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Mediators of Change in Psychosocial Interventions for Cancer Patients: A Systematic Review

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Abstract

Careful reviews and meta-analyses have made valuable contributions to understanding the efficacy of psychosocial interventions for cancer patients. An important next step is to determine the mediators that explain the influence of efficacious interventions on outcomes. This systematic review summarizes tests of mediating variables from twenty-two projects conducted from 1989–2010. Although all authors provided some type of rationale for considering particular mediating relationships, the investigations varied widely with respect to the extent to which formal theoretical constructs were tested, the type and goals of the interventions studied, and the broad types of outcomes and potential mediators examined. Although there was some evidence supporting selected mediating relationships, with positive findings often found when mediating variables represented behaviors targeted by an intervention, the findings were mixed. Expanding the focus of research to include mechanisms in psychosocial oncology intervention research is necessary for providing a unified picture of how mediating relationships may be operating in this field.

Keywords

cancer; psychosocial; intervention; treatment; quality of life

In recent decades, increasing attention has been directed at developing and testing interventions to improve the quality of life of those coping with cancer.¹ A number of careful reviews and meta-analyses have made valuable contributions to our general understanding of the efficacy of these interventions.^{2–7} Focused syntheses have concentrated on people with particular types of cancer, such as breast or gynecologic,^{8,9} stages of cancer, such as advanced,¹⁰ or particular subgroups of cancer survivors, such as men.¹¹ Other reviews have highlighted particular outcomes, such as fatigue,¹² depression and anxiety,^{13,14} or survival,^{15,16} or particular types of interventions, such as physical activity,^{17,18} mindfulness based therapy,¹⁹ or guided imagery.²⁰

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An important next step is to determine the mechanisms underlying efficacious interventions.^{2,21–23} Changes in quality of life as a result of psychosocial interventions are presumed to involve changes in mediating variables. Potential mediators include, for instance, improvements in feelings of control, increased perceptions of social support, constructive emotional processing,²⁴ and expectancies regarding symptoms.²⁵ Understanding the underlying processes by which psychosocial interventions affect quality of life also contributes to theory and to the development of superior interventions.²⁶ Theoretically, processes that have been suggested to be operating in helping individuals successfully adjust to cancer include cognitively processing threatening information about the world and oneself,²⁷ fostering a sense of hope and helping people remain engaged with life,²⁸ and reducing traumatic stress.²⁹ However, reviewers have also noted that theory-based models are somewhat rarely tested in research that examines psychosocial interventions for cancer.²³

Process research aims to provide information to increase the efficacy of therapeutic interventions by demonstrating the mechanisms through which they work.³⁰ Understanding interventions' underlying mechanisms involves studying a causal chain whereby an independent variable (the intervention) causes a change in a mediating variable (the potential mechanism) which, in turn, causes a change in the dependent variable (the outcome).³¹ Several procedures are available for conducting statistical tests of mediation.^{32–34} In addition to statistical evidence for mediation, several additional criteria are considered conceptually necessary for demonstrating that mediator is a likely mechanism of change. These include: specificity of the influence of the intervention on the mediator and the mediator on the outcome; a dose-response relationship among the purported causal relationships; a temporal relationship in the changes in intervention, mediator, and outcome; replicated results; using manipulation and frequent assessments to demonstrate a causal relationship; and findings that can be interpreted as a plausible explanation of processes of change.^{35,36} Finally, once mechanisms of change are understood, insights regarding what factors might moderate the effect of interventions may also emerge.³⁵ For instance, if an expressive writing intervention for cancer survivors is found to work through cognitive and emotional processing, then, according to social constraint theory, those who have fewer supportive resources to allow expression of their thoughts and feelings might benefit more from such an intervention.³⁷

Reviews of other psychotherapeutic literatures (e.g., treatment for alcohol use disorders, youth psychotherapy) have shown that, although studies often include assessments of potential mediating variables, full tests of statistical mediation are rarely conducted.^{38–40} Process research is likely to become more common in the literature examining psychosocial interventions for cancer patients in response to calls for theory-guided examinations of mechanisms for obtained effects in this field⁴¹ and the increasingly important role of understanding mediators in clinical research in general.³² Thus, the objective of the current review is to identify which mediating relationships have been examined in the psychosocial oncology literature and to determine which specific mediating relationships have been analyzed. Documenting the potentially mediating variables that have been empirically examined is an important step in understanding what is known thus far about how such interventions may be operating and thus identifying targets for making them more efficacious.⁴² Potential types of mediating mechanisms include changes in emotional and cognitive indices, physiological processes, social mechanisms, and coping skills. Mediators may comprise variables that represent quality of life outcomes in their own right (e.g., levels of distress) that may mediate more general quality of life outcomes, or they may comprise variables that represent skills, behaviors, or indices targeted by interventions (e.g., symptom expectancies) that are not quality of life outcomes per se. Thus, this review summarizes the findings from empirical tests of mediating variables in research investigating psychosocial

interventions for cancer survivors conducted over three decades. The second objective includes identifying particular classes of mediating relationships and patterns that have been shown to be particularly efficacious. We expect that mediating relationships based upon well-specified theoretical formulations or rationales will be most fruitful. Therefore, the review examines the extent to which examined mediating relationships are theory-based and the extent to which mediating variables are outcome-related versus related to behaviors, skills, or indices targeted by the intervention.

METHOD

The studies included were drawn from a database generated by a systematic review of psychosocial interventions for cancer survivors reported from 1980 to 2005. This review has been described elsewhere,⁴³ and it has been updated to include studies reported from 2006 through the end of 2010.

Study Identification

As described previously,⁴³ eligible studies examined psychosocial interventions designed to improve the quality of life of adult cancer survivors (aged 18 years and older). To be eligible studies must have: (1) reported quantitative outcomes on psychological, emotional, behavioral, physiological, functional, or medical status (e.g., depression, anxiety, fatigue, pain, cortisol levels, length of survival, social functioning, job functioning); (2) been first reported as a published journal article or dissertation between January 1980 and December 2010; and (3) included 10 or more individuals per group. Studies examining interventions aimed at increasing adherence to anti-cancer treatment or focusing exclusively on caregiver outcomes were outside the purview of this review. Study inclusion was deliberately broad and not constrained by study quality (aside from the criterion requiring a minimum of 10 individuals per group, noted above) with the intent of characterizing the extant literature as whole in order to describe and its purview and methodological quality. Electronic databases (PsycINFO, PubMed; and Dissertation Abstracts Online), were searched using key terms (e.g., *cancer*, *neoplasms*, *tumor*, and psychosocial intervention, psychotherapy, psychological treatment, education, cognitive behavioral, relaxation, stress management, support group, self-help group, nursing intervention, biofeedback). The reference lists of included reports and of prior reviews and meta-analyses also were examined. Searches for articles citing prior reviews and the tables of contents of several relevant journals (e.g., *Psycho-Oncology*, *Journal of Clinical Oncology*, *Cancer*, *Journal of Psychosocial Oncology*, *European Journal of Cancer*, and *Cancer Nursing*) were conducted. Initial eligibility was determined by a single investigator and was confirmed by a second trained coder; discrepancies were resolved by consensus.

Separate reports based on the same sample (e.g., separate articles reporting outcomes at 3-month and 12-month follow-ups) were consolidated and considered as a single project. The database of studies first reported from 1980 to 2005 included 488 projects and the database of studies reported from 2006 to 2010 included 444 projects. See Figure 1 for the flow of study identification, retrieval, and eligibility determination and the number of reports associated with each stage.

Project Coding

Projects were coded according to a detailed manual (available by request from the authors) with respect to numerous characteristics of the sample, intervention, study design and methodology, and statistical analyses, as described previously.⁴³ The PI and three teams of thoroughly-trained graduate-level coders met regularly to prevent coding drift, discuss coding dilemmas, and to reach consensus on independently-coded projects used for

reliability estimation. As reported,⁴³ good coding reliability was achieved for the earlier database, and for the more focused coding of the second database, the agreement for the ratings of the PI, Coder 1, and Coder 2 of the third coding team was .63 (average generalized kappa⁴⁴). For this report, the results of projects coded as conducting analyses that statistically examined the processes through which change occurs by testing the role of a mediating variable between treatment and outcome are presented. The data extraction was performed by a single investigator and confirmed by a second coder; discrepancies were resolved by consensus. We distinguished these types of analyses from another valuable type that considers the *active ingredients* of treatment or within-therapy change processes (e.g., therapeutic bond, group cohesion, types of words used in expressive writing). This type of analysis answers the related question of why an intervention might work by considering the specific components of treatment that cause the observed change, apart from the mechanisms through which these ingredients cause change^{35,36} (see^{45–47} for excellent examples in this field). Thus, we examined analyses that considered processes of change occurring within individuals undergoing interventions rather than characteristics of interventions. We included only randomized studies that compared one or more intervention conditions to a control (e.g., usual care, attention, wait list) or a comparison condition, due to the necessity of establishing a causal relationship between treatment and mediators and outcomes.

Because operational definitions and statistical procedures for mediation continue to evolve,^{42,48–51} we included evidence based upon various types of soundly conducted statistical analysis of mediation (e.g., OLS regression models, structural equation modeling). The quality of study reporting and methodology were assessed with items adapted from prior work.⁵² These considered aspects of the sample description, the rigor of randomization, intervention fidelity and delivery, and data analyses, such as whether intention-to-treat analyses were conducted. Aspects of quality conventionally considered to be important were included in the current review, such as assessing the number of participants dropping out of treatment.⁵³ However, because keeping participants and interventionists blind to treatment group assignment has low feasibility for psychosocial interventions, this factor, often considered important for study quality, was not included. Similarly, because outcomes in this area are typically based on self-report, assessments of whether blinding of outcome assessors occurred also were not included. We reported aspects of quality separately, in keeping with the notion that combining different aspects of quality is not advised.⁵⁴

RESULTS

Table 1 summarizes the characteristics of 22 projects (comprising 26 reports) that included tests for mediation. These made up 2% of the projects conducted from 1980–2010. More recent projects were more likely to report mediation analyses. Only 2 studies included in this review were first reported between 1980 and 1999, 5 studies were reported between 2000 and 2005, and the remainder were reported after 2005.

Types of Interventions

Mediator analyses were presented for a variety of types of interventions. This variety is similar to that found in the literature as a whole, including multicomponent biobehavioral intervention,^{55,56} cognitive-^{57,58} and cognitive-behavioral-oriented approaches,^{59–64} coping and communication enhancing intervention,⁶⁵ peer discussion,⁶⁶ supportive counseling,⁶⁵ cancer information mentors,⁶⁷ a comprehensive web-based health enhancement support system,⁶⁷ physical activity,^{62,68–72} relaxation and music listening,^{73,74} hypnosis,⁷⁵ education,^{57,66,73,76,77} nutrition,⁷⁷ expressive writing,⁷⁸ and mindfulness training.⁷⁹ There was also diversity in the goals of the treatments. Whereas some types of interventions were

directed at improving overall quality of life, or several aspects of psychological and physical functioning (e.g.,⁵⁵), others focused on alleviating more specific treatment-related symptoms such as pain, nausea, and fatigue (e.g.,⁷⁵). In terms of broad classes of interventions the active (non-control) treatments studied in this set of projects comprised 33% education/information, 28% cognitive, behavioral, or cognitive-behavioral therapy, 13% complementary or alternative mind-body approaches, 10% multimodal, 5% nonbehavioral counseling or psychotherapy, 3% social support by non-professionals, and 8% other approaches.

