

# Survivorship care plans for breast cancer patients: understanding the quality of the available evidence

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# ABSTRACT

**Aim** The overall goal of the present study was to contribute to consistency in the provincial approach to survivorship care planning through knowledge synthesis and exchange. Our review focused on the research concerning the physical and emotional challenges of breast cancer (Bca) patients and survivors and the effects of the interventions that have been used for lessening those challenges.

**Methods** The psychosocial topics identified in BCa survivorship care plans created by two different initiatives in our province provided the platform for our search criteria: quality of life (QOL), sexual function, fatigue, and lifestyle behaviours. We conducted an umbrella review to retrieve the best possible evidence, and only reviews investigating the intended outcomes in BCa survivors and having moderate-to-high methodologic quality scores were included.

**Results** Of 486 reports retrieved, 51 reviews met the inclusion criteria and form part of the synthesis. Our results indicate that BCa patients and survivors experience numerous physical and emotional challenges and that interventions such as physical activity, psychoeducation, yoga, and mindfulness-based stress reduction are beneficial in alleviating those challenges.

**Conclusions** Our study findings support the existing survivorship care plans in our province with respect to the physical and emotional challenges that BCA survivors often face. However, the literature concerning cancer risks specific to BCA survivors is scant. Although systematic reviews are considered to be the "gold standard" in knowledge synthesis, our findings suggest that much remains to be done in the area of synthesis research to better guide practice in cancer survivorship.

Key Words Breast cancer, survivorship, survivorship care planning, psychosocial concerns

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# **INTRODUCTION**

Breast cancer (BCa) is the most common cancer among women in both developed and developing countries<sup>1–3</sup>. Advancements in screening, diagnostic techniques, and cancer treatments have increased the survival rate for women with BCa<sup>4</sup>. Although an overwhelming menu of treatment options to fight this cancer is available, no treatment is devoid of side effects. And like other cancer survivors, BCa survivors experience numerous treatment-related challenges, the frequent ones being premature menopause, infertility, impaired physical and psychosocial functioning, and fear of a recurrence or a second primary cancer<sup>5,6</sup>. After the U.S. Institute of Medicine made its recommendation in 2006<sup>7</sup>, survivorship care plans (scPs) were introduced in North America and Europe to help cancer survivors as they move from treatment into the next phase of their lives. Substantial survivorship research and knowledge implementation efforts have occurred in the United States and the United Kingdom<sup>8–10</sup>. In the United States, the American Cancer Society, the Centers for Disease Control and Prevention, the LivesTRONG Foundation, and the National Cancer Institute have been collaborating to enhance the translation of survivorship research into evidence-based interventions<sup>11</sup>. Although the Canadian Partnership Against Cancer made survivorship and scPs a

Correspondence to: Violet D'Souza, BC Cancer Agency–Vancouver Island Centre, 2410 Lee Avenue, Victoria, British Columbia V8R 6V5. E-mail: violet.dsouza@mail.mcgill.ca 🔳 DOI: https://doi.org/10.3747/co.24.3632 practice and research priority in 2009<sup>7,12</sup>, research pertaining to the integration of survivorship care into primary care in Canada is much more recent<sup>13–19</sup>.

Survivorship care plans are personalized records of care and follow-up, which include potential post-treatment problems, signs of recurrence, guidelines for lifestyle modifications, and important community resources. The primary purpose of scPs is to improve patient-reported or health-related outcomes, or both, in cancer survivors<sup>20,21</sup>. No scP format has been universally accepted, and thus, many cancer care facilities develop their own scPs, leading to duplication of effort and scP content that varies from institution to institution. A study that evaluated 16 scPs from several developed countries found substantial variations with respect to their content and delivery approaches<sup>22</sup>.

In British Columbia, two independent initiatives led by clinician–researchers from two BC Cancer Agency centres located in two different geographic regions and funded by different external sources, created scPs for women with BCA. No or little coordination in terms of format, language, or content occurred. Thus, the overall goal of the present study was to contribute to consistency in the provincial approach to survivorship care planning through knowledge synthesis and exchange. Our review focuses on the research concerning the physical and emotional challenges of BCA patients and survivors and the effects of the interventions that have been used for lessening those challenges.

## **METHODS**

This umbrella review—that is, a systematic review of systematic reviews<sup>23</sup>—was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines<sup>24</sup>.

The electronic databases MEDLINE, PSYCINFO, Cochrane Library, CINAHL, and EMBASE were systematically searched using both key words and MeSH terms. Hand searches of reference lists in the identified articles were also conducted to gather all the available literature about the outcomes of interest. The search was conducted during April and May 2013 and was updated in December 2014 and again in April 2016 by the first author (VDS) with the support of the BC Cancer Agency–Vancouver Island Centre medical librarian. Grey literature was included only if it contained a detailed description of the included studies while also meeting the inclusion criteria.

Based on our analysis of the sCPS created by the two clinical research groups in British Columbia, we defined the outcomes of interest (presented in Table I, together with the search terms used). Systematic reviews, meta-analyses, and any kinds of reviews were included if they were conducted with at least 50 BCa patients or survivors, if they reported any of the outcomes of interest, and if they had at least a moderate quality score of 5 or greater. Studies conducted with a mixed group of cancer patients were included only if they reported the measured outcomes separately for BCa patients and survivors.

The quality of the included studies was assessed using AMSTAR<sup>25</sup>, a reliable and valid measurement tool to assess the methodologic quality of systematic reviews<sup>26</sup>. The AMSTAR score characterizes the quality of systematic reviews at

three levels, with 0–4 being considered poor quality; 5–7, moderate quality; and 8 and greater, high quality. All potentially eligible studies were scored independently by two authors (VDS, HD). Discrepancies were resolved by discussion between those authors; if necessary, the third author (AK) was consulted. Studies with a quality score of 5 or greater were included in the review.

# RESULTS

The search identified 486 citations, of which 74 scientific reviews met the inclusion criteria. Of those seventy-four reviews, twenty-three were eliminated (reasons presented in Table II). The remaining fifty-one systematic reviews or meta-analyses<sup>27–77</sup> were included in the synthesis. The details of the search for, and inclusion or exclusion of, articles are presented in Figure 1.

Of the fifty-one included reviews, twenty-six were of high quality (scores  $\geq$  8, with a mean quality score of 7.24  $\pm$  1.5). Table III presents the general characteristics of the included studies; their overall findings; the summary risk ratio estimates, odds ratios, effect sizes or standardized mean differences (when available); and the quality scores. No reviews that investigated the cancer risk in BCa patients or survivors were found. Given the diversity of the included reviews and the heterogeneity in the measured outcomes, the data were synthesized qualitatively and were summarized in categories as described in the subsections that follow.

Two streams of studies were delineated:

- Cancer- or treatment-related physical and emotional challenges in BCa patients or survivors, or both
- Interventions used in BCa patients or survivors, or both, to alleviate identified challenges and the effects of those interventions

#### Cancer- or Cancer Treatment-Related Challenges

Of the included reviews, thirteen reported challenges faced by BCa patients and survivors<sup>27–38,40</sup>. Their findings are categorized and described next.

## Anxiety, Depression, and Distress

Five reviews investigated anxiety, distress, and symptoms of depression in BCa patients and survivors<sup>30–34</sup>. According to those reviews, anxiety and distress are frequently observed in this population and seem to persist for a very long time, although the severity can vary from person to person and across time after the diagnosis.

In one review, anxiety was investigated in 1894 BCa patients receiving various types of cancer treatments. The authors reported that anxiety was a pervasive issue in BCa patients who undergo any of the three most common BCa treatment modalities (surgery, chemotherapy, and radiotherapy) and that it tends to persist beyond the acute stage of treatment<sup>31</sup>. The authors also observed higher levels of anxiety among women who underwent mastectomy than among those who underwent breast-conserving therapy. Compared with other treatments, chemotherapy was associated with higher levels of anxiety, and anxiety was highest before the first chemotherapy infusion.

