are not definite, nevertheless GRADE does provide a transparent and consistent classification of the quality of evidence for relevant comparisons and outcomes.

Potential biases in the review process

We sought to conduct a comprehensive and transparent review. The entire process of study search, study selection, data extraction and management, and assessment of risk of bias of included studies was independently performed by two authors and all results were discussed until consensus was reached.

We searched for articles in ten electronic databases using 130 key words or combinations of key words combined with checking the reference lists of included studies and selected reviews. All reasons for exclusion and inclusion of all 3652 potentially relevant studies were documented in duplicate and discussed. Information on data extraction and quality assessment was registered independently by two authors in an 8-page form for each study and combined in one consensus form with a third author giving advice in case of uncertainties. In case of any missing data or doubt on the correctness of data, the original authors were contacted. All four contacted authors replied and provided the requested data. Finally, we imposed no restrictions on language or publication date. Therefore, we think the risk of bias in the review process was small. Even though our search strategy was comprehensive and not language restricted, there is always a risk that relevant citations may have been lost in the review process.

One methodological consideration is the lack of information on baseline characteristics for the patients analysed in this review. In most studies (Ackerstaff 2009; Burgio 2006; Capone 1980; Emmanouilidis 2009; Gordon (breast) 1980; Gordon (melanoma) 1980; Hillman 1998; Kornblith 2009; Lee 1992; Lepore (PE) 2003; Lepore (PE+discus) 2003; Maguire 1983; Rogers 2009) data on return-to-work were only analysed for the patients who provided these data, i.e. the employed cancer patients in the study. However, baseline characteristics were given for the total group of cancer patients in these studies including the retired patients and homemakers. Therefore, the baseline characteristics of the patients included in this review were often unknown. As these baseline characteristics have not been reported we could not check if both groups within the studies had equal distribution of age, sex, and education which could have influenced the effects of the intervention on return-to-work. However, because most studies were randomised studies we assume that the distribution of age, sex and education in both groups of employed patients in each study were similar.

Another methodological consideration is the possibility that the Odds Ratios (ORs) could be overestimating the relative risks (RRs) because a RR approaches an OR for only small probabilities of < 10%. As the probabilities of not returning to work in the studies of this review were > 10% there might be an overestimation of

the effect. However, the OR for multidisciplinary interventions compared to care as usual was 1.87 (95% CI 1.07 to 3.27) which is a very large clinical effect.

From the risk of bias tables, it can be seen that some domains are scored "unclear", implying that the primary publications do not supply enough details to assess this point. The number of domains assessed as "unclear" should ideally be reduced by obtaining supplementary information from the primary authors, but for the course of simplicity we have chosen to complete our risk of bias tables based on information that is printed in the primary papers and information brought in from authors during preparation of earlier versions of this review.

Agreements and disagreements with other studies or reviews

This review concludes that multidisciplinary physical, psychological and vocational interventions enhance return-to-work for cancer patients. In a recent Cochrane review on persons with multiple sclerosis (MS), the effectiveness of vocational rehabilitation programmes compared to care as usual was evaluated on return-to-work (Khan 2009). Results of the studies included in their review showed that there was inconclusive evidence to support vocational rehabilitation for persons with MS because one study aimed at job retention did not find any positive effect while the other study geared towards return-to-work did report a significant positive effect. This is in line with this review, because the effective studies in this review, two of which contain a vocational rehabilitation component, were also aimed at return-to-work and not work retention.

A recent meta-analysis on the efficacy of multidisciplinary interventions on return-to-work for people on sick leave due to low back pain indicated that multidisciplinary interventions including behaviour-oriented physiotherapy, cognitive behavioural therapy, behavioural medicine, light mobilisation, rehabilitation problem-solving therapy, behavioural graded activity and / or personal information more effectively improve return-to-work than the alternatives (Norlund 2009). This result is also in agreement with our meta-analysis which showed that multidisciplinary interventions are more effective than alternative programmes in improving return-to-work in cancer patients.

The studies we found in our literature search were all person-directed interventions aimed at the patients. No work-directed vocational interventions were identified that were aimed at the workplace and including workplace adjustments such as modified work hours, modified work tasks, or modified workplace and improved communication with or between managers, colleagues and health professionals. An earlier systematic review on workplace-based return-to-work interventions found strong evidence that work disability duration is significantly reduced by work accommodation offers and contact between healthcare provider and workplace; and moderate evidence that it is reduced by interventions which include early contact with worker by workplace, ergonomic work site visits, and presence of a return-to-work coordinator (Franche 2005). Although we did find that multidisciplinary physical, psychological and vocational interventions enhance return-to-work for cancer patients, this effect might be enforced by added work-directed vocational components to the interventions.

In this review low quality evidence was found that psychosocial interventions are as effective as care as usual in enhancing return-to-work in cancer patients. This result is caused by heterogeneity in the RCTs on which the effect was assessed. We decided to exclude CBAs from our decision on the effectiveness of interventions and so the low quality evidence for a better return-to-work for psychological interventions compared to care as usual in the CBAs was not decisive. An earlier meta-analysis found that cognitive behaviour training (CBT) has a positive effect on quality of life, depression and anxiety in adult cancer survivors but that patient education (PE) does not (Osborn 2006). Results from our review show that interventions with patient education do have a positive effect in return-to-work of cancer patients, especially when they are part of a multidisciplinary intervention.

AUTHORS' CONCLUSIONS

Implications for practice

There is moderate quality evidence that multidisciplinary interventions of physical training, psychological and / or vocational elements improve the return-to-work of cancer patients. The most apparent setting for this intervention would be the hospital because all multidisciplinary providers are located there and it is the main focal point for the patients. Interventions conducted in a hospital setting are feasible for recently diagnosed cancer patients who are under treatment with curative intent and who are expected to have sufficient recovery to return to work. Other possible settings for return-to-work interventions for cancer patients would be multidisciplinary rehabilitation outpatient services in community or reintegration teams at large workplaces or multinational corporations. Thus, it should be possible to find ways to improve return-to-work of cancer survivors.

Regarding psychological, physical interventions or function conserving medical interventions the low quality evidence is limited or inconclusive.

Implications for research

Multidisciplinary physical, psychological and vocational interventions do enhance return-to-work for cancer patients. Most research so far has mainly been conducted in breast cancer patients, prostate cancer patients and gynaecological patients. Research should additionally focus on patients with other prevalent diagnoses of cancer in the working population such as colorectal cancer and blood

or lymph cancers. Other important patient characteristics such as age, education and ethnicity should also be measured. Future research on enhancing return-to-work in cancer patients should involve multidisciplinary interventions with a physical, psychological and vocational component. The vocational component should not be just patient-oriented but should be directed at the work environment (including work adjustments and supervisors) as well. With regard to psychological interventions it is unclear whether patient education and / or patient counselling is most effective. Both interventions should be compared against each other and care as usual.

No vocational interventions aimed at enhancing return-to-work in cancer patients were retrieved for this review although one would expect the largest impact on return-to-work from this kind of intervention. Future research should focus on vocational interventions which include any type of intervention focused on employment. Vocational interventions might be person-directed aiming at the patient to encourage return-to-work, vocational rehabilitation, or occupational rehabilitation, or they might be work-directed aiming at the workplace including workplace adjustments such as modified work hours, modified work tasks, or modified workplace and improved communication with or between managers, colleagues and health professionals.

So far, not all studies comparing the effect of an intervention on return-to-work with care as usual or an alternative intervention have been executed in a randomised controlled design. As a consequence, the quality of evidence in some studies was rated very low and no conclusions of the effect could be drawn. More high-quality RCTs are needed. Therefore, all studies evaluating the effect of an intervention on return-to-work should employ a randomised controlled design although this might sometimes be difficult in daily practice. In some cases, a cluster-randomised controlled design might have to be chosen in which the providers of the intervention of the settings are randomised and not the patients. In addition, the studies described in this review were relatively small and RCTs with a much greater number of patients involved are necessary.

With regard to outcome measures, many more clinical trials should incorporate return-to-work measures as an outcome measure. For instance, currently many trials are being executed evaluating the effect of physical exercise on physical fitness, fatigue or quality of life, but almost none of these studies is evaluating the effect on sick leave duration or return-to-work although it is expected these interventions are beneficial for employment. With regard to medical interventions, less radical or invasive treatments which give comparable medical outcomes are always sought. In the evaluation of these interventions not only medical outcomes or quality of life should be analysed but also work-related outcome measures. In future research, work-related outcome measures should not only include the rate of patients returning to work because this is a valid, but broad indication of return-to-work. Other work-related outcome measures such as total number of days of sick leave from first day of sick leave until first day of return, measures of work retention once back at work and work productivity should be measured. Studies also needed to define what return-to-work is: return to full-time or part-time work and return to the same job or a lesser job. Finally, studies need to invest in a much longer follow-up of work-related outcomes. Many treatments for cancer take several months and result in long-lasting side effects. Furthermore, work disability can be episodic so given these fluctuations in work absence we need long term follow-up. We also need to learn more about the natural history of work disability in cancer so we have a better idea of time frames to design studies. Therefore, the follow-up should be at least 12 months but preferably 24 months.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Ackerstaff 2009

Methods	RCT, hospital setting
Participants	34 vs 28 head and neck cancer patients Inclusion criteria: Inoperable stage IV head and neck cancer Exclusion criteria: Not reported
Interventions	Intervention group: Intra-arterial cisplatin infusion Provider: Oncologist Setting: Hospital Control group: Standard intravenous chemoradiation
Outcomes	Primary outcome measure (RTW outcomes): Return-to-work rate: Number of patients returned to work Registered by: Patient at baseline and 12 months after intervention Secondary outcome measure (QOL outcomes): Eortc-qlq c30 plus head and neck Registered by: Patient at baseline, 7 weeks, 3, 12 months
Notes	Results for working patients only in trial of 126 patients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Not reported
Incomplete outcome data addressed? All outcomes	Low risk	All reasons for drop out described
Free of selective reporting?	Low risk	All outcomes from methods are reported
ITT analysis?	High risk	Protocol violations were excluded
Baseline similarity?	Low risk	Demographics and disease characteristics similar
Co-interventions avoided or similar?	Unclear risk	Overall 25% patients had radiotherapy but unclear how many in each group
Compliance?	Low risk	After omission of 3 protocol violations