Theory or Stated Rationale for Mediator Analyses

Another aspect on which the projects varied was the extent to which the selection of proposed mediators examined was based on theory (see Table 1). Although just 6 (27%) of the projects mentioned a specific theoretical formulation, the projects universally provided some rationale for their examination of mediators. For instance, Rabin et al.'s⁷⁰ Moving Forward physical activity intervention was based on the Transtheoretical Model of Change (TTM).⁸⁰ This model proposes that various cognitive and behavioral factors are involved in individuals progressing through a series of stages of behavior change. Thus, these authors proposed that changes in these factors, such as decisional balance, behavioral processes of change, experiential processes of change, and self-efficacy, would serve as mediators of the outcome, minutes of moderate-intensity activity. Similarly, Vallance et al.⁷² used the Theory of Planned Behavior (TPB)⁸¹ to design an intervention to encourage physical activity in breast cancer survivors. The proposed mediators of the effect of the intervention on self-reported levels of physical activity were factors based upon the TPB, such as intentions to exercise. Speck et al.⁷¹ did not base their hypotheses on a formal theoretical model, but they noted that the functional ability to perform tasks is important to one's concept of body image, and thus posited that improved muscle strength, which would improve this functional ability, would lead to improved body image. Other justifications were somewhat more exploratory, such as "there are currently no studies describing a relationship between immune function and posttraumatic growth. Thus, the present intervention, which demonstrated posttraumatic growth as a result of a clinical intervention, provides an especially rich opportunity to begin looking for related changes in immune parameters"^{61(p 17)}.

Relatedly, the mediating relationships examined varied with respect to whether the proposed mediators were targets of treatment, including behaviors, skills or indices that interventions fostered or addressed directly (and which would not be considered quality of life variables in their own right) or whether the mediator was an outcome variable related to some aspect of cancer-related or cancer-treatment-related quality of life. Of the 75 different mediators tested, the majority, 67%, could be characterized as targets of treatment. For instance, Manne et al.⁶⁵ based their proposed mediators on the psychological processes that their treatments aimed to foster: for their Coping and Communication Enhancing Intervention (CCI) these were positive reappraisal, acceptance, planful problem solving, attempts to understand emotional reactions to cancer, expressing emotions, seeking emotional and instrumental support, and self-esteem; for Supportive Counseling these were expressing emotions, efforts to understand emotional reactions to cancer, and self-esteem. Similarly, Hawkins et al.⁶⁷ selected their mediators based on the rationale that they were factors intended to be influenced by their intervention; thus, they expected that quality of life improvements due to their communication intervention would be mediated by changes in the basic psychological needs of autonomy, competence, and relatedness. The remaining 33% of mediators tested could be characterized as cancer- or cancer treatment-related quality of life outcome variables. For instance, Speck et al.¹⁸ examined whether improvements in quality of life functioned as a mediator of body image as a result of strength training.

There are some methodological factors to consider when interpreting mediation results. It may be that assessing mediating variables that represent the target of treatment are more likely to reflect a priori mediation conceptualizations, as these must be considered and included in the assessments, whereas relationships among different outcome variables can be subjected to mediator analyses after the fact. Also, mediating variables that represent the target of treatment may be more conceptually closely related to outcomes. In an example of a close connection, mindful behavior (observing, describing, acting with awareness, nonjudging of inner experience, and nonreactivity to inner experience), a skill that was specifically taught, was examined as a mediator of the effect of a mindfulness training intervention on perceived stress, avoidance, and positive states of mind.⁷⁹ As an example of a more distal connection, mental quality of life (along with physical quality of life and change in strength), an outcome in its own right, was analyzed as a mediator of weight lifting strength training on body image, self-reported strength and health, and self-rated appearance and sexuality.⁷¹ Similarly, the mediator exercise self-efficacy, a target, could be considered to be quite directly linked to the outcome of minutes of moderate-intensity activity⁷⁰ whereas the link between the mediating variable symptom uncertainty, an outcome, and the outcome of social activities seems somewhat less direct.⁷³

The majority of projects assessed relationships reflecting a single mediating mechanism or a group of single mediating mechanisms. Just two projects assessed possible chains of mediating relationships (but not simultaneously). For example, Rabin et al.⁷⁰ tested whether the effect of an intervention to increase the amount of moderate intensity exercise on minutes of physical activity was mediated by the decisional balance of pros and cons of exercise adoption, exercise self-efficacy or experiential or behavioral processes of change. In addition, minutes of physical activity was tested as a mediator of vigor, fatigue, and perceived physical condition. Similarly, for another intervention designed to facilitate physical activity⁷², physical activity beliefs were tested as a mediator of the effect of the intervention on intentions to exercise, and intentions to exercise were tested as a mediator of physical activity behavior.

Timing of Assessments

As shown in Table 1, for approximately half of the projects (10, or 45%) outcomes included in mediator analyses were assessed some weeks to up to several months after the delivery of treatment (e.g.,^{65,69}) whereas for others (9, or 41%) outcomes were assessed immediately (e.g.,^{74,75}; 2 projects, or 9%, included mediator analyses that involved outcomes assessed both immediately following treatment and at a later follow up). These differences were likely related to variations in the presumed anticipated action of the intervention and the outcome(s) assessed, suggesting that mediators presumed to be working over differing spans of time were being examined in this literature. For instance, a multicomponent or an exercise intervention may work over the long term to have an impact on generalized outcomes like quality of life through a potential mechanism such as increased physical fitness, whereas a session of music therapy or hypnosis is likely to exert its effects on symptoms fairly quickly and in the short term through changes in relaxation or distress. It is also important to note that, whereas in many cases (6 projects or 27%) variables assessed at an earlier time point were tested as mediators of outcomes assessed at a later time point (e.g.,^{55,75,78}), as is recommended by some authors,^{32,42} The remainder assessed proposed mediators and outcomes at the same time point or over the same points in time (see Table 1).

Types of Mediator and Outcome Variables

As also shown in Table 1, the types of mediating and outcome variables comprised (1) variables that could be viewed as primarily psychosocial: emotional/psychological/mental functioning; social/relationship/sexual/family functioning and general quality of life; (2)

variables that could be viewed as physical: subjectively reported physical functioning/symptoms; and objectively measured; medical/physiological/physical measures; finally there were (3) variables related to navigating the treatment process; and (4) variables classified as other (e.g., perceived mastery of various skill, response expectancies) that did not fit any of these categories. The majority of projects (64%) tested at least one relationship between mediators of the same general type (psychosocial mediators of psychosocial outcomes; physical mediators of physical outcomes). However, in keeping with the mind-body focus of some interventions in the field of psychosocial oncology,⁸² 32% of projects examined causal chains that spanned psychosocial and physical parameters. For instance, one study considered the connection between physiological mediators and subjective psychological well-being outcomes in investigating whether change in peak oxygen consumption and peak power output mediated the effect of an exercise intervention on quality of life, mood, self-esteem, and fatigue.⁶⁸ Conversely, another study considered the connection between psychological and subjective mediators and a physiological outcome in investigating whether changes in depressive symptoms, mood, fatigue, and pain mediated the effect of a multicomponent biobehavioral intervention on immune measures.⁵⁶ Another study investigated both physiological (heart rate habituation, heart rate recovery) and psychological (negative mood) mediators of the effect of an intervention (expressive writing) on physical and medical symptoms (physical symptoms, medical appointments).⁷⁸ It may be that detecting mediating relationships that involve variables from different modalities (i.e., mental and physical health) is more challenging than detecting them within a single modality.

Quality of Study Reporting and Methodology

The quality of study reporting and methodology are reported in Table 2. Aspects of reporting that were strong and provided by a majority of the projects involved specifying the number of people approached, initially participating, and dropping out of treatment. The randomization procedure was also described (e.g., method to generated sequence of assignment) for a majority of projects but methods to prevent subterfuge by those making assignments of participants to conditions were documented in just 27% of projects. The delivery of treatment was guided by a manual in 60% of the projects for which this was applicable and the appropriate implementation of treatment was confirmed by monitoring in 82%. In terms of data analysis, a majority of projects (82%) examined whether groups were equivalent on baseline characteristics. Just 50% of projects reported conducting intent-to-treat analyses.

Results of Mediator Analyses

Overall, although there was some evidence supporting selected mediating relationships, the findings were mixed, among both the mediators tested within a single study and those assessed across studies. While some studies provided evidence that changes in psychological variables can serve as mediators of the effects of psychosocial interventions on changes in measures of immune function⁵⁶ and physiological variables like cortisol,⁶⁰ others did not.⁶¹ There also was mixed evidence that changes in physiological (heart rate habituation), physical activity or fitness, and immune variables may serve as mediators for psychological and symptom outcomes, with this relationship being supported for some or all outcomes assessed in some studies,^{68–70,78} but not in others.^{55,62,71} Some of this lack of findings is surprising; for example, that a reduction in fatigue could be brought about by a cognitive-behavioral intervention that focused on physical activity and psychosocial elements without an increase in physical activity.⁶² There were several examples of mediating or partially mediating relationships that were identified when the factor examined was likely to be fairly directly affected by the intervention, such as confidence in ability to relax as a result of training in stress management,⁵⁹ symptom uncertainty as a result of providing concrete

operational information,⁷³ positive reappraisal as a result of a coping and communication enhancing intervention,⁶⁵ expectations for pain and fatigue as a result of hypnosis,⁷⁵ and perceived stress management skills as a result of a stress management intervention.^{63,83}

Other Relevant Studies Not Included in This Review

There were also a small number of studies that had intentions to examine mediating relationships and had assessed relevant variables, but, as is recommended by some authors,^{33,49} did not proceed to examine mediating relationships because initial analyses did not support the effect of the intervention on outcomes. For instance, a study on the effect of cognitive behavioral therapy for insomnia seeking to examine the mediating role of changes in insomnia severity on fatigue, mood, and quality of life did not ultimately test any indirect effects because the intervention was not found to have direct effects on any of the outcomes.⁸⁴ Similarly, another study hypothesized that a decrease in symptom limitations resulting from a nurse-led cognitive-behavioral intervention that used strategies to increase self-efficacy would mediate the effect of the intervention on physical functioning.⁸⁵ This relationship was not tested because no effect of the intervention on physical functioning was identified.