Outcome type	Examples
Emotional challenges	Anxiety, apprehension, sadness, and depression
Physical challenges	Physical efficacy, fatigue, weight gain or loss, bowel function, sexual function, fertility issues, sexual dysfunction, urinary dysfunction, bowel functions
Other challenges	Body image, return to work, social functioning
Interventions tried and their impact	Physical activity, psychoeducation, cognitive therapy, and complementary therapies
Cancer risk	
Nutrition and diet	
Smoking, alcohol	
Physical activity	
Natural health products	
Herbal products	
Relaxation and meditation	
Spirituality	
	Search terms used

<b>TABLE I</b> The outcomes of interest with respect to breast cancer patients and survi
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(breast OR mammary glands) AND (cancer, carcinoma OR neoplasms) AND (quality of life, well-being, mental health, QoL, HRQOL, life quality, life qualities, qualities of life, life satisfaction OR personal satisfaction, sexual dysfunctions, bowel dysfunctions) AND (cancer patients, OR cancer survivors ) AND (physical activity, exercise) AND (diet, fiber, meat, red meat, processed meat, nutrition supplements, dairy) AND (spirituality, physiotherapy, sex therapy, education and information, cognitive therapies, psychotherapy, meditation or relaxation therapy)

According to another review that investigated depression in BCa survivors, levels of depressive symptoms were higher in younger survivors (<50 years of age) than in older survivors (>50 years of age) and in age-matched cancerfree women<sup>32</sup>. Higher levels of anxiety and depressive symptoms were found to be associated with poor social functioning<sup>30,33</sup>, poor physical functioning<sup>30,32</sup>, premature menopause, infertility concerns<sup>30,32</sup>, weight gain, body image, physical inactivity<sup>32</sup>, fear of follow-up diagnostic tests, cancer recurrence, and sexual and relationship problems<sup>34</sup>.

#### Fatigue

Three reviews reported fatigue in BCa patients and survivors<sup>28,30,38</sup>. According to those reviews, fatigue is one of the most frequently observed side effects during the active treatment period and beyond<sup>28,30</sup>. One review that investigated fatigue in 526 BCa patients and survivors reported that radiation was significantly and positively associated with fatigue, indicating that patients who received radiation treatment experienced higher levels of fatigue<sup>28</sup>. Other factors that were associated with increased fatigue were decreased appetite, nausea, vomiting, diarrhea, decreased body mass index, and anxiety and depression. Disease staging and neoadjuvant chemotherapy were not found to be associated with the level of fatigue<sup>28</sup>.

#### Quality of Life

Seven reviews reported on the quality of life (QOL) of BCa patients and survivors<sup>28,29,32–35,37</sup>, and according to those reviews, BCa patients and survivors often experience poorer QOL. Two reviews found an association between QOL and age, with considerably poorer QOL being experienced by younger ( $\leq$ 50 years of age) than by older BCa patients and

survivors<sup>32,34</sup>. In addition, positive associations were also observed for life stage; comorbid conditions; increased physical symptoms such as breast pain and fatigue; physical, emotional, and psychological dysfunctions; sexual challenges; disease stage; relapse; and active cancer treatment.

One review investigated the types of treatment given to BCa patients and their effects on QOL, finding that QOL was poorer in patients who received chemotherapy or who underwent mastectomy than in those who underwent breast-conserving surgeries<sup>34</sup>. In one review, the QOL of 2447 Latina BCa survivors was compared with that of non-Latina BCa survivors. Latina women were found to experience poorer QOL than their non-Latina counterparts<sup>33</sup>. Additionally, BCa-related lymphedema and higher levels of fatigue were significantly associated with poorer QOL<sup>28,29</sup>. The other factors that were associated with QOL were poorer mental and physical health, poor social functioning, greater distress, and greater fear of recurrence.

#### Lymphedema

Two reviews reported on Bca-related lymphedema<sup>27,29</sup>. One estimated the risk for lymphedema based on the treatment that the Bca patients received, and they observed that the risk for lymphedema was higher in patients who underwent mastectomy than in those who underwent lumpectomy; higher in those who had an axillary dissection than in those who had no axillary dissection; higher in those who underwent axillary dissection than in those who had a sentinel lymph node biopsy; and higher in those who received radiation and in those who had positive axillary nodes than in those who did not. The second review reported on the effect of lymphedema on QOL in Bca patients and survivors, finding that lymphedema was significantly associated with poor physical, psychological, and social well-being, and with poorer QOL, with the effects being more pronounced in younger survivors (<40 years of age)<sup>29</sup>.

#### Cognitive Functioning

Only one review investigated cognitive functioning in BCa survivors, and it observed significant deficits in

TABLE II Eliminated articles and the reason for elimination

Reason for elimination	References
Study was co	nducted in a general population, not in breast cancer patients or survivors
	Bagnardi V, Blangiardo M, La Vecchia C, Corrao G. Alcohol consumption and the risk of cancer: a meta-analysis. <i>Alcohol Res Health</i> 2001;25:263–70.
	Qin LQ, Xu JY, Wang PY, Hoshi K. Soyfood intake in the prevention of breast cancer risk in women: a meta-analysis of observational epidemiological studies. <i>J Nutr Sci Vitaminol (Tokyo)</i> 2006;52:428–36.
	Trock BJ, Hilakivi-Clarke L, Clarke R. Meta-analysis of soy intake and breast cancer risk. J Natl Cancer Inst 2006;98:459–71.
	van der Rhee HJ, de Vries E, Coebergh JW. Does sunlight prevent cancer? A systematic review. Eur J Cancer 2006;42:2222–32.
	Monninkhof EM, Elias SG, Vlems FA, et al., on behalf of TFPAC. Physical activity and breast cancer: a systematic review. <i>Epidemiology</i> 2007;18:137–57.
	Tempfer CB, Bentz EK, Leodolter S, et al. Phytoestrogens in clinical practice: a review of the literature. Fertil Steril 2007;87:1243–9.
	Enderlin CA, Coleman EA, Stewart CB, Hakkak R. Dietary soy intake and breast cancer risk. Oncol Nurs Forum 2009;36:531–9.
	Kim JY, Kwon O. Garlic intake and cancer risk: an analysis using the Food and Drug Administration's evidence-based review system for the scientific evaluation of health claims. <i>Am J Clin Nutr</i> 2009;89:257–64.
	Brennan SF, Cantwell MM, Cardwell CR, Velentzis LS, Woodside JV. Dietary patterns and breast cancer risk: a systematic review and meta-analysis. <i>Am J Clin Nutr</i> 2010;91:1294–302.
	Chen P, Hu P, Xie D, Qin Y, Wang F, Wang H. Meta-analysis of vitamin D, calcium and the prevention of breast cancer. <i>Breast Cancer</i> . <i>Res Treat</i> 2010;121:469–77.
	Brennan ME, Butow P, Marven M, Spillane AJ, Boyle FM. Survivorship care after breast cancer treatment—experiences and preferences of Australian women. <i>Breast</i> 2011;20:271–7.
	Chan AL, Leung HW, Wang SF. Multivitamin supplement use and risk of breast cancer: a meta-analysis. Ann Pharmacother 2011;45:476-84
	Dong JY, Qin LQ. Soy isoflavones consumption and risk of breast cancer incidence or recurrence: a meta-analysis of prospective studies. <i>Breast Cancer Res Treat</i> 2011;125:315–23.
	Jiang W, Wu Y, Jiang X. Coffee and caffeine intake and breast cancer risk: an updated dose–response meta-analysis of 37 published studies. <i>Gynecol Oncol</i> 2013;129:620–9.
	Misotti AM, Gnagnarella P. Vitamin supplement consumption and breast cancer risk: a review. eCancerMedicalScience 2013;7:365
	van der Rhee H, Coebergh JW, de Vries E. Is prevention of cancer by sun exposure more than just the effect of vitamin D? A systematic review of epidemiological studies. <i>Eur J Cancer</i> 2013;49:1422–36.
	Wu Y, Zhang D, Kang S. Physical activity and risk of breast cancer: a meta-analysis of prospective studies. <i>Breast Cancer Res Trea</i> 2013;137:869–82.
Eliminated be	ecause the original studies included in the reviews were of poor quality
	Horneber MA, Bueschel G, Huber R, Linde K, Rostock M. Mistletoe therapy in oncology. <i>Cochrane Database Syst Rev</i> 2008;:CD003297.
	Khan F, Amatya B, Ng L, Demetrios M, Zhang NY, Turner-Stokes L. Multidisciplinary rehabilitation for follow-up of women treated for breast cancer. <i>Cochrane Database Syst Rev</i> 2012;12:CD009553.
Same authors	published twice (most recent publication retained)
	Edwards AG, Hailey S, Maxwell M. Psychological interventions for women with metastatic breast cancer. <i>Cochrane Database Syst Rev</i> 2004;:CD004253.
	Mishra SI, Scherer RW, Snyder C, Geigle PM, Berlanstein DR, Topaloglu O. Exercise interventions on health-related quality of life for people with cancer during active treatment. <i>Clin Otolaryngol</i> 2012;37:390–2.
Eliminated be	ecause of publication twice by the same authors in the same year (one retained and one eliminated)
	Bagnardi V, Blangiardo M, La Vecchia C, Corrao G. Alcohol consumption and the risk of cancer: a meta-analysis. <i>Alcohol Res Health</i> 2001;25:263–70.



