A Systematic Review of Nonpharmacologic Interventions for Treatment-Related Symptoms in Women With Ovarian Cancer

Lorie L. Davis, MSN, RN, OCN®, and Janet S. Carpenter, PhD, RN, FAAN

Background: Women with ovarian cancer have a continued high symptom burden in comparison to other cancer survivors secondary to ongoing chemotherapy treatment. Prolonged or ineffective management of treatment-related symptoms can contribute to treatment noncompliance, worsening of symptoms, and reduced health-related quality of life.

Objectives: This review of the literature was conducted to describe experimental and quasi-experimental research addressing nonpharmacologic interventions for the treatment-related symptoms of sleep disturbance, pain, anxiety, depression, and low energy or fatigue in women with ovarian cancer and to critique the quality of interventions.

Methods: A systematic search of the literature was conducted in PubMed and yielded 136 articles. Eight articles met the inclusion criteria and were evaluated.

Findings: Nonpharmacologic interventions for treatment-related symptoms were complex, with an average of 4.4 components. Intervention delivery, setting, and exposure varied widely across studies. Only three studies contained details sufficient to replicate the intervention. Lack of clarity in intervention reporting may explain perceptions of clinically inefficacious symptom management in this context. Greater attention to reporting would facilitate better translation of interventions into practice and when addressing complex cancer symptom clusters.

Ovarian cancer (OC) affects more than 21,000 American women annually (American Cancer Society [ACS], 2015). OC continues to have the highest mortality rate of all cancers affecting the female reproductive system, with more than 14,000 estimated deaths expected in the United States in 2015 and a five-year survival rate of 45% for all stages (ACS, 2015; Almadrones-Cassidy, 2010; Hess & Stehman, 2012). Despite advances in treatment, women with OC have demonstrated little improvement in survival, although these women have experienced slowed progression of the disease, ultimately extending life with active disease (Hess & Stehman, 2012; Riester et al., 2014). Most women present with advanced disease at diagnosis; 61% of cases are diagnosed at a distant stage (ACS, 2015). Many women respond to initial surgery and postoperative chemotherapy; however, the majority of women experience disease recurrence, requiring ongoing chemotherapy treatment (Davis, Tinker, & Friedlander, 2014; Riester et al., 2014; Sjoquist et al., 2013). Therefore, women with OC have a continued high symptom burden in comparison to other cancer survivors (Fox & Lyon, 2007).

Alleviating treatment-related symptoms is essential in cancer care (Cleeland et al., 2013). The concept of symptom clusters, a current research priority, suggests that two or more co-occurring symptoms may not be independent entities but rather symptoms interacting synergistically (Aktas, 2013; Barsevick &
Aktas, 2013). Individuals undergoing cancer chemotherapy experience certain clusters of treatment-related symptoms (Wood & Weymann, 2013). Among all cancer survivors, frequently reported treatment-related symptoms include sleep disturbance, pain, anxiety, depression, and low energy or fatigue (SPADE) (Aktas, 2013; Cleeland et al., 2013; Oh, Seo, Jeong, & Seo, 2012; Thomas et al., 2014; Wood & Weymann, 2013; Yarbro, Wujcik, & Holmes-Gobel, 2014). Prolonged or ineffective management of treatment-related SPADE symptoms may contribute to treatment nonadherence (and poorer outcomes), worsening of symptoms, and reduced health-related quality of life (Yarbro et al., 2014). Therefore, research on interventions to address SPADE symptoms—whether as co-occurring symptom clusters or individual symptoms—in patients with cancer is critically important (Berger, Yennu, & Million, 2013).

The purpose of this article is to review the published oncology symptom management literature focusing on the quality of nonpharmacologic interventions for chemotherapy-related SPADE symptoms in women treated for a primary diagnosis of OC, an understudied population predominately affected by treatment-related symptoms. SPADE symptoms are the most prevalent and co-occurring symptoms in both cancer and non-cancer populations (Kroenke, 2014). This was recognized in developing the Patient-Reported Outcomes Measurement Information System (PROMIS), where five of seven domains are the SPADE symptoms (Cella et al., 2010). Specific aims were to (a) describe the experimental and quasi-experimental research addressing nonpharmacologic interventions for one or more treatment-related SPADE symptoms in ovarian cancer and (b) critique the quality of the interventions.