Finally, there were many projects (142, 15%) that assessed variables that could be, or were explicitly considered to be, mediators, but the analyses conducted could provide statistical evidence that was only suggestive of mediation. For instance, a study that examined the effects of progressive resistance exercise training versus standard therapeutic exercise found correlations between improvements in muscular strength and endurance and reductions in shoulder pain, but not reductions in disability.⁸⁶ Similarly, a study that randomized participants to a nurse-led pain education program or usual care examined the correlation between increases in pain knowledge and change in pain scores and found no relationship.⁸⁷ Accordingly, authors would often report that the results provided evidence consistent (or inconsistent) with a mediating hypothesis, but could not justify causal statements.

COMMENT

Current State of the Field

This systematic review of mediating relationships examined in over three decades of empirical research investigating the effects of psychosocial interventions for cancer survivors documented that, overall, these types of analyses were done infrequently, as has been suggested by other authors.⁴⁵ In addition, in this fairly small group of studies, there was much variation in the types of interventions studied, the types of outcomes and mediators assessed, and the timing of the assessment of variables. This resulted in a far from unified picture of how mediating relationships may be operating in this field and precluded empirically synthesizing the data. This is in contrast to other fields where the similarity of variables assessed has made it possible to summarize across studies that have examined comparable mediating relationships. For instance, one review aggregated the evidence provided in 10 studies regarding the hypothesis that cognitive behavioral treatment for alcohol dependence exerts its effects through increasing cognitive and behavioral coping skills.³⁹ Similarly, another review considered whether, across 19 studies, motivational interventions for substance use disorders worked through changes in client change/talk intention, readiness to change, involvement/engagement, resistance, and client experience of discrepancy.⁴⁰ One proposed reason why mediating relationships have been examined infrequently is an understandable focus on what has been considered to be most important in clinical research: testing whether an intervention works better than no intervention or another type of intervention.⁸⁸

The methodological quality of this set of projects reflected strengths with respect to completeness of reporting and treatment delivery, but with some limitations in analytic approach, such as conducting intention-to-treat analyses. This, along with other deficiencies, such as the low rate of implementing (or reporting implementing) measures to prevent subterfuge of the randomization process, may be a result of the fact that the set of studies spans three decades, and the recognition of the importance of these particular methodological quality measures has emerged fairly recently.

Implications

Nonetheless, there was some support for selected purported mechanisms, such as mind-body relationships, whereby changes in subjective psychological measures influenced physiological or health related outcomes, and physiological mediators influenced psychological outcomes. In addition, evidence supported changes in skills or behaviors closely linked to processes addressed by particular components of interventions, although it is also possible that participants exposed to such interventions would be inclined to report such skills as a result of social desirability, wishful thinking, or better understanding of the concepts behind the questions in the assessments.⁷⁹ This evidence offers some promise and suggests the value of future work using dismantling to investigate further various components of interventions.⁵⁹ These include: confidence in ability to relax as a result of training in stress management, symptom uncertainty as a result of providing concrete operational information, positive reappraisal as a result of a coping and communication enhancing intervention, expectations for pain and fatigue as a result of hypnosis, and perceived stress management skills as a result of a stress management intervention.

Furthermore, some findings spoke to how to enhance or theoretically better understand the ways interventions work. For instance, Courneya et al.⁶⁹ concluded that because out of a number of fitness indicators only the change in peak cardiovascular fitness mediated changes in physical functioning, maximizing improvements in this factor may be the best strategy for improving outcomes. In addition, because changes in psychosocial outcomes such as happiness and depression were not mediated by measures of changes in fitness, it may be that other aspects of the intervention, such as increased social interaction and distraction from cancer and its treatments, may be responsible for these positive changes. Similarly, the lack of contribution of presurgery distress to postsurgery pain once response expectancies were taken into account was surprising, but suggested that prior work that has found such a relationship for distress may have done so because response expectancies were not included.⁷⁵ Helgeson et al.⁶⁶ found that improvements in self-esteem, body image, and intrusive thoughts partially explained the effect of an educational intervention, which was unexpected, given that these were hypothesized to be mechanisms underlying the effects of an alternative intervention involving peer discussion groups. These authors reasoned that receiving information may have improved participants' ability to cope, which may have fostered improved feelings about themselves and their bodies.

Summary and Future Directions

In sum, a small proportion of studies of the effects of psychosocial interventions for cancer survivors have included examination of potential mediators of change. This diverse set of studies, reflecting a variety of types of mediating relationships, produced mixed findings, resulting in few clear general conclusions. It is important to continue the work of testing which psychosocial interventions are efficacious in improving quality of life of cancer survivors, particularly as new types of interventions are developed. In addition, potential mediating variables appear to be commonly assessed despite not often being subjected to formal statistical analyses appropriate for determining mediation. Thus, it may be possible to glean information regarding potential mediating relationships fairly readily with the types of

trials that are currently conducted. However, it is also the case that implementing particular procedures integral for the most rigorous testing of mechanisms, such as assessing multiple potential mediating variables multiple times and assessing these prior to assessing outcomes,^{32,35,36} will make study designs somewhat more complicated. Although expanding the focus of research to include the study of mechanisms in psychosocial oncology intervention research will require deliberate and sophisticated efforts, this will be necessary for providing a fuller understanding of how mediating relationships may be operating in this field.

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References

1. Institute of Medicine. Cancer Care for the Whole Patient. The National Academies Press; Washington, DC: 2008.
2. Meyer TJ, Mark MM. Effects of psychosocial interventions with adult cancer patients: a meta-analysis of randomized experiments. *Health Psychol.* 1995; 14:101–108. [PubMed: 7789344]
3. Smith MC, Stullenbarger E. An integrative review and meta-analysis of oncology nursing research: 1981-1990. *Cancer Nurs.* 1995; 18:167–179. [PubMed: 7600548]
4. Trijsburg RW, van Knippenberg FC, Rijpma SE. Effects of psychological treatment on cancer patients: a critical review. *Psychosom Med.* 1992; 54:489–517. [PubMed: 1502290]
5. Devine EC, Westlake SK. The effects of psychoeducational care provided to adults with cancer: Meta-Analysis of 116 studies. *Onc Nurs Forum.* 1995; 22:1369–1381.
6. Newell SA, Sanson-Fisher RW, Savolainen NJ. Systematic review of psychological therapies for cancer patients: overview and recommendations for future research. *J Natl Cancer Inst.* 2002; 94:558–584. 17. [PubMed: 11959890]
7. Rehse B, Pukrop R. Effects of psychosocial interventions on quality of life in adult cancer patients: meta analysis of 37 published controlled outcome studies. *Patient Educ Couns.* 2003; 50:179–186. [PubMed: 12781933]
8. Tatrow K, Montgomery GH. Cognitive behavioral therapy techniques for distress and pain in breast cancer patients: a meta-analysis. *J Behav Med.* 2006; 29:17–27. [PubMed: 16400532]
9. Hersch J, Juraskova I, Price M, Mullan B. Psychosocial interventions and quality of life in gynaecological cancer patients: a systematic review. *Psycho-Oncol.* 2009; 18:795–810.
10. Uitterhoeve RJ, Vernooy M, Litjens M, et al. Psychosocial interventions for patients with advanced cancer - a systematic review of the literature. *Br J Cancer.* 2004; 91:1050–1062. [PubMed: 15316564]
11. Dale HL, Adair PM, Humphris GM. Systematic review of post-treatment psychosocial and behaviour change interventions for men with cancer. *Psycho-Oncol.* 2010; 19:227–237.
12. Kangas M, Bovbjerg DH, Montgomery GH. Cancer-related fatigue: a systematic and meta-analytic review of non-pharmacological therapies for cancer patients. *Psychol Bull.* 2008; 134:700–741. [PubMed: 18729569]
13. Jacobsen PB, Jim HS. Psychosocial interventions for anxiety and depression in adult cancer patients: achievements and challenges. *CA Cancer J Clin.* 2008; 58:214–230. [PubMed: 18558664]
14. Sheard T, Maguire P. The effect of psychological interventions on anxiety and depression in cancer patients: results of two meta-analyses. *Br J Cancer.* 1999; 80:1770–1780. [PubMed: 10468295]
15. Chow E, Tsao MN, Harth T. Does psychosocial intervention improve survival in cancer? A meta-analysis. *Palliat Med.* 2004; 18:25–31. [PubMed: 14982204]
16. Smedslund G, Ringdal GI. Meta-analysis of the effects of psychosocial interventions on survival time in cancer patients. *J Psychosom Res.* 2004; 57:123–131. [PubMed: 15465065]

17. Schmitz KH, Holtzman J, Courneya KS, Masse LC, Duval S, Kane R. Controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. *Cancer Epidemiol Biomarkers Prev.* 2005; 14:1588–1595. [PubMed: 16030088]
18. Speck RM, Courneya KS, Masse L, Duval S, Schmitz K. An update of controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. *J Cancer Surviv.* 2010; 4:87–100. [PubMed: 20052559]
19. Hofmann SG, Sawyer AT, Witt AA, Oh D. The effect of mindfulness-based therapy on anxiety and depression: A meta-analytic review. *J Consult Clin Psychol.* 2010; 78:169–183. [PubMed: 20350028]
20. Roffe L, Schmidt K, Ernst E. A systematic review of guided imagery as an adjuvant cancer therapy. *Psychooncology.* 2005; 14:607–617. [PubMed: 15651053]
21. Redd WH. Behavioral research in cancer as a model for health psychology. *Health Psychol.* 1995; 14:99–100. [PubMed: 7789355]
22. Stanton AL. Psychosocial concerns and interventions for cancer survivors. *J Clin Oncol.* 2006; 24:5132–5137. [PubMed: 17093275]
23. Owen JE, Klapow JC, Hicken B, Tucker DC. Psychosocial interventions for cancer: review and analysis using a three-tiered outcomes model. *Psycho-Oncol.* 2001; 10:218–230.
24. Classen, C.; Sephton, SE.; Diamond, S.; Spiegel, D. Studies of life extending psychosocial interventions. In: Holland, JC., editor. *Psycho-oncology*. Oxford University Press; New York: 1998.
25. Morrow, GR.; Roscoe, JA.; Mustian, KM.; Hickok, JT.; Ryan, JL.; Matteson, S. Behavioral interventions for side effects related to cancer and cancer treatments. American Psychological Association; Washington, D.C.: 2009.
26. Meyer TJ, Mark MM. Statistical power and implications of meta-analysis for clinical research in psychosocial oncology. *J Psychosom Res.* 1996; 41:409–413. [PubMed: 9032705]
27. Schmidt JE, Andrykowski MA. The role of social and dispositional variables associated with emotional processing in adjustment to breast cancer: an internet-based study. *Health Psychol.* 2004; 23:259–266. [PubMed: 15099166]
28. Scheier, MF.; Carver, CS. Adapting to cancer: The importance of hope and purpose. In: Baum, A.; Anderson, BL., editors. *Psychosocial Interventions for Cancer*. American Psychological Association; Washington, DC: 2001.
29. Baum, A.; Posluszny, DM. Traumatic stress as a target for intervention with cancer patients. In: Baum, A.; Anderson, BL., editors. *Psychosocial interventions for cancer*. American Psychological Association; Washington, DC: 2001. p. 143-173.
30. Llewelyn SH, G. Process research in understanding and applying psychological therapy. *J Clin Psychol.* 2001; 40:1–21.
31. MacKinnon DP, Luecken LJ. How and for whom? Mediation and moderation in health psychology. *Health Psychol.* 2008; 27:S99–S100. [PubMed: 18377161]
32. Kraemer HC, Kiernan M, Essex M, Kupfer DJ. How and why criteria defining moderators and mediators differ between the Baron & Kenny and MacArthur approaches. *Health Psychol.* Mar. 2008 27:S101–108. [PubMed: 18377151]
33. Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol.* 1986; 51:1173–1182. [PubMed: 3806354]
34. Hoyle RH, Smith GT. Formulating clinical research hypotheses as structural equation models: a conceptual overview. *J Consult Clin Psychol.* 1994; 62:429–440. [PubMed: 8063970]
35. Kazdin AE, Nock MK. Delineating mechanisms of change in child and adolescent therapy: methodological issues and research recommendations. *J Child Psychol Psychiatry.* 2003; 44:1116–1129. [PubMed: 14626454]
36. Nock MK. Conceptual and design essentials for evaluating mechanisms of change. *Alcohol Clin Exp Res.* 2007; 31:4s–12s. [PubMed: 17880341]
37. Low CA, Stanton AL, Bower JE, Gyllenhammer L. A randomized controlled trial of emotionally expressive writing for women with metastatic breast cancer. *Health Psychol.* 2010; 29:460–466. [PubMed: 20658835]