Ackerstaff 2009 (*Continued*)

Similar follow-up time?	Low risk	All after 12 months

Berglund 1994

Methods	RCT, setting not reported. Efron's method for randomisation of small groups: Group sizes were forced towards equality by proportionately increasing the probability of assignment to the smaller group.
Participants	87 vs 89 cancer patients (80% breast cancer, 8% ovarian cancer). Inclusion criteria: Age below 75 years, curative treatment for a primary tumour, inclusion within 2 months after post-operative treatment with radio- or chemotherapy. Exclusion criteria: Not reported
Interventions	Intervention group: During the first 4 weeks, patients met twice a week, once for information and once for physical training. The last 3 weeks were devoted to one session of coping skills training each week. An oncology nurse specialised in psychosocial issues conducted the groups during all sessions. She was accompanied by a specialist of the theme dealt with at each session. Physical training: Exercises to increase mobility, muscle strength, fitness, relaxation. Instruction for relaxation at home. Information: Effects of treatment, diet, development trough crises, alternative treatment. Coping: Role plays, how to handle attitudes towards cancer, meeting people asking too much, problem situations at hospital, anxiety and how to handle it. Intervention lasted 7 weeks Sessions: 11 sessions of 2 hours Provider: Oncology nurse and specialist Setting: Not reported Control group: N = 36 received single information session (oncologist and dietician information included in the intervention session); N = 65: care as usual.
Outcomes	Primary outcome measure (RTW outcomes): Work status: Number not working Registered by: Patient at baseline, 3, 6, 12 months Secondary outcome measure (QOL outcomes): Problems with quality of life - 2 items Registered by: Patient at baseline, 8-12 weeks, 3, 6, 12 months
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Low risk	Efron's method for randomisation of small samples
Allocation concealment?	Unclear risk	Not reported

Berglund 1994 (*Continued*)

Blinding? All outcomes	Unclear risk	Not reported
Incomplete outcome data addressed? All outcomes	Low risk	Reasons for non-response for all assessments are reported
Free of selective reporting?	Low risk	All outcomes from methods are reported
ITT analysis?	High risk	Not performed
Baseline similarity?	Unclear risk	No baseline characteristics reported
Co-interventions avoided or similar?	Unclear risk	Not reported
Compliance?	Unclear risk	Not reported
Similar follow-up time?	Low risk	All outcomes were measured 8-12 weeks post-intervention

Borget 2007

Methods	Controlled Before-After design, hospital setting
Participants	173 vs 119 thyroid cancer patients Inclusion criteria: Thyroid carcinoma, total thyroidectomy, radioiodine ablation Exclusion criteria: Not reported Known distant metastases
Interventions	Intervention group: Recombinant human thyroid -stimulating hormone (rhTSH) 0.9 mg intramuscular for two consecutive days. Intervention lasted 2 days Provider: Specialist Setting: Hospital Control group: Hormone withdrawal
Outcomes	Primary outcome measure (RTW outcomes): a) Number returned to work b) Mean duration of sick leave in days Registered by: Patient during the month before and the month after their control visit, 6-12 months after treatment.
Notes	Funding by provider of the medicine

Burgio 2006

Methods	RCT, hospital setting
Participants	28 vs 29 prostate cancer patients Inclusion criteria: Be ambulatory, be continent, be identified for the study at least 1 week prior to surgery, elected for radical prostectomy, prostate cancer. Exclusion criteria: > 2 episodes urinary incontinence in previous 6 months, incontinence, prior prostectomy, impaired mental status, less 1 week prior to surgery.
Interventions	Intervention group: Single session of biofeedback assisted behavioral training, including pelvic floor muscle control and exercise. Use of rectal probe to provide information on rectal pressure. Feedback and verbal instructions and reinforcement. Daily home practice. Intervention lasted 6 months Sessions: 1 session + daily at home Provider: Not reported Setting: Not reported and at home Control group: Brief verbal instructions to interrupt the urinary stream during voiding
Outcomes	Primary outcome measure (RTW outcomes): RTW rate at 6 months (Results for patients with paid employment at baseline.): Number returned to work Registered by: Patient at baseline and 6 months Secondary outcome measure (QOL outcomes): MOS-SF Registered by: Patient at baseline and 6 months
Notes	Results for patients with paid employment at baseline of a total of 102 patients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Low risk	Computer generated numbers
Allocation concealment?	Low risk	Randomised schedule was implemented by research nurse, so the interventionists would be blinded to next group assignment.
Blinding? All outcomes	High risk	No blinding to patients or interventionists. Blinding of data handling persons or researchers or outcome assessors (patients) unknown.
Incomplete outcome data addressed? All outcomes	High risk	Work-related outcomes: No information was provided for patients with missing data and no non-response analysis. For the work-related data for people working at baseline no attrition / exclusion statistics were given.
Free of selective reporting?	Low risk	All outcomes from methods are reported

Burgio 2006 (*Continued*)

ITT analysis?	High risk	Work-related outcomes: No information was provided for patients with incomplete data and no ITT analysis. For the work-related data for people working at baseline no attrition / exclusion statistics were given.
Baseline similarity?	Low risk	Similarity for age, sex; unknown for education.
Co-interventions avoided or similar?	Low risk	No co-interventions.
Compliance?	Low risk	70% were still doing exercises at home after 6 months.
Similar follow-up time?	Low risk	The same time points.

Capone 1980

Methods	CBA, hospital setting
Participants	20 vs 14 gynaecologic cancer patients Inclusion criteria: Primary malignancy of the genital organs, diagnosed no more than 6 weeks prior to hospitalisation Exclusion: Unable to speak English, unable to read, mental status precluding obtaining informed consent
Interventions	Intervention group: An individual counselling programme modelled on crisis intervention was utilized with the experimental patients. The counselling programme focused on shaping reality-based expectations, facilitating attainment, encouragement of adaptive behavioral change, reintegration of the holistic self, and processing of information. Experimental patients were individually counselled a minimum of 4 times during their hospital stay. The early sessions were directed towards helping patients express feelings of concern, anger, guilt, and fears. Self-esteem and femininity were the foci of the middle sessions while the final sessions focused on interpersonal relationships. Efforts were made to encourage early return to usual familial and social roles and functions. For sexually active patients, a sexual rehabilitation component was added to the counselling. Intervention took place during hospital stay Sessions: 4 Provider: Psychologist Setting: Hospital Control group: Psychological assessment but not counselled
Outcomes	Primary outcome measure (RTW outcomes): Return-to-work rate (results for patients with paid employment at baseline.): Number returned to work Registered by: Patient at baseline and 3, 6, 12 months Secondary outcome measure (QOL outcomes):
Notes	Results only for patients with paid employment at baseline

Emmanouilidis 2009

Methods	RCT, hospital setting
Participants	7 vs 6 thyroid cancer patients, thyroidectomised. Inclusion criteria: Differentiated thyroid cancer, thyroidectomised, received K1 a/b central lymphadenectomy. Exclusion criteria: Not reported
Interventions	Intervention group: L-Thyroxine (T4) medication initiated a day after thyroidectomy, followed by the use of recombinant human TSH stimulation and subsequent radioablation therapy (RAT) at first hospitalisation immediately after surgery. Provider: Endocrinologist Setting: Hospital Control group: L-l-thyroxine medication abstinence for 4 weeks, then radioablative therapy (RAT)
Outcomes	Primary outcome measure (RTW outcomes): Sick leave time from day of discharge of department of surgery until completion of first RAT Registered by: Not reported; Follow-up time: Not reported. Secondary outcome measure (QOL outcomes):
Notes	Results for working patients only in trial of 25 patients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Not reported
Incomplete outcome data addressed? All outcomes	High risk	No drop outs reported
Free of selective reporting?	Low risk	All outcomes from methods are reported
ITT analysis?	High risk	Not reported
Baseline similarity?	High risk	They are different
Co-interventions avoided or similar?	Low risk	Scintigrapy and ultrasound identical in both groups
Compliance?	Low risk	No conversion reported

Similar follow-up time?	High risk	Length of follow-up seems to be not the same, but not reported

Gordon (breast) 1980

Methods	CBA, hospital setting
Participants	16 vs 19 breast cancer patients Inclusion criteria: Permission of primary physician, informed consent, potential breast cancer, no previous cancer history, 18-75 years of age, within 75 mile of hospital, English speaking, no psychiatric diagnosis, no prior medical treatment for cancer Exclusion criteria: Not reported
Interventions	Intervention group: First, educating the patient about how to live with the disease effectively (providing information about medical system and patient's own condition). Second, counselling, focused on the patient's reactions and feeling toward disease. Finally, environmental manipulation including consultations with other health care personnel. Intervention lasted 6 months Sessions: 13 sessions of 20 minutes Provider: Team of psychologists, social workers, and psychiatric nurse (oncology counsellor) Setting: Hospital and home Control group: Received evaluation only
Outcomes	Primary outcome measure (RTW outcomes): Employment status only for those working at baseline: Number returned to work Registered by: Patient at baseline (hospital admission) and 6 months post-hospital discharge Secondary outcome measure (QOL outcomes):
Notes	Results for working patients only in study of 197 patients