FIGURE 1 The process used to search for and select the final articles.

cognitive functioning and in verbal and visuospatial abilities for patients who received chemotherapy compared with those who did not, although the magnitude of the effect was small<sup>36</sup>. Age, education, time since treatment, and endocrine therapy did not moderate the observed deficits.

## Urinary Challenges

A single review investigated "urinary challenges" in 2500 Bca survivors<sup>37</sup>. It reported that, of their cohort, 23% experienced severe urinary dysfunctions, 12% had pain on micturition, and 58% experienced mild-to-moderate difficulties with bladder control (while laughing, crying, or performing simple tasks).

## Return to Work

Return to work was investigated in one review, according to which, BCa patients and survivors often face a miscellany of challenges that affect the return-to-work decision<sup>38</sup>. They frequently experienced extreme fatigue and fear of recurrence. Also, they were apprehensive about their physical appearance and changed body image; about disclosing the diagnosis to their employer, colleagues, and relatives; and about their ability to work, therefore fearing job loss. Some of the important observations were that the women's perception about their job or work had changed: they valued work less than before, and their motivation and priorities changed and became more goal-focused toward life. Some of the women felt discriminated against because of their cancer; some felt annoyed by questions from colleagues and heard hurtful remarks; some experienced awkward moments of social silence at workplaces; and some required changes in their work situation, such as task modifications that could marginalize them further. Also, some reported not receiving needed advice or support for returning to work, and thus found the return to work difficult, leading to job loss.

# **Religion and Spirituality**

One review investigated the relations between religious and spiritual constructs and psychological well-being in 2582 Bca survivors<sup>40</sup>. Although the findings suggest that religion and spirituality (religious coping, religious behaviours, God's image, faith) could play a role in improving or maintaining psychological well-being, multiple operational definitions for religion and spirituality and the challenges involved in quantifying "spirituality" meant that conclusions could not be drawn.

# Interventions Used to Alleviate Challenges

# **Physical Activity Interventions**

Twenty-three reviews investigated the effects on Bca patients and survivors of various physical activity interventions<sup>41–63</sup>. The types of physical activity and their effects are presented in detail in Table IV. The findings of the included reviews indicate that resistance training and aerobics provide significant benefit for physical<sup>42,44,46,48,49,52–54,56,61,63</sup> and emotional<sup>42,45,47,49,54,55,61,63</sup> functioning, and that recreational physical activities or any kind of light-to-vigorous physical activity provides a survival benefit<sup>41,51</sup>

# Psychoeducational Interventions

Of the eight scientific reviews<sup>40,60–62,73–77</sup> that reported the effects of psychoeducational interventions such as cognitive–behavioural techniques or education for Bca patients and survivors, one<sup>61</sup> reported statistically significant benefits for fatigue (p < 0.001), depression (p < 0.001), anxiety (p < 0.001), and body image (p < 0.051). Two reviews found clinically important benefits for anxiety, depression, and stress levels with moderate-intensity activity<sup>60,73</sup>; one reported benefits for mobility, muscle strength, and general fitness, and clinically important benefits for sexual functioning<sup>62</sup>; four reported short-term benefits for overall survival with low-intensity activity, and also improvements in mood and pain reduction<sup>74–77</sup>; and yet another reported significant reductions in fatigue, nausea, oral mucositis, diarrhea, constipation, pain, and insomnia, and improved qot.<sup>60</sup>.

# **Combined Interventions**

Two reviews investigated the effects on BCa patients and survivors of combinations of interventions<sup>39,64</sup>.

The first review investigated the effects of physical activity combined with psychological counselling (individually or in group sessions) provided to BCa patients and survivors for physical and social recovery from breast loss. The authors found that 75%–85% of participants returned to work by about 18 months' follow-up. However, that result might not be generalizable, because three of the four studies included in the review had been published 25 years earlier.

The second review examined the effects of combinations of interventions on Bca patients and survivors without analyzing the effects separately by intervention type<sup>64</sup>. The interventions included combinations of inpatient rehabilitation, psychological education, psychological education and information, self-help education, information support, information support plus cognitive–behavioural techniques, and exercise together with behavioural therapy.

Reference		Review characteristi	CS	Outcome	Exposure or	Findings	AMSTAR
	Type	Included studies	Sample	measured	intervention		score
Challenges for BCa patients and survivors							
Schmid-Buchi <i>et al.</i> , 2008 <sup>30</sup>	Review	20 studies: 12 with BCa patients, 8 with relatives	2344 BCa patients and their relatives	Fatigue, physical functioning, emotional distress, anxiety, and depression	BCa diagnosis	BCa patients experience treatment-related physical and social impairments such as fatigue, menopausal symptoms, and a changed body image, and emotional distresses such as fear of recurrence, anxiety, and depression.	Ŋ
Foster <i>et al.,</i> 2009 <sup>34</sup>	Systematic review	43 Studies: 16 with BCa	2857 BCa survivors	QOL, distress, and physical functioning	BCa diagnosis	Of the 26 studies, 6 investigated BCa and multivitamin use; results were contradictory and therefore inconclusive.	Ø
Tsai <i>et al.</i> , 2009 <sup>27</sup>	Meta- analysis	98 Studies: 40 prospective cohort, 10 RCTs, 5 case-control	39,753 BCa patients	Lymphedema risk	BCa treatments	The risk ratio for arm lymphedema is higher after mastectomy than after lumpectomy (RR: 1.42; 95% Cl: 1.15 to 1.76), after axillary dissection compared with no axillary dissection compared with sentinel node biopsy (RR: 3.07; 95% Cl: 2.34 to 5.15), after axillary dissection compared with sentinel node biopsy (RR: 3.07; 95% Cl: 2.20 to 4.29), after radiation therapy (RR: 1.92; 95% Cl: 1.61 to 2.28), and in the presence of positive axillary nodes (RR: 1.54; 95% Cl: 1.32 to 1.80).	ſ
Tiedtke <i>et al.</i> , 2010 <sup>38</sup>	Review	6 Qualitative, 3 retrospective studies	1584 BCa patients or survivors	Self-image and return to work	BCa diagnosis	The difficulties were disclosing the diagnosis to employers and relatives. Uncertainties with respect to physical appearance, ability to work, job loss, fatigue.	r.
Delgado-Sanz <i>et al.</i> , 2011 <sup>35</sup>	Systematic review	25 Studies	2236 Spanish BCa patients	JOD	BCa treatment	Clearly, the information available on the HRQOL of Spanish women with BCa is insufficient.	ω
Lim <i>et al.</i> , 2011 <sup>31</sup>	Meta- analysis	10 Studies: 3 RCTs	1894 BCa patients or survivors	Anxiety	BCa diagnosis and treatment	Anxiety is high in BCa patients before chemotherapy infusion and also in those who undergo a mastectomy.	~
Yanez <i>et al.,</i> 2011 <sup>33</sup>	Systematic review	22 Studies: 20 quantitative, 2 qualitative	2447 Latina BCa patients or survivors	JOD	BCa diagnosis	Relative to non-Latina women, Latina women were more likely to report poor mental, physical, and social QOL.	9
Donovan <i>et al.</i> , 2012 <sup>37</sup>	Systematic review	18 Studies: 2 RCTs, remainder observational	>2500 BCa patients	Urinary symptoms	BCa treatment	23% reported severe symptoms; 12% had pain on micturition; and 58% reported difficulty with bladder control	9