38. Weersing VR, Weisz JR. Mechanisms of action in youth psychotherapy. *J Child Psychol Psychiatry*. 2002; 43:3–29. [PubMed: 11848335]
39. Morgenstern J, Longabaugh R. Cognitive-behavioral treatment for alcohol dependence: a review of evidence for its hypothesized mechanisms of action. *Addiction*. 2000; 95:1475–1490. [PubMed: 11070524]
40. Apodaca TR, Longabaugh R. Mechanisms of change in motivational interviewing: a review and preliminary evaluation of the evidence. *Addiction*. 2009; 104:705–715. [PubMed: 19413785]
41. Stanton AL. How and for whom? Asking questions about the utility of psychosocial interventions for individuals diagnosed with cancer. *J Clin Oncol*. 2005; 23:4818–4820. [PubMed: 15939929]
42. Stanton AL, Leucken LJ, MacKinnon DP, Thompson EH. Mechanisms in psychosocial interventions for adults living with cancer: Opportunity for integration of theory, research, and practice. *J Consult Clin Psychol*. in press.
43. Moyer A, Sohl SJ, Knapp-Oliver SK, Schneider S. Characteristics and methodological quality of 25 years of research investigating psychosocial interventions for cancer patients. *Cancer Treat Rev*. 2009; 35:475–484. [PubMed: 19264411]
44. Siegel, S.; Castellan, NJ. *Nonparametric statistics for the behavioral sciences*. 2nd ed. McGraw Hill; New York: 1988.
45. Manne SL, Winkel G, Zaidler T, Rubin S, Hernandez E, Bergman C. Therapy processes and outcomes of psychological interventions for women diagnosed with gynecological cancers: A test of the generic process model of psychotherapy. *Journal of Consulting and Clinical Psychology*. 2010; 78:236–248. [PubMed: 20350034]
46. Andersen BL, Shelby RA, Golden-Kreutz DM. RCT of a psychological intervention for patients with cancer: I. mechanisms of change. *J Consult Clin Psychol*. 2007; 75:927–938. [PubMed: 18085909]
47. Creswell JD, Lam S, Stanton AL, Taylor SE, Bower JE, Sherman DK. Does self-affirmation, cognitive processing, or discovery of meaning explain cancer-related health benefits of expressive writing? *Pers Soc Psychol Bull*. 2007; 33:238–250. [PubMed: 17259584]
48. Hopwood CJ. Moderation and mediation in structural equation modeling: Applications for early intervention research. *J Early Interv*. 2007; 29:262–272.
49. MacKinnon DP, Lockwood CM, Hoffman JM, West SG, Sheets V. A comparison of methods to test mediation and other intervening variable effects. *Psychol Meth*. 2002; 7(1):83–104.
50. Shrout PE, Bolger N. Mediation in experimental and nonexperimental studies: New procedures and recommendations. *Psychol Meth*. 2002; 7(4):422–445.
51. Collins LM, Graham JW, Flaherty BP. An alternative framework for defining mediation. *Multivar Behav Res*. 1998; 33:295–312.
52. Moyer A, Finney JW, Swearingen CE. Methodological characteristics and quality of alcohol treatment outcome studies, 1970–98: an expanded evaluation. *Addiction*. 2002; 97:253–263. [PubMed: 11964099]
53. Moher D, Schulz KF, Altman D. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. *JAMA*. 2001; 285:1987–1991. [PubMed: 11308435]
54. Conn VS, Valentine JC, Cooper HM, Rantz MJ. Grey literature in meta-analyses. *Nurs Res*. 2003; 52:256–261. [PubMed: 12867783]
55. Andersen BL, Farrar WB, Golden-Kreutz D, et al. Distress reduction from a psychological intervention contributes to improved health for cancer patients. *Brain Behav Immun*. 2007; 21:953–961. [PubMed: 17467230]
56. Thornton LM, Andersen BL, Schuler TA, Carson WE III. A psychological intervention reduces inflammatory markers by alleviating depressive symptoms: Secondary analysis of a randomized controlled trial. *Psychosom Med*. 2009; 71:715–724. [PubMed: 19622708]
57. Ward S, Donovan H, Gunnarsdottir S, Serlin RC, Shapiro GR, Hughes S. A randomized trial of a representational intervention to decrease cancer pain (RIDcancerPain). *Health Psychol*. 2008; 27:59–67. [PubMed: 18230015]

58. Ward S, Serlin RC, Donovan HS, et al. A randomized trial of a representational intervention for cancer pain: Does targeting the dyad make a difference? *Health Psychol.* 2009; 28:588–597. [PubMed: 19751085]
59. Antoni MH, Lechner SC, Kazi A, et al. How stress management improves quality of life after treatment for breast cancer. *J Consult Clin Psychol.* 2006; 74:1143–1152. [PubMed: 17154743]
60. Cruess DG, Antoni MH, McGregor BA, Kilbourn KM, Boyers AE, Alferi SM, Carver CS, Kumar M. Cognitive-behavioral stress management reduces serum cortisol by enhancing benefit-finding among women being treated for early-stage breast cancer. *Psychosom Med.* 2000; 62:304–308. [PubMed: 10845343]
61. McGregor BA. The effects of a cognitive-behavioral stress management intervention on immune function and positive contributions in younger women with early stage breast cancer. *DAI.* 2000; 61:78.
62. Goedendorp MM, Peters ME, Gielissen MF, et al. Is increasing physical activity necessary to diminish fatigue during cancer treatment? Comparing cognitive behavior therapy and a brief nursing intervention with usual care in a multicenter randomized controlled trial. *Oncologist.* 2010; 15:1122–1132. [PubMed: 20930100]
63. Penedo FJ, Molton I, Dahn JR, et al. A randomized clinical trial of group-based cognitive-behavioral stress management in localized prostate cancer: Development of stress management skills improves quality of life and benefit finding. *Ann Behav Med.* 2006; 31:261–270. [PubMed: 16700640]
64. Phillips KM, Antoni MH, Lechner SC, et al. Stress management intervention reduces serum cortisol and increases relaxation during treatment for nonmetastatic breast cancer. *Psychosom Med.* 2008; 70:1044–1049. [PubMed: 18842742]
65. Manne SL, Winkel G, Rubin S, et al. Mediators of a coping and communication-enhancing intervention and a supportive counseling intervention among women diagnosed with gynecological cancers. *J Consult Clin Psychol.* 2008; 76:1034–1045. [PubMed: 19045971]
66. Helgeson VS, Cohen S, Schulz R, Yasko J. Education and peer discussion group interventions and adjustment to breast cancer. *Arch Gen Psychiatry.* 1999; 56:340–347. [PubMed: 10197829]
67. Hawkins RP, Pingree S, Shaw B, et al. Mediating processes of two communication interventions for breast cancer patients. *Patient Educ Couns.* 2010; 81:S48–53. [PubMed: 21081261]
68. Courneya KS, Mackey JR, Bell GJ, Jones LW, Field CJ, Fairey AS. Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: Cardiopulmonary and quality of life outcomes. *J Clin Oncol.* 2003; 21:1660–1668. [PubMed: 12721239]
69. Courneya KS, Sellar CM, Stevinson C, et al. Randomized controlled trial of the effects of aerobic exercise on physical functioning and quality of life in lymphoma patients. *J Clin Oncol.* 2009; 27:4605–4612. [PubMed: 19687337]
70. Rabin C, Pinto BM, Frierson GM. Mediators of a randomized controlled physical activity intervention for breast cancer survivors. *J Sport Exercise Psychol.* 2006; 28:269–284.
71. Speck RM, Gross CR, Hormes JM, et al. Changes in the Body Image and Relationship Scale following a one-year strength training trial for breast cancer survivors with or at risk for lymphedema. *Breast Cancer Res Treat.* 2010; 121:421–430. [PubMed: 19771507]
72. Vallance JK, Courneya KS, Plotnikoff RC, Mackey JR. Analyzing theoretical mechanisms of physical activity behavior change in breast cancer survivors: results from the activity promotion (ACTION) trial. *Ann Behav Med.* 2008; 35:150–158. [PubMed: 18347895]
73. Christman NJ, Cain LB. The effects of concrete objective information and relaxation on maintaining usual activity during radiation therapy. *Onc Nurs Forum.* 2004; 31:E39–45.
74. Huang S-T. The effects of music on cancer pain. *DAI.* 2006; 67:199.
75. Montgomery GH, Hallquist MN, Schnur JB, David D, Silverstein JH, Bovbjerg DH. Mediators of a brief hypnosis intervention to control side effects in breast surgery patients: response expectancies and emotional distress. *J Consult Clin Psychol.* 2010; 78:80–88. [PubMed: 20099953]
76. Johnson JE, Lauver DR, Nail LM. Process of coping with radiation therapy. *J Consult Clin Psychol.* 1989; 57:358–364. [PubMed: 2738208]