Gordon (melanoma) 1980

Methods	CBA, hospital setting
Participants	43 vs 28 melanoma skin cancer patients Inclusion criteria: Permission of primary physician, informed consent, potential melanoma skin cancer, no previous cancer history, 18-75 years of age, within 75 mile of hospital, English speaking, no psychiatric diagnosis, no prior medical treatment for cancer Exclusion criteria: Not reported
Interventions	Intervention group: First, educating the patient about how to live with the disease effectively (providing information about medical system and patient's own condition). Second, counselling, focused on the patient's reactions and feeling toward disease. Finally, environmental manipulation including consultations with other health care personnel. Intervention lasted 6 months Sessions: 13 sessions of 20 minutes Provider: Team of psychologists, social workers, and psychiatric nurse (oncology counsellor) Setting: Hospital and home Control group: Received evaluation only

Gordon (melanoma) 1980 (*Continued*)

Outcomes	Primary outcome measure (RTW outcomes): Employment status only for those working at baseline: Number returned to work Registered by: Patient at baseline (hospital admission) and 6 months post-hospital discharge. Secondary outcome measure (QOL outcomes):
Notes	Results for working patients only in study of 127 patients

Hillman 1998

Methods	RCT, hospital setting
Participants	80 vs 63 laryngeal cancer patients Inclusion criteria: Biopsy proven, previously untreated, stage 3 or 4 squamous cell carcinoma of the larynx Exclusion: T1N1 carcinoma, pyriform sinus lesions, unresectable cancers, distant metastases, prior head and neck radiotherapy, or prior malignancy with the exception of non-melanoma skin cancer
Interventions	1. Laryngectomy plus radiotherapy 2. Induction chemotherapy plus radiotherapy
Outcomes	Primary outcome measure (RTW outcomes): Number of patients: Disabled due to cancer, on sick leave, cannot find work, not seeking work, lesser job, same job Registered by: Patient at baseline (hospital admission) and 1, 6, 12, 18, 24 months after baseline Secondary outcome measure (QOL outcomes):
Notes	Results for working patients only in trial of 325 patients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	No information about randomisation procedure
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Not reported
Incomplete outcome data addressed? All outcomes	Low risk	Only seven drop-outs. Data of drop-outs was censored
Free of selective reporting?	Low risk	All outcomes from methods are reported

Hillman 1998 (*Continued*)

ITT analysis?	Low risk	ITT-analyses compared the voice assessment and employment between the two randomised groups even if the procedure was converted to the other randomisation group
Baseline similarity?	Low risk	Groups were similar in terms of age, gender, tumour size and site of lesion
Co-interventions avoided or similar?	Unclear risk	People with different voice preservation were compared
Compliance?	Low risk	Final procedure reported
Similar follow-up time?	Low risk	Same timing for each group

Johnsson (goserelin) 2007

Methods	RCT, hospital setting
Participants	55 vs 50 breast cancer patients Inclusion criteria: Invasive breast cancer, pre-menopausal status, primary surgery radical mastectomy plus axillary dissection, node-positive axillary nodes or tumour > 10 mm, no distant metastases. Exclusion criteria: Inoperable cancer, prior radiotherapy, prior neoadjuvant chemotherapy , prior or current endocrine therapy.
Interventions	Intervention group: 2. Goserelin only Duration of all endocrine treatments: 2 years Control group: No adjuvant endocrine therapy
Outcomes	Primary outcome measure (RTW outcomes): RTW rate at 24 months Registered by: Patient at baseline (hospital admission) and 12, 18, 24, 36 months after baseline Secondary outcome measure (QOL outcomes):
Notes	All patients in paid employment at baseline

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported

Johnsson (goserelin) 2007 (*Continued*)

Blinding? All outcomes	Unclear risk	Blinding of data handling persons or researchers or outcome assessors (patients) unknown
Incomplete outcome data addressed? All outcomes	Low risk	Reasons for drop out were given
Free of selective reporting?	Low risk	All outcomes from methods are reported
ITT analysis?	High risk	No ITT analysis
Baseline similarity?	Low risk	Similarity for age, sex, education, marital status
Co-interventions avoided or similar?	Low risk	Surgery, radiotherapy and chemotherapy similar
Compliance?	Unclear risk	No information about the intervention compliance
Similar follow-up time?	Low risk	The same time points

Johnsson (tamo+gose) 2007

Methods	RCT, hospital setting
Participants	64 vs 50 breast cancer patients Inclusion criteria: Invasive breast cancer, pre-menopausal status, primary surgery radical mastectomy plus axillary dissection, node-positive axillary nodes or tumour > 10 mm, no distant metastases. Exclusion criteria: Inoperable cancer, prior radiotherapy, prior neoadjuvant chemotherapy, prior or current endocrine therapy.
Interventions	Intervention group: 3. Tamoxifen + Goserelin Duration of all endocrine treatments: 2 years Control group: No adjuvant endocrine therapy
Outcomes	Primary outcome measure (RTW outcomes): RTW rate at 24 months Registered by: Patient at baseline (hospital admission) and 12, 18, 24, 36 months after baseline Secondary outcome measure (QOL outcomes):
Notes	All patients in paid employment at baseline

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Johnsson (tamo+gose) 2007 (*Continued*)

Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Blinding of data handling persons or researchers or outcome assessors (patients) unknown
Incomplete outcome data addressed? All outcomes	Low risk	Reasons for drop out were given
Free of selective reporting?	Low risk	All outcomes from methods are reported
ITT analysis?	High risk	No ITT analysis
Baseline similarity?	Low risk	Similarity for age,sex, education, marital status
Co-interventions avoided or similar?	Low risk	Surgery, radiotherapy and chemotherapy similar
Compliance?	Unclear risk	No information about the intervention compliance
Similar follow-up time?	Low risk	The same time points

Johnsson (tamoxifen) 2007

Methods	RCT, hospital setting
Participants	53 vs 50 breast cancer patients Inclusion criteria: Invasive breast cancer, pre-menopausal status, primary surgery radical mastectomy plus axillary dissection, node-positive axillary nodes or tumour > 10 mm, no distant metastases. Exclusion criteria: Inoperable cancer, prior radiotherapy, prior neoadjuvant chemotherapy , prior or current endocrine therapy.
Interventions	Intervention group: 1. Tamoxifen only Duration of all endocrine treatments: 2 years Control group: No adjuvant endocrine therapy
Outcomes	Primary outcome measure (RTW outcomes): RTW rate at 24 months Registered by: Patient at baseline (hospital admission) and 12, 18, 24, 36 months after baseline Secondary outcome measure (QOL outcomes):
Notes	All patients in paid employment at baseline

Johnsson (tamoxifen) 2007 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Blinding of data handling persons or researchers or outcome assessors (patients) unknown
Incomplete outcome data addressed? All outcomes	Low risk	Reasons for drop out were given
Free of selective reporting?	Low risk	All outcomes from methods are reported
ITT analysis?	High risk	No ITT analysis
Baseline similarity?	Low risk	Similarity for age, sex, education, marital status
Co-interventions avoided or similar?	Low risk	Surgery, radiotherapy and chemotherapy similar
Compliance?	Unclear risk	No information about the intervention compliance
Similar follow-up time?	Low risk	The same time points

Kornblith 2009

Methods	RCT, hospital setting
Participants	164 vs 73 endometrial cancer patients Inclusion criteria: Endometrial cancer, no metastatic cancer, adequate bone marrow, renal, and hepatic function, performance status 0 to 3, speaking English, French or Spanish. Exclusion criteria: Not reported
Interventions	Intervention group: Laparoscopy Provider: Surgeon Setting: Hospital Control group: Laparotomy
Outcomes	Primary outcome measure (RTW outcomes): RTW return-to-work in days Registered by: Patient at baseline (hospital admission) and 6 months* post-surgery Secondary outcome measure (QOL outcomes): FACT-G and SF-36, 1, 3, 6 weeks and 6 months post-surgery

Kornblith 2009 (*Continued*)

Notes	*6 weeks in article but authors emailed it is 6 months. Results for working patients only in trial of 653 patients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Not reported
Incomplete outcome data addressed? All outcomes	Low risk	Every loss to follow-up reason is described
Free of selective reporting?	Low risk	All outcomes from methods are reported
ITT analysis?	Low risk	21% converted to control group but ITT performed
Baseline similarity?	Low risk	Age, race
Co-interventions avoided or similar?	Low risk	None
Compliance?	Unclear risk	21% converted is acceptable?
Similar follow-up time?	Low risk	6 months post-surgery

Lee 1992

Methods	RCT, hospital setting
Participants	44 vs 47 breast cancer patients Inclusion criteria: Single invasive breast carcinoma 4 cm diameter or less in patients less than 70 years Exclusion criteria: Not reported
Interventions	Intervention group: Breast conservation comprising tumourectomy, axillary clearance, iridium implant and subsequent external beam radiotherapy. Provider: Surgeon Setting: Hospital Control group: Modified radical mastectomy
Outcomes	Primary outcome measure (RTW outcomes): Number returned to original employment (of those employed at baseline) Registered by: Patient at baseline (hospital admission) and 12 months post-operatively.

