# Cancer-Related Fatigue: A Systematic and Meta-Analytic Review of Non-Pharmacological Therapies for Cancer Patients

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Cancer-related fatigue (CRF) is a significant clinical problem for more than 10 million adults diagnosed with cancer each year worldwide. No "gold standard" treatment presently exists for CRF. To provide a guide for future research to improve the treatment of CRF, the authors conducted the most comprehensive combined systematic and meta-analytic review of the literature to date on non-pharmacological (psy-chosocial and exercise) interventions to ameliorate CRF and associated symptoms (vigor/vitality) in adults with cancer, based on 119 randomized controlled trials (RCTs) and non-RCT studies. Meta-analyses conducted on 57 RCTs indicated that exercise and psychological interventions provided reductions in CRF, with no significant differences between these 2 major types of interventions considered as a whole. Specifically, multimodal exercise and walking programs, restorative approaches, supportive–expressive, and cognitive–behavioral psychosocial interventions show promising potential for ameliorating CRF. The results also suggest that vigor and vitality are distinct phenomena from CRF with regard to responsiveness to intervention. With improved methodological approaches, further research in this area may soon provide clinicians with effective strategies for reducing CRF and enhancing the lives of millions of cancer patients and survivors.

Keywords: cancer-related fatigue, meta-analysis, systematic review, psychological therapies, exercise

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Fatigue is the most frequently reported symptom associated with cancer and its treatment (Hofmana, Ryan, Figueroa-Moseley, Jean-Pierrea, & Morrow, 2007; Lawrence, Kupelnick, Miller, Devine, & Lau, 2004; Mock, 2001; Stone, Richards, & Hardy, 1998). Up to 91% of patients have been reported to experience cancer-related fatigue (CRF; Lawrence et al., 2004). With over 10 million new cases diagnosed each year and nearly 25 million people living with cancer worldwide (Kamangar, Dores, & Anderson, 2006), CRF represents a major public health concern. Diagnostic criteria for CRF have recently been proposed in an attempt to operationalize and standardize assessment of the prevalence of this common complaint of cancer patients and survivors, but these have yet to become widely accepted (Andrykowski, Schmidt, Salsman, Beacham, & Jacobsen, 2005; Cella, Peterman, Breitbart, & Curt, 1998; Sadler et al., 2001; Van Belle et al., 2005). The prevalence rates of CRF based on such approaches are considerably lower

Correspondence concerning this article should be addressed to Maria Kangas, Centre for Emotional Health, Department of Psychology, Macquarie University, Sydney, New South Wales 2109, Australia. E-mail: maria.kangas@mq.edu.au (ranging, on average, from 17% to 21%) in comparison with CRF rates indexed by self-report fatigue measures (Young & White, 2006). Notwithstanding this discrepancy, CRF has been documented to have debilitating effects on cancer survivors' overall quality of life, which can continue to afflict patients for at least a decade after diagnosis (Bower et al., 2006).

The specific mechanism(s) that cause and maintain CRF are not yet known, although the general consensus within this field acknowledges the contribution of both physiological and psychosocial factors in the onset and/or maintenance of CRF. In particular, CRF is associated with the biological effects of a malignancy and/or its associated treatment (e.g., surgery, chemotherapy, radiotherapy), including release of cytokines, cancer-related anemia, and cachexia (Ahlberg, Ekman, Gaston-Johansson, & Mock, 2003; Schubert, Hong, Natarajan, Mills, & Dimsdale, 2007; Stasi, Abriani, Beccaglia, Terzoli, & Amadori, 2003). Mood and affective disturbances, as well as low degrees of physical functioning that may cause deconditioning (loss of physical fitness), are also factors that have been linked to the onset and maintenance of CRF (Ahlberg et al., 2003; Mock, 2001).

One continuing concern in interpreting the high prevalence rates of CRF is the absence of a universally accepted definition (Lawrence et al., 2004). Presently, most investigators refer to some variant of the definition proposed by the National Comprehensive Cancer Network (NCCN), which describes CRF as "an unusual, persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning" (Mock, 2001, p. 1700). Although this definition highlights the inherently subjective and multifaceted nature of CRF, it overlooks two important components that are distinctively associated with CRF as compared

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with fatigue in healthy individuals: (a) CRF is not necessarily alleviated by rest and sleep and (b) the symptoms are disproportionate to the person's level of actual physical exertion (Jean-Pierre et al., 2007).

The lack of consensus regarding the definition of CRF is reflected in the escalating number of self-report quantitative measures that have been designed to assess both unidimensional and multidimensional components of fatigue (see Jean-Pierre et al., 2007; and Wu & McSweeney, 2001, for reviews). Whereas the unidimensional self-report questionnaires assess the current presence and intensity of fatigue, usually within the previous 7- day period (e.g., Profile of Mood States [POMS] Fatigue subscale, McNair, Lorr, & Droppelman, 1992; Brief Fatigue Inventory [BFI], Mendoza et al., 1999), multidimensional scales assess the impact of fatigue across several dimensions, most commonly physical, emotional/affective, and cognitive components of fatigue (e.g., Revised Piper Fatigue Scale [Revised PFS], Piper et al., 1998; Schwartz Cancer Fatigue Scale [SCFS], A. L. Schwartz, 1998). Although the multidimensional measures appear to provide a more comprehensive assessment of fatigue, no gold standard assessment measure currently exists to assess overall CRF (J. E. Schwartz, Jandorf, & Krupp, 1993; Wu & McSweeney, 2001). Indeed, a common shortcoming of some of the multidimensional measures is that they are heavily focused on assessing the physical components of fatigue (which also tend to be assessed by the unidimensional scales), whereas there is high variability in the extent to which multidimensional instruments measure other dimensions of fatigue.

Essentially, measuring the effects of CRF is contingent on the specific purpose of the assessment (cf. Wu & McSweeney, 2001). That is, if the aim of the clinician/researcher(s) is to assess the presence and intensity of fatigue, then the majority of both unidimensional and multidimensional scales meet this criterion. Selection of a specific scale is then contingent on psychometric qualities and feasibility issues (e.g., brevity of the scale). However, if the primary aim of the assessment is to determine the broader effects of CRF, including various aspects of a person's overall well-being encompassing affective, cognitive, and interpersonal functioning, then the selection of a scale that measures these components would be more appropriate.

In addition to tiredness, numerous descriptors have been applied in conceptualizing CRF, including lethargy, weariness, and physical and mental exhaustion (e.g., loss of attention and concentration). CRF has also been described in terms of deficiency, such as a lack of energy, vigor, or vitality. Vigor and vitality are generally considered synonymous concepts and are defined as reflecting healthy/robust physical and mental energy, strength, and drive. The scope of terms used to describe CRF is further reflected in the diverse unidimensional and multidimensional measures that continue to be used in the oncology literature to attempt to capture this construct, which include scales assessing the incidence and/or severity of symptoms of tiredness, weariness, and exhaustion (e.g., POMS Fatigue subscale, McNair et al., 1992; Functional Assessment of Cancer Therapy Fatigue subscale, Yellen, Cella, Webster, Blendowski, & Kaplan, 1997), and/or vitality and vigor (i.e., scales measuring energy and activity levels; e.g., the Medical Outcomes Short Form Survey Instrument [MOS SF-36] Vitality subscale; POMS Vigor subscale). Interestingly, there is evidence that CRF indexed by feeling tired, exhausted, and in need of rest may be distinct from a deficiency of vigor/vitality described by feeling energetic and active. In a recent meta-analytic review examining the impact of controlled trials of exercise interventions in cancer survivors, Schmitz et al. (2005) found that physical activity had a very small effect on fatigue (during and after cancer treatment; effect size [ES] = .19) but had a large positive effect on vigor/ vitality (ES = .83).

The POMS Fatigue scale is one of the most frequently used single-dimensional subscales to measure fatigue in cancer patients (Wu & McSweeney, 2001). Moreover, the POMS Fatigue subscale was found to have better reliability and validity in assessing fatigue intensity compared with three other fatigue measures (including the Multidimensional Assessment of Fatigue, the Multidimensional Fatigue Inventory, and the Lee Fatigue Scale) in a sample of cancer patients receiving medical treatment (Meek et al., 2000). To this end, the common use of the POMS may be due, in part, to its strong psychometric properties. In addition, the POMS is a multidimensional self-report questionnaire that not only assesses the presence and intensity of fatigue but also indexes the presence and intensity of several affective components including tension-anxiety, depression-dejection, anger-hostility, and confusion-bewilderment, as well as measuring vigor-activity. Hence, preference for the POMS may also be due to its multifaceted assessment of mood and activity states.

In the absence of a consensus definition of CRF, and consistent with the current empirical literature, we have chosen to adopt a broad inclusive definition of this phenomenon for the selection of articles in this review. We have, however, separately evaluated two distinct sets of symptoms commonly assessed in the CRF literature: (a) fatigue, as indexed by scales assessing tiredness, physical and mental exhaustion, and the need for rest; and (b) vigor/vitality, as indexed by scales assessing energy and active levels of functioning.

A wide range of non-pharmacological interventions to ameliorate CRF have been evaluated. These include psychosocial interventions (e.g., cognitive-behavioral therapy [CBT]; Gaston-Johansson et al., 2000), complimentary and alternative therapies (e.g., massage; Post-White et al., 2003), and physical exercise interventions (e.g., aerobics; Coleman, Coon, et al., 2003; Coleman, Hall-Barrow, et al., 2003). Furthermore, study methodologies evaluating the effectiveness of these interventions are quite heterogeneous, ranging from one-group designs to randomized controlled trials (RCTs). Not surprisingly, conclusions across studies are highly variable, and clinical recommendations are often unsubstantiated. Synthesis of this literature is required to enlighten both future research and best clinical practice.

Given the importance of CRF, it is not surprising that there have been a plethora of narrative, nonsystematic qualitative reviews and commentaries evaluating the efficacy of various nonpharmacological interventions in managing CRF and related symptoms (e.g., Ahlberg et al., 2003; Dimeo, 2002; Galvao & Newton, 2005; Mock, 2004; Mustian et al., 2007; Stone, 2002). A notable limitation of narrative reviews is the lack of systematic identification and methodologically rigorous evaluation of published studies.

In recent years, five systematic reviews have been published that have investigated the efficacy of physical exercise interventions in managing CRF in a wide range of diverse cancer populations (Knols, Aaronson, Uebelhart, Fransen, & Aufdemkampe, 2005; Markes, Brockow, & Resch, 2006; McNeely et al., 2006; Schmitz et al., 2005; Stevinson, Lawlor, & Fox, 2004). The Markes et al. (2006), McNeely et al. (2006), and Schmitz et al. (2005) reviews also included meta-analyses of this literature. A notable limitation of all five reviews is that CRF was only a partial aim of these reviews, and the number of studies that qualified for inclusion in each of the reviews was quite limited. More specifically, Stevinson et al. (2004) systematically evaluated 25 controlled studies (including both RCTs and nonrandomized controlled clinical trials [CCTs]), which investigated the effects of physical exercise interventions in promoting general psychological well-being. Only 12 of these trials assessed fatigue outcomes. Similarly, Knols et al. (2005) examined the methodological quality and efficacy of physical exercise in 34 controlled trials (both RCTs and CCTs) in managing physical functioning and psychological well-being, but only 15 of these trials included fatigue as a primary or secondary outcome measure.

Schmitz et al. (2005) conducted a combined systematic and meta-analytic review of 32 controlled physical exercise trials in improving 25 outcome variables, including fatigue/tiredness and vigor/vitality outcomes. Whereas 9 of the 32 trials assessed fatigue/tiredness outcomes (either during or following cancer treatment) and were found to have a combined small effect size (.14), three trials assessed vigor/vitality outcomes and were found to have a moderate effect when the intervention was administered during cancer treatment (.43) and a large positive effect when the intervention was administered following cancer treatment (.83). McNeely et al. (2006) focused their review on evaluating the effectiveness of 14 physical exercise RCTs in improving quality of life and physical functioning in breast cancer patients. Six of these studies included fatigue as an outcome variable, and meta-analyses revealed a moderate to large positive effect of the intervention (.72), although only 2 of these trials were evaluated as having high internal validity. Similarly, in a recent Cochrane review, Markes et al. (2006) investigated the methodological quality and efficacy of aerobic and/or resistance exercise interventions for breast cancer patients who were concurrently undergoing adjuvant cancer treatment. Five out of the 9 trials included in this review used fatigue as an outcome measure. Interestingly, these researchers found a statistically nonsignificant effect on fatigue symptoms for exercise interventions (standard mean difference = -.12). This result is contrary to McNeely et al.'s findings. The discrepancy between these two reviews may be due in part to differences in study inclusion criteria. Whereas McNeely et al. included interventions that were administered either during or following adjuvant cancer treatment, Markes et al.'s review was explicitly based on evaluating the efficacy of exercise interventions conducted during adjuvant cancer therapy. Indeed, Markes et al.'s finding is in part comparable to the fatigue results reported by Schmitz et al. However, the fatigue results from Schmitz et al.'s and McNeely et al.'s meta-analytic findings are substantially different. Whereas Mc-Neely et al. explicitly noted the studies that were used in the meta-analysis, as did Markes et al., Schmitz et al. did not specify which studies were included. Consequently, this limits the comparisons that can be made among these three meta-analytic reviews for determining the extent to which physical exercise interventions are beneficial in reducing fatigue symptoms across various cancer patient populations.

Lawrence et al. (2004) published the first systematic review that specifically evaluated the effectiveness of psychosocial as well as physical exercise interventions in ameliorating CRF. This review, however, was limited to RCTs published prior to October 2001 in which assessed fatigue was the primary outcome, resulting in only 10 RCTs with various types of interventions (including 9 nonpharmacological studies, [comprising 6 psychosocial trials and 3 physical exercise trials] and 1 pharmacological study) for the treatment of CRF. The authors concluded that all three of these types of interventions showed promise.

Most recently, Jacobsen, Donovan, Vadaparampil, and Small (2007)<sup>1</sup> published a combined systematic and meta-analytic review article that also focused on investigating the effectiveness of non-pharmacological interventions (including psychosocial and exercise-based therapies) in managing CRF. This review explicitly evaluated non-pharmacological RCTs that were published prior to December 2005. The researchers identified and evaluated a total of 41 interventions (comprising 24 psychosocial studies and 17 exercise-based studies) in the systematic (qualitative) review, whereas only a total of 30 interventions (consisting of 18 psychosocial trials and 12 exercise-based trials) were included in the final meta-analysis. Overall, the authors found a small effect size (d =.09) across all interventions. However when the efficacy levels of the psychosocial trials were compared with the exercise interventions, the psychosocial studies were found to have a significantly larger effect size (d = .10) relative to the exercise studies (d = .10).05). A notable limitation of the Jacobsen et al. (2007) review is that the researchers combined the fatigue outcomes with the vigor outcomes when comparing the overall effect sizes between psychosocial and exercise based interventions. As noted above, although vigor and vitality are common constructs that are typically associated with CRF, it would be premature to conclude that they are identical constructs. Jacobsen et al. compared the outcomes of psychosocial interventions with regard to reducing fatigue relative to enhancing vigor and found that psychosocial interventions were significantly better at reducing fatigue (d = .09, based on n = 18trials) than at improving vigor (d = .06, based on n = 11 trials). The authors conceded that the very modest number of exercisebased intervention trials that assessed vigor precluded them from conducting a comparable analysis among these studies. The fact that these researchers found a significant difference between fatigue and vigor outcomes within the psychosocial trials attests to the shortcomings of combining these two outcomes when examining the effectiveness of psychosocial and exercise-based interventions in managing CRF and improving vigor.

Furthermore, although Jacobsen et al. (2007) indicate that their "review represents the largest and most comprehensive exploration to date of RCTs of non-pharmacological interventions for cancerrelated fatigue" (pp. 663–664), they did not identify more than 40 published non-pharmacological RCT interventions that met their inclusion criteria (publication prior to December 2005). This oversight may be due, in part, to the restricted search strategy that was utilized, including restricting the electronic search of appropriate RCTs to only three databases: PsycINFO, MEDLINE, and CINAHL. Consequently, the findings from Jacobsen et al.'s meta-analysis are preliminary and should be viewed with caution

<sup>&</sup>lt;sup>1</sup> The Jacobsen et al. (2007) review was published following the completion of the current systematic and meta-analytic review.

given that they did not include a substantial number of published RCTs that met their eligibility criteria.

Recent years have seen a mounting number of new nonpharmacological intervention studies that have included fatigue and fatigue-related variables as a primary outcome, and numerous studies have included such variables as secondary outcomes. Evaluation of this broader set of CCTs and single-group design studies is important, as it may provide additional evidence regarding the effectiveness of various types of interventions for CRF. Notably, no review to date has provided a comprehensive systematic qualitative (inclusive of RCTs, CCTs, and single-group design studies) and/or quantitative evaluation of the effectiveness of nonpharmacological interventions in ameliorating CRF as assessed by either fatigue/tiredness and/or vigor/vitality symptoms. Given the complexity of findings reported for non-pharmacological interventions, a comprehensive systematic and meta-analytic evaluation of this literature is clearly warranted and may shed new light on critical issues in the literature, including the relative efficacy of various types of non-pharmacological interventions, as well as possible selective effects for patients with particular types of cancer.

The overarching aim of the present review was to take a comprehensive approach to the systematic and meta-analytic evaluation of published non-pharmacological intervention studies, comprising both physical exercise and psychosocial interventions (with the latter including traditional psychological therapies, such as CBT and counseling, as well as behavioral and alternative treatments such as massage and yoga) to assess the effectiveness of these approaches in ameliorating CRF in adult cancer patients and survivors. The advantage of using a combined review approach in evaluating these interventions is that it enables a systematic qualitative synthesis of the data from RCT trials in which effect sizes cannot be calculated (due to limitations of reporting of study outcomes; cf. Schmitz et al., 2005) as well as synthesis of these data with the qualitative data from CCT and single-group design trials. Hence, the aim of the systematic review component here was to provide a comprehensive qualitative assessment of the efficacy of psychosocial and physical exercise interventions in reducing fatigue and improving vigor/vitality symptoms in adult cancer patients as well as comparing these findings to the quantitative results that emerged from the meta-analytic approach. The overall aim of the meta-analytic component was to quantitatively examine the effectiveness of psychosocial and physical exercise RCTs in reducing fatigue and improving vigor/vitality outcomes. Using this meta-analytic approach, we were also able to examine a broad range of methodological, design, and sample characteristics that may be important moderators in explaining the size of the effect for the fatigue and vigor/vitality outcomes, respectively.

#### **METHOD**

#### Search Strategy

The following electronic databases were searched from their respective inceptions through to the end of December 2006: CANCERLIT, CINAHL, EMBASE, MEDLINE, PubMed, and PsycINFO. The searches were conducted with the following subject headings and/or keywords and combinations: (a) *cancer* (including *tumor/tumour, neoplasm/s*); (b) fatigue-related key-

words (fatigue, vitality, vigor/vigour), tired/ness, energy, inertia, lethargy); (c) cancer-related symptoms (quality of life [QOL], physical functioning, psychological functioning, mood, distress, anxiety, depression, stress); (d) non-pharmacological interventions (counseling/counselling, psychotherapy, stress management, cognitive-behavioral (behavioural) therapy [CBT], behaviour/behavior therapy, relaxation training, exercise, massage, education); and (e) common psychosocial quantitative measures, which included fatigue-related subscales (POMS, Functional Assessment of Cancer Therapy [FACT and FACIT], the Core scale from the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire [EORTC-QLQ-C30], and the MOS-SF-36). The bibliographies of retrieved articles, narrative reviews, and commentary articles on CRF and psychosocial interventions for cancer patients were also manually searched for additional references. The abstracts of all articles identified by electronic and manual searches (4,040 in total) were carefully screened by Maria Kangas for consideration of inclusion in this review, and a random selection of 25% of the abstracts were independently assessed by Guy H. Montgomery to check for consistency in selection. All abstracts and/or titles of articles that were considered for inclusion were read independently by these two authors, applying the selection criteria stipulated below.

# Selection Criteria of Eligible Trials for Both Systematic and Meta-Analytic Reviews

We included all published trials that met the following criteria: (a) published in a scientific peer-reviewed journal in full manuscript form; (b) written in the English language; (c) included a non-pharmacological intervention as one treatment arm of the study; (d) evaluated participants who were a minimum 18 years of age, had been diagnosed with cancer (any type or stage), and were at any phase of treatment or recovery; and (e) included a specific quantitative measure of fatigue or related symptom (comprising tiredness, lethargy, vigor, vitality or energy) as a primary or secondary outcome measure, in which the measure was administered minimally at pre-intervention (baseline) and postintervention.

#### Inclusion Criteria for Systematic Review

Both RCTs and non-RCTs (encompassing CCTs that did not include a randomization procedure) were included in the systemic review. To qualify as an RCT intervention, the study must have included at least one active treatment group, which was compared with a neutral control group. Single-group design studies that included both a baseline and a post-intervention measure of a fatigue-related symptom were also included. The decision to include these three different types of research designs was made a priori on the basis that the quantity of RCTs remains limited relative to the non-RCT/CCTs and single-group design trials. Hence, we deemed it important to systematically evaluate all available evidence on the effectiveness of non-pharmacological interventions in ameliorating CRF. Case reports and single-case designs, however, were excluded from this review, as they were viewed as substantially weaker designs for drawing conclusions about the effectiveness of non-pharmacological interventions.

#### Inclusion Criteria for Meta-Analytic Review

Only RCT interventions were included in the meta-analytic review component of this article. In addition, only studies with sufficient statistical data to compute an effect size were included (see Meta-Analytic Procedure section below).

### Data Extraction and Synthesis for Systematic Review

Trials that met inclusion criteria were read in full, and relevant data were extracted independently by two of the authors using a standardized form. Any discrepancies were discussed with referral to the original manuscript until consensus was reached. Separate tables were compiled for (a) two-group design trials (RCTs and non-RCTs/CCTs) and (b) single-group designs.