Methods

Relevant studies were identified using a systematic approach. Studies with randomized or nonrandomized designs testing a nonpharmacologic intervention for any one or more of the SPADE symptoms in women treated for OC were examined. Therefore, some studies focused on a single symptom, whereas other studies focused on symptom clusters. Inclusion criteria were full-text articles in peer-reviewed journals that were specific to women with a primary diagnosis of OC (sample had to include women with a primary diagnosis of OC), featured patients who were aged 18 years or older, investigated a nonpharmacologic intervention addressing one or more treatment-related SPADE symptoms in ovarian cancer and (b) critique the quality of the interventions.

Results

Description of the Studies

As shown in Table 2, all studies were published from 2008–2014 and were conducted in four countries, consisting of Australia (Newton et al., 2011), Canada (Henry et al., 2010), the United Kingdom (Cox et al., 2008; Donnelly et al., 2011), and United States (Danhauer et al., 2008; Donovan et al., 2014; Johnson et al., 2009; McCorkle et al., 2009). Seven studies addressed different combinations of two to three SPADE symptoms, with depression being the most common symptom studied (88% of studies) (Cox et al., 2008; Danhauer et al., 2008; Donnelly et al., 2011; Henry et al., 2010; Johnson et al., 2009; McCorkle et al., 2009; Newton et al., 2011). Other SPADE symptoms that were addressed included sleep (n = 1), pain (n = 1), anxiety (n = 5), and low energy or fatigue (n = 4). Four studies used experimental designs (Donnelly et al., 2011; Donovan et al., 2014; Henry et al., 2010; McCorkle et al., 2009), and four used quasi-experimental designs (Cox et al., 2008; Danhauer et al., 2008; Johnson et al., 2009; Newton et al., 2011).

All study designs included, at a minimum, assessments at baseline and immediately after the intervention, with six studies (75%) conducting additional postintervention assessments (Danhauer et al., 2008; Donnelly et al., 2011; Donovan et al., 2014; Henry et al., 2010; Johnson et al., 2009; McCorkle et al., 2009). Intervention efficacy findings were statistically significant in three studies (Cox et al., 2008; Danhauer et al., 2008; Donovan et al., 2014), mixed results in two studies (Donnelly et al., 2011; McCorkle et al., 2009), clinically significant in two studies (Henry et al., 2010; Johnson et al., 2009), and negative in one study (Newton et al., 2011).

Quality of the Interventions

Components: An average of 4.4 components (range = 3–6) were present in the nonpharmacologic interventions in the eight studies. Components varied widely across studies and included education (Cox et al., 2008; McCorkle et al., 2009); skills building (e.g., problem solving) (Donnelly et al., 2011; Donovan...
et al., 2014; McCorkle et al., 2009); cognitive-behavioral strategies (e.g., cognitive reframing, relaxation, prayer) (Cox et al., 2008; Danhauer et al., 2008; Henry et al., 2010; Johnson et al., 2009; McCorkle et al., 2009); yoga or physical activity (Danhauer et al., 2008; Donnelly et al., 2011; Newton et al., 2011); additional screening, referrals, or nursing care (Cox et al., 2008; McCorkle et al., 2009); and self-monitoring (Donovan et al., 2014; Newton et al., 2011).

**Delivery:** Common methods for intervention delivery were telephone calls only (Cox et al., 2008), face-to-face contact only (Danhauer et al., 2008; Henry et al., 2010; Johnson et al., 2009), both calls and face-to-face contact (Donnelly et al., 2011; McCorkle et al., 2009; Newton et al., 2011), or the Internet (Donovan et al., 2014). The most common unit of delivery was to the individual, done in six studies (Cox et al., 2008; Donnelly et al., 2011; Donovan et al., 2014; Henry et al., 2010; McCorkle et al., 2009; Newton et al., 2011). One study delivered the intervention in a small-group format (Danhauer et al., 2008) and one did not specify the unit of delivery (Johnson et al., 2009). An advanced practice nurse delivered the intervention in three studies (Cox et al., 2008; Donovan et al., 2014; McCorkle et al., 2009). The majority of nonpharmacologic interventions were delivered by non-nursing professionals (Danhauer et al., 2008; McCorkle et al., 2009).