77. Scheier MF, Helgeson VS, Schulz R, et al. Interventions to enhance physical and psychological functioning among younger women who are ending nonhormonal adjuvant treatment for early-stage breast cancer. *J Clin Oncol*. 2005; 23:4298–4311. [PubMed: 15994143]
78. Low CA, Stanton AL, Danoff-Burg S. Expressive disclosure and benefit finding among breast cancer patients: Mechanisms for positive health effects. *Health Psychol*. 2006; 25:181–189. [PubMed: 16569109]
79. Bränström R, Kvillemo P, Brandberg Y, Moskowitz JT. Self-report mindfulness as a mediator of psychological well-being in a stress reduction intervention for cancer patients—A randomized study. *Ann Behav Med*. 2010; 39:151–161. [PubMed: 20177843]
80. Prochaska JO, DiClemente CC. Stages and processes of self-change of smoking: toward an integrative model of change. *J Consult Clin Psychol*. 1983; 51:390–395. [PubMed: 6863699]
81. Ajzen I. The theory of planned behavior. *Organ Behav Hum Decis*. 1991; 50:179–211.
82. Monti DA, Sufian M, Peterson C. Potential role of mind-body therapies in cancer survivorship. *Cancer*. 2008; 112:2607–2616. [PubMed: 18428193]
83. Penedo FJ, Jason R, Dahn Ivan Molton, et al. Cognitive-behavioral stress management improves stress-management skills and quality of life in men recovering from treatment of prostate carcinoma. *Cancer*. 2004; 100:192–200. [PubMed: 14692040]
84. Dirksen SR, Epstein DR. Efficacy of an insomnia intervention on fatigue, mood and quality of life in breast cancer survivors. *J Adv Nurs*. 2008; 61:664–675. [PubMed: 18302607]
85. Doorenbos A, Given B, Given C, Verbitsky N. Physical functioning: effect of behavioral intervention for symptoms among individuals with cancer. *Nurs Res*. 2006; 55:161–171. [PubMed: 16708040]
86. McNeely ML, Parliament MB, Seikaly H, et al. Effect of exercise on upper extremity pain and dysfunction in head and neck cancer survivors: a randomized controlled trial. *Cancer*. 2008; 113:214–222. [PubMed: 18457329]
87. van der Peet E, van den Beuken-van Everdingen M, Patijn J, Schouten H, van Kleef M, Courtens A. Randomized clinical trial of an intensive nursing-based pain education program for cancer outpatients suffering from pain. *Support Care Cancer*. 2009; 17:1089–1099. [PubMed: 19104843]
88. Finney JW. Treatment processes and mediators of substance use disorders treatment effects: the benefits of side road excursions. *Alcohol Clin Exp Res*. 2007; 31:80s–83s. [PubMed: 17880353]

Figure 1.
Flowchart of Study Identification, Retrieval, and Eligibility Determination

Table 1
Characteristics of Studies Investigating Mediators of the Effects of Psychosocial Interventions for Cancer Patients

Study and rationale for mediation analysis	Participants	Treatment conditions	Study design	Potential mediators	Outcomes	Findings
Andersen et al., 2007 As suggested by prior literature, a psychological intervention may improve health by reducing emotional distress or by enhancing functional immunity.	227 women newly diagnosed with regional Stage II (90%) or Stage III (10%) breast cancer who had been surgically treated for breast cancer (median 34 days post-surgery) and were awaiting adjuvant therapy (most women received radiation or chemotherapy during the study year) Average age: 51	Multicomponent biobehavioral intervention (stress conceptualization, relaxation training, social adjustment, diet, exercise, physical function and symptom management, medical provider communication) (12 months total - intensive phase lasted 4 months with 18 weekly 1.5-hour sessions; maintenance phase lasted a further 8 months with 26 weekly sessions; provided in groups of 8 to 12 patients) (M) (n=114) Assessment only control (C) (n=113)	Assessments at baseline (after surgery but before randomization), 4 months (end of intensive phase), 8 months, and 12 months (end of maintenance phase)	Emotional distress reduction – Profile of Mood States (POMS) (EI) (o) Immune function – immunity composite combining T-cell proliferation levels for ConA and PHA (MM) (o)	Health status – composite of Karnofsky Performance Status Scale (functional status) and the Southwest Oncology Collaborative Group (PF) (PF)	Health status (12 months): mediated by POMS (4 months) for women with the highest distress but not mediated by immune function
Thornton et al., 2009	45 women, from the original sample of 227 in Andersen et al. (2007), with clinically significant depressive symptoms at baseline	Same as Andersen et al. (2007) (a = 23 intervention) (n = 22 control)	Same as Andersen et al. (2007)	Depressive symptoms – Center for Epidemiologic Studies Depression Scale (CES-D) (EI) (o) Depressed mood (POMS) (EF) (o) Fatigue (POMS) (EF) (o) Pain - Medical Outcomes Study Short Form, 36 (MOS SF-36) (PF)(o)	White blood cell count (WBC) (MM) Neutrophil count (MM) T Helper/suppressor Ratio (MM)	WBC, neutrophil count, and T helper/suppressor ratio (12 months): mediated by CES-D (8 months); (repeating the analysis using depressed mood or pain as mediators produced identical results) T helper/suppressor ratio (12 months): mediated only by fatigue (8 months) (Post-hoc analyses ruled out the possibility that changes in health behaviors, such as exercise, diet, or cigarette use, mediated the effect of the intervention on outcomes)
Antoni et al., 2006 Aim to determine if changes in self-perceptions of specific skills taught in the intervention account for beneficial effects.	199 women who were diagnosed with Stage III or below breast cancer and were newly treated for non-metastatic breast cancer (surgery within the 8 weeks before the initial assessment); some women receiving	Cognitive-Behavioral Stress Management (CBSM) (aimed at teaching women to cope with daily stressors and to use social resources; e.g., relaxation exercises) (weekly 2-hour sessions for 10 weeks; provided in groups of about 8) (CB) (n = 92) Control seminar (educational version of CBSM intervention) (5–6 hours on 1	Baseline assessment completed 4 to 8 weeks postsurgery (before randomization); assessments at 6 and 12 months post-baseline	Confidence in ability to relax – Measure of Current Status (MOCS Relaxation) (EF) (t)	Recreation and pastimes – Sickness Impact Profile (SIP) (PF) Social interaction SIP (SF) Positive States of Mind (PSOM) (EF) Positive emotional experience – Affects Balance Scale (ABS) (EF)	SIP Recreation and pastimes, SIP Social interaction, PSOM, ABS Positive emotional experience, benefit finding, Benefits: lifestyle change, FACT-B Emotional well-being, FACT-B Additional concerns, IES Intrusion, interviewer rated anxiety, ABS Emotional distress (slope across baseline, 6, and 12 months); mediated by MOCS Relaxation (slope across

Study and rationale for mediation analysis	Participants	Treatment conditions	Study design	Potential mediators	Outcomes	Findings
	adjuvant chemotherapy, radiation therapy, or hormonal therapy Average age: not listed	day, at the midpoint of the 10-week period of the intervention group; provided in groups of about 8) (CB) (n=107)			Benefit finding (EF) (O) Emotional well-being - Functional Assessment of Cancer Therapy-Breast (FACT-B); FACT-B Additional concerns (EI) Thought intrusion - Impact of Events (IES - Intrusion) (EF) Interviewer rated anxiety (EF) Emotional distress - ABS (EF)	baseline, 6, and 12 months); (exploratory analyses using MOCS Coping Confidence were less supportive of meditation; and 8 other stress management skills and non-specific effects were not tested as mediators because they were not affected by the intervention)
Phillips et al., 2008 If women with breast cancer are hyperresponsive to stressful challenges, they may show decreases in cortisol if they are taught stress management techniques that increase their perceived ability to relax.	N=128	Same as Antoni et al. (2006) (n = 63 intervention) (n = 65 control)	Same as Antoni et al. (2006)	Confidence in ability to relax - Measure of Current Status (MOCS Relaxation) (O) (t)	Serum cortisol (MM)	Cortisol (slope of scores across baseline, 6, and 12 months); not mediated by MOCS (slope across baseline, 6, and 12 months)
Bränström et al., 2010 To understand the mechanisms through which mindfulness influences psychological well-being, an aim was to examine if changes in mindfulness mediate intervention effects on outcomes. To better	71 patients (70 women; 1 man) with varying cancer diagnoses who were not undergoing current radiation therapy or chemotherapy Average age: 52 years	Mindfulness training (taught the theoretical foundations of mindfulness, exercises, and meditation) (2-hour weekly sessions for 8 weeks) (CAM) (n = 32) Wait-list control (C) (n = 39)	Assessments at baseline (after randomization), 3 and 6 months post-randomization	Mindfulness - Five-facet Mindfulness Questionnaire (FFMQ) (O)(t)	Perceived stress - Perceived Stress Scale (PSS) (EF) Avoidance - Impact of Events Scale (IES) (EF) Positive emotional and cognitive experiences - PSOM (EF)	PSS, IES, and PSOM (3 months adjusted for baseline); mediated by FFMQ (baseline to 3 months change)
Christman & Cain, 2004 The congruence between expected and experienced physical sensations may be particularly important in producing the beneficial effects of Concrete Objective Information (COI). Uncertainty about sensory experiences	76 patients (52 women; 24 men) receiving radiation therapy (RT) with curative intent for gynecologic, head and neck, or lung cancer; most participants had in situ Stage II disease and were within one month of diagnosis	Concrete objective information (COI) (targeted to cancer type; described experience and symptoms of RT) (EI/I) (n = 25) Relaxation instruction (RI) (instruction for progressive and systematic muscle relaxation) (CB) (n = 25) General RT information control (E/I) (n = 26) Each group received two messages (one during first	Assessments at baseline, week 3 of RT, 2 and 4 weeks post-treatment	Symptom uncertainty - Mishel's Uncertainty in Illness Scale (UII) (o)	Social activity - visual analog scale adaptation of the Sickness Impact Profile(SI)	COI/Social activity (RT week 3); partially mediated by symptom uncertainty (RT week 3) RI (no mediating relationships tested)

Study and rationale for mediation analysis	Participants	Treatment conditions	Study design	Potential mediators	Outcomes	Findings
may disrupt regulation of coping behavior and COI may reduce symptom uncertainty, thereby enhancing coping outcomes.	Average age: 55 years	week of RT and second week during last treatment week)				
Courneya et al., 2003 It was hypothesized that changes in cardiopulmonary function would be correlated with changes in quality of life.	53 postmenopausal early-stage breast cancer survivors with no evidence of recurrent or progressive disease; completed surgery, radiotherapy, and/or chemotherapy with or without current hormone therapy Average age: 59	Supervised exercise (training on cycle ergometers 3 times a week for 15 weeks) (CAM) (n = 25) Wait-list control (C)(n = 28)	Assessments at baseline and 15-week follow-up	Change in peak oxygen consumption (MM)(t) Peak power output (MM)(t)	Overall quality of life – Functional Assessment of Cancer Therapy – Breast (FACT-B) (QL) Quality of life – FACT-G (QL) Quality of life – Trial outcome index (TOI) (QL) Self-esteem – Rosenberg Self-Esteem Scale (EF) Fatigue – Fatigue Scale of FACT (PF) Happiness – Happiness Measure (EF)	FACT-B (baseline to post-intervention change); mediated by peak oxygen consumption (baseline to post-intervention change) TOI (baseline to post-intervention change); mediated by peak oxygen consumption and peak power output (baseline to post-intervention change) Self-esteem (baseline to post-intervention change); not mediated by peak oxygen consumption or peak power output (baseline to post-intervention change) Fatigue (baseline to post-intervention change); mediated by peak power output (baseline to post-intervention change) Results for other outcomes were inconclusive
Courneya et al., 2009 Associations between changes in objective fitness and patient reported outcomes noted in prior literature.	122 patients (50 women; 72 men) with histologically confirmed lymphoma, receiving chemotherapy or no treatment; disease stage varied from no evidence of disease to Stage IV Average age: 53	Supervised aerobic exercise training (AET) (training on cycle ergometers 3 times a week for 12 weeks) (CAM) (n = 60) Usual care (UC) (C) (n = 62)	Assessments at baseline, post-intervention (12 weeks), and 6-month follow-up	Peak oxygen consumption (VO _{2peak}) (MM)(t) Cardiovascular fitness (MM)(t) Peak power output (MM) (t) Ventilatory threshold (MM)(t)	Patient-rated physical functioning – Trial Outcome Index-Anemia (TOI-An) from the Functional Assessment of Cancer Therapy-Anemia (FACT-An) (PF) Total FACT-An (QL) Fatigue – Fatigue subscale of FACT-An (PF) Happiness – Happiness scale (EF) Depression – Center for Epidemiological Studies-Depression (CES-D) (EF)	TOI-An (baseline to post-intervention change); mediated by VO _{2peak} (baseline to post-intervention change) Total FACT-An (baseline to post-intervention change); borderline significant mediation by VO _{2peak} (baseline to post-intervention change) Fatigue (baseline to post-intervention change); borderline significant mediation by VO _{2peak} (baseline to post-intervention change) Happiness (baseline to post-intervention change); not mediated by VO _{2peak} (baseline to post-intervention change) CES-D (baseline to post-intervention change); not mediated by VO _{2peak} (baseline to post-intervention change)