Two basic types of data (e.g., study methods, intervention methods) were extracted for the systematic review. Specific data extracted included research design (e.g., cross-sectional); whether a primary aim or hypothesis of the study was specifically targeting CRF (i.e., whether the authors explicitly stated in the introduction that one of the specific aims and/or hypotheses of conducting the study was to assess the efficacy of the intervention in reducing CRF and/or improving vigor/vitality); participant details (including sample size, type and stage of malignancy, and treatment status); assessment measures; primary endpoints of assessment; fatigue and fatigue-related outcomes (including vigor and vitality); type of intervention (e.g., CBT); treatment components; duration; setting; and mode of intervention (i.e., group or individual). In total, we compiled eight tables to summarize the extracted data separately according to (a) research design: two-group (RCT and non-RCTs/CCTs) and single-group designs and (b) type of intervention: psychosocial or physical exercise therapy. Psychosocial interventions comprised therapies that contained psychological and counseling components, including psychoeducation, stress management, coping strategies, counseling techniques, and relaxation training. Physical exercise interventions comprised therapies that were primarily based on physical activities, including aerobics and strength and resistance training. Studies that included a combination of psychological and physical components (e.g., stress management combined with yoga or walking) were classified as psychosocial studies. The reason for this classification is that it is not uncommon with the more traditional multimodal psychological interventions (e.g., CBT programs) to include both psychological and behavioral strategies that involve physical activity (e.g., activity scheduling that includes partaking in activities such as walking and other forms of exercise). A copy of the eight tables is available in the Supplemental Materials (http://dx.doi.org/10.1037/ 0033-2909.134.4.xxx).

On the basis of the substantial heterogeneity among studies in types of treatment interventions examined, we conducted descriptive analyses to evaluate fatigue and fatigue-related (notably vigor and vitality) outcome variables in relation to research design. Each treatment outcome variable was evaluated in terms of whether each trial found a positive effect (denoted by a plus sign), an equivocal effect (denoted by an equal sign), or no effect (denoted by a minus sign) of the intervention. For RCT and non-RCTs/ CCTs, a trial was classified as having a positive outcome (for each variable of interest evaluated. e.g., fatigue) if the intervention group was statistically significantly improved as compared with the control (for RCT designs) or alternative treatment arm (for CCT designs). Significant improvements in functioning could denote: (a) that the intervention group experienced a decline in fatigue relative to the alternative treatment arm or control group, or (b) that the control group or alternative treatment group experienced a significant increase in fatigue-related symptoms over time relative to the E group (which remained relatively consistent). This criterion was adopted in order to be consistent with the reporting of outcomes in the CRF intervention literature. For single-group design trials, the intervention was classified as having a positive outcome if a statistically significant better outcome was evident between baseline and post-intervention assessments. If more than one measure was used to assess the outcome variable of interest (e.g., use of two separate fatigue scales) for RCT, non-RCT, and single-group design studies, a trial was classified as being positive if statistically significant findings were obtained on at least one of these outcome measures.

A trial was classified as having no effect if no statistically significant differences existed between the intervention group and the control or alternative intervention treatment arm for RCT and non-RCT/CCT studies, respectively. For single-group design studies, the intervention was classified as having no effect if no statistically significant findings were evident between baseline and post-intervention assessment outcomes. If the authors of a trial did not report statistical results for an outcome measure for which data were described as being collected, we assumed that no statistical significance was found for comparisons between the primary intervention group relative to the control and/or alternative treatment arm. Accordingly, this was classified as a no-effect outcome. Furthermore, for RCT and non-RCT studies, an intervention was classified as having equivocal effects if it satisfied any of the following criteria: (a) an interactional effect existed for the intervention group on the outcome variable of interest relative to the control or alternative treatment arm while the main effect of group was not statistically significant; (b) no statistically significant differences existed between the intervention group compared with the control or alternative intervention group for the outcome variable of interest, although statistically significant within-group differences were evident for either the intervention group or control group; or (c) the intervention group exhibited significantly less amelioration of fatigue related outcomes relative to the control group.

#### Meta-Analytic Procedure

#### Fatigue

Of the 67 RCTs that assessed fatigue or tiredness as an outcome measure (50 psychosocial and 17 exercise interventions) and met inclusion criteria, 10 studies (9 psychosocial trials and 1 exercise trial) were excluded because they did not report sufficient statistical information to compute effect sizes. Hence, in total, 85% (k = 57) of RCT interventions that met the initial inclusion criteria for the meta-analysis were included in the meta-analyses.

#### Vigor/Vitality

Of the 60 RCTs that assessed vigor/vitality as an outcome measure (50 psychosocial and 10 exercise interventions) that met initial inclusion criteria, 17 trials (14 psychosocial and 3 exercise

trials) were excluded from the meta-analysis, as they did not report sufficient statistical information to compute effect sizes. Thus, in total, 72% of RCT studies were included in the meta-analyses.

Effect size (d) was calculated separately for (a) fatigue and tiredness outcome measures (henceforth referred to as fatigue outcomes and (b) vigor, vitality, and increased energy outcome measures (henceforth referred to as vigor/vitality outcomes). For study trials that reported statistical data on two or more measures of the same outcome (e.g., fatigue), consistent with the systematic review analyses, the effect size was calculated with the outcome measure that yielded more favorable findings. This latter criterion was only applicable for a couple of interventions. For each individual study trial, effect sizes (ds) for each variable of interest (i.e., fatigue and vigor/vitality outcomes) were computed by taking the difference between the control group mean and the experimental group mean, then dividing by the standard deviation (J. Cohen, 1988). For studies that did not provide this descriptive statistical information but did report relevant values from statistical tests (e.g., t test, F test, p values), effect sizes were estimated on the basis of the formulas in Smith, Glass, and Mille's (1980) text (Appendix 7). In some instances where no relevant statistical information was reported (including the specific p value), but the outcome variable (e.g., fatigue) was reported to be significant, the effect size was derived by assuming that the p values were equivalent to .05. In all other instances where insufficient statistical information was reported to estimate the group means and/or standard deviation or mean standard error term, these study trials were excluded from the meta-analysis.

The meta-analytic computations were performed with the Stata (version 9) program. To control for the wide variability in sample size, all calculations were weighted according to sample size. Weighted mean effect sizes and the 95% confidence intervals for the weighted means were calculated with a random effect approach. This approach was used for two reasons: (a) the effects for all of the outcomes were heterogeneous and (b) the random approach is more appropriate when a relatively large number of studies are to be analyzed. A notable advantage of this method is that it has a more powerful scope in generalizing to similar studies not included in the meta-analysis (cf. Frattaroli, 2007). A p value of less than .05 was considered to be a significant effect size.

#### Quality and Validity Assessment

Study qualities for RCT studies were evaluated according to the following eight validity criteria determined a priori, which were adapted from the Consolidated Standards of Reporting Trials (CONSORT) guidelines (Altman et al., 2001; Moher, Schulz, & Altman, 2001) and Delphi criteria list (Verhagen et al., 1998): randomization; allocation concealment; blinding of outcome assessments; comparability of groups at baseline; withdrawals and handling of dropouts in analyses and use of intention-to-treat (ITT) analysis; and multiple follow-up assessments. Scores were given, with one point allocated for each criterion satisfied (range = 0-8points). A study was deemed as having good internal validity/ quality if score > 4 points. This variable was used as one of the moderator analysis. The validity criteria were based primarily on the CONSORT guidelines as in recent years, the majority of peer-reviewed journals require that authors conform to these guidelines when submitting manuscripts for treatment outcome

studies. A summary of the validity ratings for the psychosocial and exercise RCT studies are presented in two tables that are available in the supplemental data (http://dx.doi.org/10.1037/0033-2909.134.4.xxx).

RCT studies were also evaluated according to four additional criteria: (a) whether the participant inclusion criteria for each identified study required individuals to be suffering from fatigue and/or related symptoms (e.g., low energy, vigor) prior to randomization; (b) whether the study was based on a specific CRF aim and/or CRF-related hypothesis (including predictions for effect of intervention(s) on fatigue, vigor and/or vitality); (c) whether the intervention was based on a specific fatigue-related theory, which the researchers made explicit in the publication; and (d) type of fatigue outcome measure used (i.e., unidimensional vs. multidimensional). These four criteria were included in the moderator analyses.

#### RESULTS

The findings from the systematic review are presented first, followed by the results from the meta-analytic component of this combined review.

#### Systematic Review

#### Search Results

A total of 119 published articles comprising 131 studies (with 8 studies that included separate follow-up publications) met the inclusion criteria. Three groups of researchers published what appear to be findings from the same databases in two distinct publications (Allison, Edgar, et al., 2004; Allison, Nicolau, et al., 2004; Coleman, Coon, et al., 2003; Coleman, Hall-Barrow, 2003; A. L. Schwartz, 1999, 2000a); accordingly, these articles were only counted once in the final tally of included studies. Seventy-one studies were RCTs (n = 52 psychosocial interventions, including 3 separate published follow-up studies, and n = 17 physical exercise interventions); 9 were non-RCTs or CCTs (n = 6 psychosocial with one separate follow-up paper; n = 2 exercise); and 36 were single-group designs (n = 21 psychosocial, including 4 separate published follow-up studies, and n = 11 exercise).

However, we excluded two trials conducted by the same researchers (Cimprich, 1993; Cimprich & Ronis, 2001), which examined the effects of a restorative psychosocial intervention in improving attentional fatigue in breast cancer patients. The reason for excluding these trials was that the fatigue outcome was based on participants' combined performance on several neurocognitive tests (including Digit Span Forward and Backward from the Weschler Intelligence Assessment Scale [WAIS)]). Therefore, we deemed that these two studies substantially deviated from the conventional unidimensional and multidimensional fatigue-related measures utilized in the non-pharmacological treatment outcome literature, thus making comparisons between these studies untenable.

#### Trial Characteristics and Outcomes

#### Psychosocial Interventions

Sixty-two articles investigated the effectiveness of various psychosocial interventions in ameliorating disease and treatment-related symptoms in which a fatigue-related measure was used as a primary or secondary outcome measure with an RCT (n = 52 studies) or a non-RCT/CCTs (n = 6 studies) group comparison design. In addition, four of the articles (Berglund, Bolund, Gustafsson, & Sjödén, 1994b; Bordeleau et al., 2003; Carlson, Ursuliak, Goodey, Angen, & Speca, 2001; Helgeson, Cohen, Schulz, & Yasko, 2001) comprised separate follow-up studies relating to 1 of the non-RCTs and 3 of the RCT studies, respectively.

Twenty-five articles (which included 4 separate follow-ups; Berger et al., 2003; Hosaka, Sugiyama, Hirai, et al., 2001; Hosaka, Sugiyama, Tokuda, & Okuyama, 2000; Hosaka, Sugiyama, Tokuda, Okuyama, Sugawara, & Nakamura, 2000) investigated a variety of psychosocial interventions using a single-group design in which a fatigue-related measure was used as an outcome variable. Eighteen of these articles reported on single-group design trials, whereas 3 presented data on more than one distinct trial (Cunningham, Edmonds, Jenkins, & Lockwood, 1995; Hosaka, 1996; Post-White, 2003).

# *Psychosocial RCTs: Sample, Design Characteristics, and Fatigue and Vigor/Vitality Outcome*

Although 42 RCT psychosocial studies were identified that included fatigue outcomes (excluding 3 separate follow-up publications), 2 of the studies included 2 separate sets of interventions (de Wit et al., 1997; F. I. Fawzy, Fawzy, & Wheeler, 1996). In addition, 6 RCT studies included 2 or more interventions that were separately evaluated against a control/comparison group (Arathuzik, 1994; Bridge, Benson, Pietroni, & Priest, 1988; Richardson et al., 1997; Sandgren & McCaul, 2003; Telch & Telch, 1986; Weintraub & Hagopian, 1990). The 42 psychosocial RCT studies comprised a total of 50 distinct trials reporting fatigue outcomes. In addition, 40 RCT psychosocial studies, comprising 53 specific trials, reported vigor or vitality outcomes.

A summary of the sample and design characteristics as well as fatigue and vigor/vitality outcomes for the psychosocial RCT interventions are presented in Table 1. Surprisingly, no trial had specific inclusion criteria limiting eligibility to fatigued individuals or those who reported low vigor/vitality. Thus, overall, there were no differences in terms of participant inclusion criteria pertaining to fatigue and/or vigor/vitality symptoms at baseline between psychosocial studies that included a specific CRF aim compared with studies that included a more generic aim (e.g., predicting improvements in general quality of life).

Only a minority of the psychosocial RCTs that reported a fatigue outcome (28%) included a specific CRF aim and/or hypothesis, and 50% of these trials reported beneficial effects for fatigue post-intervention. Overall, 24% of all psychosocial RCTs were found to have favorable outcomes in reducing CRF post-intervention. In addition, 20 of the 50 psychosocial trials reported findings for at least 1 additional follow-up period. Five of these trials showed initial positive effects for fatigue at the post-intervention assessment; however, the positive findings were not maintained for 3 of these trials at the subsequent follow-up assessment (Boesen et al., 2005; Forester, Kornfeld, & Fleiss, 1985; Wenzel, Robinson, & Blake, 1995). The remaining 8 trials that included an additional follow-up assessment showed no significant positive effects for fatigue at the initial post-assessment; however, two of these trials were found to show a significant improvement in fatigue over the longer term, at 6 months

following the completion of the intervention (Carlson et al., 2001; F. I. Fawzy et al., 1990).

Fewer than one fifth of the psychosocial RCTs that reported a vigor or vitality outcome (18%) included a specific CRF aim and/or hypothesis, and one third of these trials (33%) were found to increase vigor or vitality post-intervention. Similarly, one third of all psychosocial RCTs that reported a vigor or vitality outcome were found to have favorable outcomes in enhancing vigor or vitality in cancer patients. In addition, 21 (42%) of the psychosocial trials reported findings for vigor/vitality outcomes for at least one additional follow-up period. Seven of these trials were initially found to have positive effects for vigor/vitality at the initial post-intervention assessment; however, the beneficial effects were only maintained for three of these trials at the subsequent follow-up assessment (Carlson et al., 2001; Helgeson et al., 2001; Worden & Weisman, 1984).

Although the psychosocial interventions consisted of various types of primarily multimodal therapies, for the purposes of this review, these interventions were classified according to seven subcategories: (a) cognitive-behavioral therapy (CBT; comprising studies that used a combination of behavioral and cognitive components, including stress management and problem solving); (b) supportive-expressive therapy (which included studies involving psychotherapy that facilitated expression of emotion and fostered support from therapist and group participant members); (c) behavioral therapy (composed primarily of relaxation and/or imagery training strategies); (d) counseling (which included general supportive interventions or interventions involving a combination of psychoeducation and supportive counseling); (e) educational training (which included information about cancer symptoms, management, and/or general emotional adjustment to this experience); (f) massage therapy; and (g) restorative therapies (which included interventions that focused on restoring attention and concentration as well as prioritizing daily activities by engaging in 20- to 30-min activities that were enjoyable and/or relaxing or deemed valuable by the individual, such as sitting or walking in a park, tending to a garden, or playing with pets; one of these interventions was based on a virtual reality program that provided tranquil natural environmental scenes while participants underwent chemotherapy infusions).

Accordingly, the results were also analyzed in terms of the efficacy of specific psychotherapeutic approaches in reducing fatigue and increasing vigor/vitality. A summary of these findings is presented in Table 2. Among the psychosocial RCT interventions that included a fatigue outcome measure, the two studies that used a restorative therapeutic intervention were reported to have beneficial effects in decreasing fatigue symptoms. The one trial that used massage therapy was also found to have beneficial effects. Forty-three percent (n = 3) of the interventions that were categorized as supportive-expressive therapy programs were found to result in a significant improvement in fatigue, whereas 26% (n =5) of CBT interventions had beneficial effects in reducing fatigue. Only one of the nine counseling interventions was found to reduce fatigue symptoms, whereas no trial that used either an educational (n = 7) or a behavioral/relaxation (n = 5) intervention showed beneficial effects on fatigue.

Among the psychosocial RCTs that reported a vigor/vitality outcome, almost half (40%; n = 8) of the CBT interventions were found to significantly increase vigor/vitality. In addition, a third of the counseling and educational interventions were also found to

#### Table 1

Randomized Controlled Trials	Sample, Design	Characteristics, an	nd Fatigue and	Vigor/Vitality	Outcomes
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Variable	Psychosocial, includes fatigue outcome: Systematic review n (%)	Exercise, includes fatigue outcome: Systematic review n (%)	Psychosocial, includes vigor/vitality outcome:Systematic review n (%)	Exercise, includes vigor/vitality outcome: Systematic review n (%)
Total no. trials (published studies)	50 <sup>a</sup> (42)	17 <sup>a</sup> (17)	50 <sup>a</sup> (39)	$10^{a}(9)$
CRF aim/hypothesis				
Yes	14 (28%)	10 (59%)	9 (18%)	5 (50%)
No	36 (72%)	7 (41%)	41 (82%)	5 (50%)
Design				
CŠ	27 (54%)	7 (41%)	33 (66%)	4 (40%)
$AP^{b}$	23 (46%)	10 (59%)	17 (34%)	6 (60%)
FU <sup>c</sup>	20 (40%)		21 (42%)	
Cancer type				
BC	21 (42%)	10 (59%)	28 (56%)	7 (70%)
Mix	19 (38%)	3 (18%)	14 (28%)	2 (20%)
MM	5 (10%)		4 (8%)	0
Other	5 (10%)	4 (23%)	4 (8%)	1 (10%)
Stage				
Early	8 (16%)	6 (35%)	13 (26%)	5 (50%)
Advanced	3 (6%)	1 (6%)	6 (12%)	0
Mix	27 (54%)	8 (47%)	20 (40%)	3 (30%)
Mets.	7 (14%)	0	7 (14%)	0
NA	5 (10%)	2 (12%)	4 (8%)	2 (20%)
Treatment status				
On	25 (50%)	11 (65%)	19 (38%)	6 (60%)
Off	9 (18%)	5 (29%)	15 (30%)	4 (40%)
Mix	7 (14%)	1 (6%)	7 (14%)	0
NA	9 (18%)	0	9 (18%)	0
Includes POMS Fatigue and/or Vigor subscale	33 (66%)	6 (35%)	36 (72%)	6 (60%)
Results <sup>d</sup>				
Positive				
All	12 (24%)	6 (35%)	15 (30%)	3 (30%)
% with CRF aim/hypothesis	7 (50%)	3 (30%)	3 (33.3%)	2 (40%)
Negative				
All	32 (64%)	7 (41%)	32 (64%)	5 (50%)
% with CRF aim/hypothesis	5 (36%)	4 (40%)	4 (44.4%)	2 (40%)
Equivalent				
All	6 (12%)	4 (24%)	3 (6%)	2 (20%)
% with CRF aim/hypothesis	2 (14%)	3 (30%)	2 (22.2%)	1 (20%)

*Note.* CRF aim/hypothesis = number of studies that include a cancer-related fatigue specific aim and/or hypothesis; Design: CS = cross-sectional; AP = adjuvant prospective; FU = follow-up; cancer type: BC = breast cancer sample used; mix = heterogeneous sample of cancer patients used; MM = malignant melanoma sample used; other = includes samples based entirely on other types of cancers excluding mixed, BC, and MM samples; stage: mets. = metastatic disease; NA = not available: study did not report disease staging of sample participants; treatment status: NA = not available: study did not report treatment status of sample participants. POMS = Profile of Mood States.

<sup>a</sup> Sample size characteristics and proportions based on total number of trials. <sup>b</sup> We chose to use the term *adjuvant prospective* (AP) design given that none of the studies were strictly prospective, as baseline assessments occurred at varying intervals post–cancer diagnosis and either prior to the commencement of cancer treatment or soon after the start of treatment. Hence, study designs were categorized as AP if the intervention was administered at the same time that participants commenced either their primary or adjuvant medical/cancer treatments (i.e., radiotherapy or chemotherapy). <sup>c</sup> Includes at least one longer term follow-up in addition to the initial postintervention assessment published within the same article. <sup>d</sup> Results: As no exercise study reported on multiple follow-up assessments postintervention (i.e., excluding additional longer term follow–up assessments); all = inclusive of all studies with or without CRF aim/hypothesis; % with CRF aim/hypothesis = percentage of all studies that include CRF aim/hypothesis and that report positive, negative, and equivalent findings, respectively.

substantially improve vigor/vitality. However, only one of the supportive–expressive psychotherapies increased vigor/vitality, whereas none of the behavioral/relaxation, restorative, and massage therapies were found to enhance vigor/vitality.

# *Psychosocial non-RCTs: Sample, Design Characteristics, and Fatigue and Vigor/Vitality Outcome*

Five of the six psychosocial intervention studies included a non-RCT/CCT or group comparison design and reported on fatigue outcomes (Bailey, 1983; Berglund, Bolund, Gustavsson, & Sjödén, 1993; Courneya, Friedenreich, Sela, Quinney, Rohdes, & Handman, 2003; Petruson, Silander, & Hammerlid, 2003; Targ & Levine, 2002). None of these studies indicated that CRF was a specific study aim a priori. Similarly, no study had specific inclusion criteria limiting participation to individuals who met a set cut-off for elevated fatigue-related symptoms at baseline. Moreover, only one of the non-RCT studies was found to have an intervention that significantly reduced fatigue following the completion of the intervention. In

Table 2								
Fatigue and	Vigor/Vitality	Results	According	to	Specific	Therapeutic	Compone	nts

Intervention	No. of trials reporting fatigue outcome	% of studies reporting positive fatigue results	No. of trials reported vigor/vitality outcome	% of studies reporting positive vigor/vitality results
Psychosocial treatments: RCTs				
Cognitive-behavioral therapy	19	26%	20	40%
Supportive–expressive therapy	7	43%	6	17%
Counseling	9	11%	12	33%
Educational	7	0%	6	33%
Behavioral/relaxation	5	0%	7	0%
Massage	1	100%	1	0%
Restorative	2	100%	1	0%
Psychosocial treatments: Single-group design				
Cognitive-behavioral therapy	9	67%	6	33%
Supportive counseling	6	50%	5	60%
Educational	0		1	0%
Behavioral/relaxation	3	0%	2	0%
Massage/healing therapies	2	0%	2	0%
Restorative	4	50%	1	100%
Exercise treatments: RCTs				
Multimodal	7	43%	5	40%
Walking	3	33%	3	33%
Bicycle	2	50%	1	0%
Cardiovascular/flexibility and/or strength	4	0%	1	0%
Resistance	1	100%	0	
Exercise treatments: Single-group design				
Multimodal	7	43%	5	40%
Aerobic	4	100%	1	0%

Note. RCTs = randomized controlled trials.

particular, participants who received a combined group psychotherapy and home-based aerobic exercise intervention were found to have a significant improvement in fatigue compared with participants who only received the group psychotherapy intervention without the home-based exercise therapy component (Courneya, Friedenreich, Sela, Quinney, Rhodes, & Handman, 2003).