**Eligibility**

Records identified through PubMed database search (n = 123)

Additional records identified through spooling (n = 13)

Records after duplicates removed (n = 136)

Abstracts excluded with reasons (n = 118):
- No intervention (n = 28)
- Medical or surgical intervention (n = 17)
- Not SPADE secondary to chemotherapy (n = 9)
- Not adult or ovarian cancer (n = 31)
- Case report (n = 30)
- Review article (n = 3)

Abstracts screened (n = 136)

Full-text articles assessed for eligibility (n = 18)

Full-text articles excluded with reasons (n = 10):
- No intervention (n = 1)
- Not SPADE secondary to chemotherapy (n = 4)
- Not adult or ovarian cancer (n = 2)
- Not full text (n = 1)
- Review article (n = 2)

Studies included in synthesis (N = 8)

**SPADE**—sleep disturbance, pain, anxiety, depression, and low energy or fatigue

**Setting:** Descriptions of settings for each of the interventions also were assessed. Four studies included more than one setting (i.e., the hospital and the home) (Donnelly et al., 2011; Henry et al., 2010; McCorkle et al., 2009; Newton et al., 2011), two conducted the intervention exclusively in the home (Cox et al., 2008; Donovan et al., 2014), one conducted the intervention exclusively in the hospital (Johnson et al., 2009), and one conducted the intervention at a yoga studio in close proximity to the recruiting hospital (Danhauer et al., 2008). Privacy of the setting was described in only one study (Johnson et al., 2009), although that variable likely affected all studies.

**Exposure:** The quantity of intervention exposure was evaluated in terms of intervention dose and frequency. An exact dose of the intervention needed to achieve the results was inferred rather than explicitly identified in four studies (Cox et al., 2008; Danhauer et al., 2008; Henry et al., 2010; Johnson et al., 2009). In one study, intervention exposure was asynchronous because it was web-based, and a specific dose of the intervention was not imperative for completing the intervention. Rather, the asynchronous completion of all required intervention tasks served as the intervention dose and frequency (Donovan et al., 2014). Of studies reporting intervention dose, the range was 10–21 total sessions or contacts (Donnelly et al., 2011; McCorkle et al., 2009; Newton et al., 2011). Frequency of sessions or contacts was reported in all studies, ranging from daily to every three months.

The range of minutes per session or contact was 15–90 minutes (Cox et al., 2008; Danhauer et al., 2008; Donnelly et al., 2011; Henry et al., 2010; Johnson et al., 2009; Newton et al., 2011) or unspecified (Donovan et al., 2014; McCorkle et al., 2009). Total duration for the intervention was reported in all studies and ranged from 1–6 months.

**Compliance:** Four studies reported 100% compliance (Danhauer et al., 2008; Johnson et al., 2009; McCorkle et al., 2009; Newton et al., 2011), three reported 80% or greater compliance (Cox et al., 2008; Donnelly et al., 2011; Henry et al., 2010), and one reported 75% compliance (Donovan et al., 2014) with completion of the intervention. The asynchronous, web-based intervention (Donovan et al., 2014) reported the lowest compliance with completion compared to all other studies despite being a less time-intensive and more accessible intervention.

**Replication:** Three studies provided adequate detail to replicate the intervention (Danhauer et al., 2008; Donovan et al., 2014; Johnson et al., 2009). Each provided a precise overview of all intervention elements (and an example of a goal or activity accomplished for each element of the intervention in the case of tailored interventions) in addition to the proper order of the elements or tasks. Only one of these three studies, a randomized, controlled trial with a wait-list control group, included adequate descriptions of the processes for both the intervention and usual care group (Donovan et al., 2014).