Reference		Review characteristi	cs	Outcome	Exposure or	Findings	AMSTAR
	Type	Included studies	Sample	measured	intervention		score
Challenges for BCa patients and survivors continued							
Howard-Anderson <i>et al.</i> , 2012 <sup>32</sup>	Systematic review	28 Studies: 15 cross-sectional, 8 longitudinal, and 5 interventional	>1324 BCa patients and survivors less than 50 years of age	QOL, menopausal symptoms, fertility, weight gain, physical inactivity, and behavioural	BCa diagnosis, and being 50 years of age or younger	Younger women with breast cancer were found to experience distinct psychosocial and menopause-related concerns, weight gain, and physical inactivity, poor QOL, fear of cancer recurrence, depressive symptoms.	٩
Jim <i>et al.</i> , 2012 <sup>36</sup>		RCTs	807 BCa patients treated with chemotherapy	Cognitive functioning	Chemotherapy	Compared with patients who did not receive chemotherapy, those who received chemotherapy had deficits in cognitive functioning, verbal ability, and visuospatial ability.	Γ
Schreiber and Brockopp, 2012 <sup>40</sup>	Systematic review	18 Studies: 1 RCT, 13 cross-sectional, 4 longitudinal	2582 BCa patients	Religion, spirituality, and well-being	BCa diagnosis	The relationships between religion, spirituality, and psychological well-being are limited and unclear.	œ
Alcantara-Silva <i>et al.</i> , 2013 <sup>28</sup>	Systematic review	12 Studies: 9 clinical trials, 3 observational); 9 studies with BCa	Of 2127 patients with gynecologic cancer, 526 had BCa	Fatigue, QOL	BCa diagnosis	Fatigue was common in BCa patients and more common with radiation therapy.	IJ
Pusic <i>et al.</i> , 2013 <sup>29</sup>	Systematic review	<ul><li>39 Studies:</li><li>8 RCTs,</li><li>14 prospective cohort,</li><li>14 cross-sectional,</li><li>3 retrospective</li></ul>	7074 BCa patients or survivors	QOL of cancer survivors	BCa-related lymphedema	BCa-related lymphedema significantly affects the HRQOL of BCa survivors.	IJ
PA interventions in BCa patients or survivors							
Oldervoll <i>et al.</i> , 2004 <sup>42</sup>		<ul><li>12 Studies</li><li>involving all types</li><li>of cancers</li><li>(6 with BCa patients,</li><li>3 with patients</li><li>having mixed cancers)</li></ul>	>371 BCa patients	Physical functioning and fatigue	Resistance exercise and aerobics	Improvements in physical functioning, peak oxygen consumption, and QOL, and a decrease in fatigue.	Ŋ
Stricker <i>et al.</i> , 2004 <sup>55</sup>	Systematic review	20 Studies	Patients with all types of cancer (>369 BCa patients)	Fatigue	Walking, aerobics, strength and resistance training	Cumulative evidence strongly supports that exercise decreases cancer-related fatigue in selected patients.	ę

TABLE III Continued

TABLE III Continued							
Reference		Review characteristi	ics	Outcome	Exposure or	Findings	AMSTAR
	Type	Included studies	Sample	measured	intervention		score
PA interventions in BCa patients or survivors continued							
Galvao and Newton, 2005 <sup>50</sup>	Review	<ul><li>18 Interventional studies</li><li>(9 with BCa patients, 3 with patients having mixed-cancers)</li></ul>	Patients with all types of cancer, but predominantly BCa patients (n>511)	Nausea, fatigue, distress, QOL	Cardiovascular training, resistance training, or flexibility training	Positive physiological and psychological benefits from exercise when undertaken during or after traditional cancer treatment.	Ю
Markes <i>et al.</i> , 2006 <sup>53</sup>	Systematic review	9 Studies	452 BCa patients	Physical fitness and fatigue	Aerobics or resistance training	Improved cardiorespiratory fitness (SMD: 0.66; 95% CI: 0.20 to 1.12). The decrease in fatigue was statistically insignificant.	6
McNeely <i>et al.</i> , 2006 <sup>54</sup>	Systematic review	14 Studies	717 BCa patients	QOL, physical functioning, fatigue	Aerobics or resistance training	Improved QOL, cardiorespiratory fitness, physical functioning, and fatigue in BCa patients and survivors.	6
Cheema <i>et al.,</i> 2008 <sup>46</sup>	Systematic review	<ul><li>10 Intervention studies:</li><li>5 RCTs, 1 non-RCT, 4 non-controlled studies</li></ul>	538 BCa patients receiving chemotherapy and radiation treatment	JOD	Progressive resistance training	Women surgically treated for BCa can derive health-related and clinical benefits by performing progressive resistance training after surgery for BCa	Ю
Bicego <i>et al.,</i> 2009 <sup>44</sup>	Systematic review	9 Interventional studies	373 BCa patients	TOÒ	Physical activity (aerobic, resistance training)	Exercise positively influences QOL in women living with BCa	œ
De Backer <i>et al.</i> , 2009 <sup>48</sup>	Systematic review	24 Studies: 10 RCTs, 4 controlled trials, 10 non-controlled trials	Patients with all types of cancer [54% BCa patients (n≥716)]	Physical functioning	Resistance training	Benefited cardiopulmonary function and muscle mass.	М
Karki <i>et al.</i> , 2009 <sup>58</sup>	Systematic review	14 RCTs	658 BCa patients with lymphedema	Management of lymphedema	Physiotherapy	Compression bandages are likely to reduce upper limb lymphedema in BCa patients. No effect for physiotherapy on lymphedema.	6
Kim <i>et al.</i> , 2009 <sup>52</sup>	Meta- analysis	10 Controlled trials	588 BCa patients or survivors	Cardiopulmonary function and body composition	Mainly aerobics	Aerobics improved cardiopulmonary function and body composition in BCa patients.	8
Barbaric <i>et al.</i> , 2010 <sup>41</sup>	Systematic review	10 Prospective cohorts (7 with BCa patients)	13844 BCa and other-cancer patients	Overall survival	Light-to-vigorous activity of any kind	Participation in PA was found to improve rates of breast cancer survival in 4 of the 7 studies.	ω

Reference		Review characterist	2	Outcome	Exposure or	Findings	AMSTAR
				measured	intervention		score
	Type	Included studies	Sample				
A interventions in BCa patients or survivors continued							
Velthuis <i>et al.,</i> 2010 <sup>43</sup>	Meta- analysis	18 Studies (12 with BCa patients)	1109 Participants in total (>700 with BCa)	Fatigue	Exercise (home based, self-monitored, supervised exercise programs)	Supervised home-based aerobic program produced a significant, medium reduction in cancer-related fatigue. (SMD: 0.30; 95% CI: 0.09 to 0.51)	ω
Bract <i>et al.</i> , 2011 <sup>59</sup>	Systematic review	2 RCTS	68 BCa patients	QOL and fatigue	Formal dance or movement therapy	Because of the small sample and high risk for bias, the positive outcomes observed (for QOL and fatigue) are not conclusive.	6
Ibrahim and Al-Homaidh, 2011 <sup>51</sup>	Meta- analysis	6 Studies	12,108 BCa survivors	Survival after BCa diagnosis	Recreational physical activity	Post-diagnosis PA was associated with a 34% reduction in BCa death ( <i>p</i> =0.00001), a 41% reduction in all-cause mortality ( <i>p</i> =0.00001), and a 24% reduction in disease recurrence ( <i>p</i> =0.00001).	ъ
Pastakia and Kumar, 2011 <sup>56</sup>	Systematic review	9 RCTs	Not available	JOD	Aerobic or resistance training	Exercise programs had a positive effect on the QOL outcomes of BCa patients and survivors.	~
Cramp and Byron-Daniel, 2012 <sup>47</sup>	Systematic review	56 studies (28 with BCa patients)	Patients with all types of cancer (4068 with BCa)	Fatigue, QOL	Aerobics, resistance training, or walking	Statistically significant improvements in fatigue were identified for BCa patients.	6
Fong <i>et al.</i> , 2012 <sup>49</sup>	Meta- analysis	34 RCTs (22 with BCa patients)	Patients or survivors with all types of cancer (>3869 with BCa)	QOL, fatigue, depression	Aerobics or resistance training	Improved QOL and decreased depression and fatigue in BCa patients after the treatment.	ω
Ridner <i>et al.</i> , 2012 <sup>57</sup>	Systematic review	14 Studies	1288 BCa patients or survivors	Lymphedema and related outcomes	Physiotherapy and compression bandages	Compression bandages are likely to reduce upper limb lymphedema in BCa patients. Physiotherapy methods and their combinations are limited because of the poor quality of the trials.	ъ
Carayol <i>et al.</i> , 2013 <sup>45</sup>	Meta- analysis	17 Interventional studies	748 BCa patients	Fatigue, anxiety, and depression	Supervised and home-based flexibility exercise	Exercise intervention significantly reduced fatigue, anxiety, and depression	10