Only half of the non-RCT psychosocial group comparison studies included vigor/vitality as an outcome measure (Bailey, 1983; Hernandez-Reif, Field, Ironson, Beutler, & Vera, 2005; Targ & Levine, 2002). Two of these studies documented a significant improvement in vigor for two of the interventions. Specifically, Bailey (1983) found that a live music intervention significantly improved vigor compared with taped music, whereas Hernandez-Reif et al. (2005) reported that massage therapy significantly increased vigor compared with participants who received progressive muscle relaxation training.

# *Psychosocial Single-Group Design Interventions: Fatigue and Vigor/Vitality Outcomes*

A summary of the sample, design characteristics, and fatigue and vigor/vitality outcomes for the psychosocial single-group design trials is presented in Table 3. In particular, 24 trials reported outcomes for fatigue, whereas 42% of these trials included CRF as a specific aim and/or hypothesis of the study. Almost half of the single-design trials (46%) were reported to have beneficial effects for fatigue, and more than one third of these trials (40%) included a specific CRF aim and/or hypothesis. Five of the 11 studies that reported an improvement in fatigue included an additional longer term follow-up assess-

ment; however, only two of these trials were found to maintain the reduction in fatigue at 3 months following completion of the intervention (Allison, Edgar, et al., 2004; Allison, Nicolau, Edgar, et al., 2004; Cunningham, Lockwood, & Edmonds, 1993).

Seventeen psychosocial single-group design trials reported outcomes for vigor/vitality, and only one third of these interventions included CRF as a specific aim and/or hypothesis of the study. About one third of the single-group design trials (29%) reported positive outcomes for vigor/vitality, and only one of these trials included a specific CRF aim. Two of the six studies that reported an improvement in vigor/vitality included an additional longer term follow-up assessment; however, only one of these trials was found to maintain improvements at 3 months following completion of the intervention (Cunningham et al., 1993).

The single-group design psychosocial interventions were also classified according to their primary therapeutic approaches. The categories were the same as those used for the RCT psychosocial interventions. Two thirds of single-group designs that were CBT programs (n = 6) were found to significantly reduce fatigue. In addition, 50% of supportive counseling (n = 3) and restorative therapies (n = 2) were found to improve fatigue symptoms. However, none of the behavioral/relaxation (n = 3) and alternative (massage and body healing; n = 2) therapies were found to have significantly beneficial effects on fatigue outcomes. Furthermore, the majority (60%; n = 3) of the supportive counseling and one third (n = 2) of the CBT intervention studies reported improved vigor/vitality. The one restorative therapeutic trial was also found to increase vigor/vitality, although none of the behavioral/relaxation (n = 2), massage and body

Single-Design Studies: Sample, Design Characteristics, and Fatigue and Vigor/Vitality Outcomes

Variable	Psychosocial includes fatigue outcome: Systematic review n (%)	Exercise includes fatigue outcome: Systematic review n (%)	Psychosocial includes vigor/ vitality outcome: Systematic review n (%)	Exercise includes vigor/ vitality outcome: Systematic review n (%)
Total no trials (published studies)	$24^{a}(20)$	$11^{a}(10)$	$17^{a}(13)$	$6^{a}(5)$
CRF aim/hypothesis	2: (20)	(10)	(10)	0 (0)
Yes	10 (42%)	7 (64%)	6 (35%)	2 (33%)
No	14 (58%)	4 (36%)	4 (24%)	4 (67%)
Design				
CS	16 (67%)	6 (54.5%)	13 (76%)	4 (67%)
$AP^{b}$	8 (33%)	5 (45.5%)	4 (24%)	2 (33%)
FU <sup>c</sup>	5 (21%)		3 (18%)	
Cancer type				
BC	8 (33%)	5 (45.5%)	4 (24%)	1 (17%)
Mix	15 (63%)	5 (45.5%)	13 (76%)	5 (83%)
MM	0	0	0	0
Other	1 (4%)	1 (9%)	0	0
Stage				
Early	3 (12%)	0	2 (125)	0
Advanced	0	1 (9%)	0	0
Mix	10 (42%)	7 (64%)	7 (41%)	4 (67%)
Mets.	0	0	0	0
NA	11 (46%)	3 (27%)	8 (47%)	2 (33%)
Treatment status				
On	10 (42%)	5 (45.5%)	6 (35%)	2 (33.3%)
Off	5 (21%)	3 (27.3%)	2 (12%)	1 (17.7)
Mix	3 (12%)	1 (9%)	2 (12%)	1 (17.7)
NA	6 (25%)	2 (18.2%)	7 (41%)	2 (33.3)
Includes POMS Fatigue and/or	14 (58%)	3 (27%)	13 (76%)	3 (50%)
Vigor subscale				
Results				
Positive	11 (460)		5 (20%)	2 (22)
	11 (46%)	6 (54.5%)	5 (29%)	2 (33%)
% with CRF aim/hypothesis	4 (40%)	6 (86%)	1 (1/%)	1 (50%)
Negative	12 (540)	5 (45 50)	10 (716)	4 ((70))
	13 (54%)	5 (45.5%) 1 (14%)	12(/1%)	4 (6/%)
% with CRF aim/hypothesis	6 (60%)	1 (14%)	5 (83%)	1 (50%)

*Note.* CRF aim/hypothesis = number of studies that included a cancer-related fatigue specific aim and/or hypothesis. POMS = Profile of Mood States. All = inclusive of all studies with or without CRF aim/hypothesis; % with CRF aim/hypothesis = percentage of studies that include CRF aim/hypothesis; Design: CS = cross-sectional; AP = adjuvant prospective; FU = includes at least one longer-term follow-up, in addition to initial post-intervention assessment; Cancer Type: BC = breast cancer sample used; Mix = heterogeneous sample of cancer patients used; MM = malignant melanoma sample used; Other = includes samples based entirely comprising of other types of cancers excluding mixed, BC, and MM samples; Stage: Mets = metastatic disease; NA = not available: study did not report disease staging of sample participants; treatment status: NA = not available: study did not report treatment status of sample participants.

<sup>a</sup> Sample size characteristics and proportions based on total number of trials. <sup>b</sup> We chose to use the term *adjuvant prospective* (AP) design given that none of the studies were strictly prospective, as baseline assessments occurred at varying intervals post–cancer diagnosis and either prior to the commencement of cancer treatment or soon after the start of treatment. Hence, study designs were categorized as AP if the intervention was administered at the same time that participants commenced either their primary or adjuvant medical/cancer treatments (i.e., radiotherapy or chemotherapy). <sup>c</sup> Includes at least one longer term follow-up in addition to the initial postintervention assessment published within the same article. <sup>d</sup> Results: As no exercise study reported on multiple follow-up assessments postintervention (i.e., excluding additional longer term follow–up assessments); all = inclusive of all studies with or without CRF aim/hypothesis; % with CRF aim/hypothesis = percentage of all studies that include CRF aim/hypothesis and that report positive, negative, and equivalent findings, respectively.

healing (n = 2), or educational (n = 1) interventions improved vigor/vitality outcomes.

#### **Exercise Interventions**

Nineteen articles reported effectiveness of various physical exercise interventions with a fatigue-related outcome measure using an RCT (n = 17 studies) or non-RCT/CCT (n = 2) group com-

parison design. One of the RCT studies included two separate types of exercise interventions, which were separately evaluated against a control group (Segal et al., 2001). Accordingly, the 17 RCT studies comprised 18 distinct trials in total.

Eleven publications investigated the effectiveness of various physical exercise interventions in which a fatigue-related measure was included as an outcome in a single-group design. One article evaluated two distinct single-group intervention trials (Christopher & Morrow, 2004); hence, the single-group design interventions consisted of 12 distinct trials.

# *Exercise RCTs: Sample, Design Characteristics, and Fatigue and Vigor/Vitality Outcomes*

Whereas 17 exercise trials reported fatigue outcomes, only 10 exercise trials reported vigor or vitality outcomes. Notably, in concordance with the psychosocial interventions, not one of the exercise RCT trials had specific inclusion criteria limiting participation to individuals who met a set cut-off for elevated fatiguerelated symptoms and/or reduced energy levels at baseline. A summary of the sample, design characteristics, and fatigue and vigor/vitality outcomes for the exercise RCT interventions are presented in Table 1. Although more than half of the exercise trials that reported a fatigue outcome (59%) included CRF as a specific aim or hypothesis of the study, less than one third of these interventions were found to have favorable outcomes in reducing fatigue. Similarly, whereas 50% of the exercise trials that reported a vigor or vitality outcome included a specific CRF aim and/or hypothesis, only 40% of these interventions were found to enhance vigor or vitality. Interestingly, no exercise RCT intervention reported data on any additional follow-up assessment intervals after collection of the postassessment data, following the cessation of the intervention period.

The physical exercise trials were classified according to five main therapeutic approaches for the purposes of this review: (a) multimodal exercise programs (which included multiple exercise components/activities); (b) walking intervention (which explicitly involved walking); (c) bicycle/cycling program (which explicitly involved cycling with exercise bicycles or cycle ergometers); (d) cardiovascular, flexibility and/or strength training; and (e) resistance training. The results were also analyzed in terms of the efficacy of specific exercise modalities in reducing fatigue and increasing vigor or vitality, and a summary of these findings is presented in Table 2. Among the exercise RCT interventions that included a fatigue outcome measure, the only exercise intervention that was explicitly based on a resistance training program reported significant beneficial effects on fatigue. In addition, 43% of multimodal exercise programs were found to reduce fatigue symptoms. One of the walking programs, as well as one of the bicycle interventions, led to a reduction in fatigue; however, none of the cardiovascular/flexibility and strength training programs (n = 4)led to significant reductions in fatigue. Furthermore, 40% (n = 2) of the multimodal exercise programs and one third (n = 1) of the walking interventions were found to significantly increase vigor/ vitality, whereas none of the cardiovascular/flexibility training or cycling programs were found to have beneficial effects on vigor/ vitality.

# *Exercise Non-RCTs: Sample, Design Characteristics, and Fatigue and Vigor/Vitality Outcomes*

Two non-RCT physical exercise interventions were identified, both of which included CRF as a specific aim and/or hypothesis (Dimeo, Thomas, Raabe-Menssen, Propper, & Mathias, 2004; Galantino et al., 2003). Moreover, both of these studies reported fatigue outcomes, but neither study utilized vigor or vitality as an outcome measure. In particular, the Galantino et al. (2003) study found no significant improvement in fatigue among groups of participants who received either a walking exercise intervention or a tai chi intervention. In contrast, participants in both intervention groups (the aerobic exercise intervention and the progressive muscle relaxation intervention) in the Dimeo et al. (2004) study were found to have a reduction in fatigue postassessment; however, the benefit did not differ between the two interventions.

# *Exercise Single-Group Design Interventions: Sample, Design Characteristics, and Fatigue and Vigor/Vitality Outcomes*

A summary of the sample, design characteristics, fatigue, and vigor/vitality outcomes for the exercise single-group design trials is presented in Table 3. Eleven trials reported outcomes for fatigue. Almost two thirds (64%) of the trials included a specific CRF aim and/or hypothesis, and the majority of these studies (86%) were reported to have beneficial effects in reducing fatigue. A smaller proportion of exercise trials (n = 6) reported outcomes for vigor or vitality. Moreover, only two of these trials included a specific CRF aim and/or hypothesis, and only one of the studies reported beneficial results in increasing vigor.

The exercise single-group design interventions were classified according to two main categories: (a) aerobic (which consisted of interventions that instructed individuals to partake in an aerobic activity of choice) and (b) multimodal exercise programs. The results were also analyzed in terms of the efficacy of specific exercise modalities in reducing fatigue and increasing vigor or vitality, and a summary of these findings is also presented in Table 2. Among the exercise interventions that included a fatigue outcome, all four of the aerobic interventions had beneficial effects on fatigue, whereas 43% (n = 3) of the multimodal exercise programs reported significant declines in fatigue symptoms. Additionally, only two trials, both involving multimodal exercise programs, were found to enhance vigor/vitality.

#### Meta-Analytic Review

#### Methodological Quality of RCT Interventions

Standard criteria (Altman et al., 2001) regarding methodological quality of the psychosocial and exercise RCT studies included in the meta-analyses (including studies that reported fatigue and/or vigor/vitality outcomes) were evaluated. The quality scores for the psychosocial RCTs (n = 43 publications) ranged from 1.5 to 7 out of a maximum of 8 points. (As one might imagine, blinding of participants to psychosocial or exercise interventions is almost impossible, as participants must actively engage in these interventions; hence, no study received a perfect score of 8). All trials specified participant inclusion criteria; however, 54% (n = 24) did not specify method of randomization used. In addition, for 74% of the studies (n = 32), participants were comparable at baseline or adjustments were made to control for baseline differences; 63% (n = 27) included at least 80% of participants at the first follow-up assessment following completion of the intervention; and 65% (n = 28) included multiple follow-up assessments. The main limitations for the psychosocial RCTs were nonreporting or use of blinding of outcome assessors (n = 37; 86%); concealment of allocation (n = 31; 72%); and use of ITT analyses and/or handling of missing data (n = 28; 65%). Interestingly, there was no evidence that methodological quality of the psychosocial trials has improved in recent years. Forty-nine percent (n = 21) of the RCTs were published prior to 2000, and 67% of these (n = 14) scored 4.5 points or greater. Similarly, 51% of the RCTs (n = 22) were published in the past 8 years (2000 through December 2006), and almost two thirds of these (n = 14; 64%) scored 4.5 points or greater.

The quality scores for the exercise RCTs (n = 17 publications) ranged from 2 to 7 out of a maximum of 8 points. For 29% of the RCTs (n = 5), there was no mention of method of randomization used. The main limitations for the exercise-based RCTs were the following: (a) no study reported findings for at least one multiple follow-up assessment, (b) 47% of trials (n = 8) did not report or use ITT analyses, and (c) 41% (n = 7) of the studies did not describe concealment of allocation. Only 3 studies were published prior to 2001, and all 3 of these studies were found to have poor quality in reporting of study procedures and outcomes (i.e., scoring less than 4.5 points).

# The Effects of Psychosocial and Physical Exercise Interventions for Fatigue—Overall Analyses

Fifty-seven separate trials (N = 4,621) were included in the overall analyses, including 41 psychosocial (N = 3,620) and 16 physical exercise (N = 1,001) interventions. The individual effect sizes for the psychosocial interventions ranged from 0.43 to -1.10 (where negative indices indicated lower fatigue symptoms post-intervention), with a weighted pooled mean effect size of -.31. This effect was significant (z = -9.62; p < .001). According to J. Cohen (1988), effect sizes of less than .20 are considered small, those of less than .50 are considered medium/moderate, and those of .80 or greater are considered large; Revicki et al. (2006) indicated that effect sizes greater than .20 are clinically meaningful. Hence, the overall effect of psychosocial interventions on CRF was in the small to moderate range and clinically meaningful. The overall effect sizes for exercise interventions ranged from 0.33 to -1.09, with a weighted pooled mean effect size of -.42. This effect was also significant (z = -4.41, p < .001). The overall effect of physical exercise interventions on fatigue was on the edge of moderate and also clinically meaningful. However, in comparing the effects of exercise interventions with psychosocial interventions on fatigue, no significant group difference emerged (z =-0.95, p > .05).

Possible publication bias was assessed by conducting meta-bias analyses for both the psychosocial and exercise RCTs included in the meta-analytic review. The results showed that there were no publication biases for either the psychosocial, t(40) = -1.09, p > .05, or the exercise, t(15) = -0.81, p > .05, interventions. These findings provide no support for the possibility that the significant effect sizes reported for fatigue outcomes are due to publication bias, or what is commonly referred to in the literature as the "file-drawer problem."

# Moderators of the Relation of Fatigue to Psychosocial and Physical Exercise Interventions

Table 4 presents a summary of the meta-analytic results comparing the effects of exercise interventions to psychosocial interventions on fatigue outcomes according to 14 main sets of potential moderating variables. Notably, given that it would be expected that studies including a CRF aim/hypothesis would have a stronger effect size compared with studies that did not stipulate a specific CRF aim/hypothesis, the CRF aim/hypothesis status was also included in each set of moderator analyses. Furthermore, on the basis of the observation that no exercise study reported data for multiple follow-up assessment intervals, the effect sizes that were computed for psychosocial interventions in this section of the review were based on the initial assessment conducted following the completion of the intervention trials. For the psychosocial interventions that also reported fatigue outcomes for multiple follow-up assessment intervals, these findings are presented separately in a later section of this article.

#### CRF-Specific Aim and/or Hypothesis

More than half of the exercise interventions (56%) that reported a fatigue outcome included a specific CRF aim/hypothesis, although less than one quarter of psychosocial interventions (22%) indicated a specific CRF aim/hypothesis. Interestingly, however, psychosocial interventions that included a CRF specific aim/ hypothesis had a somewhat stronger weighted (although moderate) effect size (-.48) than the psychosocial interventions that did not include a CRF specific aim/hypothesis (-.23). The reverse pattern emerged for exercise interventions, where a somewhat stronger effect was noted for interventions that did not include a CRF specific aim/hypothesis (-.47) compared with exercise studies that included a CRF aim/hypothesis (-.38). The group interaction effect, however, was found to be nonsignificant.

#### Fatigue-Related Theory

Only a minority of psychosocial (15%) and exercise (19%) studies specified a fatigue-related theory in substantiating the intervention(s) evaluated to reduce fatigue. Psychosocial interventions that reported a specific fatigue-related theory were found to have a significantly smaller effect size (-.27) than exercise interventions that reported a fatigue-specific theory (-.83, p < .05). Both psychosocial and exercise interventions that did not report a fatigue-specific theory were found to have moderately small effect sizes (-.32). Psychosocial studies that did not report a fatigue-specific theory but included a CRF aim/hypothesis were found to have a moderate effect size (-.58) compared with the exercise interventions that included a CRF aim/hypothesis (-.15); this interaction was significant (p < .01).

#### Fatigue-Related Outcome Measures

No significant difference in effect sizes emerged between studies that used the POMS Fatigue scale compared with those studies that used other types of fatigue measures to assess fatigue outcomes. In addition, the effect size for fatigue-related outcome measures was not influenced by whether studies included a specific CRF aim/hypothesis.

#### Methodological Quality and Reporting of Study Outcomes

Quality of study. Psychosocial interventions that were classified as having good methodological validity had a slightly larger (text continues on page 716)

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# Table 4

Sample Size, Effect Size, Confidence Interval, and Significance for Fatigue Outcome for Each Study Variable

		Eff ( <i>ES</i> ;	ect size weighted)	95% CI (random effects)		
Variable	No. of study trials: <i>K</i>	ES	p (random)	Lower	Upper	Interaction: p
Overall (psychological and exercise studies)	57 ( $N = 4,621$ )	-0.341	.000	-0.402	-0.280	
Group comparison						
Psychological	41 (N = 3,620)	-0.313	.000	-0.377	-0.249	.342
Exercise	16 (N = 1,001)	-0.415	.000	-0.599	-0.231	
CRF aim						
Psychological	13	-0.484	.000	-0.571	-0.398	
Exercise	9	-0.375	.005	-0.637	-0.114	.102
Non-CRF aim						
Psychological	28	-0.234	.000	-0.318	-0.150	
Exercise	7	-0.465	.000	-0.711	-0.219	
Fatigue-specific theory						
Psychological (all)	6	-0.268	.005	-0.454	-0.081	
Exercise (all)	3	-0.826	.000	-1.100	-0.551	.036*
No-fatigue specific theory						
Psychological (all)	35	-0.321	.000	-0.395	-0.247	
Exercise (all)	13	-0.319	.001	-0.510	-0.128	
Fatigue-specific theory						
Psychological (CRF aim/hypothesis)	4	-0.292	.000	-0.365	-0.218	
Psychological (non-CRF aim/hypothesis)	2	-0.220	.700	-1.337	0.897	
Exercise (CRF aim/hypothesis)	3	-0.826	.000	-1.100	-0.551	
Exercise (non-CRF aim/hypothesis)	0					
No fatigue-specific theory						
Psychological (CRF aim/hypothesis)	9	-0.575	.000	-0.706	-0.444	
Psychological (non-CRF aim/hypothesis)	26	-0.234	.000	-0.311	-0.158	.002**
Exercise (CRF aim/hypothesis)	6	-0.150	.346	-0.462	0.162	
Exercise (non-CRF aim/hypothesis)	7	-0.465	.000	-0.711	-0.219	
POMS Fatigue subscale used						
Psychological (all)	25	-0.328	.000	-0.392	-0.265	
Exercise (all)	5	-0.387	.031	-0.737	-0.036	.699
Non-POMS fatigue measure used						
Psychological (all)	16	-0.286	.000	-0.406	-0.165	
Exercise (all)	11	-0.428	.000	-0.649	-0.207	
POMS Fatigue subscale used						
Psychological (CRF aim/hypothesis)	4	-0.605	.000	-0.812	-0.398	
Psychological (non-CRF aim/hypothesis)	21	-0.279	.000	-0.346	-0.213	.588
Exercise (CRF aim/hypothesis)	4	-0.410	.047	-0.816	-0.005	
Exercise (non-CRF aim/hypothesis)	1	-0.290	.000	-0.372	-0.208	
Non-POMS fatigue measure used						
Psychological (CRF aim/hypothesis)	9	-0.435	.000	-0.535	-0.336	
Psychological (non-CRF aim/hypothesis)	7	-0.093	.322	-0.277	0.091	.121
Exercise (CRF aim/hypothesis)	5	-0.347	.064	-0.715	0.020	
Exercise (non-CRF aim/hypothesis)	6	-0.495	.000	-0.766	-0.223	
Treatment modality: individual therapy						
Psychological (all)	23	-0.315	.000	-0.382	-0.249	
Exercise (all)	15	-0.393	.000	-0.583	-0.203	.355
Treatment modality: group therapy						
Psychological (all)	18	-0.308	.000	-0.442	-0.175	
Exercise (all)	1	-0.744	.000	-0.847	-0.641	
Treatment modality: individual therapy						
Psychological (CRF aim/hypothesis)	11	-0.507	.000	-0.597	-0.416	
Psychological (non-CRF aim/hypothesis)	12	-0.143	.001	-0.224	-0.061	.048*
Exercise (CRF aim/hypothesis)	9	-0.375	.005	-0.637	-0.114	
Exercise (non-CRF aim/hypothesis)	6	-0.419	.001	-0.675	-0.162	
Treatment modality: group therapy						
Psychological (CRF aim/hypothesis)	2	-0.360	.317	-0.360	-1.066	
Psychological (non-CRF aim/hypothesis)	16	-0.302	.000	-0.442	-0.161	
Exercise (CRF aim/hypothesis)	0					
Exercise (non-CRF aim/hypothesis)	1	-0.744	.000	-0.847	-0.641	
Baseline compatibility and/or adjustment made						
Psychological (all)	29	-0.285	.000	-0.341	-0.229	
Exercise (all)	12	-0.307	.004	-0.515	-0.100	.147