Lee 1992 (*Continued*)

Notes	Results for working patients only in trial of 197 patients

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation process not reported
Allocation concealment?	Unclear risk	Not clear who and how the randomisation was carried out
Blinding? All outcomes	Unclear risk	Not reported
Incomplete outcome data addressed? All outcomes	Low risk	All drop-outs and reasons for refusal reported
Free of selective reporting?	Low risk	All outcomes from methods are reported
ITT analysis?	High risk	Analyses done in anxiety and depression between participants and refusals, but not in return-to-work
Baseline similarity?	Unclear risk	No data given, but groups were similar in terms of sociodemographic factors except social class
Co-interventions avoided or similar?	Low risk	All patients aged less than 65 years who had axillary nodal metastases were further randomised to receive 12 cycles of adjuvant therapy or no further treatment
Compliance?	Low risk	Attitudes toward treatment procedures measured
Similar follow-up time?	Low risk	Same timing in both groups

Lepore (PE) 2003

Methods	RCT, hospital setting
Participants	41 vs 40 prostate cancer patients Inclusion criteria: Localised prostate cancer, no history of other cancer, primary residence within 1 hour driving, nonmetastatic disease. Exclusion criteria: Not reported
Interventions	Intervention group: 1. Education only: Six weekly 1hour lectures delivered by an expert: Prostate cancer biology (oncologist), control physical side effects (urologist), nutrition (dietician), stress and coping (oncology nurse), relationships and sexuality (clinical psychologist), follow-up care and future health concerns (urologist). Printed material. Intervention lasted 6 weeks

Lepore (PE) 2003 (*Continued*)

	Sessions: 6 sessions of 1 hour Providers: Oncologist, urologist, dietician, oncology nurse, clinical psychologist. Setting: Not reported Control group: Nothing beyond standard medical care.
Outcomes	Primary outcome measure (RTW outcomes): Employment status only for those working at baseline: Number returned to work and in steady employment Registered by: Patient at baseline (2 months post-treatment), 2 weeks, 6 months, 12 months Secondary outcome measure (QOL outcomes): SF-36 Registered by: Patient at baseline (2 months post-treatment), 2 weeks, 6 months, 12 months
Notes	Results for working patients only in trial of 250 patients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Sealed envelope
Allocation concealment?	Low risk	Randomisation was carried out by an interviewer who was blinded to experimental condition and did not participate in the interventions
Blinding? All outcomes	Low risk	Interviewer blinded at baseline; patients were not informed about the hypothesis
Incomplete outcome data addressed? All outcomes	Low risk	Attrition was unrelated to experimental condition. Reasons for drop out given.
Free of selective reporting?	Low risk	All outcomes from methods are reported
ITT analysis?	High risk	No ITT-analyses conducted in work-related outcomes
Baseline similarity?	Low risk	Groups were similar in all important background variables
Co-interventions avoided or similar?	Low risk	No reported co-intervention
Compliance?	Unclear risk	No report of patients' compliance about the intervention
Similar follow-up time?	Low risk	Timing of outcomes same in each group

Lepore (PE+discus) 2003

Methods	RCT, hospital setting
Participants	43 vs 40 prostate cancer patients Inclusion criteria: Localised prostate cancer, no history of other cancer, primary residence within 1 hour driving, nonmetastatic disease. Exclusion criteria: Not reported.
Interventions	Intervention group: 2. Education plus discussion: Lecture series and 45 additional min of group discussion (male clinical psychologist) , discussion on how lecture topic was relevant to group. Female family members' own discussion with female oncology nurse. Intervention lasted 6 weeks Sessions: 6 sessions of 1 hour 45 minutes Providers: Oncologist, urologist, dietician, oncology nurse, clinical psychologist Setting: Not reported Control group: Nothing beyond standard medical care
Outcomes	Primary outcome measure (RTW outcomes): Employment status only for those working at baseline: number returned to work and in steady employment Registered by: Patient at baseline (2 months post-treatment), 2 weeks, 6 months, 12 months Secondary outcome measure (QOL outcomes): SF-36 Registered by: Patient at baseline (2 months post-treatment), 2 weeks, 6 months, 12 months
Notes	Results for working patients only in trial of 250 patients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Sealed envelope
Allocation concealment?	Low risk	Randomisation was carried out by an interviewer who was blinded to experimental condition and did not participate in the interventions
Blinding? All outcomes	Low risk	Interviewer blinded at baseline; patients were not informed about the hypothesis
Incomplete outcome data addressed? All outcomes	Low risk	Attrition was unrelated to experimental condition. Reasons for drop out given.
Free of selective reporting?	Low risk	All outcomes from methods are reported
ITT analysis?	High risk	No ITT-analyses conducted in work-related outcomes

Lepore (PE+discus) 2003 (*Continued*)

Baseline similarity?	Low risk	Groups were similar in all important background variables
Co-interventions avoided or similar?	Low risk	No reported co-intervention
Compliance?	Unclear risk	No report of patients' compliance about the intervention
Similar follow-up time?	Low risk	Timing of outcomes same in each group

Maguire 1983

Methods	RCT, hospital setting
Participants	42 vs 46 breast cancer patients Inclusion criteria: Breast cancer, mastectomy Exclusion criteria: Not reported
Interventions	Intervention group: Within a few days of surgery the nurse advised on exercise, look at her scar, discussed how she felt about losing a breast, demonstrated breast prothesis. After discharge at home, the nurse examined arm movements, checked exercises, clarified how patient felt about scar, encouraged being open with her partner. Nurse encouraged return-to-work and become socially active. She followed the patient up every two months to monitor the progress until patient adapted well. Intervention lasted several months Sessions: 2 or more sessions Provider: Oncology nurse Setting: Hospital, home Control group: Care normally given by the surgical unit
Outcomes	Primary outcome measure (RTW outcomes): Employment status rate: Number returned to work Registered by: Patient at 12-18 months post-surgery Secondary outcome measure (QOL outcomes): not reported
Notes	Results for working patients only in trial of 152 patients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Low risk	Half of the weeks were designed as counselling weeks and the other half as control weeks using a random number table
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Not reported

Maguire 1983 (*Continued*)

Incomplete outcome data addressed? All outcomes	Low risk	Reasons for drop out reported
Free of selective reporting?	Low risk	All outcomes from methods are reported
ITT analysis?	High risk	No ITT analysis
Baseline similarity?	Low risk	Stated in the article that baseline characteristics were similar
Co-interventions avoided or similar?	Low risk	No co-interventions or similar visits to social worker
Compliance?	Low risk	Stated in the article that each patient in the counsel group was advised and counselled by the nurse
Similar follow-up time?	Unclear risk	Broad follow-up measurement point: 12 to 18 months

Rogers 2009

Methods	RCT, community setting
Participants	14 vs 14 breast cancer patients. Inclusion criteria: English speaking, female, breast cancer survivor, 18-70 years, stage I, II or IIIA, expected on hormonal therapy of the duration of the study (8 months), medical clearance by physician, at least 8 weeks after surgery. Exclusion criteria: Dementia, organic brain syndrome, medical / psychological / social problems, contradiction for physical activity (angina etc), breast cancer recurrence or metastatic, inability to ambulate, planning to relocate, or engaged in > 60 min of vigorous physical activity or >150 min of moderate vigorous activity per week.
Interventions	Intervention group: 12 week physical activity behaviour change intervention. Goal: 150 min of moderate walking per week. Six discussion group sessions with clinical psychologist. 12 individual supervised exercise sessions + 3 face to face counselling sessions with exercise specialist. Home-based exercises.(40). Intervention lasted 12 weeks Sessions: 21 sessions Provider: Clinical psychologist, exercise specialist Setting: Not reported and home Control group: Provision of written materials from the Internet
Outcomes	Primary outcome measure (RTW outcomes): Sick leave days missed from work in past month. Registered by: Patient at baseline and 3 months after the intervention Secondary outcome measure (QOL outcomes): FACT-General + breast Registered by: Patient at baseline and 3 months after the intervention
Notes	Results for working patients only in trial of 39 patients

Rogers 2009 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Low risk	Computer generated
Allocation concealment?	Low risk	Sealed envelope
Blinding? All outcomes	Unclear risk	Not reported
Incomplete outcome data addressed? All outcomes	Low risk	Reasons for drop-out are given
Free of selective reporting?	Low risk	All outcomes from methods are reported
ITT analysis?	Low risk	ITT analysis performed
Baseline similarity?	Low risk	Groups were compared on demographic, medical, diet, physical activity, other health-related outcomes
Co-interventions avoided or similar?	Low risk	Vigorous exercise excluded
Compliance?	Low risk	Intervention adherence monitored
Similar follow-up time?	Low risk	3 months after baseline

vs: versus; RCT: randomised controlled trial; RTW: return-to-work; QOL: quality of life; MOS-SF: Medical Outcomes Studies-Short Form;

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Adamsen 2009	No return-to-work outcomes reported.
Berglund 1993	No RCT or CBA.
Berglund 2003	No return-to-work outcomes reported.
Bloom 2008	No return-to-work outcomes reported.
Budin 2008	Outcome is not sick leave or return-to-work but vocational environment scale.

(*Continued*)

Burak 2002	Outcome is not sick leave or return-to-work but return to normal activity.
Cain 1986	Outcome is not sick leave or return-to-work but vocational environment scale.
Chan 2005	No return-to-work outcomes reported.
Cho 2006	No return-to-work outcomes reported.
Fassoulaki 2000	No return-to-work outcomes reported.
Gordon 2005	No return-to-work outcomes reported.
Greer 1992	Outcome is not sick leave or return-to-work but vocational environment scale.
Griffith 2009	No return-to-work outcomes reported.
Harrison-Paul 2006	No return-to-work outcomes reported.
Hartmann 2007	No return-to-work outcomes reported.
Heim 2007	No return-to-work outcomes reported.
Janson 2005	No return-to-work outcomes reported for intervention.
Jiang 2009	Outcome is not sick leave or return-to-work but includes normal routine activity.
Jones 2005	No return-to-work outcomes reported.
Jorgensen 2009	No return-to-work outcomes reported.
Korstjens 2008	No return-to-work outcomes reported.
Lee 2009	No cancer.
May 2009	No return-to-work outcomes reported.
McNeely 2008	No return-to-work outcomes reported.
Meneses 2007	No return-to-work outcomes reported.
Mock 1994	No return-to-work outcomes reported.
Norager 2007	No return-to-work outcomes reported.
Nowrouzi 2009	No intervention.
Poppelreuter 2009	No return-to-work outcomes reported.