TABLE III Continued

TABLE III Continued							
Reference		Review characteristi	CS	Outcome	Exposure or	Findings	AMSTAR
	Type	Included studies	Sample	measured	intervention		score
PA interventions in BCa patients or survivors continued							
Mishra <i>et al.</i> , 2014 <sup>63</sup>	Systematic review	40 Studies (20 with BCa patients, 12 in patients having mixed cancers)	Patients with all types of cancer (3694 with BCa)	QOL, anxiety, depression, fatigue, social functioning, and body image	Prescribed physical activity (aerobic, anaerobic, or combinations)	Exercise was associated with improved QOL, decreased anxiety and fatigue, and social functioning and body image.	o
Psychoeducational interventions							
Edwards <i>et al.</i> , 2004 <sup>74</sup>	Systematic review	5 RCTs	511 Women with BCa	Survival, mood, pain	Education, psychotherapy, cognitive behavioural therapy, and group interventions	Short-term benefit (pain and anxiety reduction). Insufficient evidence to advocate for group psychological therapies.	o
Naaman <i>et al.</i> , 2009 <sup>73</sup>	Meta- analysis	18 RCTs	14 Studies with 1278 subjects (692 in a treatment group, 586 in a control group)	QOL, anxiety, depression	Cognitive, behavioural, supportive, biofeedback, educational (group or individualized)	Clinically important benefits: moderate effect for anxiety (-0.40; 95% CI: $-0.72$ to $-0.08$ ; $n=1278$ ), moderate-to-strong effect for depression (-1.01; 95% CI: $-1.48$ to $-0.54$ ; $n=1324$ ), and a moderate effect for QOL (0.74; 95% CI: 0.12 to $1.37$ ; $n=623$ )	ω
Fors <i>et al</i> ,,2011 <sup>77</sup>	Systematic review	18 RCTs (only 3 of high quality; rest were moderate quality)	3272 BCa patients or survivors	Social functioning	Psycho- education, cognitive behavioural therapy	Cognitive behavioural therapy had some beneficial effect on anxiety and depression, and improvements in QOL. No differences with psychoeducation or other interventions.	<b>o</b>
Galway <i>et al.</i> , 2012 <sup>75</sup>	Systematic review	32 Publications (30 trials)	5155 Patients with all types of cancer (sample size for BCa alone not available)	QOL, distress, and mood	Supportive human interaction in all psychological interventions	Small improvements in QOL stress at 6-month follow-up; no effect on depression or anxiety. Psychoeducational and nurse-delivered interventions produced significant small positive effects on QOL (2 studies, SMD: 0.23; 95% CI: 0.04 to 0.43).	<b>б</b>
Mustafa <i>et al.,</i> 2013 <sup>76</sup>	Systematic review	10 Included in meta-analysis	1378 BCa patients	QOL, survival	Education; individual psychotherapy, cognitive behavioural ther- apy, and group interventions	Survival benefit was found at 12 months (OR: 1.46; 95% CI: 1.07 to 1.99), but not at 5-year follow-up (OR: 1.03; 95% CI: 0.42 to 2.52). Improved pain scores, with a mean difference of -0.58 (95% CI: -0.98 to -0.18).	Ν

Reference		Review characterist	ics	Outcome	Exposure or	Findings	AMSTAR
	Type	Included studies	Sample	measured	intervention		score
Combination intervention (PA and psychoeducational)							
Hoving et al., 2009 <sup>39</sup>	Systematic review	4 Studies	1324 BCa patients or survivors	Physical exercise and psychological counselling and their effect on return to work	BCa and treatment	Return-to-work rates of approximately 75%–85% after up to 18 months' follow-up seem favourable. Of the 4 studies, 3 were published 25 years earlier. Recent and sound evidence is lacking.	Ν
Duijts <i>et al.,</i> 2011 <sup>61</sup>		56 Studies	>5464 BCa patients or survivors	Fatigue, depression, anxiety, body image, stress, and HRQOL	Behavioural technique, physical exercise	Behavioural techniques significantly decreased anxiety, depression, fatigue [effect size: $0.158$ (95% CI: $0.233$ to $0.082$ ), $p$ =0.001], and stress in BCa patients and survivors. Physical activity significantly decreased fatigue and depression, and improved body image and HRQOL, although the intensity of the effect was moderate.	ω
Taylor <i>et al.</i> , 2011 <sup>62</sup>	Systematic review	21 Studies: 15 randomized trials, 6 nonrandomized trials	Not available (not possible to compute, because some studies had mixed survivors)	Sexual functioning	Exercise (n=2), medical (n=2), and psycho- educational (n=17) interventions	Because of methodologic flaws, the findings are not conclusive, but suggest that targeted sexual counselling or therapy might help patients and their partners.	ى
Wanchai <i>et al.</i> , 2011 <sup>60</sup>	Systematic review	28 Studies (17 with BCa patients)	2369 BCa patients	Fatigue, QOL	Physical activity, psycho- education, counselling, sleep therapy, complementary therapy	Exercise, education, and counselling, sleep therapy, and complementary therapy appear to be helpful methods in improving QOL in patients with BCa experiencing cancer-related fatigue.	Ŋ
Mewes <i>et al.</i> , 2012 <sup>64</sup>	Systematic review	22 Studies (5 with BCa patients)	Survivors of all types of cancer (517 with BCa)	Fatigue and physical functioning	Multi- dimensional rehabilitation programs	Statistically significant difference for multidimensional interventions compared with usual care for the outcomes of fatigue and physical functioning	Ν

e456

TABLE III Continued

Reference		Review characteristic	S	Outcome	Exposure or	Findings	AMSTAR
	Type	Included studies	Sample	measured	intervention		score
Complementary or alternative therapy							
Kim <i>et al.</i> , 2010 <sup>71</sup>	Systematic review	4 Clinical trials (1 RCT)	281 BCa patients	QOL, mood	Reflexology	All of the included studies suggest that reflexology generates beneficial effects. However, high risks for bias in the 3 included studies, and small sample prevents any firm conclusions from being drawn.	Γ
Lee <i>et al.</i> , 2010 <sup>70</sup>	Systematic review	7 Studies: 3 RCTs, 4 clinical trials	201 BCa patients	QOL, fatigue, BMI, mood, depression, pain, anxiety, muscle strength, flexibility	Tai chi	Inconclusive findings because of the small sample and high risk for bias.	Г
Matchim <i>et al.</i> , 2011 <sup>72</sup>	Review	16 Studies (7 with BCa patients)	470 BCa patients	Anxiety, depression, stress	Mindfulness- based stress reduction	Significant improvements in anxiety, depression, and stress. Studies with larger samples are warranted.	6
Buffart <i>et al.</i> , 2012 <sup>68</sup>	Systematic review	16 Publications (13 RCTs)	700 BCa patients or survivors	QOL, and physical and social functioning	Yoga	Reduction in distress, anxiety, and depression ( <i>d</i> : -0.69 to -0.75), reduction in fatigue ( <i>d</i> : -0.51), increase in QOL, and emotional and social functioning ( <i>d</i> : 0.33 to 4.49). No effect on physical functioning or sleep.	6
Cramer <i>et al.</i> , 2012 <sup>66</sup>	Systematic review	10 RCTs	742 BCa patients	QOL, and functional, social, and spiritual well-being	Yoga	Short-term improvements in QOL, and functional, social, and spiritual well-being.	6
Cramer <i>et al.</i> , 2012 <sup>67</sup>	Systematic review	6 RCTs	362 BCa survivors	Fatigue	Yoga	Yoga significantly decreased fatigue (p=0.04) in BCa patients	8
Harder <i>et al.</i> , 2012 <sup>65</sup>	Systematic review	18 Studies	952 BCa patients or survivors	Fatigue, QOL, and psychosocial and physical functioning	Yoga	Reduction in distress, anxiety, depression, and fatigue, and improvements in emotional well-being and QOL.	6
Zhang <i>et al.</i> , 2012 <sup>69</sup>	Meta- analysis	6 Clinical trials with wait list controls	382 Patients	QOL, anxiety, depression, distress, sleep	Yoga	Statistically significant effect on QOL ( <i>p</i> =0.03). No significant effect on anxiety, depression, distress, and sleep.	Ŀ
BCa = breast cancer; QOL = quality of life ratio; BMI = body mass index.	; RCT = random	ized controlled trial; RR =	= relative risk; Cl =	: confidence interval;	PA = physical acti	vity; SMD = standardized mean difference; C	DR = odds