		Eff (ES;	ect size weighted)	95% CI (random effects)		Internetion	
Variable	No. of study trials: K	ES	p (random)	Lower	Upper	Interaction: <i>p</i>	
No baseline compatibility and/or adjustment							
made	10	0.000	001	0.444	0.1.50		
Psychological (all)	12	-0.383	.001	-0.614	-0.153		
Exercise (all)	4	-0.742	.001	-1.173	-0.312		
Baseline compatibility and/or adjustment made	0	0.250	000	0.444	0.256		
Psychological (CRF aim/nypotnesis)	8 21	-0.350	.000	-0.444	-0.256	804	
Eventies (CDE sim/humothesis)	21	-0.201	.000	-0.552	-0.189	.804	
Exercise (CKF alli/liypothesis)	5	-0.320	.032	-0.013	-0.027		
No baseline compatibility and/or adjustment	5	-0.289	.030	-0.551	-0.028		
made							
Psychological (CRF aim/hypothesis)	5	-0.721	000	-0.797	-0.645		
Psychological (non-CRF aim/hypothesis)	7	-0.149	.000	-0.425	0.127	.036*	
Exercise (CRF aim/hypothesis)	2	-0.570	.164	-1.374	0.233	1020	
Exercise (non-CRF aim/hypothesis)	$\frac{1}{2}$	-0.914	.000	-1.253	-0.575		
ITT and/or handling of missing data	_						
Psychological (all)	11	-0.523	.000	-0.638	-0.407		
Exercise (all)	9	-0.154	.194	-0.386	0.078	.000**	
No ITT or handling of missing data							
Psychological (all)	30	-0.235	.000	-0.305	-0.165		
Exercise (all)	7	-0.753	.000	-0.989	-0.518		
ITT and/or handling of missing data							
Psychological (CRF aim/hypothesis)	5	-0.557	.000	-0.688	-0.426		
Psychological (non-CRF aim/hypothesis)	6	-0.494	.000	-0.662	-0.325	.854	
Exercise (CRF aim/hypothesis)	6	-0.192	.239	-0.511	0.127		
Exercise (non-CRF aim/hypothesis)	3	-0.065	.203	-0.164	0.035		
No ITT or handling of missing data							
Psychological (CRF aim/hypothesis)	8	-0.431	.000	-0.512	-0.350		
Psychological (non-CRF aim/hypothesis)	22	-0.163	.001	-0.255	-0.070	.257	
Exercise (CRF aim/hypothesis)	3	-0.743	.001	-1.194	-0.292		
Exercise (non-CRF aim/hypothesis)	4	-0.758	.000	-0.933	-0.583		
More than 80% retention at postassessment	•	0.040	000	0.404	0.054		
Psychological (all)	28	-0.340	.000	-0.424	-0.256	101	
Exercise (all)	12	-0.345	.001	-0.554	-0.136	.124	
Less than 80% retention at postassessment	12	0.055	000	0.270	0 121		
Psychological (all)	15	-0.255	.000	-0.379	-0.131		
Exercise (all) More than 80% retention at postassessment	4	-0.029	.008	-1.090	-0.108		
Psychological (CPE aim/hypothesis)	8	-0.512	000	-0.622	-0.402		
Psychological (non-CRE aim/hypothesis)	20	-0.271	.000	-0.367	-0.174	221	
Exercise (CRE aim/hypothesis)	20	-0.320	.000	-0.613	-0.027	.221	
Exercise (exercise (ann/hypothesis)	5	-0.379	008	-0.658	-0.100		
Less than 80% retention at postassessment	5	0.577	.000	0.020	0.100		
Psychological (CRF aim/hypothesis)	5	-0.445	.001	-0.701	-0.188		
Psychological (non-CRF aim/hypothesis)	8	-0.141	.139	-0.329	0.046	.331	
Exercise (CRF aim/hypothesis)	2	-0.570	.164	-1.374	0.233		
Exercise (non-CRF aim/hypothesis)	2	-0.688	.085	-1.472	0.096		
AP design							
Psychological (all)	15	-0.223	.000	-0.332	-0.114		
Exercise (all)	9	-0.546	.000	-0.726	-0.367	.031*	
CS design							
Psychological (all)	26	-0.366	.000	-0.453	-0.278		
Exercise (all)	7	-0.243	.084	-0.520	0.033		
AP design							
Psychological (CRF aim/hypothesis)	5	-0.422	.000	-0.569	-0.276		
Psychological (non-CRF aim/hypothesis)	10	-0.123	.134	-0.284	0.038	$.008^{**}$	
Exercise (CRF aim/hypothesis)	7	-0.447	.000	-0.647	-0.247		
Exercise (non-CRF aim/hypothesis)	2	-0.904	.000	-1.256	-0.551		
CS design	-		<b>A</b>				
Psychological (CRF aim/hypothesis)	8	-0.528	.000	-0.709	-0.347	e	
Psychological (non-CRF aim/hypothesis)	18	-0.295	.000	-0.398	-0.192	.237	
Exercise (CRF aim/hypothesis)	2	-0.125	.784	-1.017	0.767		
Exercise (non-CRF aim/hypothesis)	5	-0.283	.000	-0.442	-0.124		

(table continues)

		Eff ( <i>ES</i> ;	ect size weighted)	95% (random	95% CI (random effects)	
Variable	No. of study trials: <i>K</i>	ES	p (random)	Lower	Upper	Interaction: <i>p</i>
Type of cancer: 100% breast cancer sample						
Psychological (all)	18	-0.281	.000	-0.391	-0.171	
Exercise (all)	9	-0.618	.000	-0.850	-0.386	$.010^{*}$
Type of cancer: mixed or non-BC sample						
Psychological (all)	23	-0.338	.000	-0.421	-0.256	
Exercise (all)	7	-0.155	.330	-0.467	0.157	
Type of cancer: 100% breast cancer sample	-	0.610	000	0.000	0.404	
Psychological (CRF aim/hypothesis)	5	-0.619	.000	-0.833	-0.404	17.4
Psychological (non-CRF aim/hypothesis)	13	-0.155	.007	-0.267	-0.042	.1/4
Exercise (CKF alm/nypolnesis)	4	-0.679	.000	-1.000	-0.359	
Type of capacr	5	-0.370	.008	-0.992	-0.147	
Mixed or non BC sample						
Psychological (CRE aim/hypothesis)	8	-0.406	000	-0.506	-0.306	
Psychological (CRF ann/hypothesis)	15	-0.303	.000	-0.429	-0.176	577
Exercise (CRF aim/hypothesis)	5	-0.132	531	-0.545	0.281	.577
Exercise (non-CRE aim/hypothesis)	2	-0.212	440	-0.751	0.327	
On treatment at initial assessment	-	0.212		0.751	0.527	
Psychological (all)	26	-0.243	.000	-0.327	-0.159	
Exercise (all)	10	-0.566	.000	-0.736	-0.396	.003**
Not on treatment at initial assessment						
Psychological (all)	15	-0.437	.000	-0.542	-0.332	
Exercise (all)	6	-0.161	.282	-0.454	0.132	
On treatment at initial assessment						
Psychological (CRF aim/hypothesis)	9	-0.477	.000	-0.575	-0.379	
Psychological (non-CRF aim/hypothesis)	17	-0.118	.033	-0.226	-0.009	.001**
Exercise (CRF aim/hypothesis)	7	-0.447	.000	-0.647	-0.247	
Exercise (Non-CRF aim/hypothesis)	3	-0.844	.000	-1.025	-0.664	
Not on treatment at initial assessment						
Psychological (CRF aim/hypothesis)	4	-0.509	.015	-0.917	-0.100	
Psychological (non-CRF aim/hypothesis)	11	-0.413	.000	-0.531	-0.295	.692
Exercise (CRF aim/hypothesis)	2	-0.125	.784	-1.017	0.767	
Exercise (non-CRF aim/hypothesis)	4	-0.164	.008	-0.286	-0.042	
Good validity"	00	0.255	000	0.422	0.277	
Psychological (all)	23	-0.355	.000	-0.432	-0.277	071
Exercise (all)	8	-0.275	.030	-0.555	-0.018	.071
Poor valually Psychological (all)	19	-0.260	000	-0.282	-0.127	
Exercise (all)	18	-0.200	.000	-0.383	-0.137 -0.238	
Good validity <sup>a</sup>	0	0.557	.001	0.075	0.250	
Psychological (CRF aim/hypothesis)	6	-0.513	000	-0.658	-0.368	
Psychological (non-CRF aim/hypothesis)	17	-0.298	.000	-0.382	-0.214	531
Exercise (CRF aim/hypothesis)	6	-0.376	.022	-0.699	-0.054	.001
Exercise (non-CRF aim/hypothesis)	2	0.027	.400	-0.036	0.091	
Poor validity <sup>b</sup>						
Psychological (CRF aim/hypothesis)	7	-0.461	.000	-0.592	-0.330	
Psychological (non-CRF aim/hypothesis)	11	-0.132	.143	-0.310	0.045	.041*
Exercise (CRF aim/hypothesis)	3	-0.373	.258	-1.020	0.274	
Exercise (non-CRF aim/hypothesis)	5	-0.665	.000	-0.888	-0.442	
Setting: institution						
Psychological (all)	31	-0.345	0.000	-0.424	-0.266	
Exercise (all)	6	-0.336	0.016	-0.609	-0.063	.259
Setting: home or combination						
Psychological (all)	10	-0.216	0.001	-0.345	-0.086	
Exercise (all)	10	-0.462	0.001	-0.731	-0.194	
Setting: institution						
Psychological (CRF aim/hypothesis)	11	-0.490	.000	-0.585	-0.396	
Psychological (non-CRF aim/hypothesis)	20	-0.265	.000	-0.365	-0.165	.225
Exercise (CRF aim/hypothesis)	2	-0.250	0.354	-0.779	0.279	
Exercise (non-CRF aim/hypothesis)	4	-0.380	0.032	-0.726	-0.034	

		Eff ( <i>ES</i> ;	ect size weighted)	95% CI (random effects)		Internetion	
Variable	No. of study trials: K	ES	p (random)	Lower	Upper	Interaction: <i>p</i>	
Setting: home or combination							
Psychological (CRF aim/hypothesis)	2	-0.455	0.075	-0.945	0.045		
Psychological (non-CRF aim/hypothesis)	7	0.411	0.010	0.745	0.000	.301	
Exercise (CRF aim/hypothesis)	/	-0.411	0.019	-0.745	-0.068		
Treatment duration: $< 6$ weeks							
Psychological (all)	12	-0.402	0.000	-0.560	-0.245		
Exercise (all)	0						
Treatment duration: 6 to 8 weeks							
Psychological (all)	21	-0.264	0.000	-0.357	-0.170		
Exercise (all)	3	-0.346	0.080	-0.735	0.042		
Treatment duration: >8 weeks							
Psychological (all)	8	-0.313	0.000	-0.458	-0.168		
Exercise (all)	13	-0.431	0.000	-0.644	-0.218		
Development duration: <0 weeks	7	-0.499	000	-0.601	-0.275		
Psychological (CKF ann/hypothesis)	5	-0.488	.000	-0.001	-0.573		
Exercise (CRE aim/hypothesis)	0	0.272	.243	0.759	0.187		
Exercise (non-CRF aim/hypothesis)	0						
Treatment duration: -6 to 8 weeks	0						
Psychological (CRF aim/hypothesis)	3	-0.321	.062	-0.657	0.016		
Psychological (non-CRF aim/hypothesis)	18	-0.254	.000	-0.357	-0.151		
Exercise (CRF aim/hypothesis)	2	-0.155	.376	-0.498	0.188		
Exercise (non-CRF aim/hypothesis)	1	-0.730	.000	-0.773	-0.687		
Treatment duration: >8 weeks							
Psychological (CRF aim/hypothesis)	3	-0.638	.000	-0.778	-0.497		
Psychological (non-CRF aim/hypothesis)	5	-0.103	.000	-0.158	-0.048		
Exercise (CRF aim/hypothesis)	7	-0.638	.000	-0.778	-0.497		
Exercise (non-CRF aim/hypothesis)	6	-0.413	.000	-0.596	-0.231		
Specific treatment approaches: psychosocial (all)	17	0.204	000	0.447	0.161		
CB1 Supportive expressive	1/	-0.304	.000	-0.447	-0.161		
Behavioral/ relavation	0	-0.443	.000	-0.038	-0.232		
Counseling	7	-0.294	003	-0.487	-0.100		
Educational	4	-0.110	.124	-0.250	0.030		
Massage	1	-0.680	.000	-0.739	-0.621		
Restorative	2	-0.524	.107	-1.161	0.113		
Specific treatment approaches: psychosocial							
(CRF aim/hypothesis)							
CBT	3	-0.431	.000	-0.512	-0.350		
Supportive- expressive	2	-0.617	.000	-0.813	-0.422		
Behavioral/ relaxation	2	-0.328	.320	-0.975	0.319		
Counseling	2	-0.540	.002	-0.873	-0.206		
Educational	1	-0.250	.000	-0.261	-0.239		
Massage	1	-0.680	.000	-0.739	-0.621		
Specific treatment approaches: psychosocial	2	-0.324	.107	-1.101	0.115		
(non-CRF aim)							
CBT	14	-0.270	.001	-0.432	-0.107		
Supportive- expressive	4	-0.354	.000	-0.504	-0.204		
Behavioral/ relaxation	2	-0.095	.317	-0.281	0.091		
Counseling	5	-0.193	.015	-0.349	-0.038		
Educational	3	-0.063	.274	-0.176	0.050		
Massage	0						
Restorative	0						
Specific treatment approaches: exercise (all)							
Walking only	3	-0.496	.006	-0.849	-0.143		
Multimodal	6	-0.627	.000	-0.785	-0.469		
Bicycle	2	.004	.757	-0.020	0.027		
Cardiovascular and/or flexibility	4	-0.219	.262	-0.601	0.163		
RESISTANCE	1	-0.520	.000	-0.555	-0.507	(4-1.1	

(table continues)

Variable		Effe (ES; )	ect size weighted)	95% CI (random effects)		
	No. of study trials: <i>K</i>	ES	p (random)	Lower	Upper	Interaction: p
Specific treatment approaches: exercise						
(CRF aim/hypothesis)						
Walking only	3	-0.496	.006	-0.849	-0.143	
Multimodal	2	-0.372	.077	-0.783	0.040	
Bicycle	1	0.020	.238	-0.013	0.053	
Cardiovascular and/or flexibility	2	-0.325	.620	-1.608	0.959	
Resistance	1	-0.520	.000	-0.533	-0.507	
Specific treatment approaches: Exercise						
(non-CRF aim/hypothesis)						
Walking only	0					
Multimodal	4	-0.758	.000	-0.933	-0.583	
Bicycle	1	-0.005	.610	-0.024	0.014	
Cardiovascular and/or flexibility	2	-0.113	.520	-0.456	0.230	
Resistance	0					

*Note.* CRF = cancer-related fatigue; POMS = Profile of Mood States: ITT = intention to treat; AP = adjuvant prospective; CS = cross-sectional. <sup>a</sup> Good validity is represented by a score above 4 points (out of 8). <sup>b</sup> Poor validity is represented by a score of less than 4.5 points.

(although modest) effect size (-.36) than did the psychosocial interventions that were found to have poor methodological quality (-.26). The reverse pattern emerged for exercise interventions, where a moderately stronger effect was noted for interventions that were classified as having poor methodological quality (-.56)compared with exercise studies that were found to have good methodological quality (-.28). This group interaction effect was found to be nonsignificant. However, a significant interaction effect emerged between poor methodological quality and whether studies included a CRF aim/hypothesis (p < .05). Specifically, psychosocial studies with poor methodological quality that included a CRF aim were found to have a moderate effect size (-.46) in comparison with psychosocial studies with no CRF aim (-.13). Conversely, exercise studies with poor methodological quality that did not have a CRF aim were found to have a moderately larger effect size (-.67) than exercise studies that included a CRF aim (-.37). No significant interaction effect was found between good methodological quality and CRF aim/ hypothesis status.

*Baseline compatibility.* Both psychosocial (-.38) and exercise (-.74) interventions that did not specify whether participants allocated to the two groups (active intervention vs. control arm) were compatible at baseline assessment on demographic and outcome variables, or did not report whether adjustments were made in the analyses when baseline differences emerged, were found to have larger effect sizes than psychosocial (-.29) and exercise (-.31) interventions that did address these considerations. Furthermore, a significant interaction effect was found between those studies that did not control or report sample baseline compatibility and inclusion of a CRF aim/hypothesis (p < .05). In particular, psychosocial studies that did not control or report sample baseline compatibility but did include a CRF aim/hypothesis were found to have a larger effect size (-.72) than psychosocial studies that did not report a CRF aim/hypothesis (-.15). In contrast, exercise interventions that did not control or report sample baseline compatibility but did include a CRF aim/hypothesis were found to have a smaller effect size (-.57) than exercise studies that did not include a CRF aim/hypothesis (-.91).

ITT analyses and handling of missing data. Psychosocial interventions that reported use of ITT analyses and/or reported how participant attrition or missing data were handled were found to have a moderately stronger effect size (-.52) than the psychosocial interventions that did not (-.24). The opposite pattern emerged for exercise interventions, where a stronger effect was noted for interventions that did not report the use of ITT analyses and/or handling of missing data (-.75) compared with exercise studies that did (-.15). This group interaction effect was found to be significant (p < .001), but no significant interaction effect was evident between studies' use of ITT analyses, reporting of handling missing data, and dropouts and CRF aim/hypothesis status.

Participant retention rates at the initial assessment following completion of intervention. Psychosocial interventions that included postassessment data for at least 80% of participants who were recruited and assessed at both baseline and postassessment were found to have a stronger (although moderately small) effect size (-.34) than the psychosocial interventions in which less than 80% of participants completed the post-assessment (-.26). Once again, the opposite pattern was evident for exercise interventions; a stronger effect was noted for interventions where fewer than 80% of participants completed the postassessment (-.63) compared with exercise studies with data for more than 80% of participants at postassessment (-.35). However, this group interaction effect was found to be nonsignificant. Similarly, no significant interaction was evident between intervention category, participant retention rates, and whether studies included a CRF aim/hypothesis.

### Study Design

Psychosocial interventions that used a cross-sectional (CS) design were found to have a moderately stronger effect size (-.37) than the psychosocial interventions that used an adjuvant prospective (AP) design (-.22). In contrast, a stronger effect size was

 $p^* p < .05. p^* < .01.$ 

evident for exercise interventions that were based on an AP design (-.55) compared with exercise studies that utilized a CS design (-.24). This group effect was significant (p < .05).

A significant interaction was also found between intervention category, AP design, and whether studies included a CRF aim/hypothesis. Specifically, psychosocial studies that used an AP design and included a CRF aim/hypothesis were found to have a moderately larger effect size (-.42) than those studies that did not include a CRF aim (-.12). The reverse pattern was evident for the exercise interventions that used an AP design. That is, exercise studies that did not include a CRF aim/hypothesis were found to have a larger effect size (-.90) than those studies that did include a CRF aim/hypothesis (-.45). No interaction effect, however, was found between those studies that used a CS design and CRF aim/hypothesis status.

#### Participant Characteristics

*Cancer type.* Psychosocial interventions that solely included breast cancer patients were found to have a smaller effect size (-.28) than psychosocial interventions that included mixed samples (including breast cancer patients) or focused explicitly on non-breast cancer samples (e.g., prostate or head and neck malignancies; -.34). Conversely, exercise interventions that explicitly included only breast cancer patients were found to have a stronger effect size (-.62) than exercise studies that included mixed samples (including breast cancer patients) or explicitly focused on non-breast cancer samples (-.16). The group interaction effect was found to be significant (p < .05), although no significant interaction effect emerged between intervention category, cancer type, and whether studies included a CRF aim/hypothesis.

Medical/cancer treatment status. Psychosocial studies that explicitly included participants who were receiving primary or adjuvant medical treatment (e.g., radiation or chemotherapy) at the time of the psychosocial intervention were found to have a smaller effect size (-.24) than psychosocial interventions that included participants who were not on primary or adjuvant treatment at the time of the intervention or included mixed samples of participants (of whom some were on treatment and others had completed treatment; -.44). Once again, the opposite pattern emerged for exercise interventions, where a moderate effect size was revealed for studies that explicitly included participants receiving primary or adjuvant medical treatment at the time the exercise program was administered (-.57) compared with exercise studies that included participants who were not on primary or adjuvant treatment at the time of the intervention or included mixed samples of participants (of whom some were on treatment and others had completed treatment) at the time of the intervention (-.16). The group interaction effect was found to be significant (p < .05). In addition, a significant interaction effect was found between studies that included participants who were receiving primary or adjuvant treatment at the time of the intervention and whether they included a CRF aim/hypothesis (p < .01). In particular, psychosocial studies that included participants who were receiving primary or adjuvant treatment at the time of the intervention and also included a CRF aim/hypothesis were found to have moderately larger effect size (-.48) than psychosocial interventions that did not include a CRF aim/hypothesis (-.12). In contrast, exercise studies that included participants who were receiving primary or adjuvant

treatment at the time of the intervention and also included a CRF aim/hypothesis were found to have a smaller effect size (-.45) than the exercise interventions that did not include a CRF aim/ hypothesis (-.84).

#### Intervention Variables

Treatment modality. The effect size for psychosocial interventions that were administered on an individual basis (-.32) was comparable to the effect size for interventions administered in a group format (-.31). Only one exercise study included a group exercise format, and a relatively strong effect size (-.74) was found compared with individually administered exercise programs, which were found to have a relatively moderate effect size (-.39). Moreover, a significant interaction effect was found between studies that relied on individually administered interventions and a CRF aim/hypothesis status (p < .05). Specifically, psychosocial studies that included a CRF aim/hypothesis were found to have a moderately larger effect size (-.51) than psychosocial studies that did not include a CRF aim/hypothesis (-.14). Conversely, exercise studies that did not include a CRF aim/hypothesis were found to have a slightly larger, moderate effect size (-.42) than exercise interventions that did include a CRF aim/hypothesis (-.38).