(*Continued*)

Rotstein 1989	Only half of the patients was employed at baseline.
Seibaek 2009	No return-to-work outcomes reported.
Seiler 2005	Outcome is not sick leave or return-to-work but return to normal daily activity.
Semple 2009	No return-to-work outcomes reported.
Shelton 2009	No return-to-work outcomes reported.
Sherer 1997	No RCT or CBA.
Shimada 2007	No return-to-work outcomes reported.
Vos 2006	No return-to-work outcomes reported.
Wenzel 2009	Outcome is not sick leave or return-to-work but vocational environment scale.
Wiggins 2009	No return-to-work outcomes reported.

Characteristics of ongoing studies *[ordered by study ID]*

Bunnell 2010

Trial name or title	Quality of life, employment and informal care costs in women who are receiving chemotherapy for breast cancer
Methods	Observational
Participants	Patients with histologically confirmed invasive carcinoma of the breast with 0-3 positive axillary nodes
Interventions	Adjuvant cyclophosphamide and doxorubicin versus paclitaxel
Outcomes	Quality of life, employment, informal care costs, peripheral neuropathy
Starting date	October 2005
Contact information	C.A. Bunnell, Dana-Farber Institute, USA
Notes	

Saarto 2010

Trial name or title	Breast cancer and exercise
Methods	RCT, multicenter
Participants	Breast cancer patients, female, 35-68 years
Interventions	Intervention: Supervised training once a week in groups of 10-15 subjects, guided by an experienced physical therapist. Control group: Standard care
Outcomes	Return-to-work, osteoporosis, quality of life, weight control
Starting date	September 2005
Contact information	T. Saarto, Helsinki University Central Hospital, Department of Oncology
Notes	

Tamminga 2010

Trial name or title	To enhance return-to-work in cancer patients - a randomised controlled trial
Methods	RCT, multicenter
Participants	Primary diagnosis of cancer with a one year survival rate of approximately 80% and treatment with curative intent; age between 18 and 60 years, paid employment at the time of diagnosis, sick listed.
Interventions	Intervention: Vocational rehabilitation intervention according to a specially developed protocol. Control group: Usual care.
Outcomes	Return-to-work and quality of life
Starting date	March 2009
Contact information	S.J.Tamminga@amc.uva.nl
Notes	

Velthuis 2010

Trial name or title	Physical Activity during Cancer Treatment study
Methods	RCT, multicenter
Participants	Patients diagnosed with breast or colon cancer (M0) who will be treated with chemotherapy. Age 25-75 years.
Interventions	Intervention: 18 week supervised group exercise programme based on Bandura's social cognitive theory (SCT) during cancer treatment. The exercise programme will start earliest one week after surgery and at least within

	six weeks (breast cancer) or ten weeks (colon cancer) after definitive cancer diagnosis. The control group will receive care as usual (no exercise programme).
Outcomes	Fatigue, health service utilization, sick leave
Starting date	January 2010
Contact information	mvelthuis@ikmn.nl
Notes	

DATA AND ANALYSES

Comparison 1. Psychological versus Care as usual - RCTs

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Return to work	2	124	Odds Ratio (M-H, Fixed, 95% CI)	2.32 [0.94, 5.71]
1.1 Patient education	1	61	Odds Ratio (M-H, Fixed, 95% CI)	1.33 [0.40, 4.38]
1.2 Patient education, group discussion	1	63	Odds Ratio (M-H, Fixed, 95% CI)	5.71 [1.26, 25.96]
2 Quality of life - Physical functioning	2	330	Mean Difference (IV, Fixed, 95% CI)	1.43 [-0.71, 3.57]
2.1 Patient education	1	164	Mean Difference (IV, Fixed, 95% CI)	0.80 [-2.31, 3.91]
2.2 Patient education and group discussion	1	166	Mean Difference (IV, Fixed, 95% CI)	2.0 [-0.95, 4.95]
3 Quality of life - Mental functioning	2	330	Mean Difference (IV, Fixed, 95% CI)	0.14 [-1.62, 1.91]
3.1 Patient education	1	164	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-2.78, 2.18]
3.2 Patient education and group discussion	1	166	Mean Difference (IV, Fixed, 95% CI)	0.60 [-1.91, 3.11]

Comparison 2. Psychological versus Care as usual - CBAs

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Return to work	3	140	Odds Ratio (M-H, Fixed, 95% CI)	4.67 [2.04, 10.70]
1.1 Individual counselling	1	34	Odds Ratio (M-H, Fixed, 95% CI)	4.2 [0.98, 17.95]
1.2 Patient education, counselling	2	106	Odds Ratio (M-H, Fixed, 95% CI)	4.91 [1.79, 13.46]

Comparison 3. Physical versus Care as usual - RCTs

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Return to work	1		Odds Ratio (Fixed, 95% CI)	Totals not selected
1.1 Physical activity	1		Odds Ratio (Fixed, 95% CI)	Not estimable
2 Quality of life	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 4. Medical function conserving versus Medical more radical - RCTs

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Return to work	8		Odds Ratio (Random, 95% CI)	1.53 [0.95, 2.45]
1.1 Chemoradiation	1		Odds Ratio (Random, 95% CI)	0.73 [0.25, 2.14]
1.2 Early thyroid hormones	1		Odds Ratio (Random, 95% CI)	11.36 [1.17, 110.34]
1.3 Minimal surgery	3		Odds Ratio (Random, 95% CI)	1.52 [0.74, 3.14]
1.4 Adjuvant endocrine	3		Odds Ratio (Random, 95% CI)	1.56 [0.61, 3.99]
2 Quality of life	2	1028	Mean Difference (IV, Fixed, 95% CI)	1.37 [-0.62, 3.36]
2.1 Chemoradiation	1	126	Mean Difference (IV, Fixed, 95% CI)	4.0 [-4.04, 12.04]
2.2 Minimal surgery	1	902	Mean Difference (IV, Fixed, 95% CI)	1.20 [-0.85, 3.25]

Comparison 5. Medical function conserving versus Medical more radical-CBAs

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Return to work	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Early thyroid hormones	1		Odds Ratio (M-H, Fixed, 95% CI)	Not estimable

Comparison 6. Multidisciplinary physical, psychological and vocational interventions versus Care as usual-RCTs

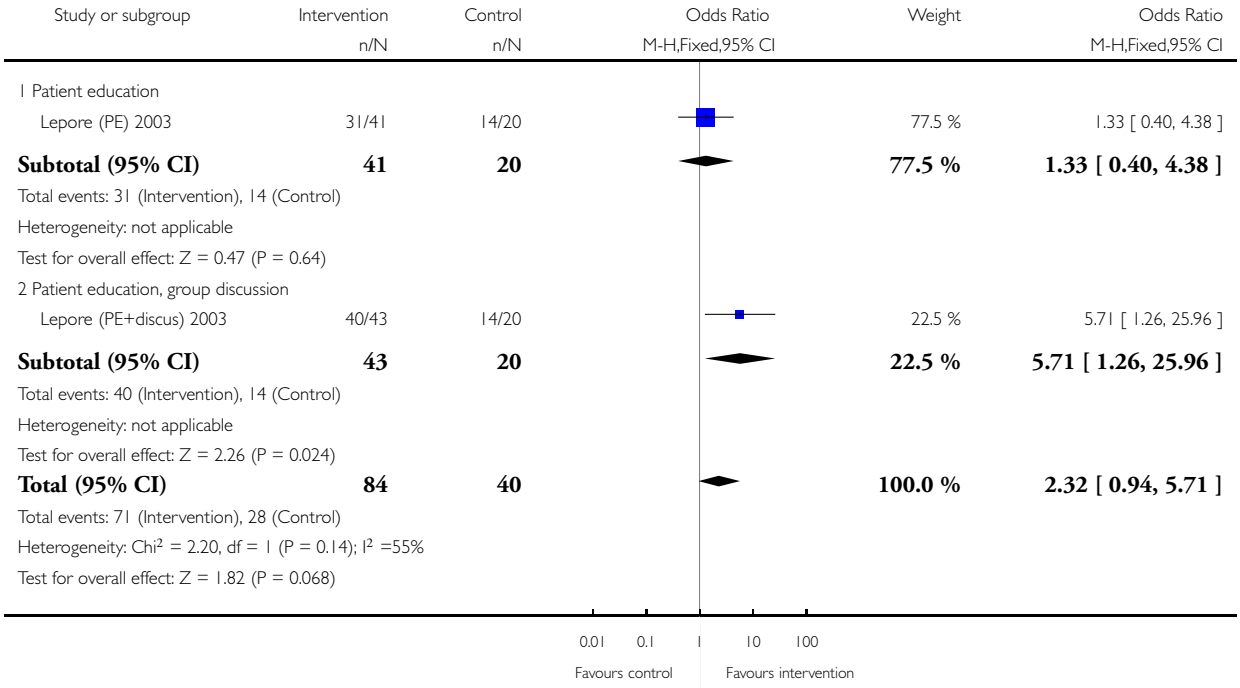
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Return to work	3	299	Odds Ratio (M-H, Fixed, 95% CI)	1.87 [1.07, 3.27]
1.1 Physical training, patient education and coping with RTW	1	154	Odds Ratio (M-H, Fixed, 95% CI)	1.84 [0.77, 4.39]
1.2 Physical exercise, counselling, encouragement of RTW	1	88	Odds Ratio (M-H, Fixed, 95% CI)	2.69 [1.07, 6.72]
1.3 Physical exercise, patient education and biofeedback	1	57	Odds Ratio (M-H, Fixed, 95% CI)	0.96 [0.27, 3.42]
2 Quality of life	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Physical training, patient education and coping with RTW	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable

Analysis 1.1. Comparison 1 Psychological versus Care as usual - RCTs, Outcome 1 Return to work.