Study and rationale for mediation analysis	Participants	Treatment conditions	Study design	Potential mediators	Outcomes	Findings
Cruess et al., 2000 Positive growth experiences might promote beneficial physiological changes.	34 women currently being treated for early stage (I or II) breast cancer; recruited within 8 weeks of surgery Average age: 46	Cognitive-Behavioral Stress Management (CBSM) (groups of 4 to 6 with training in stress management and relaxation) (weekly 2-hour sessions for 10 weeks) (CB) (n = 24) Control condition (received a 1-day seminar regarding stress management after a 10-week waiting period) (CB) (n=10)	Assessments at baseline (4–8 weeks post-surgery and before randomization) and post-intervention (10 weeks)	Benefit finding – Benefit Finding Scale (BFS) (EF) (o)	Serum cortisol (MM)	Other objective fitness measures did not mediate the effects of AET on outcomes <i>Cortisol (post-treatment adjusted for baseline)</i> ; mediated by BFS (baseline to post-treatment change)
McGregor, 2000 If distress is contributing to decrements in immune function, and if the quality of the immune system is an important factor in breast cancer disease progression, stress management interventions might improve physical as well as the emotional health of women being treated for breast cancer.	29 women being treated for early-stage (0,1 or II) breast cancer who volunteered to be studied for immune function	Same as Cruess et al. (2000) (n=18 intervention) (n = 11 control)	Assessments at baseline and at 3 months post-intervention (6 months osturgery)	Interleukin 2 (IL2) production (MM)(o) Serum cortisol (MM)(o) Feelings of positive contributions from being diagnosed with breast cancer-Positive Contributions Scale (PCS) (EF) (o)	Proliferative response to anti-CD3 (MM)	<i>Proliferative response to anti-CD3 (baseline to 6 months change)</i> ; not mediated by cortisol (post-treatment adjusted for baseline) or PCS (baseline to post-treatment change); because there was no effect of the intervention on IL2, a full test of mediation was not pursued
Goedendorp et al., 2010 Intervening with physical activity to reduce fatigue is based on the assumption that a lack of physical activity and deconditioning during cancer treatment can worsen fatigue.	220 patients (139 women; 81 men) diagnosed with a primary tumor and scheduled to receive treatment with curative intent Average age: 57	Brief nursing intervention focusing on physical activity (BNI) (2 1-hour sessions, 3 months apart) (E/I) (n = 72). Extensive cognitive-behavior therapy (CBT) (same physical activity information as BNI but also had an emphasis on cognitive restructuring, education, and emotional support) (up to 10 1-hour sessions during 6 months; average of 6.2 sessions) (CB) (n = 76) Usual care (UC) (C) (n = 72)	Assessments at baseline and 6 months after baseline (if patients received treatment in the 5 th or 6 th month, they were assessed at least 2 months after the treatments were finished); 26% of participants assessed after surgery or start of hormone therapy but always before adjuvant chemotherapy or radiotherapy	Physical activity – actigraphy (MM)(t) Physical activity – Daily Observed Activity (DOA) (PF)(t) Compliance with advice concerning physical activity (QPA) (O)(t)	Fatigue severity – fatigue subscale of the Checklist Individual Strength (CIS) (PF)	<i>Fatigue (baseline to at least 2 months post-cancer treatment change)</i> ; not mediated by physical activity, DOA, or QPA (baseline to at least 2 months post-cancer treatment change)

Study and rationale for mediation analysis	Participants	Treatment conditions	Study design	Potential mediators	Outcomes	Findings
Hawkins et al., 2010 Self-Determination Theory posits that quality of life is based on the extent to which three basic needs for autonomy, competence, and relatedness are met. These needs are likely to be affected by the diagnosis and treatment of breast cancer and the interventions tested may help recover these.	434 women newly diagnosed with primary breast cancer (within the past 2 months)	Web-based Comprehensive Health Enhancement Support System (CHES); breast cancer information and discussion group) and Internet training and access (M) ($n = 111$) Mentor (10 phone calls over 6 months) and Internet training and access (E/I) ($n = 106$) CHES, Mentor, and Internet training and access (M) ($n = 105$) Internet training and access (E/I) ($n = 112$)	Assessments at baseline and 6 weeks into the intervention (total intervention was 6 months)	Self-determination constructs including the following: Autonomy (EF) (t) Competence (EF) (t) Relatedness (EF) (t)	Quality of life – World Health Organization Quality of Life (WHOQOL-BREF) (QL)	CHES + Mentor (vs. Internet only condition) <i>Quality of life (6 weeks adjusted for baseline):</i> mediated by autonomy, competence, and relatedness (baseline to 6 weeks change) CHES + Mentor (vs. CHES) <i>Quality of life (6 weeks adjusted for baseline):</i> mediated by relatedness but not autonomy or competence (baseline to 6 weeks change) CHES + Mentor (vs. Mentor) <i>Quality of life (6 weeks adjusted for baseline):</i> not mediated by autonomy, competence, or relatedness (baseline to 6 weeks change)
Helgeson et al., 1999 Education and informational support was expected to enhance sense of control over the illness and reduce feelings of uncertainty and confusion. Peer discussion and its associated provision of emotional support was expected to enhance self image and positive social comparisons. Both interventions were expected to reduce	312 women being treated for early stage breast cancer (Stage I, II, or III) with surgery and adjuvant chemotherapy (two-thirds were undergoing chemotherapy during the intervention) Average age: 48	Education-based group intervention (emphasis on how to enhance patient control of illness; e.g., exercise, adverse effects of chemotherapy) (weekly meetings for 8 weeks for 45 minutes; facilitators called once per month for 3 months post-intervention to reinforce principles of the group) (E/I) ($n = 79$), Peer discussion-based group intervention (focused on expression of feelings) (weekly meetings for 8 weeks for 60 minutes; 3 additional monthly meetings held) (SS) ($n = 74$) Combination of Education and Peer discussion (M) ($n = 82$) Control (C) ($n = 77$)	Assessments at baseline, 1–2 weeks post-intervention, and 6 months post-intervention	Illness uncertainty (TP) (o) Frequency of discussing illness with network members (SF) (o) Self-esteem – Rosenberg Self-Esteem Scale (EF) (o) Body image – based on the Cancer Rehabilitation Evaluation System (EI) (o) Intrusive thoughts Impact of Event Scale (IES) (EF) (o) Vicarious control (EF) (o) Personal control (EF) (o)	Physical component score (PCS) of the MOS SF-36 (PF) Mental component score (MCS) of the MOS SF-36 (EF) Positive Affect (PA) – Positive and Negative Affect Scale (EF)	Education-based group intervention <i>PCS (1–2 weeks post-intervention adjusted for baseline):</i> mediated by self-esteem and body image but not by frequency of discussing illness or illness uncertainty (post-intervention adjusted for baseline) <i>MCS (1–2 weeks post-intervention adjusted for baseline):</i> mediated by self-esteem but not frequency of discussing illness, uncertainty, or body image (post-intervention adjusted for baseline) <i>PA and MCS (6 months post-intervention adjusted for baseline):</i> mediated by intrusive thoughts but not by vicarious control or personal control (6 months adjusted for baseline) <i>PCS (6 months post-intervention adjusted for baseline):</i> not mediated by intrusive thoughts, vicarious control, or personal control (6 months adjusted for baseline) Peer discussion-based group (no mediating relationships were tested) Combination of Education and Peer discussion (no mediating relationships were tested)

Study and rationale for mediation analysis	Participants	Treatment conditions	Study design	Potential mediators	Outcomes	Findings
<p>invasive thoughts about the illness.</p> <p>Huang, 2006 Previous authors posit that the mechanisms of the effects of music on pain relate to mind-body effects related to changes in the autonomic nervous system that work through distraction (consuming some attentional capacity to perceive pain) and the relaxation response (that evokes a hypometabolic state and an endomorphinergic mechanism).</p>	<p>126 hospitalized cancer (e.g., leukemia, lymphoma, oral cancer, etc.) patients (38 women; 88 men) who reported pain in the past 24-hour period; admitted for treatment or complications or palliative care; Stage of diagnosis varied (54% Stage IV); 64% metastatic cancer</p>	<p>Music listening (choice of four music intervention tapes) (1 30-minute session) (CAM) ($n = 62$) Control (rested in bed for 30 minutes) (C) ($n = 64$)</p>	<p>Assessments at baseline and post-intervention (after the 30-minute intervention or control)</p>	<p>Relaxation – Relaxation Mastery Scale (RMS) (O)(t) Relaxation – Relaxation visual analogue scale (R-VAS) (PF)(t) Distraction – Activity Attention visual analogue scale (AA-VAS) (O)(t)</p>	<p>Pain sensation – visual analogue scale (VAS) (PF) Pain distress – VAS (PF)</p>	<p><i>Pain sensation VAS (post-test):</i> mediated by R-VAS and distraction VAS but not by RMS (post-test) <i>Pain distress VAS (post-test):</i> mediated by R-VAS and AA-VAS but not by RMS (post-test)</p>
<p>Johnson et al., 1989 Self-regulation theory posits that directing attention away from the emotional dimensions of a stressful experience is associated with reduced distress. A schema of an impending experience that includes concrete objective, rather than emotional features can dampen emotional responses, facilitate the processing of incoming information, and increase confidence in coping. A concrete objective informational intervention was hypothesized to affect outcomes by influencing attention focus and informational processing as reflected in perceptions of the degree of similarity between expectations and experience and a</p>	<p>84 male outpatients receiving radiation therapy (RT) as curative therapy for localized prostate cancer Average age: 68</p>	<p>Concrete objective information intervention (audiotapes describing a phase of the RT experience) (4 occasions: prior to the treatment planning session, prior to the first treatment, at the fifth treatment, and during the last week of treatment) (E/I) ($n = 42$) Routinely received information (4 occasions) (E/I) ($n = 42$)</p>	<p>Assessments during RT (third treatment, which was 5–10 days after the treatment planning session – 1 week, 3 weeks into treatment, and last week of treatment), 1 month post-RT, and 3 months post-RT</p>	<p>Similarity between expectations and experience (TP) (t) Sense of understanding one's experience (TP) (t)</p>	<p>Disruption in usual activities – Recreation and pastime (RP) subscale of the Sickness Impact Profile (SIP) (PF)</p>	<p><i>RP (sum over 1st, 3rd, and last week of radiation treatment and 1 month and 3 months post-treatment):</i> mediated by understanding of one's experience and by the similarity between expectations and experience when these mediators were considered together but this effect was primarily attributable to understanding of one's experience (post-treatment planning session and post-first treatment)</p>