Treatment setting. Psychosocial interventions that were administered in a hospital setting were found to have a slightly larger moderate effect size (-.35) than psychosocial interventions that were administered in the home or were administered in combined settings (i.e., some sessions were conducted at the hospital while others were conducted at home; -.22). Exercise interventions that were conducted at home or were administered in combined settings were found to have a moderate effect size (-.46) compared with the smaller effect size found for exercise programs that were explicitly administered in a hospital setting (-.34). This group interaction effect was not significant. Similarly, no significant interaction effect was found between intervention category, setting location, and CRF aim/hypothesis status.

*Treatment duration.* Psychosocial interventions that consisted of fewer than six sessions were found to have a moderate effect size (-.40) compared with the smaller effect for psychosocial interventions that included between 6 and 8 sessions (-.26) as well as those with more than 8 sessions (-.31). None of the exercise interventions consisted of fewer than 6 sessions. Exercise programs that consisted of more than 8 sessions were found to have a moderate effect size (-.43) compared with the smaller effect size for interventions that consisted of 6 to 8 sessions (-.35).

#### Psychosocial Treatment Components

In order to evaluate the effects of specific types of psychosocial interventions, and to ensure consistency between the systematic and meta-analytic reviews, we categorized the psychosocial interventions according to the same seven treatment approaches utilized in the systematic/qualitative analyses. The one study that investigated massage therapy for CRF (and which, based on a CRF aim/hypothesis) was found to have the strongest effect size (-.68) was followed by the two restorative interventions that included a CRF specific aim/hypothesis (-.52). The effect sizes for the counseling, CBT, supportive–expressive, and educational inter-

ventions were considerably larger for those studies that included a CRF aim/hypothesis than for the interventions that were not based on an explicit CRF aim/hypothesis. In particular, supportive–expressive psychotherapies that included a CRF aim/hypothesis were found to have a moderately large effect size (-.62). Similarly, counseling (-.54) and CBT (-.43) approaches that included a CRF aim/hypothesis were found to have a moderate effect size, followed by smaller effect sizes for behavioral/relaxation therapies (-.33). The weakest effect emerged for educational interventions with (-.25) and without a CRF aim/hypothesis (-.06).

#### **Exercise Treatment Components**

The most effective type of exercise intervention was a multimodal exercise program, which had a moderately strong effect on fatigue (-.63). However, multimodal studies that did not include a CRF aim/hypothesis were found to have a larger effect size (-.76) than those that included a CRF aim/hypothesis (-.37). The only intervention that included resistance training was found to have a moderate effect on fatigue (-.52), and this study included a CRF aim/hypothesis. Similarly, walking interventions (-.50) were also found to have a moderate effect, and all three walking interventions included a CRF aim/hypothesis. The cardiovascular and flexibility training programs were found to have a moderately smaller effect (-.22), although the interventions that were based on a CRF aim/hypothesis were found to have a moderately larger effect size (-.33) than the cardiovascular and flexibility training programs that did not include a CRF aim/hypothesis (-.11). The two interventions that were based explicitly on bicycle exercise programs were found to have no effect in reducing fatigue (-.004), and this lack of effect was applicable to both the study that included a CRF aim (.02) and the second bicycle study that did not include a CRF aim (-.01).

# Psychosocial Interventions That Reported Multiple Follow-up Assessments for Fatigue

Table 5 presents a summary of the meta-analytic results for the weighted effect sizes of the 13 psychosocial intervention trials that included at least 1 additional follow-up assessment for fatigue outcomes following the initial post-intervention assessment. Seven of these studies reported on a short-term follow-up within 4 months; 5 reported on a 6-month follow-up; and 1 reported on a follow-up longer than 6 months. The overall effect sizes for the follow-up psychosocial interventions ranged from 0.38 to -1.95, with a weighted pooled mean effect size of -.32. This effect was significant (z = -5.05; p < .001). Thus, the overall effect of the follow-up psychosocial interventions in reducing fatigue was in the small to moderate range and clinically meaningful. The number of studies was too few to conduct formal statistical assessments of possible main effects for the set of potential moderating variables or interactions with the timing of the follow-up assessments. Generally, however (see Table 5), the effect sizes for the intervention were consistent across studies, with some differences in the moderator variables.

# The Effects of Psychosocial and Physical Exercise Interventions for Vigor/Vitality—Overall Effects

As shown in Table 6, a total of 43 separate trials (N = 3,855) were included in the overall analyses evaluating the effects of

psychosocial and exercise interventions on vigor/vitality outcomes. The overall effect sizes for the 36 psychosocial intervention trials (N = 3,460) ranged from -.19 to 1.45 (where positive indices indicated higher vigor/vitality symptoms postintervention), with a weighted pooled mean effect size of .37. This effect was significant (z = 10.49; p < .001) and clinically meaningful. Thus, the overall effect of psychosocial interventions on vigor/vitality was small to moderate. The overall effect sizes for the seven exercise intervention trials (N = 395) ranged from .27 to 1.42, with a weighted pooled mean effect size of .69. This effect was also significant (z = -5.28, p < .001) and clinically meaningful. Hence, the overall effect of physical exercise interventions on vigor/vitality was in the moderate to strong range. In comparing the difference in effects on vigor/vitality for exercise interventions with psychosocial interventions, we found a significant group difference showing that exercise interventions were stronger than psychosocial interventions (p < .05).

Possible publication bias was also evaluated; no evidence of bias was found for either the psychosocial, t(35) = 1.07, p > .05, or the exercise, t(6) = 0.79, p > .05 trials. These results provide no support for the possibility that the significant effect sizes reported for vigor/vitality outcomes were due to publication bias.

# Moderators of the Relation of Vigor/Vitality to Psychosocial and Physical Exercise Interventions

Table 6 presents meta-analytic results comparing the effects of exercise interventions with psychosocial interventions on vigor/ vitality outcomes in conjunction with 14 potential moderating variables. Once again, the CRF aim/hypothesis status was also included in each set of moderator analyses. In addition, considering that no exercise study reported data for multiple follow-up assessment intervals for vigor/vitality outcomes, the meta-analysis computed for psychosocial interventions in this section was based on the initial assessment conducted following the completion of the psychosocial intervention trials. For the psychosocial interventions that also reported vigor/vitality outcomes for multiple follow-up assessment intervals, these findings are presented separately in a later section.

#### CRF Specific Aim

Psychosocial interventions that included CRF as a specific aim/ hypothesis had a moderately larger effect size (.50) than did the psychosocial interventions that did not include a CRF aim/ hypothesis (.33). Similarly, exercise interventions that included a CRF-specific aim/hypothesis had a strong effect (.79) compared with the moderately high effect size that was found for exercise studies that did not include a CRF aim a priori (.61). This group interaction effect was found to be nonsignificant.

#### Vigor/Vitality-Related Theory

Only a minority of psychosocial (8%) and exercise (29%) studies specified a vigor/vitality-related theory in substantiating the intervention(s) evaluated to enhance vigor/vitality. Psychosocial (text continues on page 726)

# Table 5

Psychological Interventions: Sample Size, Effect Size, Confidence Interval, and Significance for Fatigue Outcome for Each Study Variable at Longer Term Follow-ups

		Eff ( <i>ES</i> ;	ect size weighted)	95% CI (random effects)	
Variable	No. of study trials: <i>K</i>	ES	p (random)	Lower	Upper
Psychological studies with additional follow-ups <sup>a</sup>	13	-0.421	.000	-0.600	-0.242
Within 4 months	7	-0.514	0.006	-0.881	-0.147
6 months	5	-0.304	0.000	-0.464	-0.144
>6 months	1	-0.360	0.000	-0.377	-0.343
CRF aim					
Within 4 months	2	-0.785	0.500	-3.068	1.498
6 months	0				
>6 months	0				
Non-CRF aim					
Within 4 months	5	-0.405	0.000	-0.618	-0.193
6 months	5	-0.304	0.000	-0.464	-0.144
>6 months	1	-0.360	0.000	-0.377	-0.343
Fatigue-specific theory					
Within 4 months, with CRF aim	1	0.380	0.000	0.364	0.396
Within 4 months, with non-CRF aim	1	-1.050	0.000	-1.093	-1.007
No fatigue-specific theory		1.050	0.000	1.001	1 000
Within 4 months, with CRF aim	1	-1.950	0.000	-1.991	-1.909
Within 4 months, with non-CRF aim	4	-0.245	0.001	-0.383	-0.106
6 months, with non CDE aim	0	0.204	0.000	0.464	0.144
o months, with CPE aim	5	-0.304	0.000	-0.404	-0.144
>6 months, with non CPE sim	0	-0.260	0.000	-0.277	-0.242
POMS Estique subscale	1	-0.300	0.000	-0.377	-0.343
Within 4 months with CRF aim	0				
Within 4 months, with con-CRF aim	3	-0.290	0.000	-0.431	-0.149
6 months, with CRF aim	0	0.290	0.000	0.151	0.119
6 months, with non-CRF aim	5	-0.304	0.000	-0.464	-0.144
>6 months, with CRF aim	0	01001	0.000	00.	01111
>6 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343
Non-POMS fatigue measure					
Within 4 months, with CRF Aim	2	-0.785	0.500	-3.068	1.498
within 4 months, with non-CRF aim	2	-0.580	0.217	-1.501	0.341
Treatment modality: individual therapy					
Within 4 months, with CRF aim	1	-1.950	0.000	-1.991	-1.909
Within 4 months, with non-CRF aim	2	-0.358	0.000	-0.374	-0.343
6 months, with CRF aim	0				
6 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343
>6 months, with CRF aim	0				
>6 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343
Treatment modality: group therapy		0.000	0.000	0.044	0.004
Within 4 months, with CRF aim	1	0.380	0.000	0.364	0.396
Within 4 months, with non-CRF aim	3	-0.439	0.018	-0.803	-0.075
6 months, with CRF aim	0	0.000	0.002	0 401	0.000
6 months, with non-CRF aim	4	-0.290	0.003	-0.481	-0.098
> 6 months, with non CPE sim	0				
> 0 III0IIIIIS, WIII II0II-CKF allII Pasalina compatibility and/or adjustment made	0				
Within 4 months, with CPE aim	1	-1.050	0.000	-1.001	-1.000
Within 4 months, with pon-CRE aim	1	-0.245	0.000	-0.383	-0.106
6 months with CRF aim	0	0.245	0.001	0.505	0.100
6 months, with non-CRF aim	5	-0.304	0.000	-0.464	-0.144
>6 months, with CRF aim	0	01001	0.000	01101	01111
>6 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343
No baseline compatibility and/or adjustment					
made					
Within 4 months, with CRF aim	1	0.380	0.000	0.364	0.396
Within 4 months, with non-CRF aim	1	-1.050	0.000	-1.093	-1.007
ITT and/or handling of missing data					
Within 4 months, with CRF aim	1	-1.950	0.000	-1.991	-1.909
Within 4 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343 (table continues)

		Eff (ES;	ect size weighted)	95% CI (random effects)	
Variable	trials: K	ES	p (random)	Lower	Upper
6 months, with CRF aim	0				
6 months, with non-CRF aim	2	-0.475	0.000	-0.700	-0.249
>6 months, with CRF aim	0				
>6 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343
No ITT and/or handling of missing data					
Within 4 months, with CRF aim	1	0.380	0.000	0.364	0.396
Within 4 months, with non-CRF aim	4	-0.417	0.005	-0.706	-0.128
6 months, with CRF aim	0				
6 months, with non-CRF aim	3	-0.188	0.000	-0.270	-0.105
>6 months, with CRF aim	0				
>6 months, with non-CRF aim	0				
More than 80% retention at postassessment					
Within 4 months, with CRF aim	1	-1.950	0.000	-1.991	-1.909
Within 4 months, with non-CRF aim	2	-0.235	0.060	-0.480	0.010
6 months, with CRF aim	0				
6 months, with non-CRF aim	4	-0.340	0.001	-0.548	-0.131
>6 months, with CRF aim	0				
> 6 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343
Less than 80% retention at postassessment					
Within 4 months, with CRF aim	1	0.380	0.000	0.364	0.396
Within 4 months, with non-CRF aim	3	-0.520	0.038	-1.011	-0.028
6 months, with CRF aim	0				
6 months, with non-CRF aim	1	-0.160	0.000	-0.181	-0.139
>6 months, with CRF aim	0				
>6 months, with non-CRF aim	0				
AP design	0				
Within 4 months, with CRF aim	0	0.2(0	0.000	0.277	0.242
Within 4 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343
6 months, with CRF aim	0	0.2(0	0.000	0.277	0.242
6 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343
>6 months, with CRF aim	0	0.2(0	0.000	0.277	0.242
>6 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343
Within 4 months, with CDE sim	2	0.795	0.500	2 069	1 409
Within 4 months, with non CDE sim	ے 4	-0.785	0.500	- 5.008	1.496
Within 4 months, with Ion-CKF and	4	-0.417	0.005	-0.700	-0.128
6 months, with non CPE sim	0	-0.200	0.002	-0.491	_0.008
>6 months, with CPE sim	4	-0.290	0.005	-0.461	-0.098
>6 months, with non CPE aim	0				
100% breast cancer sample	0				
Within 4 months with CRE aim	2	-0.785	0.500	-3.068	1 /08
Within 4 months, with non-CRF aim	3	-0.520	0.038	-1.011	-0.028
6 months with CRF aim	0	0.520	0.050	1.011	0.020
6 months, with non-CRF aim	2	-0.229	0.001	-0.366	-0.092
>6 months, with CRF aim	0	0.22)	0.001	0.500	0.072
>6 months, with non-CRF aim	0				
Mixed or non-BC sample:	0				
Within 4 months with CRF aim	0				
Within 4 months, with non-CRF aim	2	-0.235	0.060	-0.480	0.010
6 months, with CRF aim	0				
6 months, with non-CRF aim	3	-0.353	0.006	-0.607	-0.099
>6 months, with CRF aim	0				
>6 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343
On treatment at initial assessment					
Within 4 months, with CRF aim	2	-0.785	0.500	-3.068	1.498
Within 4 months, with non-CRF aim	4	-0.479	0.001	-0.755	-0.204
6 months, with CRF aim	0				
6 months, with non-CRF aim	2	-0.260	0.009	-0.456	-0.064
>6 months, with CRF aim	0				
>6 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343
6 months, with CRF aim	0				

		Eff (ES;	ect size weighted)	95% CI (random effects)		
Variable	No. of study trials: K	ES	p (random)	Lower	Upper	
Not on treatment at initial assessment						
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	1	-0.110	0.000	-0.120	-0.100	
6 months, with CRF aim	0					
6 months, with non-CRF aim	3	-0.333	0.040	-0.651	-0.015	
>6 months, with CRF aim	0					
>6 months, with non-CRF aim	0					
Good validity scores <sup>b</sup>						
Within 4 months, with CRF aim	1	-1.950	0.000	-1.991	-1.909	
Within 4 months, with non-CRF aim	2	-0.235	0.060	-0.480	0.010	
6 months, with non-CRF aim	4	-0.340	0.001	-0.548	-0.131	
>6 months, with CRF aim	0	0.040	0.000	0.055	0.040	
>6 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343	
Poor validity		0.200	0.000	0.264	0.207	
Within 4 months, with CRF aim	1	0.380	0.000	0.364	0.396	
Within 4 months, with non-CRF aim	3	-0.520	0.038	-1.011	-0.028	
6 months, with CRF aim	0	0.1(0	0.000	0 101	0.120	
6 months, with non-CRF aim	1	-0.160	0.000	-0.181	-0.139	
>6 months, with CRF aim						
>6 months, with non-CRF aim						
Institutional setting	0					
Within 4 months, with new CDE sime	0	0.210	0.010	0.260	0.051	
Within 4 months, with non-CKF and	3	-0.210	0.010	-0.309	-0.031	
6 months, with non CDE sim	0	0.204	0.000	0.464	0.144	
o months, with CDE sim	3	-0.304	0.000	-0.404	-0.144	
>6 months, with non CPE aim	0	-0.360	0.000	-0.377	-0.343	
Home or combined home and institution setting	1	0.500	0.000	0.377	0.545	
Within 4 months, with CPE aim	2	-0.785	0.500	-3.068	1 /08	
Within 4 months, with non-CRE aim	2	-0.700	0.046	-1 386	-0.014	
6 months, with CRE aim	0	0.700	0.040	1.500	0.014	
6 months, with non-CRF aim	0					
>6 months, with CRF aim	0					
>6 months, with non-CRF aim	0					
Treatment duration: Less than 6 sessions	0					
Within 4 months with CRF aim	0					
Within 4 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343	
6 months with CRF aim	0	0.500	0.000	0.577	0.515	
6 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343	
>6 months with CRF aim	0	01000	0.000	01077	010 10	
>6 months, with non-CRF aim	1	-0.360	0.000	-0.377	-0.343	
Treatment duration: 6 to 8 sessions						
Within 4 months, with CRF aim	2	-0.785	0.500	-3.068	1.498	
Within 4 months, with non-CRF aim	2	-0.605	0.174	-1.477	0.267	
6 months, with CRF aim	0					
6 months, with non-CRF aim	4	-0.290	0.003	-0.481	-0.098	
>6 months, with CRF aim	0					
> 6 months, with non-CRF aim	0					
Treatment duration: >8 sessions						
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	2	-0.229	0.056	-0.465	0.006	
Specific treatment approaches: within 4 months						
CBT	6	-0.275	0.051	-0.550	0.001	
Counseling	1	-1.950	0.000	-1.991	-1.909	
Specific treatment approaches: 6 months						
CBT	5	-0.304	0.000	-0.464	-0.144	
Specific treatment approaches:						
>6 months						
CBT	1	-0.360	0.000	-0.377	-0.343	

*Note.* CRF = cancer-related fatigue; POMS = Profile of Mood States; CBT = cognitive-behavioral therapy. <sup>a</sup> The effects from the psychological studies which included at least one additional following assessment were categorized according to short-term (i.e., follow-up within 4 months), medium-range (6-month follow-up), and longer term (follow-up of more than 6 months) effects. <sup>b</sup> Good validity = score above 4 points (out of 8). <sup>c</sup> Poor validity = less than 4.5 points. \* p < .05. \*\* p < .01.

# Table 6

Sample Size, Effect Size, Confidence Interval, and Significance for Vigor/Vitality Outcome for Each Study Variable

		Effec (w	et size ( <i>ES</i> ) eighted)	95% cor inter (random	nfidence rval effects)	
Variable	No. of study trials: <i>K</i>	ES	p (random)	Lower	Upper	Interaction: p
Overall (psychological and exercise studies)	43 ( <i>N</i> = 3,855)	0.421	.000	0.354	0.489	
Group comparison						
Psychological	36 (N = 3,460)	0.369	.000	0.300	0.438	.023*
Exercise	7 (N = 395)	0.692	.000	0.435	0.949	
CRF aim	2	0.500	000	0.001	0.614	
Psychological	8	0.502	.000	0.391	0.614	
Exercise	3	0.790	.000	0.443	1.137	.991
Non-CRF aim						
Psychological	28	0.332	.000	0.243	0.421	
Exercise	4	0.613	.000	0.385	0.840	
Vigor/vitality specific theory	2	0.000	000	0.404	0.446	
Psychological (all)	3	0.290	.000	0.134	0.446	1.00
Exercise (all)	2	0.974	.000	0.788	1.160	.169
No vigor/vitality specific theory	22	0.277	000	0.005	0.460	
Psychological (all)	33	0.377	.000	0.295	0.460	
Exercise (all)	5	0.570	.000	0.399	0.742	
Vigor/vitality specific theory	2	0.000	000	0.124	0.446	
Psychological (CRF aim/hypothesis)	3	0.290	.000	0.134	0.446	
Psychological (non-CRF aim/hypothesis)	0	0.074	000	0.500	1.1.00	
Exercise (CRF aim/hypothesis)	2	0.974	.000	0.788	1.160	
Exercise (non-CRF aim/hypothesis)	0					
No vigor/vitality specific theory	-	0 ( 10	000	0.427	0.042	
Psychological (CRF aim/hypothesis)	5	0.640	.000	0.437	0.842	221
Psychological (non-CRF aim/hypothesis)	28	0.332	.000	0.243	0.421	.231
Exercise (CRF aim/hypothesis)	1	0.420	.000	0.387	0.453	
Exercise (non-CRF aim/hypothesis)	4	0.613	.000	0.385	0.840	
POMS vigor subscale used	27	0.207	000	0.0(5	0.500	
Psychological (all)	27	0.387	.000	0.265	0.508	
Exercise (all)	3	0.660	.005	0.202	1.119	(00
Non-POINS vigor/vitality measure used	0	0.217	000	0.252	0.292	.090
Psychological (all)	9	0.317	.000	0.232	0.382	
DOMS Vicer subseels used	4	0.710	.000	0.555	1.077	
POINS Vigor subscale used	4	0.585	000	0.400	0.771	
Psychological (CKF ann/hypothesis)	- 4	0.365	.000	0.400	0.771	066
Everging (CPE aim/hypothesis)	25	0.333	.000	0.220	1 2 9 2	.900
Exercise (CKF ann/hypothesis)	2	0.743	.022	0.108	0.572	
Non POMS vigor/vitality measure used	1	0.490	.000	0.408	0.372	
Psychological (CPE aim/hypothesis)	4	0.425	000	0.277	0.573	
Psychological (CRF ann/hypothesis)	+ 5	0.425	.000	0.277	0.373	052
Exercise (CPE aim/hypothesis)	1	0.238	.000	0.172	0.004	.952
Exercise (CRF ann/hypothesis)	1	0.654	.000	0.382	0.905	
Treatment modality: individual therapy	5	0.054	.000	0.362	0.720	
Psychological (all)	22	0 294	000	0.225	0 364	
Exercise (all)	7	0.294	.000	0.435	0.949	
Treatment modality:	1	0.072	.000	0.435	0.747	
group therapy						
Psychological (All)	14	0.484	000	0 355	0.613	
Exercise (All)	0	0.404	.000	0.555	0.015	
Treatment modality:	0					
individual therapy						
Psychological (CRF aim/hypothesis)	7	0.470	000	0 355	0.585	
Psychological (non-CRF aim/hypothesis)	15	0 214	.000	0.121	0.308	748
Exercise (CRF aim/hypothesis)	3	0.790	.000	0.443	1 137	.7-0
Exercise (non-CRF aim/hypothesis)	5 4	0.613	.000	0 385	0.840	
Treatment modality	т Т	0.015	.000	0.505	0.040	
group therapy						
Psychological (CRF aim/hypothesis)	1	0.720	000	0.655	0 785	
Psychological (non-CRF aim/hypothesis)	13	0.466	.000	0.332	0.600	
Exercise (CRF aim/hypothesis)	0	0100	.000	0.332	0.000	
Exercise (non-CRF aim/hypothesis)	Ő					