Review: Interventions to enhance return-to-work for cancer patients

Comparison: 1 Psychological versus Care as usual - RCTs

Outcome: 1 Return to work

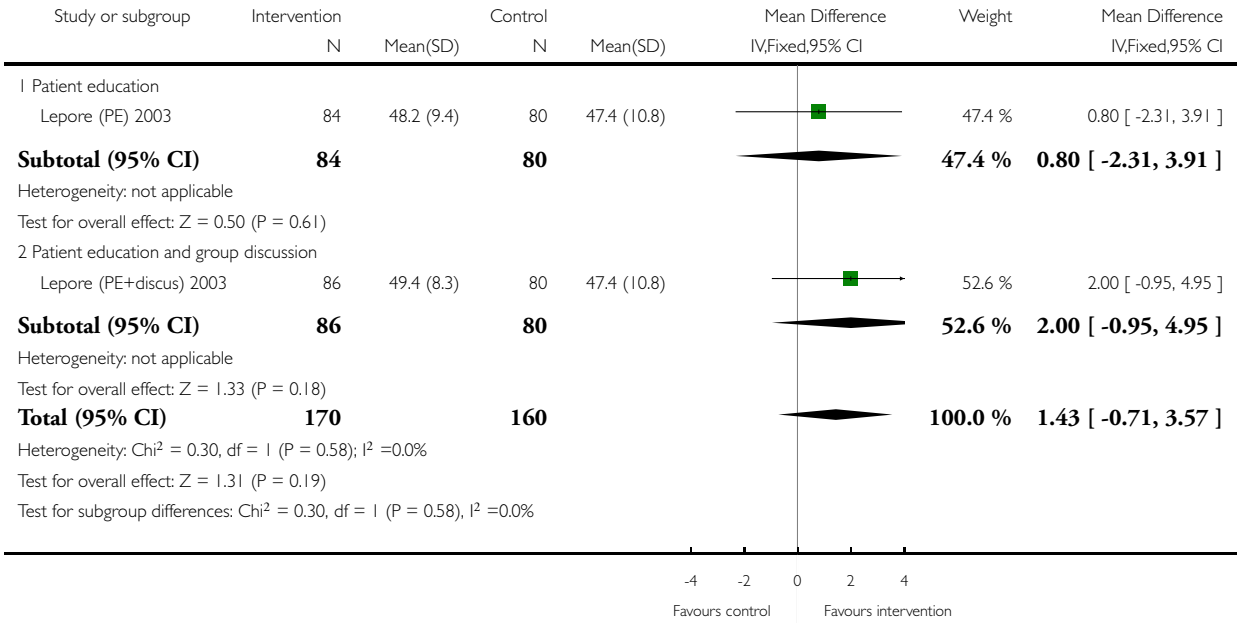


Analysis 1.2. Comparison 1 Psychological versus Care as usual - RCTs, Outcome 2 Quality of life - Physical functioning.

Review: Interventions to enhance return-to-work for cancer patients

Comparison: 1 Psychological versus Care as usual - RCTs

Outcome: 2 Quality of life - Physical functioning

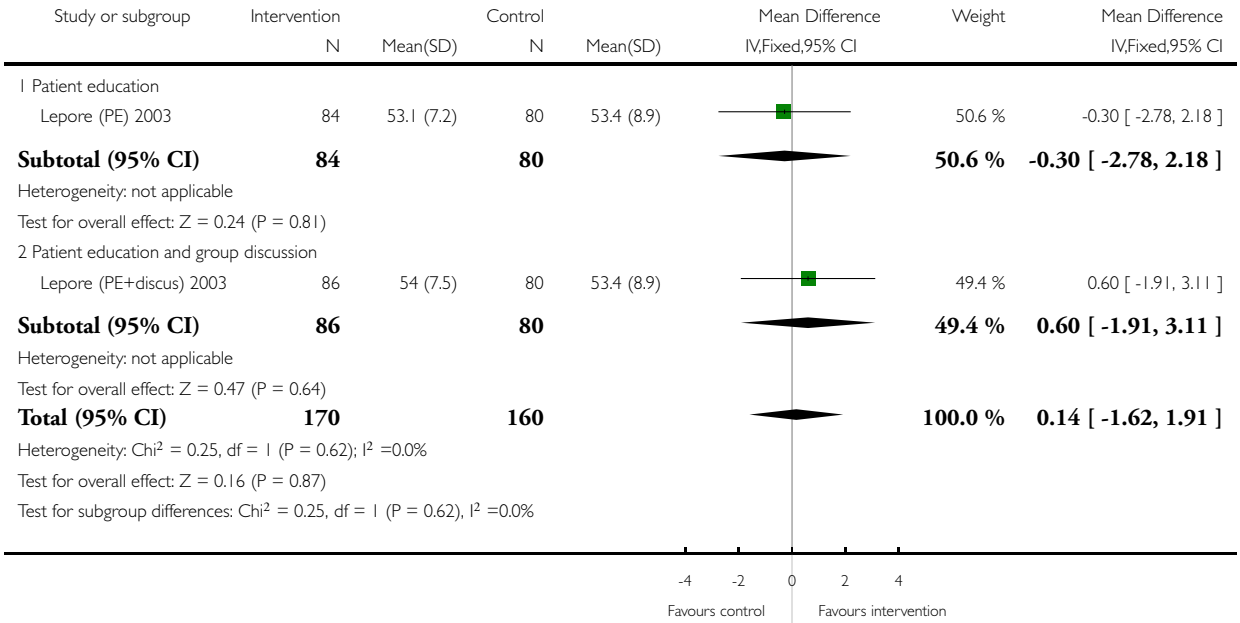


Analysis 1.3. Comparison 1 Psychological versus Care as usual - RCTs, Outcome 3 Quality of life - Mental functioning.

Review: Interventions to enhance return-to-work for cancer patients

Comparison: 1 Psychological versus Care as usual - RCTs

Outcome: 3 Quality of life - Mental functioning

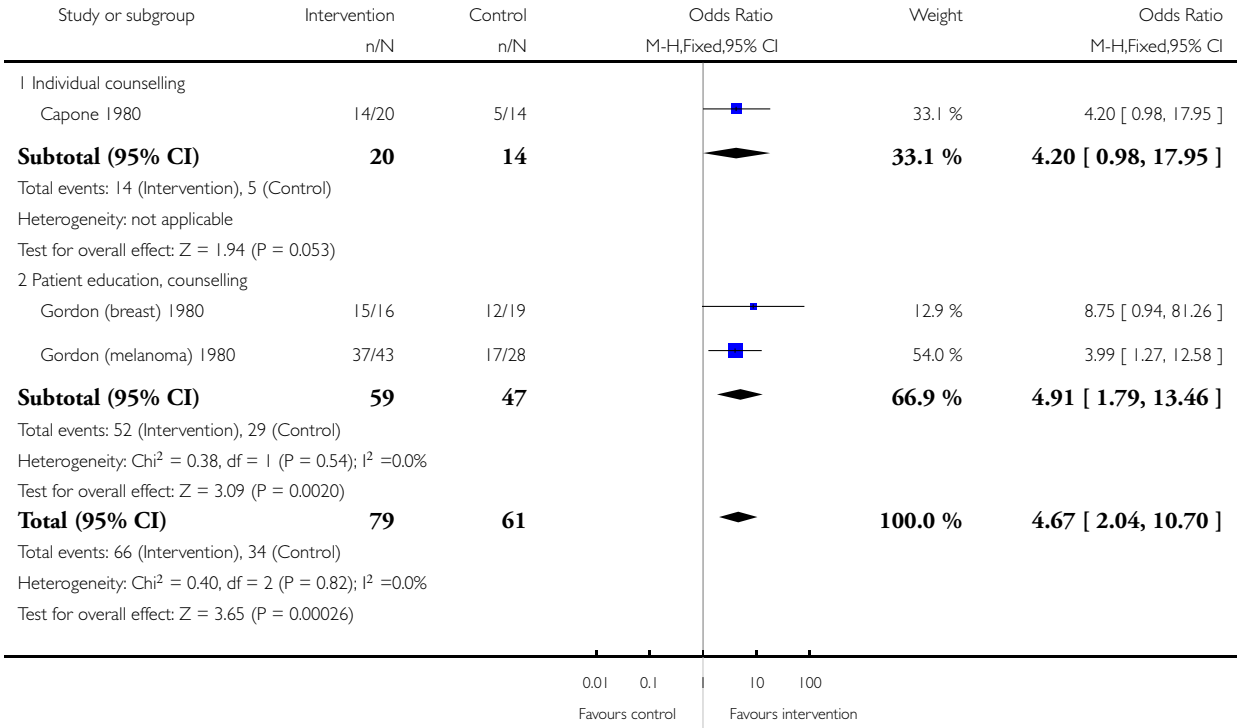


Analysis 2.1. Comparison 2 Psychological versus Care as usual - CBAs, Outcome 1 Return to work.

Review: Interventions to enhance return-to-work for cancer patients

Comparison: 2 Psychological versus Care as usual - CBAs

Outcome: 1 Return to work

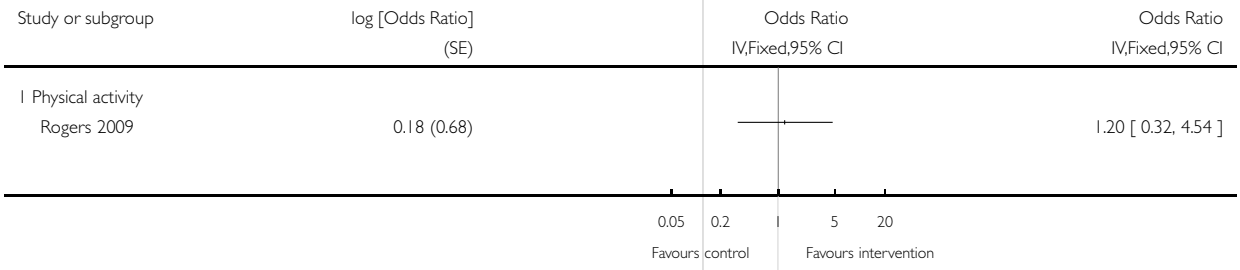


Analysis 3.1. Comparison 3 Physical versus Care as usual - RCTs, Outcome 1 Return to work.