	0					
Reference	Type of PA	Supervision	Duration	Frequency	Intensity	Effect
Oldervoll <i>et al.</i> , 2004 <sup>42</sup>	Strength training, cardio, walking, treadmill	Some supervised and some guided	10–35 Minutes, for 2–26 weeks	2–5 Sessions weekly	Varied	Improvements in physical functioning, peak oxygen consumption, QOL; decrease in fatigue.
Stricker <i>et al.,</i> 2004 <sup>55</sup>	Walking, treadmill, aerobics, bicycling	Institution-based	10–90 Minutes, for 4–20 weeks	2–5 Sessions weekly	Varied	Cumulative evidence strongly supports that exercise decreases cancer-related fatigue in selected patients.
Galvao and Newton, 2005 <sup>50</sup>	Cardiovascular training	Supervised and some home-based	20–35 Minutes, for 2–28 weeks	3–6 Sessions weekly	Unclear	Positive physiologic and psychological ben- efits from exercise when undertaken during or after traditional cancer treatment.
Markes <i>et al.</i> , 2006 <sup>53</sup>	Aerobics in 7 studies, aerobics and resistance training in 2 studies	Supervised	6-12 Weeks	Not available	Not available	Improved cardiorespiratory fitness (SMD: 0.66; 95% CI: 0.20 to 1.12). The decrease in fatigue was statistically nonsignificant.
McNeely <i>et al.</i> , 2006 <sup>54</sup>	Mixed aerobic and resistance exercise	Some supervised and some home-based	15–60 Minutes per session, for 15 weeks	2–5 Sessions weekly	Not stated	Improved QOL, cardiorespiratory fitness, physical functioning, and fatigue in BCa patients and survivors.
Cheema <i>et al.</i> , 2008 <sup>46</sup>	Progressive resistance training with aerobics	Some supervised, some partially supervised, and 1 not supervised	20–60 Minutes, for 16 weeks to 6 months	3 Sessions weekly	Moderate- to high-intensity	Improved physical functioning and cardiorespiratory fitness.
Bicego <i>et al.</i> , 2009 <sup>44</sup>	Aerobics, resistance training	Yes	50–60 Minutes each session, for 6–12 weeks	2 Sessions weekly	Light	Exercise positively influenced QOL.
De Backer <i>et al.,</i> 2009 <sup>48</sup>	Prescribed resistance training	Yes	3–24 Weeks, for 12 weeks	2–3 Sessions weekly	Moderate, as tolerated	Improvements in physical functioning.
Karki <i>et al.</i> , 2009 <sup>58</sup>	Resistance training, compression pumps, mechanical compression therapy	Supervised	1–12 Months	Not available	Not available	Compression bandages are likely to reduce upper limb lymphedema in breast cancer patients. No effect for physiotherapy on lymphedema.
Kim <i>et al.</i> , 2009 <sup>52</sup>	Aerobics in 8 studies, and aerobics with resistance training in 2 studies	5 Supervised, 2 home-based, 3 supervised and home-based	30–40 Minutes per session, for 6–26 weeks	2–5 Sessions weekly	Moderate	Aerobics improved cardiopulmonary function and body compositions in BCa patients.
Barbaric <i>et al.</i> , 2010 <sup>41</sup>	Activity of any kind (swimming, playing, walking, and so on)	°N N	1 Year before d lifetime level o level of PA after	iagnosis, f PA, and diagnosis	Light to vigorous	Significantly decreased BCa-related mortality.
Bradt <i>et al.</i> , 2011 <sup>59</sup>	Dance or movement therapy	Yes	3 Hours per session, for 12 weeks	6 Weekly sessions	Light	A large beneficial effect on QOL and fatigue for participants.
Duijts et al., 2011 <sup>61</sup>	Any kind	Information not available	Information not available	Information not available	Information not available	Significantly decreased fatigue, anxiety, and depression; improved QOL and body image.

TABLE IV Continued						
Reference	Type of PA	Supervision	Duration	Frequency	Intensity	Effect
Ibrahim and Al-Homaidh, 2011 <sup>51</sup>	Recreational PA	Information not available	Not available	Not available	Moderate to vigorous	Post-diagnosis PA was associated with reductions of 34% in BCa deaths ( $p$ =0.00001), 41% in all-cause mortality ( $p$ =0.00001), and 24% in disease recurrence ( $p$ =0.00001).
Velthuis <i>et al.</i> , 2010 <sup>43</sup>	Walking, resistance training	Some supervised and some home-based	10–45 Minutes per week, 2–6 months	3–6 Times weekly	Varied (at personal pace to high- intensity)	Supervised home-based aerobic program produced a significant medium reduction in cancer-related fatigue (SMD: 0.30; 95% CI: 0.09 to 0.51).
Pastakia and Kumar, 2011 <sup>56</sup>	Aerobics	Institution-based	14–60 Minutes, for 5–24 weeks	3 Sessions weekly	Moderate	Intervention had a positive effect on the QOL of BCa patients and survivors.
Taylor <i>et al.</i> , 2011 <sup>62</sup>	Strength training	Institution-based	90-Minute sessions, for 13 weeks	Twice weekly	Not	The findings were not conclusive.
Wanchai <i>et al.</i> , 2011 <sup>60</sup>	Aerobics	Supervised and some home-based	10–50 Minutes per session, for 1–12 weeks	1–5 Sessions weekly	Moderate	Because of methodologic flaws, the find- ings are not conclusive, but they suggest that targeted sexual counselling or therapy might help patients and their partners.
Cramp and Byron-Daniel, 2012 <sup>47</sup>	Aerobics, walking, cycling, resistance training,	<ul><li>37 Institution-based and</li><li>19 home-based</li><li>exercise programs</li></ul>	10-120 Minutes, for 3 weeks to 1 year	2 Sessions weekly	Varied widely	Aerobics was associated with a significant reduction in fatigue.
Fong <i>et al.,</i> 2012 <sup>49</sup>	Aerobic and resistance training	Information not available	10–90 Minutes, for 3–30 weeks	3–7 Sessions weekly	Information not available	Improvements in physical, emotional, and functional well-being; improved QOL; lower levels of fatigue and depression.
Ridner <i>et al.</i> , 2012 <sup>57</sup>	Full-body exercise, physiotherapy, and compression bandages	Institution-based	13-26 Weeks	Information not available	Moderate	Compression bandages are likely to reduce upper limb lymphedema in BCa patients. Physiotherapy methods and their combinations are limited because of the poor quality of the trials.
Carayol <i>et al.</i> , 2013 <sup>45</sup>	Aerobics and strength-training	No	23–60 Minutes, for 6–26 weeks	2–6 Sessions weekly	Moderate- to low-intensity	Inverse dose-response relationships were observed for fatigue and QOL.
Mishra <i>et al.,</i> 2014 <sup>63</sup>	Prescribed PA (aerobics, walking, stretching, cardiovascular activity, or resistance training (or combinations)	Some supervised and some guided	20–90 Minutes, for 7–12 weeks	20–90 Minutes, for 7–12 weeks	Not specified	Exercise was associated with improved QOL, decreased anxiety, fatigue, social functioning, body image.