		Effec (w	et size (ES) eighted)	) 95% confidence interval (random effects)		Interaction	
Variable         aseline compatibility and/or adjustment made         Psychological (all)         Exercise (all)         o baseline compatibility and/or adjustment made         Psychological (all)         Exercise (all)         aseline compatibility and/or adjustment made         Psychological (CRF aim/hypothesis)         Psychological (non-CRF aim/hypothesis)         Exercise (non-CRF aim/hypothesis)         Psychological (CRF aim/hypothesis)         Psychological (non-CRF aim/hypothesis)         Psychological (non-CRF aim/hypothesis)         Tand/or handling of missing data         Psychological (all)         Exercise (all)         o ITT or handling of missing data         Psychological (CRF aim/hypothesis)         Exercise (CRF aim/hypothesis)         Psychological (CRF aim/hypothesis)         Psychological (CRF aim/hypothesis)         Exercise (CRF aim/hypothesis)         Exercise (CRF aim/hypothesis)         Exercise (CRF aim/hypothesis)      <	No. of study trials: K	ES	p (random)	Lower	Lower Upper		
Baseline compatibility and/or adjustment made							
Psychological (all)	27	0.340	.000	0.246	0.433		
Exercise (all)	7	0.692	.000	0.435	0.949		
No baseline compatibility and/or adjustment made							
Psychological (all)	9	0.453	.000	0.373	0.532		
Exercise (all)	0						
Baseline compatibility and/or adjustment made			000	0.404	0.455		
Psychological (CRF aim/hypothesis)	4	0.320	.000	0.184	0.455		
Psychological (non-CRF aim/hypothesis)	23	0.343	.000	0.216	0.471	.578	
Exercise (CRF aim/hypothesis)	3	0.790	.000	0.443	1.137		
Exercise (non-CRF aim/hypothesis)	4	0.613	.000	0.385	0.840		
No baseline compatibility and/or adjustment made	4	0.707	000	0.504	0.010		
Psychological (CRF aim/hypothesis)	4	0.707	.000	0.594	0.819		
Psychological (non-CKF alm/nypotnesis)	5	0.279	.000	0.199	0.360		
Exercise (CKF ann/hypothesis)	0						
ITT and/or handling of missing data	0						
Psychological (all)	12	0.512	000	0.412	0.614		
Exercise (all)	12	0.313	.000	0.412	0.014	000**	
No ITT or handling of missing data	5	0.474	.000	0.210	0.738	.000	
Psychological (all)	24	0.207	000	0.108	0 307		
Evercise (all)	24	1 241	.000	0.198	1 584		
ITT and/or handling of missing data	2	1.241	.000	0.898	1.564		
Psychological (CRE aim/hypothesis)	4	0.425	000	0.277	0 573		
Psychological (non-CRE aim/hypothesis)	8	0.557	.000	0.277	0.713	285	
Exercise (CRE aim/hypothesis)	2	0.650	.000	0.199	1 101	.205	
Exercise (non-CRE aim/hypothesis)	3	0.341	.000	0.270	0.412		
No ITT or handling of missing data	5	0.511	.000	0.270	0.112		
Psychological (CRF aim/hypothesis)	4	0.585	.000	0.400	0.771		
Psychological (non-CRF aim/hypothesis)	20	0.241	.000	0.132	0.350	065	
Exercise (CRF aim/hypothesis)	1	1.070	.000	1.025	1.115		
Exercise (non-CRF aim/hypothesis)	1	1.420	.000	1.311	1.529		
More than 80% retention at postassessment							
Psychological (all)	21	0.387	.000	0.239	0.535		
Exercise (all)	6	0.726	.000	0.443	1.008	.619	
Less than 80% retention at postassessment							
Psychological (all)	15	0.333	.000	0.285	0.382		
Exercise (all)	1	0.490	.000	0.408	0.572		
More than 80% retention at postassessment							
Psychological (CRF aim/hypothesis)	3	0.557	.000	0.377	0.736		
Psychological (non-CRF aim/hypothesis)	18	0.358	0.000	0.193	0.523	.866	
Exercise (CRF aim/hypothesis)	3	0.790	.000	0.443	1.137		
Exercise (non-CRF aim/hypothesis)	3	0.654	.000	0.382	0.926		
Less than 80% retention at postassessment							
Psychological (CRF aim/hypothesis)	5	0.467	.000	0.334	0.599		
Psychological (non-CRF aim/hypothesis)	10	0.278	.000	0.231	0.326		
Exercise (CRF aim/hypothesis)	0						
Exercise (non-CRF aim/hypothesis)	1	0.490	.000	0.408	0.572		
AP design							
Psychological (all)	14	0.219	.000	0.120	0.318		
Exercise (all)	4	0.517	.000	0.242	0.791	.543	
CS design							
Psychological (all)	22	0.466	.000	0.376	0.556		
Exercise (all)	3	0.928	.000	0.551	1.304		
AP design							
Psychological (CRF aim/hypothesis)	1	0.420	.000	0.397	0.443		
Psychological (non-CRF aim/hypothesis)	13	0.203	.000	0.102	0.304	.562	
Exercise (CRF aim/hypothesis)	2	0.745	.022	0.108	1.382		
Exercise (non-CRF aim/hypothesis)	2	0.290	.000	0.251	0.329		
CS design	_	0	~ ~ ~	0.000	0		
Psychological (CRF aim/hypothesis)	7	0.515	.000	0.394	0.635		
Psychological (non-CRF aim/hypothesis)	15	0.443	.000	0.320	0.565	./44	

(table continues)

		Effec (w	et size ( <i>ES</i> ) eighted)	95% cor inter (random	nfidence rval effects)	
Variable	No. of study trials: K	ES	p (random)	Lower	Upper	Interaction: <i>p</i> .959 .159 .05 <sup>†</sup> .479 .693 .925
Exercise (CRF aim/hypothesis)	1	0.880	.000	0.857	0.903	
Exercise (non-CRF aim/hypothesis)	2	0.954	.040	1.866	2.052	
Type of cancer: 100% breast cancer sample						
Psychological (all)	20	0.224	.000	0.144	0.303	
Exercise (all)	5	0.604	.000	0.285	0.923	.959
Type of cancer: mixed or non-BC sample		0.540	000	0.110	0.656	
Psychological (all)	16	0.549	.000	0.443	0.656	
Exercise (all)	2	0.919	.066	-0.061	1.899	
Prove of cancer: 100% breast cancer sample:	5	0.467	000	0.224	0.500	
Psychological (CKF alm/nypoinesis)	5 15	0.467	.000	0.334	0.399	150
Exercise (CPE aim/hypothesis)	13	0.143	.000	0.042	0.248	.139
Exercise (CRF ann/hypothesis)	23	0.974	.000	0.788	0.412	
Type of cancer: Mixed or non BC sample	5	0.341	.000	0.270	0.412	
Psychological (CRF aim/hypothesis)	3	0.557	000	0.377	0.736	
Psychological (non-CRF aim/hypothesis)	13	0.537	.000	0.427	0.750	05†
Exercise (CRF aim/hypothesis)	15	0.420	.000	0.387	0.453	.05
Exercise (con-CRF aim/hypothesis)	1	1 420	.000	1 311	1 529	
On treatment at initial assessment		11120	1000	11011	110 27	
Psychological (all)	20	0.272	.000	0.194	0.350	
Exercise (all)	4	0.517	.000	0.242	0.791	.479
Not on treatment at initial assessment						
Psychological (all)	16	0.492	.000	0.372	0.612	
Exercise (all)	3	0.928	.000	0.551	1.304	
On treatment at initial assessment						
Psychological (CRF aim/hypothesis)	3	0.557	.000	0.377	0.736	
Psychological (non-CRF aim/hypothesis)	17	0.222	.000	0.140	0.304	.693
Exercise (CRF aim/hypothesis)	2	0.745	.022	0.108	1.382	
Exercise (non-CRF aim/hypothesis)	2	0.290	.000	0.251	0.329	
Not on treatment at initial assessment						
Psychological (CRF aim/hypothesis)	5	0.467	.000	0.334	0.599	
Psychological (non-CRF aim/hypothesis)	11	0.500	.000	0.319	0.681	.925
Exercise (CRF aim/hypothesis)	1	0.880	.000	0.857	0.903	
Exercise (non-CRF aim/hypothesis)	2	0.954	.040	0.043	1.866	
Good validity <sup>a</sup>						
Psychological (all)	23	0.408	.000	0.317	0.498	
Exercise (all)	4	0.632	.001	0.268	0.996	.401
Poor validity <sup>6</sup>	12	0.000	000	0.001	0.207	
Psychological (all)	13	0.299	.000	0.201	0.397	
Exercise (all)	3	0.774	.002	0.273	1.275	
Doughological (CPE sim/hypothesis)	5	0.422	000	0.200	0.554	
Psychological (CKF ann/hypothesis)	19	0.422	.000	0.290	0.534	088
Exercise (CPE sim/hypothesis)	10	0.405	.000	0.280	1 160	.088
Exercise (CRI <sup>+</sup> ann/hypothesis)	$\frac{2}{2}$	0.974	.000	0.788	0.320	
Poor validity <sup>b</sup>	2	0.290	.000	0.231	0.329	
Psychological (CRE aim/hypothesis)	3	0.661	000	0.580	0.743	
Psychological (non-CRF aim/hypothesis)	10	0.001	.000	0.095	0.308	007**
Exercise (CRF aim/hypothesis)	1	0.420	.000	0.387	0.453	.007
Exercise (contraining pointesis)	2	0.954	.000	0.043	1.866	
Setting: institution	2	0.951	.010	0.015	1.000	
Psychological (all)	26	0.444	.000	0.341	0.548	
Exercise (all)	4	0.653	.000	0.398	0.907	.217
Setting: home or combination						
Psychological (all)	10	0.180	.000	0.093	0.267	
Exercise (all)	3	0.740	.002	0.264	1.216	
Setting: institution						
Psychological (CRF aim/hypothesis)	5	0.640	.000	0.437	0.842	
Psychological (non-CRF aim/hypothesis)	21	0.399	.000	0.283	0.514	.220
Exercise (CRF aim/hypothesis)	1	0.420	.000	0.387	0.453	
Exercise (non-CRF aim/hypothesis)	3	0.738	.009	0.185	1.290	

		Effect (we	t size ( <i>ES</i> ) eighted)	95% con inter (random	nfidence rval effects)	
Variable	No. of study trials: <i>K</i>	ES	p (random)	Lower	Upper	Interaction:
Setting: home or combination						
Psychological (CRF aim/hypothesis)	3	0.290	.000	0.134	0.446	
Psychological (non-CRF aim/hypothesis)	7	0.133	.026	0.016	0.249	.014*
Exercise (CRF aim/hypothesis)	2	0.974	.000	0.788	1.160	
Exercise (non-CRF aim/hypothesis)	1	0.270	.000	0.246	0.249	
Treatment duration: <6 weeks						
Psychological (all)	9	0.473	.000	0.367	0.579	
Exercise (all)	0					
Treatment duration: $-6$ to 8 weeks						
Psychological (all)	15	0.362	.000	0.171	0.552	
Exercise (all)	2	0.745	.022	0.108	1.382	
Treatment duration: >8 weeks						
Psychological (all)	12	0.296	.000	0.237	0.355	
Exercise (all)	5	0.671	.000	0.356	0.986	
Treatment duration: <6 weeks						
Psychological (CRF aim/hypothesis)	6	0.479	.000	0.355	0.604	
Psychological (non-CRF aim/hypothesis)	3	0.460	.002	0.162	0.757	
Exercise (CRF aim/hypothesis)	0					
Exercise (non-CRF aim/hypothesis)	0					
Treatment duration: -6 to 8 weeks	0					
Psychological (CRF aim/hypothesis)	0					
Psychological (non-CRF aim/hypothesis)	15	0.362	000	0.171	0.552	
Exercise (CRF aim/hypothesis)	2	0.745	022	0.108	1 382	
Exercise (one-CRF aim/hypothesis)	0	0.715	.022	0.100	1.502	
Treatment duration: >8 weeks	0					
Psychological (CRF aim/hypothesis)	2	0 568	000	0 274	0.862	
Psychological (non-CRF aim/hypothesis)	10	0.242	.000	0.185	0.299	
Exercise (CRF aim/hypothesis)	1	0.880	.000	0.857	0.903	
Exercise (exer ann/hypothesis)	1	0.613	.000	0.385	0.840	
Specific treatment approaches: psychosocial (all)	7	0.015	.000	0.565	0.040	
CBT	14	0.472	000	0 362	0.583	
Supportive_ expressive	5	0.377	.000	0.120	0.634	
Behavioral/ relaxation	4	0.136	220	-0.082	0.355	
Counseling	8	0.130	.220	0.171	0.462	
Educational	3	0.183	107	-0.039	0.402	
Massage	1	0.330	.107	0.272	0.388	
Restorative	1	0.850	.000	0.785	0.915	
Specific treatment approaches: psychosocial	1	0.050	.000	0.765	0.715	
(CRE aim/hypothesis)						
CBT	2	0.501	000	0.306	0.696	
Supportive_ expressive	1	0.720	.000	0.655	0.785	
Behavioral/ relayation	1	0.720	.000	0.055	0.732	
Counseling	2	0.010	.000	-0.009	0.752	
Educational	1	0.320	.000	0.313	0.327	
Massage	1	0.520	.000	0.515	0.327	
Pastorative	1	0.850	000	0.785	0.015	
Specific treatment enpressions: neuclassical	1	0.850	.000	0.785	0.915	
(non CPE aim)						
(IIOII-CKI <sup>*</sup> aIIII)	12	0.467	000	0.247	0.587	
CD1 Supportive expressive	12	0.407	.000	0.047	0.565	
Papavioral/ relevation	4	-0.010	.030	-0.247	0.303	
Counseling	5	-0.010	.934	-0.247	0.227	
Educational	2	0.332	.009	0.064	0.361	
Educational	<u>∠</u> 1	0.115	.333	-0.207	0.495	
Nassage Destorative	1	0.330	.000	0.272	0.388	
Residiate transmission and the second	U					
Well-in a sub-	2	0.540	004	0 171	0.029	
waiking only	3	0.549	.004	0.171	0.928	
Nuumodai Biavala	4	0.800	.000	0.469	1.131	
Dicycle	U					
Desistence	0					
DEMNIQUE	U					

(table continues)

Variable		Effec (w	t size (ES) eighted)	95% con inter (random		
	No. of study trials: K	ES	p (random)	Lower	Upper	Interaction:
Specific treatment approaches: exercise (CRF aim/hypothesis)						
Walking only	1	1.070	.000	1.025	1.115	
Multimodal	2	0.650	.005	0.199	1.101	
Bicycle	0					
Cardiovascular and/or flexibility	0					
Resistance	0					
Specific treatment approaches: exercise (non-						
CRF aim/hypothesis)						
Walking only	2	0.290	.000	0.274	0.307	
Multimodal	2	0.954	.040	0.043	1.866	
Bicycle	0					
Cardiovascular and/or flexibility	0					
Resistance	0					

*Note.* CRF = cancer-related fatigue; POMS = Profile of Mood States; ITT = intention to treat; AP = adjuvant prospective: CS = cross-sectional; CBT = cognitive-behavioral therapy.

<sup>a</sup> Good validity is represented by a score above 4 points (out of 8). <sup>b</sup> Poor validity is represented by a score of less than 4.5 points.  $^{\dagger}p = .05$ .  $^{*}p < .05$ .  $^{**}p < .01$ .

interventions that reported a specific vigor/vitality-related theory and also included a CRF aim/hypothesis were found to have a much smaller effect size (.29) than exercise interventions reporting a vigor/vitality-specific theory that also included a CRF aim/ hypothesis (.97). Similarly, psychosocial interventions that did not report a vigor/vitality-specific theory were found to have moderately small effect sizes (.38) compared with exercise interventions that did not report a vigor/vitality-specific theory (.57).

#### Vigor/Vitality-Related Outcome Measures

No significant difference in effect sizes emerged between studies that used the POMS Vigor scale compared with those studies that used other types of vigor/vitality measures to assess outcomes. In addition, the effect size for vigor/vitality-related outcome measures was not influenced by whether studies included a CRF aim/hypothesis.

#### Methodological Quality and Reporting of Study Outcomes

Quality of study. Psychosocial intervention studies that were classified as having good methodological quality had a somewhat larger effect size (.41) than the psychosocial interventions that were found to have poor methodological quality (.30). The reverse pattern emerged for exercise interventions, where a stronger effect was evident for studies classified as having poor methodological quality (.77) compared with the moderately strong effect size that was found for exercise studies coded as having good methodological quality (.63). The group interaction effect was found to be nonsignificant. However, a significant interaction effect emerged between intervention category, poor methodological quality, and whether studies included a CRF aim/hypothesis (p < .01). Psychosocial studies with poor methodological quality that included a CRF aim/hypothesis were found to have a moderately large effect size (.66) compared with psychosocial studies with no CRF aim/

hypothesis (.42). The reverse pattern was found for exercise interventions. That is, exercise studies with poor methodological quality that did not specify a CRF aim/hypothesis were found to have a much larger effect size (.95) than exercise studies that included a CRF aim/hypothesis (.20). Although no significant interaction effect was found between good methodological quality and CRF aim/hypothesis status (p = .08), exercise studies with good methodological quality that did not specify a CRF aim/hypothesis were found to have a much larger effect size (.97) than those that did stipulate a CRF aim/hypothesis (.29). Psychosocial studies with good methodological quality were found to have a moderate effect size regardless of whether they did (.42) or did not (.40) specify a CRF aim/hypothesis.

*Baseline compatibility.* Psychosocial intervention studies that did not specify whether participants allocated to the two groups (active intervention vs. control arm) were comparable at baseline assessment on demographic and outcome variables, or did not report whether adjustments were made in the analyses when baseline differences emerged, were found to have a somewhat larger effect size (.45) than those that did (.34). In contrast, all of the exercise interventions that reported a vigor/vitality outcome documented that participants were comparable at baseline or made appropriate adjustments for group differences on demographic and/or baseline variables.

ITT analyses and handling of missing data. The effect size for psychosocial interventions that reported the use of ITT analyses and/or reported participant attrition or handling of missing data was moderately larger (.51) than the psychosocial interventions that did not (.30). The two exercise studies that did not report the use of ITT analyses and/or handling of missing data were found to have very strong effect sizes (1.24) compared with the exercise interventions that did (.47). The interaction of this variable with intervention category was significant (p < .001). However, no significant interaction effect was found between intervention category, ITT, and CRF aim/hypothesis status.

Participant retention rates at the initial assessment following completion of intervention. Psychosocial intervention studies that included postassessment data for at least 80% of participants were found to have an effect size (.39) comparable to that of psychosocial interventions in which fewer than 80% of participants completed the postassessment (.34). For exercise interventions that included postassessment data for at least 80% of particiipants, a stronger effect size (.73) was found compared with the only exercise study in which fewer than 80% of participants completed the postassessment (.49). The group interaction effect was found to be nonsignificant. Additionally, no significant interaction effect was found between intervention category, participant retention rate, and whether interventions were based on a CRF aim/hypothesis.

### Study Design

Psychosocial interventions that used a cross-sectional (CS) design were found to have a somewhat larger effect size (.47) compared with psychosocial interventions that were based on an AP design (.22). Similarly, a much stronger effect size was evident for exercise interventions that were based on a CS design (.93) compared with exercise studies that utilized an AP design (.52). Additionally, no significant interaction effect was found between intervention category, study design, and whether interventions were based on a CRF aim/hypothesis.

#### Participant Characteristics

Cancer type. Psychosocial intervention studies that only included breast cancer patients were found to have a smaller effect size (.22) compared with psychosocial interventions with mixed samples (including breast cancer patients) or those explicitly focused on other non-breast cancer samples (e.g., head and neck malignancies; .55). Similarly, exercise interventions that included mixed samples (including breast cancer patients) or explicitly included other non-breast cancer samples (.92) were found to have a much stronger effect size than exercise studies that included only breast cancer patients (.60). Moreover, a significant interaction effect was found between intervention category, heterogeneous cancer sample, and whether the intervention was based on a CRF aim/hypothesis (p = .05). In particular, the one exercise study that did not specify a CRF aim/hypothesis was found to have a substantially larger effect size (1.42) relative to the exercise interventions that included a CRF aim (.42). Psychosocial interventions that included heterogeneous cancer samples were found to have moderate effect sizes regardless of whether they included a CRF aim/hypothesis.

*Medical/cancer treatment status.* Psychosocial intervention studies that were conducted while patients were still undergoing primary or adjuvant cancer treatment (e.g., radiation or chemotherapy) were found to have a small to moderate effect size (.27), whereas studies that included interventions with patients after treatment (some participants who were on treatment combined with others who had completed their treatment) had a somewhat larger effect size (.49). A similar pattern emerged for exercise interventions. That is, studies that included participants not in

treatment at the time of the intervention were found to have a very large effect size (.93) compared with exercise studies that were conducted while patients were undergoing cancer treatment (.52). No significant interaction effects were found between this variable, intervention category, and whether studies included a CRF aim/ hypothesis.

#### Intervention Variables

*Treatment modality.* The effect size for psychosocial interventions that were administered on an individual basis (.29) was relatively small compared with effect sizes for interventions administered in a group format (.48). All of the exercise interventions used individual-based programs, which were found to have a moderately strong effect (.69).

Treatment setting. The effect size for psychosocial interventions administered in a hospital setting was moderately strong (.44) compared with those administered in the home or across settings (i.e., some sessions were conducted at the hospital while others were conducted at home; .18). In contrast, exercise interventions that were conducted at home or were administered in combined settings were found to have a slightly better effect size (.74) compared with exercise programs that were explicitly administered in a hospital setting (.65). Additionally, a significant interaction effect was found between intervention category, homebased treatments, and whether the intervention was based on a CRF aim/hypothesis (p < .05). Exercise interventions that included a CRF aim/hypothesis and were conducted at home were found to have a significantly larger effect size (.97) relative to psychosocial interventions that were home-based and included a CRF aim/hypothesis (.29). Both exercise and psychosocial studies that were conducted primarily at home and did not include a CRF aim/hypothesis were found to have a moderately small effect size (.27 to .29).