Study and rationale for mediation analysis	Participants	Treatment conditions	Study design	Potential mediators	Outcomes	Findings
<p>Low et al., 2006</p> <p>Both written expressive disclosure and benefit finding were hypothesized to improve health outcomes by enhancing regulation of stress-related physiological, affective, and cognitive experience. Writing about one's deepest thoughts and feelings about cancer might do so by autonomic habituation, or a decrease in physiological arousal, to negative thoughts and memories about cancer. Writing about one's positive thoughts and feelings about cancer might do so through the experience and expression of positive emotions, "undoing" arousal associated with these stressful thoughts and renewing engagement with meaningful life goals.</p>	<p>60 women with a first diagnosis of Stage I or II breast cancer who had completed primary medical treatment (surgery, radiotherapy, and/or chemotherapy) in the last 5 months</p>	<p>Writing about deepest thoughts and feelings about breast cancer (EMO) (4 sessions lasting 20 minutes within a 3-week period) (O)</p> <p>Writing about positive thoughts and feelings about breast cancer (POS) (4 sessions) (O) ($n = 21$),</p> <p>Control condition that involved writing about facts of the breast cancer experience (CTL) (4 sessions) (O) ($n = 18$)</p>	<p>Assessments at baseline and 3 months after the end of treatment</p>	<p>Heart rate habituation during writing (MM)(t)</p> <p>Heart rate recovery (MM)(t)</p> <p>Negative mood – POMS Distress (EF) (o)</p>	<p>Physical symptoms (PD)</p> <p>Medical appointments for cancer-related morbidities (prospective recording over 3 months post-treatment and verified by medical records if possible) (MM)</p>	<p><i>Physical symptoms (3 months adjusted for baseline):</i> mediated by heart rate habituation (within session baseline to post-writing change, averaged across sessions) for EMO group; no mediating effects of heart rate recovery or negative mood <i>Medical appointments (3 months):</i> no mediating effects</p>
<p>Manne et al., 2008</p> <p>The effects of a coping and communication enhancing intervention would be mediated by psychological processes targeted: increased positive reappraisal, acceptance, planful problem solving, emotional processing, emotional expression, seeking emotional and instrumental support, and self-esteem. The effects of a supportive counseling intervention</p>	<p>353 women diagnosed with primary gynecological cancers (more than half with Stage III or IV disease; 33% with Stage I; 121 patients metastatic) and undergoing active medical treatment Average age: 55</p>	<p>Coping and Communication-Enhancing Intervention (CCI) (e.g., enhancing coping skills, evaluating and altering life priorities, dealing with emotional reactions to cancer) (6 1-hour sessions plus one booster session that took place one week after the sixth session) (C/P) ($n = 122$)</p> <p>Supportive Counseling (SC) (enhancing adaptation by encouraging emotional expression and coping behaviors) (6 sessions plus one booster session) (C/P) ($n = 120$)</p>	<p>Assessments at baseline (preintervention), 3 months, 6 months, and 9 months post-baseline</p>	<p>Positive reappraisal – COPE (EF) (t)</p> <p>Acceptance – COPE (EF) (t)</p> <p>Planful problem-solving – COPE (EF)</p> <p>Seeking support for emotional reasons – COPE (EF) (t)</p> <p>Seeking support for instrumental reasons – COPE (EF) (t)</p> <p>Emotional processing – Emotional expression scale (EF) (t)</p> <p>Expression of positive emotion – Emotional</p>	<p>Depression – Beck Depression Inventory (BDI) (EF)</p>	<p>CCI BDI (over baseline, 3, 6, and 9 months): mediated by positive reappraisal, planful problem solving, and self-esteem, and partly mediated by expression of positive emotion and expression of intimacy but not the other potential mediators (over baseline, 3, 6, and 9 months)</p> <p>SC BDI (over baseline, 3, 6, and 9 months): partially mediated by positive reappraisal but not by other potential mediators</p>

Study and rationale for mediation analysis	Participants	Treatment conditions	Study design	Potential mediators	Outcomes	Findings
would be mediated by processes that it fostered: increasing emotional expression, increasing attempts to understand emotional reactions to cancer, and improve self-esteem. The first intervention taught specific adaptive coping strategies whereas the second supported existing adaptive coping.		Usual Care (UO) (C) (n = 111)		Expressivity Questionnaire (EEQ) (EF) (t) Expression of intimacy – EEQ (EF) (t) Expression of negative emotion – EEQ (EF) (t) Cancer-related emotional expression – Emotional expression scale (EF) (t) Self-esteem – Rosenberg Self-Esteem Inventory (EF) (t)		
Montgomery et al., 2010 Previous research suggests that specific expectancies for nonvolitional outcomes (reflecting automatic rather than behavioral or external processes) and emotional distress mediate the benefits of presurgical hypnosis on postsurgical side effects.	200 women immediately prior to breast-conserving surgery (i.e., excisional breast biopsy or lumpectomy) Average age: 49	Hypnosis (one 15-minute session within 1 hour of before surgery) (CB) (n = 105) Attention control (C) (n = 95)	Assessments prior to surgery (baseline expectations, prior to intervention), following the intervention, and following surgery	Response expectancies for post-surgical pain (O) (t) Response expectancies for post-surgical nausea (O) (t) Response expectancies for post-surgical fatigue (O) (t) Emotional distress – Short Version of the Profile of Mood States (SV-POMS) (EF) (O)	Postsurgical pain (VAS) (PF) Postsurgical nausea (VAS) (PF) Postsurgical fatigue (VAS) (PF)	<i>Pain (post-surgery)</i> : partially mediated by response expectancies for pain (post-intervention adjusted for pre-intervention) but not by SV-POMS <i>Nausea (post-surgery)</i> : partially mediated by SV-POMS but not by response expectancies for nausea (post-intervention adjusted for pre-intervention) <i>Fatigue (post-surgery)</i> : partially mediated by both response expectancies for fatigue (post-intervention adjusted for pre-intervention) and SV-POMS
Penedo et al., 2004 Intervention-associated improvements in quality of life were expected to be mediated by increased stress-management skills gained through a stress management intervention.	92 localized prostate cancer (Stage I or II) patients who underwent either radiation therapy or radical prostatectomy (RP) within past 18 months; no adjuvant treatment for prostate cancer Average age: 63	Cognitive-behavioral stress management (CBSM) (emphasized education and relaxation) (2-hour group sessions weekly for 10 weeks) (CB) (n = 52) Seminar control (emphasized relaxation; one 4-hour session; occurred during weeks 5 and 6 after baseline assessments) (CB) (n = 40)	Assessment at baseline; CBSM participants reassessed 2–3 weeks post-intervention (7–8 weeks after seminar); control participants reassessed 12–13 weeks after baseline assessment	Perceived stress-management skills (PSMS) – Measure of Current Status (MOCS) (O) (t)	Quality of life (QOL) – Functional Assessment of Cancer Therapy-General (FACT-G) (QL)	<i>QOL (post-intervention adjusted for baseline)</i> : mediated by PSMS (pre- to post-intervention change)
Penedo et al., 2006 Individuals who are able to share their cancer experience with empathetic others may be more likely to begin cognitive restructuring and a search for meaning.	191 men who had undergone radical prostatectomy or radiation therapy for localized prostate cancer Average age: 65	Same as Penedo et al. (2004) (n = 107 intervention) (n = 84 control)	Same as Penedo et al. (2004)	PSMS – MOCS (O) (t)	QOL – FACT-G (QL) – Benefit Finding (BF) – Positive Contributions Scale – Cancer (PCS-C) (EF)	<i>Post-intervention BF and QOL (post-intervention adjusted for baseline)</i> : mediated by change in PSMS (pre- to post-intervention change)

Study and rationale for mediation analysis	Participants	Treatment conditions	Study design	Potential mediators	Outcomes	Findings
Interventions that emphasize cognitive coping skills such as reframing and replacement of irrational thoughts may foster processing difficult material. Interventions that include affect regulation, anxiety reduction, stress management exercises like muscle relaxation, guided imagery, and deep breathing may decrease vigilance and equip participants with tools to manage the emotions associated with traumatic experiences.	86 sedentary breast cancer survivors who had been diagnosed with Stage 0-II BRCA over past 5 years and had completed treatment (surgery, chemotherapy, and/or radiation therapy) for Stage I or II breast cancer. Average age: 53	Home-based, moderate-intensity physical activity (PA) program (instruction on how to exercise, based on stage of change from Transtheoretical Model; goals for length and frequency of exercise increased over study period) (12 weeks; received telephone call each week for counseling and help) (E/I) (<i>n</i> = 43) Contact control condition (told not to change exercise behavior over the 12 study weeks; received phone call each week) (C) (<i>n</i> = 43)	Assessments at baseline, post-intervention (12 weeks), 6 months post-baseline, and 9 months post-baseline	Decisional balance – Pros and Cons of exercise adoption (O) (t) Exercise self-efficacy (EF) (t) Processes of behavior change Exercise Processes of Change questionnaire (included experiential and behavioral processes) (O) (t) Fitness – Rockport One-Mile Walk Test (MM) (o) Minutes of moderate-intensity physical activity – 7-day Physical Activity Recall – 7-day PAR (MM) (t)	Minutes of moderate-intensity physical activity (MM) Vigor – POMS (EF) Fatigue – POMS (EF) Perceived physical condition – Body Esteem Scale (PF)	<i>Minutes of moderate-intensity physical activity (post-intervention adjusted for baseline);</i> not mediated by decisional balance, self-efficacy, or experiential or behavioral processes of change (baseline to post-intervention) <i>Vigor (post-intervention adjusted for baseline);</i> mediated by minutes of moderate-intensity physical activity but not fitness (baseline to post-intervention) <i>Fatigue (post-intervention adjusted for baseline);</i> marginally mediated by fitness but not minutes of moderate-intensity physical activity (baseline to post-intervention) <i>Perceived physical condition (post-intervention adjusted for baseline);</i> not mediated by fitness or minutes of moderate-intensity physical activity (baseline to post-intervention)