Of the remaining five studies, all were classified as providing detail appropriate for partial replication of the intervention. Classification as partial was made because of ambiguity with regard to the intervention in more than one of the previously discussed content areas, excluding compliance (i.e., detail of components, delivery, setting, or exposure). Based on this...
TABLE 1. Quality of Nonpharmacologic Interventions for Treatment-Related Symptoms in Ovarian Cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>Components</th>
<th>Delivery</th>
<th>Setting</th>
<th>Quantity and Duration</th>
<th>Compliance</th>
<th>Replication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cox et al., 2008</td>
<td>Content on detection of recurrent disease; implications of recent blood tests; assessment of current symptoms; tailored information, advice, coping strategies in physical, psychological (i.e., anxiety and/or depression), and social domains; referrals for medical care and specialist</td>
<td>Follow-up calls individually administered by a clinical nurse specialist</td>
<td>Approached in clinics; intervention delivered from nurse phone clinics; home-based for participants</td>
<td>Calls every three months, with about 20 minutes per call (extra time allocated if needed); lasting 10 months</td>
<td>46 (82%) completed the intervention</td>
<td>Partial</td>
</tr>
<tr>
<td>Danhauer et al., 2008</td>
<td>Restorative yoga sessions: physical postures, breathing, and deep relaxation along with reinforcement to be gentle to oneself; no home practice required, and no home practice information provided</td>
<td>Restorative yoga classes in a closed-group format; an average of 7.3 women (range = 5–12) per group; classes moderated by a certified yoga instructor with cancer-specific training</td>
<td>Yoga studio near the medical center</td>
<td>Classes were held once per week (Monday afternoon) for 75 minutes per class for 10 weeks.</td>
<td>51 (100%) completed all time points; average of 5.9 (of 10) classes attended; participants were given a $20 gift card for completing all time points</td>
<td>Full</td>
</tr>
<tr>
<td>Donnelly et al., 2011</td>
<td>Physical activity intervention with walking and strengthening exercises, based on the Transtheoretical Model: initial, individual face-to-face consult with physiotherapist; calls to address barriers and goals; final face-to-face consult; follow-up calls to address barriers and goals; final follow-up call</td>
<td>Physical activity consult with follow-up calls, with both physical activity consult and follow-up calls done individually; consults were provided by physiotherapist; deliverer of follow-up calls was not specified</td>
<td>Setting for consults not specified; otherwise, home-based</td>
<td>Weekly calls for 10 weeks following initial consult; two monthly follow-up calls after final consult; calls lasted 15 minutes in duration but differed significantly between groups (p &lt; 0.001); duration of consults was not specified; the final follow-up call was at six months</td>
<td>Initial and final consults received by 15 (94%) and 13 (81%), respectively; 16 were in the intent-to-treat group, 4 did not receive the intervention, and 1 dropped out</td>
<td>Partial</td>
</tr>
<tr>
<td>Donovan et al., 2014</td>
<td>Approach to symptom management based on Common Sense and Conceptual Change models, including: representational assessment, identifying gaps, creating conditions for change, replacement information, summary, goal setting and planning, and goal and strategy review; three target symptoms were selected by each participant as focus for all content</td>
<td>Private web-based message boards provided individual interactions for the intervention and target symptoms; administered by two master’s-prepared nurse interventionists with a background in oncology</td>
<td>Web-based</td>
<td>Asynchronous; nurse interventionists responded within 24 hours; average of 79 days for all elements of the intervention</td>
<td>25 (76%) women completed the intervention</td>
<td>Full</td>
</tr>
<tr>
<td>Henry et al., 2010</td>
<td>Facilitate search for meaning following cancer diagnosis by reviewing impact and meaning of cancer diagnosis, exploring past significant life events and successful coping (as related to cancer), and discussing life priority and goal changes that give meaning to one’s life while considering cancer-related limitations</td>
<td>Therapeutic sessions individually administered by a psychologist</td>
<td>Sessions conducted at the hospital or at home</td>
<td>1–4 sessions were offered, with individual sessions lasting 30–90 minutes; the number and length of sessions were individualized to each participant’s psychological and physical needs; sessions took place during a two-month period (range = 1–3 months)</td>
<td>12 (80%) women completed the intervention</td>
<td>Partial</td>
</tr>
</tbody>
</table>

(Continued on the next page)
criteria, two of the five remaining studies were deemed partial for ambiguity in components and setting (Donnelly et al., 2011; Newton et al., 2011), two were deemed partial for ambiguity in components and exposure (Henry et al., 2010; McCorkle et al., 2009), and one was deemed partial for ambiguity in components, setting, and exposure (Cox et al., 2008).

### Discussion

This systematic review is the first to critique the quality of nonpharmacologic interventions addressing SPADE symptoms in women treated for OC. Other reviews have focused on interventions in other cancer types with different symptom burden. Those reviews specific to women with OC have addressed evidence to support survivorship issues, suggesting the continued need for quality interventions addressing treatment-related symptoms (Berger et al., 2013; Trivers, Patterson, Roland, & Rodriguez, 2013).