Review: Interventions to enhance return-to-work for cancer patients

Comparison: 3 Physical versus Care as usual - RCTs

Outcome: 1 Return to work



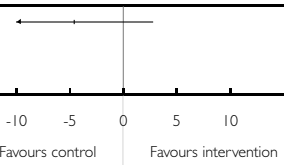
Analysis 3.2. Comparison 3 Physical versus Care as usual - RCTs, Outcome 2 Quality of life.

Review: Interventions to enhance return-to-work for cancer patients

Comparison: 3 Physical versus Care as usual - RCTs

Outcome: 2 Quality of life

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Rogers 2009	21	87.4 (13.1)	20	92 (11)		-4.60 [-11.99, 2.79]



Analysis 4.1. Comparison 4 Medical function conserving versus Medical more radical - RCTs, Outcome 1 Return to work.

Review: Interventions to enhance return-to-work for cancer patients

Comparison: 4 Medical function conserving versus Medical more radical - RCTs

Outcome: 1 Return to work

Study or subgroup	log [Odds Ratio] (SE)	Odds Ratio IV,Random,95% CI	Weight	Odds Ratio IV,Random,95% CI
1 Chemoradiation				
Ackerstaff 2009	-0.315 (0.55)		13.5 %	0.73 [0.25, 2.14]
Subtotal (95% CI)			**13.5 %**	**0.73 [0.25, 2.14]**
Heterogeneity: not applicable				
Test for overall effect: Z = 0.57 (P = 0.57)				
2 Early thyroid hormones				
Emmanouilidis 2009	2.43 (1.16)		4.0 %	11.36 [1.17, 110.34]
Subtotal (95% CI)			**4.0 %**	**11.36 [1.17, 110.34]**
Heterogeneity: not applicable				

(*Continued* . . .)

(. . . *Continued*)

Study or subgroup	log [Odds Ratio] (SE)	Odds Ratio IV,Random,95% CI	Weight	Odds Ratio IV,Random,95% CI
Test for overall effect: Z = 2.09 (P = 0.036)				
3 Minimal surgery				
Hillman 1998	1.01 (0.43)		18.7 %	2.75 [1.18, 6.38]
Kornblith 2009	0.53 (0.26)		29.9 %	1.70 [1.02, 2.83]
Lee 1992	-0.58 (0.58)		12.6 %	0.56 [0.18, 1.75]
Subtotal (95% CI)			**61.1 %**	**1.52 [0.74, 3.14]**
Heterogeneity: Tau^2 = 0.24; Chi^2 = 4.89, df = 2 (P = 0.09); I^2 =59%				
Test for overall effect: Z = 1.14 (P = 0.25)				
4 Adjuvant endocrine				
Johnsson (goserelin) 2007	0.247 (0.85)		6.8 %	1.28 [0.24, 6.77]
Johnsson (tamo+gose) 2007	0.647 (0.81)		7.4 %	1.91 [0.39, 9.34]
Johnsson (tamoxifen) 2007	0.425 (0.83)		7.1 %	1.53 [0.30, 7.78]
Subtotal (95% CI)			**21.4 %**	**1.56 [0.61, 3.99]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.12, df = 2 (P = 0.94); I^2 =0.0%				
Test for overall effect: Z = 0.93 (P = 0.35)				
Total (95% CI)			**100.0 %**	**1.53 [0.95, 2.45]**
Heterogeneity: Tau^2 = 0.13; Chi^2 = 9.91, df = 7 (P = 0.19); I^2 =29%				
Test for overall effect: Z = 1.75 (P = 0.080)				

Analysis 4.2. Comparison 4 Medical function conserving versus Medical more radical - RCTs, Outcome 2 Quality of life.

Review: Interventions to enhance return-to-work for cancer patients

Comparison: 4 Medical function conserving versus Medical more radical - RCTs

Outcome: 2 Quality of life

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Chemoradiation							
Ackerstaff 2009	60	79.4 (23)	66	75.4 (23)		6.1 %	4.00 [-4.04, 12.04]
Subtotal (95% CI)	**60**		**66**			**6.1 %**	**4.00 [-4.04, 12.04]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.97 (P = 0.33)							
2 Minimal surgery							
Kornblith 2009	635	91.9 (14)	267	90.7 (14.5)		93.9 %	1.20 [-0.85, 3.25]
Subtotal (95% CI)	**635**		**267**			**93.9 %**	**1.20 [-0.85, 3.25]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.15 (P = 0.25)							
Total (95% CI)	**695**		**333**			**100.0 %**	**1.37 [-0.62, 3.36]**
Heterogeneity: Chi^2 = 0.44, df = 1 (P = 0.51); I^2 =0.0%							
Test for overall effect: Z = 1.35 (P = 0.18)							
Test for subgroup differences: Chi^2 = 0.44, df = 1 (P = 0.51), I^2 =0.0%							

Analysis 5.1. Comparison 5 Medical function conserving versus Medical more radical-CBAs, Outcome 1 Return to work.

Review: Interventions to enhance return-to-work for cancer patients

Comparison: 5 Medical function conserving versus Medical more radical-CBAs

Outcome: 1 Return to work

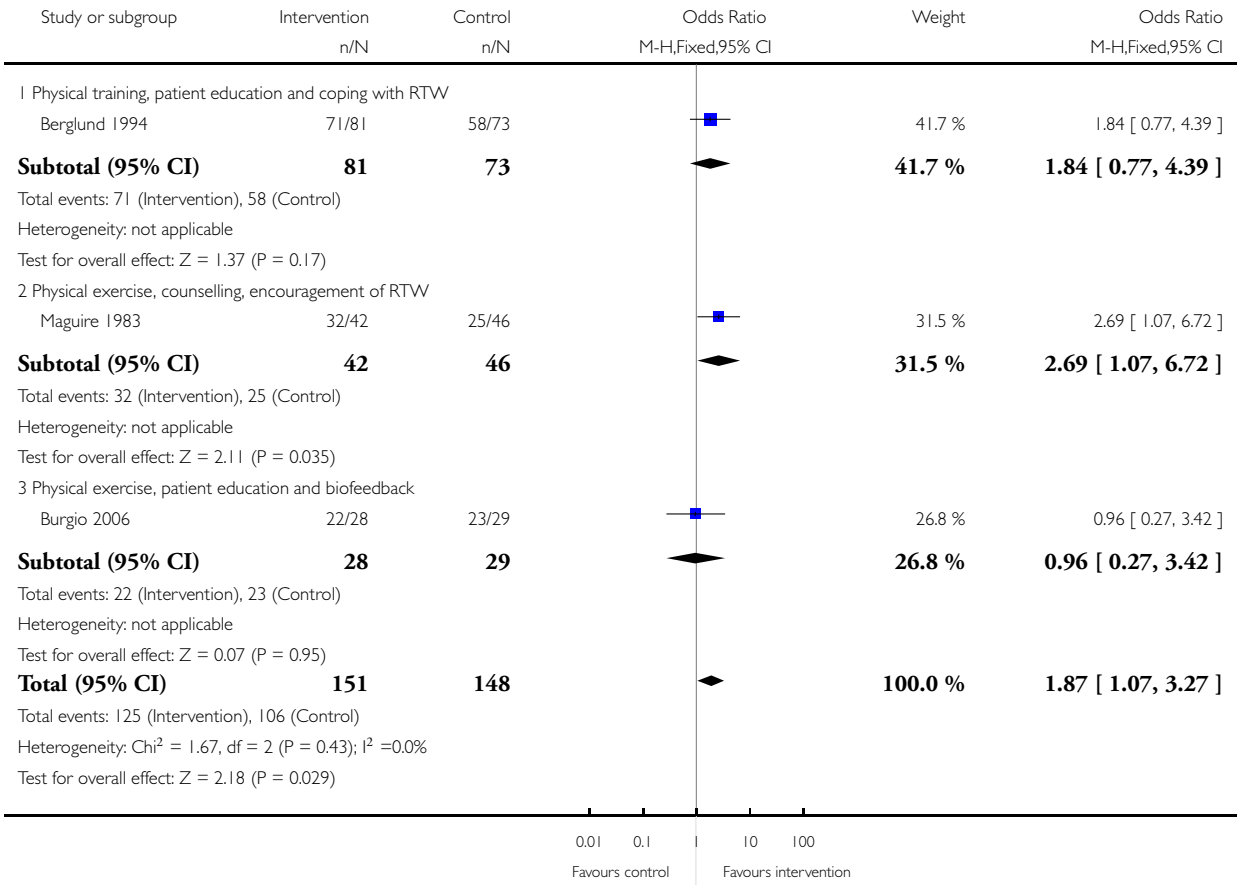
Study or subgroup	Intervention n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
1 Early thyroid hormones				
Borget 2007	110/173	66/119		1.40 [0.87, 2.26]

Analysis 6.1. Comparison 6 Multidisciplinary physical, psychological and vocational interventions versus Care as usual-RCTs, Outcome 1 Return to work.