Study and rationale for mediation analysis	Participants	Treatment conditions	Study design	Potential mediators	Outcomes	Findings
Scheier et al., 2005 Five variables that represented mechanisms targeted by the intervention were examined: knowledge and skills to increase confidence in self-care were expected to increase self-efficacy; information and skills were expected to decrease distress surrounding the illness and thus reduce intrusive thoughts; coping skills were thought to enhance aspects of actual coping; information was thought to enhance feelings about appearance and therefore enhance levels of femininity and sexual desirability; information and skills were also thought to reduce cancer-related worries.	252 women (50 years or younger) who had completed active nonhormonal adjuvant therapy within the past 2 months and had been diagnosed with Stage 0, I, or II breast cancer with 10 or fewer positive lymph nodes (mean time since diagnosis: 6 months) Average age: 44	Educational intervention (emphasized psychosocial issues for younger women with breast cancer; groups ranged from 2 to 11) (4 group sessions meeting once a month for 2 hours) (E/I) ($n = 85$) Nutritional intervention (4 group sessions meeting once a month for 2 hours) (E/I) ($n = 83$) Standard medical care control (C) ($n = 84$)	Assessments at baseline, 4 months post-baseline (post-intervention), and 13 months post-baseline (9 months post-intervention)	Intrusive thoughts – Intrusive Thoughts subscale of the IES (EF) (O) Self-efficacy expectancies (O) (I) Cancer concerns – Profile of Concerns about Breast Cancer Scale (EF) (O) Self-concept perceptions (EF) (O) Coping – abbreviated version of the situational COPE scale (EF) (I)	Depressive symptoms – CES-D (EF) Physical functioning – Total physical functioning score (PCS) of the MOS SF-36 (PF)	Educational intervention <i>CES-D (9 months post-intervention)</i> : mediated by intrusive thoughts, concerns regarding cancer recurrence and mortality, self-concept perceptions, and planning coping; (when considered simultaneously, only intrusive thoughts, self-concept perceptions, and self-efficacy expectancies were independent mediators) <i>PCS (post-intervention)</i> : no mediating effects <i>PCS (9 months post-intervention)</i> : mediated by cancer concerns regarding recurrence and mortality and marginally mediated by intrusive thoughts and self-concept perceptions, but not self-efficacy expectancies and planning coping; (when considered simultaneously, only cancer concerns regarding recurrence and mortality was an independent mediator) Nutritional intervention <i>CES-D (9 months post-intervention)</i> : mediated by intrusive thoughts, self-efficacy expectancies, cancer concerns regarding recurrence and mortality, self-concept, and denial coping; (when considered simultaneously, only intrusive thoughts, self-concept perceptions, and self-efficacy expectancies were independent mediators) <i>PCS (post-intervention)</i> : marginally mediated by self-concept perceptions but not by intrusive thoughts <i>PCS (9 months post-intervention)</i> : mediated by intrusive thoughts, cancer concerns regarding recurrence and mortality, self-concept perceptions, and self-efficacy expectancies; (when considered simultaneously only cancer concerns regarding recurrence

Study and rationale for mediation analysis	Participants	Treatment conditions	Study design	Potential mediators	Outcomes	Findings
Speck et al., 2010 The functionality and ability of the body to perform tasks are believed to be important to one's body image; thus an increase in muscle strength as a result of a strength training intervention would lead to improved perceived body image.	234 breast cancer survivors (history of unilateral non-metastatic breast cancer diagnosis 1 year or more before study entry; currently cancer free) with or at risk for lymphedema Average age: 57	Weight lifting strength training (instructed twice-weekly for the first 13 treatment weeks in weight training in groups of 2-6) (Total intervention lasted 12 months) (CAM) (<i>n</i> = 113) Wait list control (instructed to not change activity level) (C) (<i>n</i> = 121)	Assessments at baseline and 12 months	Quality of life - SF 36 Version 2 Physical Composite Score (PCS) and Mental Composite Score (MCS) (QL) (o) Bench press and leg press percent change (from baseline to 12-month follow-up) (MM) (t)	Body image - Body Image and Relationships Scale (BIRS) total and subscales: Strength and health; Social barriers; Appearance and sexuality (EF)	<i>BIRS total and subscale scores (baseline to 12 months):</i> not mediated by PCS and MCS, or bench and leg press percent change (baseline to 12 months)
Vallance et al., 2008 An intervention designed to facilitate physical activity based upon the Theory of Planned Behavior would influence physical activity behavior through specific constructs related to the theory, belief changes and planning strategies (i.e., implementation intentions).	377 breast cancer survivor (histologically confirmed Stages I to IIIa breast cancer, postadjuvant therapy except hormone therapy, and no current disease) Average age: 58	Theory of Planned Behavior (TPB)-based physical activity behavior change intervention (one session in which given print materials that focused on belief change and planning strategies for PA) or a combination of the intervention and a pedometer (INT) (E/I) (<i>n</i> = 187) Standard public health recommendation for physical activity (SR) (C) (<i>n</i> = 96) (an additional condition, <i>n</i> = 94, was not included in the analyses)	Assessments at baseline, 4 weeks, and 12 weeks post-intervention	Intention to exercise (O) (t)Planning to exercise (O) (t) Physical Activity beliefs (normative, behavioral, and control), norms, attitudes, and perceived behavioral control (O) (t)	Physical Activity (PA) - Leisure score index (LSI) of the Godin Leisure-Time Exercise Questionnaire (GLTEQ) (PF) Intention to exercise (O)	<i>LSI (12 weeks):</i> partially mediated by intentions to exercise and planning to exercise (4 weeks) (possible mediating effects of remaining TPB variables were not tested due to weak correlations between them and the intervention and PA behavior) <i>Intention to exercise (12 weeks):</i> mediated by the behavioral and control beliefs of "live longer," "reduce the risk of my cancer recurring," "had no support," "additional responsibilities," and "didn't fit routine" (4 weeks)
Ward et al., 2008 An intervention based on a Representation Approach (based on theory regarding cognitive representations of illness and the process of conceptual change), which assesses a patient's representation about a health problem and can change misconceptions (barriers) that are embedded in that representation.	176 metastatic cancer patients (101 women; 75 men) with cancer-related pain during the past two weeks Average age: 55	Repre sensation Intervention to Decrease Cancer Pain (RIDCancerPain) (identifying and changing the patient's misconceptions of pain) (1 session lasting 20 minutes to one hour; follow-up telephone call 2-3 days after the session) (CB) (<i>n</i> = 118) Standard Educational Intervention Control (SEI) (booklet discussing pain medication and follow-up telephone call to answer questions 2-3 days after reading the booklet) (E/I) (<i>n</i> = 104)	Assessments at baseline, 1 month, and 2 months later	Beliefs about reporting pain and analgesic use - Barriers Questionnaire II (BQ) (O)(t)	Pain - Usual Severity (PF) Pain - Usual Severity (baseline to 2 months) (PF) Pain - Usual Severity (baseline to 1 month); not mediated by BQ (baseline to 1 month) (The mediating role of coping was not examined because there was no effect of the intervention on coping)	<i>Pain - Usual Severity (baseline to 2 months):</i> mediated by BQ (baseline to 2 months) <i>Pain - Usual Severity (baseline to 1 month):</i> not mediated by BQ (baseline to 1 month) (The mediating role of coping was not examined because there was no effect of the intervention on coping)
Ward et al., 2009 An intervention based on a Representational	161 cancer patients (96 women; 65 men) with moderate	Repre sensation educational intervention delivered to patient-significant other pairs	Randomly assigned to Dyad (<i>n</i> = 51),	BQ-II (O)(t)	Pain severity - Brief Pain Inventory Short Form (BPI) (PF)	Dyad and Solo Patients' pain severity, pain relief, pain interference, negative mood, and

Study and rationale for mediation analysis	Participants	Treatment conditions	Study design	Potential mediators	Outcomes	Findings
Approach, which elicits and seek to understand a patient's representation of an illness before providing new information, can overcome attitudinal barriers to reporting pain and using analgesics and thereby decrease pain severity and improve quality of life.	to severe pain in the past two weeks Average age: 59	(Dyad) (RID) Cancer Pain intervention involved identifying and replacing misconceptions about pain in a single session that lasted 20–80 minutes; in dyad condition, received intervention with SO; follow-up phone calls to help with planning at 2 and 4 weeks after the first session (received intervention with SO) (CB) (n = 51) Representational intervention delivered to patient (Solo) (CB) (n = 53) Care as usual (C) (n = 57)	Solo (n = 53), or control (n = 57) Assessments at baseline, 5 weeks later, and 9 weeks later		Pain relief (from pain management) (PF) Pain interference – BPI (PI) Negative mood – subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (QLQ-C30) (EF) Global quality of life (QOL) – items from the FACT-G and the QLQ-C30 (QL)	global QOL (baseline to 9 weeks); mediated by BQ (baseline to 9 weeks); (other mediating relationships were not tested because the intervention-mediator paths were not significant for patients' or significant others' for baseline to 5 weeks, or for significant others' for 9 weeks)

Note: N's refer to number of participants initially included in study. Studies presented in same cell outlined with solid borders represent overlapping samples or samples combined in other project publications. Studies measured multiple outcome variables. Only outcome variables relevant to mediation analyses are included in the table. Intervention types: C= No treatment or treatment as usual control; CAM = Complementary or alternative mind-body approach; CB = Cognitive, behavioral, or cognitive-behavioral therapy; C/P = Counseling or Psychotherapy (nonbehavioral); E/I = Education/Information; M = Multimodal intervention; O = Other type of intervention; SS = Social support by non-professionals. Mediator/Outcome types: EF = Emotional/Psychological/Mental Functioning;; MM = Medical/Physiological/Physical Measures; O = Other outcome; PF = Physical Functioning/Symptoms ; QL = Quality of life; SF = Social/Relationship/Sexual/Family Functioning; TP = Navigating the cancer treatment process. Types of mediators: (o) outcome-related; (t) intervention- or target of treatment-related.

Table 2

Quality of Study Methodology and Reporting

	Projects (<i>n</i> = 22)
	%
Sample description	
Reported number approached to participate	54.5
Reported number initially participating	100.0
Compared characteristics of participants to eligible non-participants	13.6
Reported number dropping out of treatments	72.7
Research Design	
Quality of randomization	
Method only stated to be randomized	31.8
Randomization procedure described but no measures to prevent subterfuge included	27.3
Randomization procedure described and measures to prevent subterfuge included	40.9
Intervention provision and specification	
Manuals used to guide treatment (where applicable, <i>N</i> =15 applicable intervention conditions)	60.0
Intervention implementation assessed	
Intervention monitored	81.8
Assessed immediate effects of intervention	18.3
Additional unintended intervention monitored	18.2
Contamination monitored	4.5
	%
Data Analyses	
Groups compared for equivalence at baseline	81.8
Interaction between treatment condition and participant baseline characteristics in relation to dropout status (where applicable <i>N</i> = 21)	33.3
Intention-to-treat analyses conducted	50.0