Very few experimental or quasi-experimental research studies (n = 8) were identified in the current authors’ search. Although studies were conducted in several countries, a significant portion (50%) were conducted in the United States (Danahauer et al., 2008; Donovan et al., 2014; Johnson et al., 2009; McCorkle et al., 2009), and, therefore, results may not be generalizable to other groups of OC survivors. This small number of available and potentially nongeneralizable studies suggests a need for further studies addressing treatment-related SPADE symptoms in women with OC.

Little consistency was noted across studies in terms of which SPADE symptoms were addressed, although most studies addressed a symptom cluster of two or more SPADE symptoms. Research suggests that all five SPADE symptoms were likely present and could have been measured and addressed (Aktas, 2013; Cleeland et al., 2013; Oh et al., 2012; Thomas et al., 2014; Wood & Weymann, 2013; Yarbro et al., 2014), indicating that it will be important to more consistently address all five symptoms as the larger SPADE symptom cluster in future research.

Another major finding of the current authors’ review was the lack of clarity in intervention reporting. Although many interventions appeared efficacious in alleviating SPADE symptoms, ambiguity in descriptions of two or more content areas of the

<table>
<thead>
<tr>
<th>Study</th>
<th>Components</th>
<th>Delivery</th>
<th>Setting</th>
<th>Quantity and Duration</th>
<th>Compliance</th>
<th>Replication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johnson et al., 2009</td>
<td>Centering prayer sessions: preparation, centering prayer (i.e., posture and relaxation, choosing a centering word, centering on the word, and closure), and debriefing</td>
<td>Centering prayer sessions, unit not specified, administered by a centering prayer teacher from a local religious community. The teacher was credentialed in spiritual direction and trained in centering prayer.</td>
<td>Private room during infusion visit</td>
<td>During three consecutive infusion visits, 60 minutes per session, for nine weeks</td>
<td>10 (100%) completed the intervention, and 7 completed the intervention and all time points</td>
<td>Full</td>
</tr>
<tr>
<td>McCorkle et al., 2009</td>
<td>Tailored, specialized care to assist participants in developing and maintaining self-management skills: symptom management and monitoring, emotional support, patient education, coordination of resources, referrals, and direct nursing care; those indicating significant distress also received psychiatric evaluation of emotional needs and screening for possible disorders</td>
<td>Nursing contact of individuals; contacts were led by an oncology advanced practice nurse; psychiatric evaluations were conducted by an advanced practice nurse in mental health nursing</td>
<td>Home visits, calls, and clinic visits</td>
<td>18 total contacts (8 home visits, 7 calls, and 3 clinic visits); two contacts per week in month 1, two per month in months 2–6; duration of contacts was not specified but total program length was six months</td>
<td>63 (100%) completed the intervention at all time points</td>
<td>Partial</td>
</tr>
<tr>
<td>Newton et al., 2011</td>
<td>Walking intervention: An educational booklet including topics such as how to monitor walking intensity, when not to walk, and monitoring changes in treatment-related side effects; a walking prescription; a logbook for recording details of walking activity</td>
<td>Face-to-face contact or phone delivery via individual contacts by an exercise physiologist with tertiary training in exercise science and specialist training in exercise prescription for patients with cancer</td>
<td>Single medical center; those participating face-to-face; home-based for phone contacts; offered face-to-face if participant was local</td>
<td>Weekly for both contacts; 11–21 total contacts at 20–60 minutes per contact (when meeting with exercise physiologist); duration of phone contacts was not specified; program was the duration of the chemotherapy treatment (11–21 weeks)</td>
<td>17 (100%) completed the intervention at all time points</td>
<td>Partial</td>
</tr>
</tbody>
</table>
TABLE 2. Literature Review: Description of the Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Purpose</th>
<th>Symptom(s)</th>
<th>Sample and Setting</th>
<th>Methods and Design</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cox et al., 2008</td>
<td>Acceptability of nurse-led phone intervention; define psychosocial areas discussed during intervention</td>
<td>Anxiety and depression</td>
<td>46 women with OC of all stages from a single center in the United Kingdom</td>
<td>Quasi-experimental, pilot, single group with pre- and post-assessment</td>