Review: Interventions to enhance return-to-work for cancer patients

Comparison: 6 Multidisciplinary physical, psychological and vocational interventions versus Care as usual-RCTs

Outcome: 1 Return to work



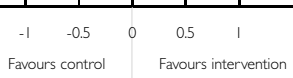
Analysis 6.2. Comparison 6 Multidisciplinary physical, psychological and vocational interventions versus Care as usual-RCTs, Outcome 2 Quality of life.

Review: Interventions to enhance return-to-work for cancer patients

Comparison: 6 Multidisciplinary physical, psychological and vocational interventions versus Care as usual-RCTs

Outcome: 2 Quality of life

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Physical training, patient education and coping with RTW						
Berglund 1994	87	2.29 (0.9)	101	2.36 (0.9)		-0.07 [-0.33, 0.19]



APPENDICES

Appendix 1. MEDLINE search strategy

1. neoplasms (MeSH Terms)
2. cancer* (Text Word)
3. neoplasm* (Text Word)
4.carcinoma* (Text Word)
5. oncolog* (Text Word)
6. malignan* (Text Word)
7. tumor (Text Word)
8. tumour (Text Word)
9. tumors (Text Word)
10. tumours (Text Word)
11. leukemia* (Text Word)
12. sarcoma* (Text Word)
13. lymphoma* (Text Word)
14. melanoma* (Text Word)
15. blastoma* (Text Word)
16. radiotherapy (Text Word)
17. chemotherapy (Text Word)
18. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
19. "return-to-work" (Text word)
20. employment (MeSH Terms)
21. employment (Text Word)
22. unemployment (MeSH Terms)
23. unemployment (Text Word)
24. unemployed (Text Word)
25. retirement (Text Word)
26. "sick leave" (MeSH Terms)

27. sick leave (Text Word)
28. Sickness absence (Text Word)
29. absenteeism (MeSH Terms)
30. absenteeism (Text word)
31. "work" (MeSH Terms)
32. occupations (MeSH Terms)
33. "occupational medicine" (MeSH Terms)
34. "occupational health" (MeSH Terms)
35. "occupational health services" (MeSH Terms)
36. "disability management" (Text word)
37. "rehabilitation, vocational" (MeSH Terms)
38. occupation* (Text Word)
39. rehabilitation (MeSH Terms:NoExp)
40. "neoplasms/rehabilitation" (MeSH Terms)
41. vocational* (Text Word)
42. "work ability" (Text Word)
43. "work capacity" (Text Word)
44. "work activity" (Text Word)
45. "work disability" (Text Word)
46. "work rehabilitation" (Text Word)
47. "work status" (Text Word)
48. "work retention" (Text Word)
49. workability (Text Word)
50. employability (Text Word)
51. employable (Text Word)
52. employee* (Text Word)
53. 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52
54. randomized-controlled-trial (pt)
55. controlled clinical trial (pt)
56. randomized controlled trials (mh)
57. random allocation (mh)
58. double blind method (mh)
59. single blind method (mh)
60. clinical trial (pt)
61. clinical trials (mh)
62. (clin* adj25 trial*) (ti,ab)
63. ((singl*(tw) OR doubl*(tw) OR trebl*(tw) OR tripl*(tw)) AND (mask*(tw) OR blind*(tw)))
64. placebos (mh)
65. placebo*(tw)
66. random*(tw)
67. research design(mh:noexp)
68. comparative study(pt)
69. evaluation studies(pt)
70. follow-up studies(mh)
71. prospective studies(mh)
72. cross-over studies(mh)
73. control*(tw)
74. prospectiv*(tw)
75. volunteer*(tw))
76. Evaluate* (tw)
77. Compare* (tw)
78. Program* (tw)

79. 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78
80. “primary prevention” (MeSH Terms)
81. “Neoplasms/prevention and control”(MeSH Terms)
82. “Smoking/prevention and control”(MeSH)
83. “smoking cessation” (MeSH Terms)
84. Smoking/adverse effects“(MeSH Terms)
85. “occupational exposure” (MeSH Terms)
86. occupational exposure (Text Word)
87. “occupational diseases” (MeSH Terms)
88. occupational risk factor (Text Word)
89. “protective clothing” (MeSH Terms)
90. “inhalation exposure” (MeSH Terms)
91. exposure (Text Word)
92. exposed (Text Word)
93. body mass (tw)
94. tobacco (tw)
95. occupational vitiligo (Text Word)
96. ”Antineoplastic Agents“(Mesh)
97. ”Molecular Structure“(Mesh)
98. ”Immunoconjugates“(Mesh)
99. ”Mutagenesis“(Mesh)
100. ”Apoptosis“(Mesh)
101. apoptosis (Text Word)
102. ”Tumor Markers, Biological“(Mesh)
103. marker* (tw)
104. genet* (tw)
105. ”Signal Transduction“(Mesh)
106. toxin (Text Word)
107. toxin* (Text Word)
108. toxic* (Text Word)
109. toxic (Text Word)
110. ”Toxicology“(Mesh)
111. “case control” (tw)
112. epidemiol* (tw)
113. ”Carcinogens, Environmental/adverse effects“(MeSH)
114. “Mass Screening” (MeSH Terms)
115. screening (tw)
116. “Palliative Care” (MeSH Terms)
117. “end of life” (tw)
118. palliative (tw)
119. “Neoplasm Metastasis” (MeSH Terms)
120. “Mortality” (MeSH Terms)
121. “aged, 80 and over” (MeSH Terms)
122. “terminal care” (MeSH Terms)
123. “geriatric assessment” (MeSH Terms)
124. “non-cancer” (tw)
125. “non-malignant” (tw)
126. “gene expression profiling” (MeSH Terms)
127. ”Radiology/education“(MeSH Terms)
128. 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113 or 114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127

129. (18 and 53 and 79) not 128
130. (animal(mh) NOT human(mh))
131. 129 not 130

Appendix 2. EMBASE, CINAHL, OSH-ROM & PsycINFO: identical search strategy via Ovid

1. cancer.mp. (*)
2. *Neoplasm/ or neoplasm*.mp.
3. carcinoma*.mp.
4. oncolog*.mp.
5. malignan*.mp.
6. tumor*.mp.
7. tumour*.mp.
8. leukemi*.mp.
9. sarcom*.mp.
10. lymphom*.mp.
11. melanom*.mp.
12. blastom*.mp.
13. radiotherapy.mp.
14. chemotherapy.mp.
15. 6 or 11 or 3 or 7 or 9 or 12 or 2 or 14 or 8 or 1 or 4 or 13 or 10 or 5
16. exp Work Resumption/ or return to work.mp.
17. exp Employment/ or exp Employment Status/ or employment.mp.
18. exp Unemployment/ or unemployment.mp.
19. unemployed.mp.
20. retirement.mp.
21. (sick leave or Sickness absence or absenteeism).mp.
22. (vocational* or work ability or work capacity or work activity or work disability or work rehabilitation or work status or work retention or workability or employability or employable or employee*).mp.
23. randomized controlled trial.mp.
24. controlled clinical trial.mp.
25. (random allocation or double blind method or single blind method or clinical trial or placebo* or random* or comparative study or follow-up study or cross-over study or control* or prospectiv* or volunteer* or Evaluate* or Compare* or Program*).mp.
26. (primary prevention or smoking cessation or occupational disease* or occupational risk factor or protective clothing or exposure or exposed or body mass or tobacco or occupational vitiligo or Antineoplastic Agents or Molecular Structure or Immunoconjugates or Mutagenesis or Apoptosis or genet* or Signal Transduction or toxin or toxin* or toxic* or toxic or case control or epidemiol* or screening or end of life or palliative or Metastas* or terminal care or geriatric assessment or non-malignant or gene expression).mp.
27. animal.mp. or exp Animal/
28. 24 or 25 or 23
29. occupation.mp.
30. exp Vocational Rehabilitation/ or exp Work Disability/
31. disability management.mp.
32. exp Vocational Rehabilitation/ or work rehabilitation.mp.
33. 21 or 30 or 17 or 20 or 32 or 18 or 22 or 31 or 16 or 19
34. 33 and 28 and 15
35. 34 not 26
36. 35 not 27
* ([mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name])

Appendix 3. DARE search strategy

DARE: (more terms not possible)
(cancer OR neoplasm* OR carcinoma* OR oncolog* OR malignan* OR tumor* OR tumour* OR leukemi* OR sarcom* OR lymphom* OR melanom* OR blastom* OR radiotherapy OR chemotherapy) AND (return to work OR employment OR unemployment OR unemployed OR retirement OR sick leave OR Sickness absence OR absenteeism OR occupation* OR vocational* OR work ability OR work capacity OR work activity OR work disability OR work rehabilitation OR work status OR work retention OR workability OR employability OR employable OR employee*) NOT (primary prevention OR smoking cessation OR palliative OR Metastasis OR terminal)

HISTORY

Protocol first published: Issue 1, 2009

Review first published: Issue 2, 2011

Date	Event	Description
14 April 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

AdB is the main author and has been involved with all aspects of the protocol. She wrote the protocol and the review. She designed and conducted the search strategy. TT, ST, MF-D, MF and JV contributed to the draft version of the protocol and review and will contribute to subsequent versions and revisions of the review. AdB and TT included eligible studies, conducted the quality assessment of eligible studies and extracted the data from the original studies. JV and AdB conducted the data synthesis.

DECLARATIONS OF INTEREST

None.

SOURCES OF SUPPORT

Internal sources

- Coronel Institute of Occupational Health, Netherlands.
- Cochrane Occupational Safety and Health Review Group, Finland.
- University of Birmingham, UK.
- Uniformed Services University of the Health Sciences, USA.

External sources

- SIG Pathways to Work. University Research Programme, Netherlands.
- Finnish Work Environment Fund, Finland.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The Journal of Cancer Survivorship was not handsearched but included in the electronic search instead, because the journal is now in MEDLINE.