*Treatment duration.* Psychosocial interventions that consisted of fewer than 6 sessions were found to have a moderate effect size (.47) compared with those containing 6 to 8 sessions (.36) as well as those with more than 8 sessions (.30). Exercise programs with between 6 and 8 sessions were found to have a moderately strong effect size (.75), which was comparable to the moderately strong effect size for programs with more than 8 sessions (.67).

#### Psychosocial Treatment Components

The interventions were classified according to the same seven categories that were used in the meta-analysis for fatigue outcomes. Once again, the one study that utilized a restorative therapy program and was based on a CRF aim/hypothesis was found to have the largest effect size (.85), followed by the moderate effect that emerged for CBT interventions (.47). Supportive-expressive therapies (.38), counseling interventions (.33), and massage therapies (.33) were found to have relative moderate effects, followed by the small effect sizes that were found for educational (.18) and behavioral/relaxation (.14) therapies. Comparable to the fatigue outcomes, psychosocial interventions that included a CRF aim/ hypothesis were found to have larger effect sizes than interventions that were not based on a CRF aim/hypothesis. In particular, supportive-expressive therapies (.72), behavioral/relaxation (.61), and CBT (.50) approaches that included a CRF aim/hypothesis were found to have moderate to large effect sizes.

#### Exercise Treatment Components

The interventions that consisted of multimodal physical exercise components were found to have the strongest effect sizes (.80), whereas the walking interventions were found to have a moderate effect (.55). Interestingly, however, the two multimodal interventions that did not include a CRF aim/hypotheses had a larger effect size (.95) than did the two multimodal interventions that specified a CRF aim/hypothesis (.65). The reverse effect emerged for the walking interventions, whereby the walking intervention study that include a CRF aim/hypothesis had a larger effect size (1.07) than did the two walking interventions that did not include a CRF aim/hypothesis had a larger effect size (1.07) than did the two walking interventions that did not include a CRF aim/hypothesis (.29).

# Psychosocial Interventions That Reported Multiple Follow-up Assessments for Fatigue

Table 7 presents a descriptive summary of the meta-analytic results, comparing the weighted effect sizes of psychosocial interventions that included at least one additional follow-up assessment for vigor/vitality outcomes after the initial post-intervention. Thirteen separate trials were included in the overall analyses consisting of 2 psychosocial studies that reported a short-term follow-up within 4 months following completion of the intervention and initial postassessment; 5 studies that reported a 6-month follow-up; and 6 trials that reported a longer term follow-up (more than 6 months following the completion of the intervention and initial postassessment). The overall effect sizes for the follow-up psychosocial interventions ranged from .07 to .85, with a weighted pooled mean effect size of .29 (p < .001). Thus, the overall effect of the follow-up psychosocial interventions in improving vigor/ vitality was in the small to moderate range. The sample size was too small to conduct formal statistical assessments of possible main effects for the set of potential moderating variables or interactions with the timing of the follow-up assessments. Generally, however (see Table 7), the effect sizes for the intervention were consistent across studies, with some differences in the moderator variables.

#### DISCUSSION

A total of 119 articles in scientific peer-reviewed journals published in the English language were identified that explored the effectiveness of non-pharmacological interventions for fatiguerelated variables as either primary or secondary outcomes. Because there is currently no universal gold standard measure of CRF and the literature includes studies defining CRF as (a) a loss of energy, feelings of tiredness, and exhaustion (including loss of focus and concentration) and/or (b) an increase in energy, as indexed by measures of vigor and vitality, we chose to separately assess the efficacy of non-pharmacological interventions according to their effect on (a) reducing fatigue/tiredness and (b) enhancing vigor/ vitality and energy levels.

# Effects of Psychosocial and Exercise Interventions on Reducing Fatigue

Effect sizes for both psychosocial and exercise interventions for reducing fatigue were significant and clinically meaningful. No significant differences were evident between psychosocial and exercise interventions in the overall effect for reducing fatigue; however, psychosocial interventions were found to have a small to moderate effect size in reducing fatigue (.31), whereas physical exercise interventions were found to have a moderate effect in reducing fatigue (.42; J. Cohen, 1988). These results are consistent with systematic/qualitative reviews of both RCT and single-group design interventions (e.g., Mustian et al., 2007). That is, a greater proportion of both RCT and single-group design physical exercise interventions were found to have a beneficial effect in decreasing fatigue and tiredness symptoms in cancer patients.

It is noteworthy that no psychosocial or exercise study included specific participant inclusion criteria limiting eligibility to individuals who were assessed as fatigued at baseline. This outcome concurs with Jacobsen et al.'s (2007) review findings. Moreover, given that 53% (n = 27) more studies were included in the current meta-analysis for fatigue outcomes compared with the Jacobsen et al. (2007) meta-analysis, the present finding accentuates a significant gap in the treatment outcome literature for the specific management of clinical levels of CRF. The lack of studies on predefined "cases" of CRF is most likely due to the lack of consensus pertaining to the definition of CRF itself as well as to the pervasiveness of fatigue in cancer patients (Bower et al., 2006). However, the fact that fatigue is the most frequently reported symptom associated with cancer and its treatment perhaps attests to the relevancy of the methodological approach of including all cancer patients in trials rather than focusing on CRF cases exclusively. Accordingly, the findings from the present review are instrumental in highlighting the types of non-pharmacological interventions that have been found to be effective in reducing fatigue across a wide spectrum of cancer populations. The conclusions drawn from the comparisons of psychosocial and exercise intervention effect sizes, however, should be tempered by a number of methodological issues, discussed below.

First, although there was no significant difference in the effect sizes between psychosocial and exercise interventions contingent on whether the studies included a CRF aim/hypothesis as well as the methodological quality of the study, the effect size for psychosocial interventions tended to be greater than the exercise interventions when methodological parameters were considered. In particular, psychosocial interventions that included a CRF aim/ hypothesis were found to have significantly larger effect sizes in comparison with exercise interventions that included a CRF aim/ hypothesis when (a) the methodological study quality was fair to poor, (b) the study did not report and/or adjust for sample baseline compatibility, (c) the intervention was conducted while patients were undergoing medical treatment, and (d) the intervention was administered in an individualized format. This finding is particularly noteworthy given that more than half (56%) of the exercise interventions that reported a fatigue outcome included a CRF aim/hypothesis in comparison with less than one third of psychosocial studies (28%). This indicates that psychosocial interventions that are specifically intended to alleviate CRF are methodologically stronger than exercise interventions specifically designed to manage CRF. Furthermore, irrespective of whether a study included a CRF aim/hypothesis, the psychosocial interventions were found to have a significantly greater effect size when they reported the use of appropriate statistical methods, including ITT analyses and handling of attrition and missing data relative to the exercise interventions. Collectively, these findings suggest that more rig-

### CANCER-RELATED FATIGUE

# Table 7

Psychological Interventions: Sample Size, Effect Size, Confidence Interval, and Significance for Vigor/Vitality Outcome for Each Study Variable at Longer Term Follow-ups

		Effec (w	ct size (ES) veighted)	95% confidence interval (random effects)		
Variable	No. of study trials: <i>K</i>	ES	p (random)	Lower	Upper	
Psychological studies with additional follow-ups <sup>a</sup>	13	0.289	0.000	0.206	0.371	
Psychological: Within 4 months	2	0.280	0.000	0.123	0.437	
Psychological: 6 months	5	0.370	0.001	0.370	0.147	
Psychological: >6 months	6	0.224	0.000	0.124	0.324	
CRF aim						
Within 4 months	0					
6 months	0					
> 6 months	2	0.130	0.030	0.012	0.248	
Non-CRF aim						
Within 4 months	2	0.280	0.000	0.123	0.437	
6 months	5	0.280	0.001	0.370	0.147	
>6 months	4	0.271	0.002	0.101	0.440	
Vigor/vitality specific theory						
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	0					
6 months, with CRF aim	0					
6 months, with non-CRF aim	0					
>6 months, with CRF aim	2	0.130	0.030	0.012	0.248	
>6 months, with non-CRF aim	0					
No vigor/vitality specific theory	0					
Within 4 months, with CRF aim	0	0.000	0.000	0.400	0.425	
Within 4 months, with non-CRF aim	2	0.280	0.000	0.123	0.437	
6 months, with CRF aim	0	0.070	0.001	0.4.45	0.500	
6 months, with non-CRF aim	5	0.370	0.001	0.147	0.593	
>6 months, with CRF aim	0	0.071	0.002	0 101	0.440	
>6 months, with non-CRF aim	4	0.271	0.002	0.101	0.440	
POMS vigor subscale	0					
Within 4 months, with CKF aim	0	0.290	0.000	0 102	0 427	
Within 4 months, with non-CRF aim	2	0.280	0.000	0.123	0.437	
6 months, with non CDE aim	0	0.270	0.001	0.147	0.502	
6 months, with CDE sim	3	0.570	0.001	0.147	0.393	
>6 months, with non CPE sim	0	0.208	0.008	0.053	0.262	
Non POMS vigor measure	5	0.208	0.008	0.055	0.302	
Within 4 months with CRE aim	0					
Within 4 months, with non-CRE aim	0					
6 months with CRF aim	0					
6 months, with non-CRF aim	0					
>6 months, with CRF aim	2	0.130	0.030	0.012	0 248	
>6 months, with con-CRF aim	1	0.460	0.000	0.445	0.240	
Treatment modality: individual therapy	Ĩ	0.100	0.000	0.115	0.175	
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	1	0.360	0.000	0.343	0.377	
6 months, with CRF aim	0	01000	01000	010 10	01077	
6 months, with non-CRF aim	2	0.266	0.005	0.080	0.452	
>6 months, with CRF aim	$\overline{2}$	0.130	0.030	0.012	0.248	
>6 months, with non-CRF aim	2	0.231	0.075	-0.024	0.486	
Treatment modality: group therapy						
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	1	0.200	0.000	0.179	0.221	
6 months, with CRF aim	0					
6 months, with non-CRF aim	3	0.440	0.049	0.001	0.879	
>6 months, with CRF aim	0					
>6 months, with non-CRF aim	2	0.310	0.039	0.016	0.604	
Baseline compatibility and/or adjustment made						
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	2	0.280	0.000	0.123	0.437	
6 months, with CRF aim	0					
6 months, with non-CRF aim	5	0.370	0.001	0.147	0.593	
>6 months, with CRF aim	2	0.130	0.030	0.012	0.248	
>6 months, with non-CRF aim	4	0.271	0.002	0.101	0.440	
				(tab	le continues)	

		Effec (v	Effect size (ES) (weighted)		95% confidence interval (random effects)	
Variable	No. of study trials: <i>K</i>	ES	p (random)	Lower	Upper	
No baseline compatibility and/or adjustment made	0					
ITT and/or handling of missing data	0					
Within 4 months, with CRF aim	0	0.260	0.000	0.242	0 277	
6 months, with CPE sim	1	0.360	0.000	0.343	0.377	
6 months, with non-CRE aim	2	0.605	0.014	0.125	1.085	
>6 months, with CRF aim	2	0.130	0.030	0.012	0.248	
>6 months, with non-CRF aim	2	0.410	0.000	0.312	0.508	
No ITT and/or handling of missing data						
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	1	0.200	0.000	0.179	0.221	
6 months, with CRF aim	0					
6 months, with non-CRF aim	3	0.212	0.000	0.136	0.289	
>6 months, with CRF aim	0	0.125	0.000	0.077	0 102	
>6 months, with non-CRF aim	2	0.135	0.000	0.077	0.193	
Within 4 months with CRE aim	0					
Within 4 months, with non-CRF aim	1	0.360	0.000	0 343	0.377	
6 months, with CRF aim	0	0.500	0.000	0.010	0.577	
6 months, with non-CRF aim	3	0.503	0.003	0.174	0.833	
>6 months, with CRF aim	0					
>6 months, with non-CRF aim	3	0.327	0.001	0.129	0.525	
Less than 80% retention at postassessment						
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	1	0.200	0.000	0.179	0.221	
6 months, with CRF aim	0	0.170	0.000	0.152	0.100	
6 months, with non-CKF aim	2	0.170	0.000	0.152	0.188	
>6 months with non-CRE sim	2	0.130	0.030	0.012	0.248	
AP design	1	0.100	0.000	0.051	0.149	
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	1	0.360	0.000	0.343	0.377	
6 months, with CRF aim	0					
6 months, with non-CRF aim	1	0.360	0.000	0.343	0.377	
>6 months, with CRF aim	0					
>6 months, with non-CRF aim	2	0.231	0.075	-0.024	0.486	
CS design	0					
Within 4 months, with CRF aim	0	0.000	0.000	0.170	0.001	
Within 4 months, with non-CRF aim	1	0.200	0.000	0.179	0.221	
6 months, with non CPE sim	0	0 373	0.030	0.035	0.710	
>6 months, with CRF aim	2	0.130	0.030	0.033	0.710	
>6 months, with non-CRF aim	2	0.310	0.039	0.012	0.604	
100% breast cancer sample	_					
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	1	0.200	0.000	0.179	0.221	
6 months, with CRF aim	0					
6 months, with non-CRF aim	3	0.212	0.000	0.136	0.289	
>6 months, with CRF aim	2	0.130	0.030	0.012	0.248	
>6 months, with non-CRF aim	2	0.281	0.119	-0.072	0.634	
Mixed or non-breast cancer sample	0					
Within 4 months, with cor CPE aim	0	0.260	0.000	0.242	0 277	
6 months, with CRE aim	1	0.300	0.000	0.343	0.377	
6 months, with non-CRF aim	2	0.605	0.014	0.125	1.085	
>6 months, with CRF aim	0	0.005	0.014	0.125	1.005	
>6 months, with non-CRF aim	2	0.260	0.009	0.064	0.456	
On treatment at initial assessment						
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	2	0.280	0.000	0.123	0.437	
6 months, with CRF aim	0				_	
6 months, with non-CRF aim	3	0.234	0.001	0.092	0.375	
>6 months, with CRF aim	0	0.210	0.000	0.100	0.420	
>o months, with non-CKF aim	3	0.310	0.000	0.180	0.439	

		Effec (v	ct size (ES) veighted)	95% confidence interval (random effects)		
Variable  Vortice of the second secon	No. of study trials: <i>K</i>	ES	p (random)	Lower	Upper	
Not on treatment at initial assessment						
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	0					
6 months, with CRF aim	0	0.555	0.027	0.007		
6 months, with non-CRF aim	2	0.575	0.036	0.036	1.114	
>6 months, with non CDE sim	2	0.150	0.030	0.012	0.248	
Cood validity <sup>b</sup>	1	0.100	0.000	0.132	0.108	
Within 4 months, with CPE aim	0					
Within 4 months, with non-CRF aim	1	0.360	0.000	0 343	0 377	
6 months with CRF aim	0	0.500	0.000	0.545	0.577	
6 months, with non-CRF aim	3	0.503	0.003	0.174	0.833	
>6 months, with CRF aim	2	0.130	0.030	0.012	0.248	
>6 months, with non-CRF aim	4	0.271	0.002	0.101	0.440	
Poor validity <sup>c</sup>						
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	1	0.200	0.000	0.179	0.221	
6 months, with CRF aim	0					
6 months, with non-CRF aim	2	0.170	0.000	0.152	0.188	
>6 months, with CRF aim	0					
>6 months, with non-CRF aim	0					
Institutional setting						
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	2	0.280	0.000	0.123	0.437	
6 months, with CRF aim	0					
6 months, with non-CRF aim	4	0.420	0.002	0.160	0.680	
>6 months, with CRF aim	0	0.071	0.002	0.101	0.440	
>6 months, with non-CRF aim	4	0.271	0.002	0.101	0.440	
Within 4 months, with CDE sim	0					
Within 4 months, with non CPE sim	0					
6 months, with CPE aim	0					
6 months, with non-CRE aim	1	0.170	0.000	0 133	0.207	
>6 months, with CRF aim	2	0.130	0.000	0.012	0.207	
>6 months, with non-CRF aim	0	0.150	0.050	0.012	0.240	
Treatment duration: less than 6 sessions	0					
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	1	0.360	0.000	0.343	0.377	
6 months, with CRF aim	0					
6 months, with non-CRF aim	1	0.360	0.000	0.343	0.377	
>6 months, with CRF aim	2	0.130	0.030	0.012	0.248	
>6 months, with non-CRF aim	2	0.231	0.075	-0.024	0.486	
Treatment duration: 6 to 8 sessions						
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	1	0.200	0.000	0.179	0.221	
6 months, with CRF aim	0					
6 months, with non-CRF aim	3	0.440	0.049	0.001	0.879	
>6 months, with CRF aim	0					
>6 months, with non-CRF aim	1	0.160	0.000	0.152	0.168	
Treatment duration: >8 sessions						
Within 4 months, with CRF aim	0					
Within 4 months, with non-CRF aim	0					
6 months, with CRF aim	0	0.170	0.000	0.122	0.207	
o months, with OPE aim	1	0.170	0.000	0.133	0.207	
>6 months, with non CPE sim	0	0.460	0.000	0.445	0 475	
>0 monules, with non-CKF allin Specific treatment approaches: within 4 months	1	0.400	0.000	0.443	0.475	
CBT	2	0.280	0.000	0 123	0 / 37	
Specific treatment approaches: 6 months	2	0.200	0.000	0.123	0.437	
CBT	5	0.370	0.001	0.147	0.593	
				1 mil		

Table 7	(continued)
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		Effec (w	Effect size (ES) (weighted)		95% confidence interval (random effects)		
Variable	No. of study trials: <i>K</i>	ES	p (random)	Lower	Upper		
Specific treatment approaches: >6 months							
CBT	2	0.260	0.009	0.064	0.456		
Supportive-expressive	0						
Behavioral/relaxation	0						
Counseling	2	0.075	0.000	0.053	0.096		
Educational	2	0.325	0.016	0.060	0.590		

*Note.* CRF = cancer-related fatigue; ITT = intention to treat; CBT = cognitive-behavioral therapy.

<sup>a</sup> The effects from the psychological studies that included at least one additional following assessment were categorized according to short (i.e., within 4 months follow-up), medium (6-month follow-up), and longer term (more than 6 months) effects. <sup>b</sup> Good validity is represented by a score above 4 points out of 8. <sup>c</sup> Poor validity is represented by a score of less than 4.5 points.

p < .05. p < .01.

orous study designs favor psychosocial interventions in reducing fatigue in cancer patients. This conclusion is consistent with the present systematic review findings in which we found that half (50%) of the psychosocial RCTs that included a CRF aim had a beneficial effect in reducing fatigue, whereas only 30% of exercise RCTs that included a CRF aim found a reduction in fatigue.

On the basis of the available studies, there also appears to be a potential difference between exercise and psychosocial interventions with regard to their effectiveness when used during adjuvant cancer therapy. Physical exercise interventions during adjuvant therapy (including radiation and chemotherapy) tended to have a moderately stronger effect in decreasing fatigue compared with exercise interventions that were administered following treatment completion. The reverse pattern of results was evident for psychosocial interventions. Overall, these results suggest that psychosocial interventions may be more beneficial in reducing fatigue when administered following cancer treatment, whereas exercise interventions are more effective when administered at the same time as radiation and/or chemotherapy. Furthermore, the findings revealed that whereas exercise may benefit breast cancer patients more than non-breast cancer patients, psychosocial interventions are more beneficial in reducing fatigue across various cancer populations.

Several additional differences between the effect sizes for psychosocial and exercise therapies emerged according to design characteristics, specifically pertaining to treatment modality, setting, and duration. Although these effects were not significantly different between the two main interventions groups, these findings are suggestive with regard to conditions under which exercise and psychosocial interventions may be more or less effective in ameliorating fatigue. Notably, only one exercise study included in this meta-analytic review utilized a group approach for administering the physical intervention. The strong outcome in that trial tentatively suggests that group exercise programs may be quite beneficial in reducing fatigue, as the effect was substantially greater than that seen with exercise interventions administered on an individual basis. However, as this result is based on only one study, this finding needs to be interpreted cautiously. In addition, the findings indicated that exercise interventions administered at least partially in a home or a non-institution setting and including 8 or more weeks of therapy were found to be more effective in reducing fatigue. Conversely, psychosocial interventions conducted in hospital settings and conducted within 5 sessions were found to be more beneficial than interventions conducted in a home setting and scheduled over 6 and 8 weekly sessions. There seem to be minimal differences, however, between psychosocial interventions administered in an individual versus a group format.

Considering the heterogeneity of the specific interventions used in both the psychosocial and exercise trials, in order to gain a better understanding as to which particular treatment orientations were more effective in reducing fatigue, we evaluated the efficacy of psychosocial interventions according to seven specific therapeutic orientations and the efficacy of the exercise programs according to five specific treatment components. The most effective psychosocial therapies were restorative treatment and massage programs, which were found to have a moderately strong effect size; notably all three of these studies included a CRF aim/hypothesis. Specifically, two RCT studies utilized restorative interventions. For one of the studies, patients were required to prioritize their activities and engage in valuable and/or pleasurable activities in natural environmental settings, whereas the other study involved observing a natural/environmental setting using a virtual reality intervention. Though promising, the results for restorative and massage therapy need to be interpreted with caution as they are based on a very limited number of studies. Overall, CBT, supportiveexpressive psychotherapy, and counseling programs were found to have a moderate effect in reducing fatigue, whereas smaller effect sizes were found for educational and behavioral interventions based primarily on relaxation and/or imagery training. However, considerably stronger effect sizes were evident for supportiveexpressive psychotherapies, counseling, CBT, and behavioral therapies that were based on a CRF aim/hypothesis. In fact, the weakest effects emerged for educational interventions (regardless of whether they included a CRF aim/hypothesis), which is further consistent with the present systematic review findings where no RCT or single-group design trial that used an educational approach was found to be beneficial in decreasing fatigue symptoms in cancer patients.

Within the set of physical exercise interventions, those that utilized multimodal treatment components were found to have the strongest effect in reducing fatigue. Interestingly, however, multimodal intervention studies that were not based on a CRF aim/ hypothesis were found to have a considerably larger effect size

than multimodal exercise interventions that included a CRF aim/ hypothesis. Exercise interventions that were based explicitly on walking programs were found to have a moderate effect in reducing fatigue, and all three walking interventions were based on a CRF aim/hypothesis. The only trial that used a resistance therapy program and which included a CRF aim/hypothesis, was also found to have a moderate effect size, although, as this effect is based on one study, this result is preliminary in terms of supporting the efficacy of resistance training in managing fatigue. Physical interventions that were based on cardiovascular training and/or flexibility and strength training were also found to have a moderate effect in decreasing fatigue. In particular, cardiovascular and flexibility training programs that included a CRF aim/hypothesis were found to have stronger effect sizes than those that did not. Programs that explicitly utilized exercise bicycles were found to have minimal effect in reducing fatigue.