<td>Anxiety and depression were discussed by 42%; 71% were referred for counseling. A significant increase was noted in emotional well-being with reduced emotional problems at T2 (t[44] = –2.5, p = 0.016).</td>
</tr>
<tr>
<td>Danhauer et al., 2008</td>
<td>Feasibility of yoga intervention in OC and BC; measure changes in fatigue, psychological distress, positive affect, and quality of life</td>
<td>Anxiety, depression, and energy or fatigue</td>
<td>51 women with OC (n = 37) and BC (n = 14) of all stages from multiple centers in the United States</td>
<td>Quasi-experimental, pilot, single group with pre- and post-assessment (follow-up at two months)</td>
<td>Significant decrease between T1 and T2 for depression (p ≤ 0.01); significant decrease between T1 and T3 for anxiety (p ≤ 0.01); and significant decrease between T1 and T2 for fatigue (p ≤ 0.05)</td>
</tr>
<tr>
<td>Donnelly et al., 2011</td>
<td>Feasibility and efficacy of a PA behavioral change intervention for managing fatigue</td>
<td>Sleep, depression, and energy or fatigue</td>
<td>33 women with non-metastatic OC or endometrial cancer, 16 in the intervention arm and 17 in the control arm, at a single center in the United Kingdom</td>
<td>Two-group, single-blind pilot RCT (random numbers tables) with pre- and post-assessment (a follow-up at six months)</td>
<td>Significant decrease in fatigue for intervention group between T1 and T2 (p = 0.046, d = 0.13) and T1 and T3 (p = 0.01, d = 0.2); significant difference between groups at T2 (p = 0.04, d = 0.14) for sleep. No significant difference was found for depression.</td>
</tr>
<tr>
<td>Donovan et al., 2014</td>
<td>Feasibility, usability, acceptability, and efficacy of web-based message board intervention on symptom outcomes</td>
<td>Pain and energy or fatigue</td>
<td>56 women in the United States with recurrent OC, 33 in the intervention arm and 33 in the control group, using a web-based platform</td>
<td>Two-group pilot RCT (1:1 ratio allocation); pre- and post-assessment (at two and six weeks follow-up)</td>
<td>Significant between-group effect for distress at T2 with less distress in intervention group (t[88.4] = –2.57, p = 0.012); significant group effect in favor of intervention on distress (p = 0.037)</td>
</tr>
<tr>
<td>Henry et al., 2010</td>
<td>Acceptability, feasibility, and usefulness of a meaning-making intervention on negative outcomes</td>
<td>Anxiety and depression</td>
<td>24 women with stage III–IV OC, 12 in the intervention group and 12 in the control group, at multiple centers in Canada</td>
<td>Two-group, single-blind pilot RCT (blocking); pre- and post-assessment (at one and three months follow-up)</td>
<td>No statistically significant group difference for anxiety and depression; clinical levels of anxiety and depression in control were more than twice as high (42%) as intervention (17%) at three months post-intervention</td>
</tr>
<tr>
<td>Johnson et al., 2009</td>
<td>Feasibility and influence of centering prayer intervention on mood, spiritual well-being, and quality of life</td>
<td>Anxiety, depression, and energy or fatigue</td>
<td>10 women with recurrent OC at a single center in the United States</td>
<td>Pilot, quasi-experimental single-group; pre- and post-assessment (at three and six months follow-up)</td>
<td>No statistically significant results; clinically significant decrease in anxiety from T1 to T2 (X difference score of 10); decreased anxiety maintained at three and six months postassessment (X difference scores of 11.99 and 10, respectively); clinically significant decrease in depression from T1 to T2 (X difference score of 9.4); decreased depression not maintained at three and six months (X difference scores of 5.6 and 6.7, respectively); no clinically significant results for fatigue</td>
</tr>
<tr>
<td>McCorkle et al., 2009</td>
<td>Effects of a nursing intervention on health-related quality-of-life outcomes</td>
<td>Depression</td>
<td>63 women with OC in the intervention group and 60 in the attention control group, from a single center in the United States</td>
<td>Two-group, single-blind RCT (sealed envelope); pre- and post-assessment (at one, three, and six months follow-up)</td>
<td>Mixed-effect regression model with statistically significant within-groups difference in depression scores over time (p &lt; 0.0001); no between-groups difference found</td>
</tr>
<tr>
<td>Newton et al., 2011</td>
<td>Feasibility, safety, and effect of a walking intervention on health-related quality-of-life outcomes in women undergoing chemotherapy</td>
<td>Anxiety and depression</td>
<td>17 women with OC of all stages at a single center in Australia</td>
<td>Quasi-experimental, pilot, single group with pre- and post-assessment</td>
<td>No clinically significant or statistically significant changes found between T1 and T2 for anxiety or depression (p = 0.63 and 0.16, respectively)</td>
</tr>
</tbody>
</table>