Such interventions were beneficial with respect to cognition, health-related QOL, and social well-being.

### **Complementary and Alternative Therapies**

Ten reviews reported on the effects of complementary and alternative therapies in BCa patients and survivors<sup>40,60,65-72</sup>. Of those ten, six investigated the effects of a yoga intervention<sup>60,65–69</sup>; two, the effect of *tai chi*<sup>60,70</sup>; one, the effect of reflexology<sup>71</sup>; one, the effect of polarity therapy<sup>60</sup>; and one, the effect of mindfulness-based stress reduction therapy<sup>72</sup>. In addition, one review that had investigated psychosocial well-being, religion, and spirituality in eighteen observational studies had included one randomized controlled trial (181 women with BCa) using meditation, affirmation, imagery, and ritual as the test intervention, comparing that group with a control group receiving cognitivebehavioural therapy<sup>40</sup>. The test intervention was associated with improvements in spiritual integration (p = 0.001)and higher satisfaction (p = 0.006). Yoga was significantly associated with lower levels of fatigue67, anxiety, and depression, and with better QOL<sup>65,66,68,69</sup>. Mindfulness-based stress reduction was associated with significant reductions in stress, anxiety, and depression in BCa patients and survivors<sup>72</sup>. Although polarity treatment, *tai chi*, and reflexology showed important benefits for cancer-related fatigue in Bca survivors, those results are inconclusive because of small sample sizes and high risk for bias.

# DISCUSSION

The overall goal of the present study was to contribute to a consistent, province-wide, evidence-based approach to survivorship care planning by synthesizing the published literature about care for BCa survivors and by updating the evidentiary base used for the SCPS created in our province. To our knowledge, this umbrella review is the first to comprehensively summarize the scientific evidence about the psychosocial aspects of Bca survivorship. It is important to note that, although scps aim to support people with cancer as they complete treatment and usually provide information and recommendations to lessen subsequent cancer risk, our review did not find any systematic reviews that investigated the risk of a second primary cancer or BCa recurrence. Within the limits of the study design, our findings suggest that, compared with the general population, вса patients and survivors frequently experience higher levels of anxiety and depression, poorer QOL, higher levels of fatigue, poorer physical functioning, and urinary dysfunction. Interventions such as physical activity, psychoeducation, yoga, and mindfulness-based stress reduction are beneficial with respect to fatigue, anxiety, depression, stress, fatigue, QOL, and physical functioning.

This synthesis project, which forms a part of our quality improvement initiatives, aimed to support the production of evidence-based scPs and information materials that health care providers can share with BCa survivors in our province. Thus, our goal was to use a systematic review of systematic reviews to synthesize, within a short timeframe, the best available evidence to inform a more comprehensive project on scPs. The findings of this umbrella review accord with the existing BCa sCPs in our province with respect to the physical and emotional challenges of BCa survivors and the dietary and physical activity recommendations (Table v). However, literature concerning the cancer risks specific to BCa survivors is lacking.

Although BCa is one of the well-studied cancers, the serious dearth in the systematically synthesized literature concerning cancer risk in BCa patients and survivors raises a serious question about the extent to which the recommendations made by BCa clinicians and SCPS concerning cancer prevention are evidence-based. Interestingly, Norman *et al.*<sup>78</sup> described a similar challenge when reviewing the evidence for the effect of lifestyle factors on BCa recurrence in early 2007. Although the authors mentioned a number of trials focused on survivors being conducted at that time, we found no systematic reviews that reported on the risk of recurrence or a second primary cancer.

In spite of the serious knowledge gap concerning lifestyle modifications, many BCa SCPS—including the sCPS from our province—continue to recommend lifestyle modifications to lower future BCa risk<sup>79–81</sup>. Nevertheless, we identified eighteen reviews (not included in the present umbrella review) of mild-to-moderate quality that investigated BCa risk in general populations (Table II). According to those reviews, alcohol and caffeine intake increase the risk, and healthy diet, fish (those containing long-chain fatty acids), and vitamin D and calcium intake lower the BCa risk in the general population; findings for soy intake and multivitamin supplements were inconclusive. Although those findings are important in the primary prevention of BCa, can that knowledge be applied for secondary prevention in BCa patients and survivors?

Systematically conducted reviews have been considered the "gold standard" in knowledge synthesis<sup>24,82,83</sup>, but we have identified a significant gap in the scientific literature that is crucial to BCa survivorship care planning. Much has to be done in the area of synthesis research on survivorship, confirming what Luctkar-Flude et al.16 recently reported. We are therefore highlighting the urgent need for appropriate studies targeting secondary prevention of cancer for BCa survivors, especially studies that explore lifestyle and behavioural factors, including diet. Campbell et al.<sup>84</sup> indicated that support for patient self-management and use of evidence-based health promotion interventions were areas of relative weakness when survivorship models of care were analyzed in 8 Livestrong Survivorship Centers of Excellence Network sites in the United States, corroborating our statement.

Our study findings concerning fatigue, anxiety, depression, and QOL in BCa patients and survivors further confirm what was reported recently by Sisler *et al.*<sup>19</sup>. It is typical that, when faced with certain degrees of physical or functional challenge, a person's psychological adjustment and QOL can be impaired<sup>85,86</sup>.

Our umbrella review included a large number of scientific reviews that investigated the effects of various types of interventions on BCa patients and survivors. Of those interventions, physical activity and psychoeducation seem promising with respect to fatigue, anxiety, depression, stress, physical functioning, and QOL in BCa patients and survivors<sup>42,54,61,63</sup>. The findings concerning physical activity are in line with a recent report published by Segal

TABLE V	Outcomes	of interest	retrieved	from th	he survivo	rship	care p	olans	(SCPs)	
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Outcome	SCP 1	SCP 2					
Anxiety, de	Anxiety, depression, stress, and quality of life						
	Stress can affect you physically, emotionally, and behaviourally. Ongoing physical problems can be associated with anxiety, and anxiety can lead to loss of control, feeling alone. Anxiety and depression are frequently seen, and they can reduce your quality of life.	Many people will experience depression at some point in their lives. It is an illness that can affect anyone at any age. Depression is very common in cancer patients and can and should be treated. Eat well and be as physically active as possible. Exercise releases endorphins, which are natural mood-boosters					
Fatigue							
	Fatigue can be a side effect of cancer treatment that may last for some time. Try breaking tasks into smaller, more manageable steps. Ask for help when needed.	During and after cancer treatment, you may feel very tired and have no energy. Take short naps or breaks, rather than one long rest period. Eat as well as you can and drink plenty of fluids. Take short walks or do light exercise if possible. Try easier or shorter versions of activities that you enjoy					
Memory an	d concentration						
	Many women do notice minor changes in their memory and concentration. It can also be due to stress and fatigue. Unhealthy diet also can contribute this. Daily mental and physical activity can improve memory and other mental functions (reading, puzzles, new hobbies, etc.).	(No information)					
Intimacy an	nd sexual function						
	Breast cancer surgery may lessen your sex drive. The scars and the changes in appearance may make you nervous.	Loss of your sex drive is common during cancer treatment. Cancer treatments may cause a variety of changes that could lead to vaginal dryness or narrowing, ulcers, and infection. Sex drive usually returns sometime after treatment is over.					
Fertility and	l birth control options						
	Some cancer treatments affect a woman's reproductive capabilities. Some chemotherapies can cause early menopause resulting in infertility.	Some cancer treatments can affect the ovaries and may cause temporary or permanent failure of the ovaries (menopause). Sometimes the ovaries are removed altogether. As a result, women go through menopause and experience menopausal symptoms (hot flashes and vaginal dryness). These symptoms can be more severe than those from natural menopause					
Self-image,	appearance						
	Breast cancer surgery may be very traumatic. Reconstruction may be an option for some. Low self-esteem has a negative influence on the quality of life. Many women may gain weight.	Some common changes include weight loss or weight gain, hair loss (including pubic hair), loss of a body part, and surgery scars.					
Lympheden	na						
	Once it occurs, it rarely goes away. Avoid injections in the arm, and use compression sleeves while exercising and doing strenuous work.	Lymphedema can be temporary or a long-term condition. Avoid lifting the arm to carry heavy things on the same side as the surgery. Exercise regularly, do not overdo.					
Return to w	rork						
	Returning to work can help resume normal routines, focus on other challenges, and reconnect with friends and coworkers. For some, returning to work provides an opportunity to resume a normal routine, to be back in control.	Many women return to work. Plan a gradual return to work in order to ease into work, especially if your work is physical.					
Spirituality							
	You may be looking to find meaning in your life. Some people find their religion and faith helpful. You may try meditation or express through art.	Some women find relief through prayers; others renew their faith again after being diagnosed with cancer, which helps them feel good about themselves. Faith may make them stronger and healthier, giving them strength.					
Physical activity							
	Being physically active maintains optimal bone health and decreases the risk of a bone fracture by improving bone mass and increasing muscular strength, coordination and balance and thereby reducing falls. Physical activity that is weight-bearing is best. Examples include walking, dancing, aerobics, skating, and weightlifting. Aerobic exercise targets your cardiovascular fitness and helps to maintain health.	Physical activity helps you to feel better and less stressed, gives you more energy for daily activities, and improves your quality of life, sleep, and appetite. It promotes self-confidence and a feeling of control over your health. It also helps you cope with discomfort and manage weight.					
Sun exposu	re						
	Radiated skin may be sensitive, avoid the sun.	(No information)					