With regard to longer term beneficial effects, only psychosocial interventions included long-term follow-up data, and effect sizes were consistent with clinically meaningful effects on fatigue. No exercise study included follow-up data, so at this time the effect of exercise interventions on fatigue over the longer term is unknown.

# Effects of Psychosocial and Exercise Interventions on Increasing Vigor/Vitality

Overall, physical exercise interventions were clearly found to have a stronger effect on improving vigor/vitality in cancer patients (.69) compared with the small to moderate effect that emerged for psychosocial interventions (.37). The significant difference in effect sizes was independent of the methodological quality of the study designs, participant retention rates at the completion of the intervention, baseline compatibility, and adjustment of any baseline differences, as well as participant and study characteristics, including study design, cancer type and treatment status, modality, setting, and duration of intervention.

There were no significant group interactions between type of intervention (psychosocial vs. exercise) and methodological study design variables on vigor/vitality, with the exception of reporting and using ITT analyses and managing attrition and dropout data. Specifically, exercise interventions that did not explicitly report the use of ITT analyses and/or the handling of missing data had a notably stronger effect compared with exercise studies that did report the use of ITT analyses and/or handling of missing data. In contrast, psychosocial studies that explicitly reported the use of ITT and/or handling of missing data were found to have a moderately greater effect size compared with the studies that did not, although these effects were considerably smaller than the exercise interventions that did report appropriate handling of statistical analyses.

No significant group interactions emerged between psychosocial and exercise interventions reporting vigor/vitality outcomes contingent on whether studies included a CRF aim/hypothesis. However, psychosocial studies that did include a CRF aim/ hypothesis were found to have larger effect sizes when methodological study quality was fair to poor compared with exercise studies that included a CRF aim/hypothesis. This outcome is comparable to the fatigue results, which further attests to the methodological quality of the psychosocial interventions that were explicitly based on a CRF aim/hypothesis.

Looking more closely at psychosocial therapy modalities, we found that the one study that used a restorative approach to improve vigor/vitality and reported a CRF aim/hypothesis had a particularly large effect size, which is comparable to the fatigue outcomes for restorative approaches. Collectively, these results suggest that a restorative approach holds promise for both reducing fatigue and improving vigor/vitality, but until replicated with more studies utilizing this approach, more firm conclusions cannot be drawn at this time. CBT and supportive-expressive therapy approaches also moderately enhanced vigor/vitality, a pattern of findings that concurs with the present systematic review findings examining both the RCT and single-group design studies. Moreover, supportive-expressive psychotherapies, CBT, and behavioral interventions that included a CRF aim/hypothesis were found to have moderate to large effect sizes in improving vigor/vitality. Once again, educational interventions were found to have the weakest effect size. Therefore, it seems that education about managing CRF and associated symptoms is not sufficient to reduce fatigue and improve vigor/vitality.

Physical exercise interventions that reported vigor/vitality outcomes utilized two broad types of approaches: multimodal exercise programs and walking interventions. Whereas the walking interventions were found to have a moderate effect in improving vigor/vitality, multimodal exercise programs were found to have a strong effect in enhancing vigor/vitality. Interestingly, consistent with the fatigue outcomes, multimodal interventions that did not include a CRF aim/hypothesis were found to have considerably larger effect sizes than multimodal studies that did not report a CRF aim/hypothesis.

The present findings are generally consistent with Schmitz et al.'s (2005) findings. In particular, their meta-analytic analyses found that exercise interventions had a large positive effect (.83) for improving vigor/vitality when administered following cancer treatment. Although these findings were based on only two studies, and therefore need to be interpreted with caution, our results were comparable nonetheless. In particular, we found that exercise interventions (k = 3) that were administered following cancer treatment were clearly stronger (.93) in improving vigor/vitality than the moderate effect of exercise therapies (k = 4) administered while patients were still receiving radiation and/or chemotherapy (.52).

Schmitz et al. (2005) also found an extremely small effect for exercise therapies in reducing fatigue both during and following the completion of cancer treatment (.14), a finding that was based on 9 studies with variable methodological quality. In contrast, on the basis of 16 studies, we found a moderate effect for exercise interventions in managing fatigue (.42). Interestingly, we found that exercise programs conducted during medical treatments tended to have a larger effect size (.57) than exercise programs administered following the completion of cancer therapies (.16). The reason for this discrepancy between the present review and Schmitz et al.'s review may be attributable to the difference in studies included in the analyses. Schmitz et al. did not explicitly report which studies were included in the fatigue and vigor/vitality analyses and given that their review aim (and hence study inclusion criteria) differed from the aim of this review, their analyses likely included several different trials from those in our review.

In addition, our findings pertaining to the effects of exercise therapies in reducing fatigue are partly comparable with McNeely et al.'s (2004) meta-analytic findings in which they reported a moderate to large effect (.72) for exercise interventions (k = 6) in reducing fatigue in breast cancer patients. Indeed, our results revealed that exercise interventions (k = 9) when administered to breast cancer patients were moderately stronger in effect in decreasing fatigue (.62) than were exercise programs (k = 7) administered with mixed and non-breast cancer patients (.16). On the basis of these three meta-analytic reviews, a consistent pattern emerged indicating that exercise interventions are more effective in improving vigor/vitality in various cancer patient populations, particularly when administered at the completion of cancer treatment.

Our findings, however, differ from the small fatigue effects reported in Markes et al.'s (2006) review. This disparity seems to be due primarily to the differences in study inclusion criteria. Notably, Markes et al. used more limited inclusion criteria restricting the analyses to studies that were conducted with breast cancer patients undergoing adjuvant treatment, whereas our analyses with breast cancer patients included both patients who were receiving adjuvant therapy as well as individuals who had completed their cancer treatments.

For the most part, our meta-analytic findings also differ from the small combined fatigue and vigor/vitality effects reported in Jacobsen et al.'s (2007) review. We found considerably larger effect sizes for both psychosocial and exercise interventions in both reducing fatigue and enhancing vigor/vitality than the effect sizes reported in Jacobsen et al.'s review, which were very small. Whereas Jacobsen et al. found that, overall, psychological interventions had a significantly stronger although small effect size (d = .10) in reducing fatigue and improving vigor compared with exercise interventions (d = .05), our results indicated the reverse pattern. Although the study inclusion criteria between our review and Jacobsen et al.'s review were the same, there are at least three notable methodological differences between the two reviews that may account for the disparity in findings. First, as previously noted, Jacobsen et al. merged the results for fatigue and vigor/ vitality outcomes when analyzing the effects between psychological and exercise interventions. As our current findings, as well as Schmitz et al.'s (2005) results, attest, interventions that are beneficial in reducing fatigue may not necessarily be equally effective in enhancing vigor/vitality. Merging the results from fatigue and vigor/vitality outcome studies may minimize the effects for both outcomes. Further, although vigor and vitality are two concepts that are commonly related to CRF, until further research delineates the specific mechanisms underlying CRF, it would be premature to conclude that studies that reduce fatigue will also enhance vigor/ vitality and vice versa.

A second notable difference between our review and Jacobsen et al.'s (2007) review concerns the post-intervention outcome used for the psychosocial studies. Because no exercise-based RCT intervention study had a longer term post-intervention follow-up assessment, to ensure that we comparably evaluated the effects of exercise and psychosocial interventions, we used the initial postintervention assessment fatigue and vitality/vigor outcome scores for those psychosocial intervention studies that had multiple postintervention follow-up assessments. Hence, the findings from our meta-analysis were specifically based on comparing the effects between psychosocial and exercise interventions in reducing fatigue and improving vigor/vitality in the short-term, following treatment completion. In contrast, Jacobsen et al. utilized the final outcome score reported by all studies in determining treatment effects between exercise and psychological interventions. As a consequence, the effects of psychosocial interventions that reported longer term follow-up outcomes were merged with those psychosocial and exercise interventions that only reported outcomes immediately after treatment completion. A third notable difference is that our meta-analysis for fatigue outcomes alone was based on 52% more studies than were included in Jacobsen et al.'s (2007) combined fatigue and vigor meta-analysis. The smaller sample size may have further contributed to the considerably smaller effect sizes reported in their review relative to our current findings.

#### Conclusions and Implications

The findings from this combined systematic and meta-analytic review indicate that both psychosocial and exercise interventions can produce clinically meaningful benefits for reducing cancer patients' levels of fatigue. Physical exercise interventions have an advantage when one considers the effectiveness of these interventions for also improving vigor/vitality. These results provide some guidance in the recommendation of specific types of psychosocial and exercise interventions for managing CRF. First, several integrative intervention trials that were evaluated in this combined review included a combination of both psychosocial (including counseling, stress management, and coping strategies) and exercise-based (i.e., physical activity, such as walking and yoga) treatment elements. Indeed, even restorative interventions that include activity scheduling can be likened to these integrative approaches. The positive findings that emerged from some of these integrative studies (Courneya, Friedenreich, Sela, Quinney, Rhodes, & Handman, 2003; Speca, Carlson, Goodey, & Angen, 2000) suggest that perhaps the best way to address CRF, which is a multiply determined construct, is to take a multimodal therapeutic approach that would address both reducing fatigue and increasing vigor/vitality.

The present data supporting the view that psychosocial and exercise interventions may be effectively administered either during or after adjuvant therapy further bolsters the position that a therapeutic approach integrating exercise and psychosocial approaches may best serve patients clinically. Indeed, the positive 6-month follow-up data for psychosocial approaches such as CBT argue strongly for their inclusion in a multimodal approach. Of course, these approaches warrant further investigation in order to delineate the optimum balance of each therapeutic component for effectively ameliorating the constellation of CRF symptoms. More specifically, additional studies are warranted to further discriminate specific intervention components in multimodal interventions that are most effective in controlling CRF as well as to determine the optimum timing and duration of treatment. As some multimodal interventions were found to be effective in managing CRF, integrative approaches would appear to show promise for controlling CRF. Moreover, there is a general need to improve the methodology (including participant selection criteria; sample size calculations; randomization procedures, including concealment of allocation and blinding of assessors; prospectively defined assessment outcome endpoints; use of ITT analyses; handling of attrition and missing data; and inclusion of longer term follow-up assessments) for additional randomized large-scale clinical trials within this field of research.

It is interesting to note that in comparing the effect sizes of psychosocial and exercise therapies in which CRF was a specific aim, there was minimal difference (.10) between these two interventions in terms of managing fatigue symptoms. That is, both types of interventions appear to have relative moderate effects on fatigue. Furthermore, whereas psychosocial interventions that included a CRF aim also showed a moderate effect size in improving vigor/vitality, exercise therapies that included a CRF aim had a strong effect in improving vigor/vitality. These findings provide further evidence that exercise interventions may be more beneficial for improving vigor/vitality, but not for reducing fatigue symptoms, compared with psychosocial interventions.

In consideration of the wide range of psychosocial and exercise therapeutic orientations that have been used to manage CRF, a finer grained analysis of specific types of therapies provides further clarity in determining which interventions are most beneficial in managing CRF. In particular, on the basis of studies that included a CRF aim, the present findings suggest that among the psychosocial interventions, restorative approaches, supportiveexpressive psychotherapies, CBT, and counseling therapies have a moderate to strong effect in reducing fatigue. Moreover, restorative, supportive-expressive, CBT, and behavioral therapies that are expected to manage CRF also have a moderate to strong effect in increasing vigor/vitality. Among the exercise interventions that were expected to manage CRF, walking and multimodal exercise programs would appear to have the greatest potential in both reducing fatigue and enhancing vigor/vitality. In conjunction, these findings suggest that the effectiveness of nonpharmacological interventions in managing CRF likely depend on the specific subtypes of interventions compared. Notably, there is minimal difference between exercise and psychosocial therapies in both managing fatigue and improving vigor/vitality symptoms when comparing the most effective specific therapeutic orientations that were specifically intended to manage CRF from these two broad approaches. However, given that only a minority of studies that used these specific psychosocial and exercise intervention approaches were based on CRF aims, these findings are preliminary and need to be replicated in future research. Indeed, considering that CRF is a subjective and multiply determined phenomenon, comparative trials evaluating different components from multimodal psychosocial and exercise therapeutic approaches in managing CRF are warranted. Moreover, the integration of effective components from psychosocial and exercise approaches, and the combination of these with pharmacological approaches, are also likely to show promise for managing the multiple effects of CRF.

The findings from the current review highlight a number of conceptual and methodological issues that need to be considered in interpreting the outcomes from studies in this area of research. First, the present findings revealed that effect sizes for both the fatigue and vigor/vitality outcomes were not significantly influenced by whether fatigue and vigor/vitality were measured using generic versus cancer-specific unidimensional as well as more multidimensional instruments. Notably, no differences emerged between those studies that utilized the POMS Fatigue and/or Vigor subscales compared with studies that used other types of fatiguerelated outcome measures. This finding concurs with the Meek et al. (2000) study, which demonstrated that the POMS Fatigue subscale had strong psychometric properties in detecting changes in CRF symptoms compared with multidimensional fatigue measures.

Second, a large number of studies used separate scales to assess fatigue and vigor/vitality outcomes within the same trial. However, only a small proportion of studies that used two different fatiguerelated variables (e.g., fatigue and vigor, or fatigue and vitality) reported an improvement in both domains. Specifically, 35 psychosocial and 6 exercise trials reported outcomes for both fatigue and vigor/vitality within the same study, but only 6 of these psychosocial trials and 2 of the exercise studies were found to have a significant improvement in both of these symptoms. These outcomes suggest that a reduction in fatigue does not necessarily entail an improvement in vigor or vitality (or vice versa). That is, an intervention that may reduce fatigue symptoms may not make an individual feel more energetic or vigorous. This pattern of results further reinforces the notion that the CRF phenomenon appears to be a broad construct and also accentuates the need for additional research to investigate the specific mechanisms pertaining to the onset and maintenance of fatigue at different stages throughout an individual's experience with cancer from diagnosis to treatment, as well as the short- and longer term recovery from both disease and treatment effects.

Furthermore, the varying outcomes between fatigue and vigor/ vitality measures raise the issue of whether the conceptualization and assessment of CRF needs to be considered as a continuum ranging from normal levels of fatigue to more clinical levels associated with noticeable interference with general functioning and well-being. This latter proposition is in accord with the International Classification of Diseases (10th ed. [ICD-10]) criteria for CRF (Cella et al., 1998; Cella, Davis, Breitbart, & Curt, 2001). For those intervention trials that were found to be associated with an improvement in vigor/vitality but did not lead to a decline in fatigue symptoms, it is possible that participants' baseline levels of fatigue were within the normal range of functioning, hence only accounting for improvements in energy levels. Therefore, these interventions may be indicative of preventative approaches in curbing the onset of chronic elevated levels of fatigue, whereas interventions that were found to reduce fatigue may be suggestive of therapeutic approaches in managing CRF. However, as noted, on the basis that not a single RCT intervention included participant inclusion criteria restricting eligibility to individuals specifically suffering from acute or clinical levels of fatigue, future studies are needed that evaluate the effectiveness of different approaches in both reducing fatigue and enhancing vigor in patients suffering from clinical levels of fatigue compared with cancer patients that do not report debilitating symptoms of fatigue. This type of research should be instrumental in delineating therapeutic approaches from preventative methods in overcoming as well as preventing chronic CRF.

#### Limitations

The present review has several potential limitations. First, by excluding articles that were not published in scientific peerreviewed journals and those not printed in the English language, it is probable that a number of relevant treatment intervention studies were omitted. Similarly, akin to any review, although thorough search strategies were utilized in identifying all relevant empirical articles, it is possible that some trials were missed in the selection process. Given the large number of studies included in this review, however, in the event that several trials were overlooked, this is unlikely to have substantially altered the present findings. The robust nature of the findings of this review was further supported by the nonsignificant results that emerged from the meta-bias analyses for both the fatigue and vigor/vitality outcomes. Indeed, a notable strength of this review was the comprehensive inclusion criterion in evaluating RCTs, non-RCT and CCT group comparisons, and single-group design interventions in the systematic review. Because RCTs are considered the "gold standard" in evaluating the effectiveness of interventions, the meta-analytic review was explicitly based on evaluating the treatment outcomes for the RCT studies. This combined review approach therefore had the advantage of allowing a comparison within and between different design types and therapeutic approaches.

Second, our examination of moderating influences (e.g., study methodological quality) on effect sizes was at times based on relatively few articles. This small cell size could potentially have led to an underpowered approach for detecting moderator effects. Therefore, we recommend that as this literature continues to grow, a re-analysis of moderating influences be undertaken. Third, our examination of different variants of methodological quality was, for the most part, based on the CONSORT criteria. It is possible that other aspects of methodological quality (e.g., participant adherence rates to treatment/homework compliance, interventionist expertise) may have influenced the effect of different treatment components. However, some of these further in-depth moderator analyses would also have suffered from small cell size comparisons, particularly when evaluating differences between psychosocial and exercise interventions contingent on whether they include a CRF aim/hypothesis. Additionally, given that in recent years the majority of high-quality peer-reviewed scientific journals require authors to adhere to the CONSORT criteria in reporting treatment outcome research, our adherence to this set of criteria enabled us to determine the specific criteria that have not been adequately reported and/or commonly utilized in the CRF treatment outcome literature to date. To this end, on the basis of the current state of the CRF non-pharmacological intervention literature, improvements are required in reporting of statistical analyses, using concealment of allocation in randomization procedures, and blinding of assessors.

#### Summary

The present systematic evaluation of the quality and outcomes of non-pharmacological interventions indicates that both psychosocial and exercise-based therapies show strong potential for effectively ameliorating CRF, particularly when specific therapeutic orientations (notably, multimodal exercise and walking interventions as well as restorative, supportive–expressive, and CBT psychosocial therapies) are considered. This is a noteworthy conclusion given the increasing impression in the literature in recent years emphasizing the potential benefits of exercise-based interventions in managing CRF relative to other non-pharmacological types of interventions (e.g., Lawrence et al., 2004; Mock, 2004; Stasi et al., 2003). To our knowledge this is the most comprehensive review conducted to date that has systematically evaluated the methodological quality and outcomes of both exercise-based and psychosocial interventions that included fatigue or related outcome measures, notably vigor and vitality. It is therefore premature to conclude that there is stronger or more promising evidence to support the effectiveness of one type of intervention over the other. Rather, on the basis of our findings, there appears to be support for the effectiveness of both types of interventions in controlling CRF symptoms, especially when the interventions tested were expected to reduce CRF and/or enhance vigor/vitality. Moreover, the present findings suggest that perhaps multimodal approaches that include both more promising psychosocial approaches (e.g., restorative, CBT, supportive-expressive components) with exercise may lead to the greatest benefit for cancer patients. These results show commonality with findings from Whiting et al.'s (2001) systematic review evaluating the effectiveness of all types of interventions (including psychosocial, exercise, and pharmacological studies) in the management of chronic fatigue syndrome (CFS) and found that CBT and graded exercise therapy showed the most promising results in reducing CFS. Examination of the utility of integrative psychological and exercise interventions combined with pharmacological treatments in effectively controlling CRF would be a particularly promising avenue for future research in this area.

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## **Correction to Karelaia and Hogarth (2008)**

In the article, "Determinants of Linear Judgment: A Meta-Analysis of Lens Model Studies," by Natalia Karelaia and Robin M. Hogarth (*Psychological Bulletin*, 2008, Vol. 134, No. 3, pp. 404–426), in Table 1 (p. 411), two columns of data were inadvertently transposed and thus listed under their incorrect column headers,  $I^2$  (%) and  $\tau^2$ . The correct version is presented below.

Furthermore, in Table 6 (p. 417), one data entry was inadvertently omitted. In the row "Log(learning trials)," the entry in the corresponding  $SE_{\rm B}$  column for  $R_{\rm s}$  (M2) should be listed as .02. An additional typographical error occurred on p. 415 in the left-hand column, second line of text from the bottom; the phrase should read "a measure of sample size."

#### Table 1

Descriptive Statistics of Lens Model Indices

								Correlations				
Lens model index	M (weighted)	95% confidence interval	п	Q	$I^{2}$ (%)	$ au^2$	r <sub>a</sub>	G	R <sub>e</sub>	$R_{\rm s}$	С	GR <sub>e</sub>
r_	.56	.53–.59	249	17.319*	99	.057	_					
Ğ	.80	.7683	236	19,829*	99	.067	$.78^{**}$	_				
R	.81	.7984	246	$10,706^{*}$	98	.035	.43**	.10	_			
R <sup>e</sup> s	.80	.7982	237	5,644*	96	.019	.56**	.43**	.14*	_		
Ċ	.04	.0206	204	6,249*	97	.023	.23**	.03	23**	05	_	
GR	.65	.6168	236	20,668*	99	.070	.91**	.82**	.63**	.41**	08	
GR <sup>e</sup>	.66	.6369	236	17,469*	99	.060	.83**	.92**	.12	.72**	03	$.78^{**}$
$GR_{e}^{"}-r_{a}$	.10	.0911	236	2,461*	90	.008						

*Note.* See "The Mathematical Formulation of Brunswik's Lens Model" section of the text for a description of the lens model indices. Q represents within-group heterogeneity;  $f^2$  is the percentage of variation attributable to between-study heterogeneity;  $\tau^2$  is the DerSimonian and Laird (1986) estimate of between-study variance.

 $p^* < .05. p^* < .01.$ 

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# Correction to Kangas, Bovbjerg, and Montgomery (2008)

In the article "Cancer-Related Fatigue: A Systematic and Meta-Analytic Review of Non-Pharmacological Therapies for Cancer Patients" by Maria Kangas, Dana H. Bovbjerg, and Guy H. Montgomery (*Psychological Bulletin*, 2008, Vol. 134, No. 5, pp. 700–741), the URL to the Supplemental Materials for the article is listed incorrectly in two places in the text. The incorrect listings appear on p. 704 (in the last two lines of the third paragraph) and on p. 705 (in the third and fourth lines of the first paragraph in the second column). The correct URL for the Supplemental Materials is http://dx.doi.org/10.1037/a0012825.supp, which is provided on the first page of the article beneath the abstract.