BC—breast cancer; d—Cohen’s measure of sample effect size; OC—ovarian cancer; PA—physical activity; RCT—randomized, controlled trial; T—time

Note: All studies evaluated efficacy of the intervention.
intervention was present in all studies classified as providing only enough detail for partial replication of the intervention (63%). Lack of clarity in intervention reporting can be problematic in building science for two important reasons: (a) The interventional component most related to an important effect cannot be easily identified and, therefore, repeated or emphasized, and (b) replication of the intervention becomes challenging both for scientists trying to perform additional research and providers interested in implementing the intervention in clinical practice. When faced with these challenges, as a result of less than optimal intervention reporting, building the scientific basis for interventions addressing treatment-related SPADE symptoms is difficult and progress can be impeded. Understandably, one review concluded that OC survivors are frustrated by the lack of OC-specific information and continue to experience common and unaddressed treatment-related symptoms, including pain and fatigue (Trivers et al., 2013). Therefore, healthcare providers should consider two gaps emphasized by the current review: (a) Gaps in knowledge about the quality of the interventions may not be caused by a lack of efficacy but rather by a lack of detailed reporting (i.e., details are not sufficient for replication), and (b) a deficiency in the quality of intervention reporting directly affects the ability to translate interventions into clinical practice, ultimately inhibiting the potential to positively address treatment-related SPADE symptoms in OC.

Existing interventions to address SPADE symptoms are complex even when addressing only two or three, rather than all, SPADE symptoms simultaneously. A review conducted in cancer populations other than OC suggests that interventions should be recommended if they are capable of successfully relieving the sentinel symptom (i.e., the indicator of a cluster, leading to assessment of other relevant symptoms) (Aktas, 2013; Berger et al., 2013). However, this recommendation is temporary because the push for research addressing the mechanism(s) behind co-occurring symptoms is a continuing effort. As translational science becomes more sophisticated and intervention complexity increases to holistically address symptom clusters, attention to intervention reporting will be paramount.

Limitations

Limitations to this review exist. First, only PubMed was searched, and some articles may have been missed. PubMed provides access to more than 24 million citations (National Center for Biotechnology Information, 2014); therefore, it was reasonable that the search strategy effectively captured most, if not all, of the relevant evidence, and any additional articles acquired from searching other databases would not significantly alter the conclusions of the review. Second, the review had a narrow focus by only critiquing articles addressing SPADE symptoms in women treated for OC and not for other cancers. This led to the inclusion of only eight studies. However, women with OC are an understudied population, and their trajectory of symptoms is likely to be different than other cancers; therefore, research from other cancer populations is not likely to generalize to women with OC. Finally, although only studies investigating SPADE symptoms after chemotherapy treatment were included in the review, it was not possible to determine whether these symptoms may also have existed prior to treatment.

Implications for Practice

- Increase awareness of the treatment-related SPADE symptoms (sleep disturbance, pain, anxiety, depression, and low energy or fatigue) in women with ovarian cancer.
- Identify potentially efficacious nonpharmacologic interventions and the quality of these interventions for treatment-related SPADE symptoms.
- Call for improvements in intervention reporting to better facilitate translation of findings into clinical practice.

Conclusions and Implications for Practice

Research on nonpharmacologic interventions to manage treatment-related SPADE symptoms is important in cancer care and in individuals with advanced disease experiencing ongoing treatment, such as women with OC. A larger review including multiple databases is likely needed to ascertain the full extent of this literature. However, in the current review, the authors identified a limited number of studies and gaps in the quality of intervention reporting which may negatively impact replication in larger trials and translation into clinical practice. Attention to the reporting of interventions is necessary in future research to increase the implementation of interventions by providers and to positively affect the symptom management needs of women with OC. In addition, this review serves as a call to action for increased attention to intervention reporting by research scientists. Improved reporting will be even more essential as the understanding of SPADE symptoms as clusters of two or more co-occurring symptoms becomes more sophisticated and interventions become ever more complex.

References

Berger, A.M., Yennu, S., & Million, R. (2013). Update on interventions focused on symptom clusters: What has been tried and what have we learned? Current Opinion in Supportive and Palliative Care, 7, 60–66. doi:10.1097/SPC.0b013e32835c7d88