#### TABLE V Continued

Outcome	SCP 1	SCP 2
Торассо		
	Smoking is associated with many illnesses. If you smoke, consider quitting.	Smoking is related to poor bone and general health. If you smoke, consider quitting.
Caffeine		
	Excess caffeine can have a negative effect on bone. Limit coffee to fewer than 4 cups daily.	For optimal bone health, limit coffee to fewer than 4 cups daily.
Alcohol		
	The link between alcohol consumption and breast cancer recurrence is not as strong.	(No information)
Bone health	1	
	You may be at a higher risk for bone loss whether you have treatment-induced menopause or whether you had cancer treatments such as aromatase inhibitors. Bones depend on calcium and vitamin D to stay strong and healthy. Protein, calcium, and vitamin D play important roles in maintaining bone health.	Postmenopausal women have an increased risk of osteoporosis. The risk can also be further increased by factors such as family history, smoking, diet, early menopause, chemotherapy, long-term corticosteroids, and some hormonal therapies that lower estrogen.
Diet and he	althy eating	
	Healthy eating decreases your risk of breast cancer recurrence. A lower fat diet may also help women to achieve weight loss. Breast cancer is linked to obesity, a high-fat diet, and alcohol consumption. One third of these cancers are linked to diet. Vegetables, fruits, and whole grains are healthy foods that should be the base of a balanced diet.	When following a low-fat diet, it is important to focus on both the total amount and quality (type) of fat you eat. Choosing fats found in plant-based foods such as nuts, seeds, avocados, and vegetable oils is preferred to saturated fat from animals. When eating a low-fat diet, it is also important to focus on replacing fat with foods that are minimally processed or refined.
Natural hea	Ith products	
	Natural health products are vitamins, minerals, herbs, and other supplements that you take on a regular basis as a natural medicine rather than using them as a food. Sometimes they are taken in higher amounts than can be obtained through your diet.	There is concern about whether vitamins, minerals, and herbal supplements may affect your treatments. These natural health products are therefore not recommended during chemotherapy or radiation treatments.
Calcium an	d vitamin D	
	Calcium and vitamin D are essential for strong bones. A daily intake of calcium is 1200 mg. A daily supplement of 1000 IU vitamin D is recommended for bone health and the prevention of cancer.	Calcium and vitamin D are essential for strong bones. A daily dose is a sum of what you consume from food sources and from supplements. The recommended daily intake of calcium is 1200 mg. Vitamin D intake from all sources should not exceed 4000 IU daily.
Organic foc	od .	
	The research concerning organic food and its association with cancer risk has not been studied accurately. To reduce your risk, buy locally grown foods that are in season and be sure to peel and wash vegetables and fruits well.	(No information)
Saturated fa	t and cholesterol	
	Choose lean cuts of meat, poultry without skin, and low-fat milk products. Choose an unsaturated fat. Choose low-fat milk products and lean cuts of meat. Limit high cholesterol foods such as eggs and shellfish.	Low-fat food may reduce the risk of cancer recurrence. Choose fat from plant-based foods such as nuts, seeds, avocados, and vegetable oils rather than the saturated fat from animals.
Soy		
	Soy contains a form of plant estrogen. Up to 2–3 servings of soy foods daily are safe in women with a history of breast cancer whether they had estrogen receptor–positive disease or use tamoxifen hormonal therapy.	Soy may contain plant estrogen.
Hormones i	n food	
	Hormones may stimulate breast cancer growth or affect hormonal treatments such as tamoxifen. Confusion exists concerning the potential harm of hormones in foods, specifically milk and other dairy products, poultry, and beef. Hormonal growth products are not present in dairy and poultry products, including turkey, in Canada.	The potential benefits and risks of foods such as flax and soy, which contain plant estrogens, are not well known at this time.
Salt intake		
	Limit your salt intake. Salt can have a negative effect on bone. Limit salt intake.	Salt can have a negative effect on bones. Check the nutrition label on processed foods, and limit salt to less than 2100 mg daily.

*et al.*<sup>18</sup>. Treatments for BCa—such as ovarian suppression, chemotherapy, and endocrine therapies—can lead to severe menopausal symptoms in women<sup>87,88</sup>, and it has been postulated that estrogen deficiency might be leading to atrophy of the urinary tract, leading to urinary symptoms and sexual dysfunctions<sup>88,89</sup>. Although sexual dysfunction is a frequently observed side effect of treatment in BCa patients and survivors, we found only one review that investigated the effects of exercise, counselling, and information interventions on sexual functioning<sup>90</sup>. The review reported that counselling seemed to be beneficial, but its findings remain inconclusive because of methodology flaws and a high risk for bias found both in the review itself and in the included primary studies.

The following limitations should be kept in mind in interpreting our results. Although our umbrella review included only moderate- or high-quality systematic reviews and meta-analyses, we had no control over the studies that were included in those publications. The systematic reviews—but not the original studies included in those reviews—can be assessed using AMSTAR. Even when quality assessments were performed in the included reviews, the tools used for those assessments varied widely. We came across many reviews that reported inconclusive findings because of the heterogeneities that they observed. And heterogeneities were not restricted to measured outcomes alone; they also pertained to the measuring tools used, to follow-up periods, to the populations studied, and to the contradictory findings observed.

While recognizing those limitations, a major strength of our study is that the umbrella review was very rigorously conducted. Decision-makers are increasingly required to make evidence-informed policy decisions and often require evidence within short timeframes. In our umbrella review, we collated and highlighted the existing scientific evidence that is of superior quality, and we present a snapshot of the events and challenges that are important in BCA survivorship. The AMSTAR tool used here to assess the quality of the included reviews is reliable for quality assessment, giving us confidence in the results we have reported.

Our umbrella review combines data from high-quality systematic reviews and summarizes the best evidence available to inform clinicians delivering SCPS to people affected by Bca. Our findings also accord with the recently published American Cancer Society and American Society of Clinical Oncology вса survivorship guideline<sup>10</sup>. We postulate that, in the absence of more germane systematic reviews on cancer risk for BCa patients and survivors, the information presented here is current and reliable, and can help clinicians in making recommendations to women completing treatment for BCa and living with or beyond cancer, complementing those recently published BCa survivorship guidelines. Furthermore, our review has generated more research questions and hypotheses, thus pointing to the need for more studies that are important in survivorship care planning for women with Bca.

# CONCLUSIONS

Our study findings support existing SCPS in our province concerning the physical and emotional challenges that BCa

survivors often face. However, literature concerning the cancer risks specific to Bca survivors is sparse. Although systematically conducted reviews are the "gold standard" in knowledge synthesis, our findings suggest that much remains to be done in the area of synthesis research to better guide practice in cancer survivorship.

#### CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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