Advancements in chemotherapy have greatly increased breast cancer survival, leading to an increased focus on the management of long-term effects of treatment. Chemotherapy-related cognitive impairment, one such long-term effect, is experienced by as many as 90% of breast cancer survivors (BCS) and negatively affects employment, daily function, and quality of life. Chemotherapy-related cognitive impairment is a top research and clinical practice priority.

Objectives: The aim of this article is to review computer-based cognitive training intervention studies tested in BCS, present implications for practice and directions for future research, and discuss neuroplasticity and cognitive reserve, the mechanisms by which computer-based cognitive training produces physiologic changes in the brain.

Methods: A search of PubMed, CINAHL®, and PsycINFO® databases yielded two computer-based cognitive training intervention studies in BCS.

Findings: This review suggests that computer-based cognitive training may enhance cognitive function in BCS with chemotherapy-related cognitive impairment. Oncology nurses are in a unique position to support BCS experiencing chemotherapy-related cognitive impairment. In addition to acknowledging BCS’ concerns, screening for other potential factors, and providing education on healthy living, nurses may suggest computer-based cognitive training as an approach to managing chemotherapy-related cognitive impairment. Future research should use imaging and larger populations.
Although multifactorial, the specific cause of cognitive impairment is unknown. Some studies have reported cognitive impairment occurring in BCS before treatment (Ahles et al., 2008; Jansen et al., 2011; Phillips et al., 2012), suggesting that the problem may be a result of the tumor itself or a response to the stress of diagnosis (Ahles et al., 2008; Denlinger et al., 2015; Jansen et al., 2011). Underlying mechanisms most likely include stress, fatigue, depression, brain tissue injury, oxidative stress, inflammation, and vascular injury (Ahles & Saykin, 2007). In addition, some of these mechanisms may be mediated by low levels of estrogen, which may affect BCS who experience acute menopause related to treatment (Fallowfield & Jenkins, 2015). Other factors that affect cognitive impairment include age, education, anxiety, and genetics (Vance et al., 2016). Although some investigators report cognitive impairment to improve or even resolve over time (Fan et al., 2005; Weis, Poppelreuter, & Bartsch, 2009), others found that cognitive impairment persisted for many years, or even decades, in survivorship (Koppelmans et al., 2012; Yamada, Denburg, Beglinger, & Schultz, 2010).

Effective interventions to enhance cognitive function in BCS with chemotherapy-related cognitive impairment are needed. The National Comprehensive Cancer Network (NCCN) guidelines identified occupational therapy (with strategies focused on improvement of cognitive function) as a first-line intervention for cognitive impairment in cancer survivors (Denlinger et al., 2015). The Oncology Nursing Society issued its review of evidence-based interventions for cancer and treatment-related cognitive impairment; the recommendation deemed likely to be effective was cognitive training (Von Ah, Jansen, & Allen, 2014). In addition, literature reviews conducted on studies of interventions for cognitive impairment in BCS reported that cognitive training interventions aimed at improving speed of processing, attention, and memory are the most promising for BCS (Morean, O’Dwyer, & Cherney, 2015; Vance et al., 2016). Computer-based cognitive training refers to a method of improving cognitive function through repeated practice on computer-based cognitive exercises that target specific cognitive processes, such as attention, memory, speed of processing, or executive functioning (Conklin et al., 2015).

The purpose of this focused literature review is to describe the use of computer-based cognitive training to enhance cognitive function in BCS with chemotherapy-related cognitive impairment. This focused review provides: (a) an overview of the concepts of cognitive reserve and neuroplasticity, (b) an overview of computer-based cognitive training interventions tested in healthy older adults, (c) a review of computer-based cognitive training interventions tested in BCS, and (d) implications for future practice and research.

Cognitive Reserve and Neuroplasticity

Within the framework of cognitive reserve and neuroplasticity, computer-based cognitive training creates physiologic changes in the brain that increase cognitive reserve (Lampit, Hallock, Suo, Naismith, & Valenzuela, 2015). Cognitive reserve refers to the number and strength of neural connections in the brain (Vance, Kaur, et al., 2012). The more cognitive reserve that one has, the better the brain is able to function. Neuroplasticity refers to physiologic changes that occur in neurons as a result of stimuli or lack thereof (Mahnke, Bronstone, & Merzenich, 2006); therefore, neuroplasticity can be positive or negative.

Positive neuroplasticity is a process that enhances the stimulation and health of neurons so that they grow and form new or stronger connections to other neurons, increasing cognitive reserve (Vance, Kaur, et al., 2012). Examples of positive neuroplasticity include computer-based cognitive training, physical activity (e.g., cardiovascular workout), proper nutrition (e.g., omega-3 fatty acids), and good sleep hygiene. Negative neuroplasticity is a process that inhibits the stimulation and health of neurons so that the connections between other neurons weaken and atrophy, reducing cognitive reserve (Vance, Kaur, et al., 2012). Examples of negative neuroplasticity in BCS include chemotherapy, radiation therapy, and endocrine therapy.

Two studies conducted in healthy older adults demonstrated the effects of positive and negative neuroplasticity on cognitive reserve and, thereby, cognitive function (Boyke, Driemeyer, Gaser, Büchel, & May, 2008; Lampit et al., 2015). Using a physical activity (i.e., juggling) to assess whether positive and negative neuroplasticity create physiologic changes in the brain, Boyke et al. (2008) conducted a randomized, controlled trial with 69 healthy older adults. Participants were randomized into a juggling training group (n = 44) or control group (n = 25). Those in the juggling group were instructed on how to juggle three balls at a time. Magnetic resonance imaging (MRI) scans were conducted on all participants at three time points: time 1 (at baseline, before juggling instruction); time 2 (after three months when participants were able to juggle for at least one minute); and time 3 (three months later, when participants had not juggled for three months). Of the 44 participants in the juggling group, only 25 were able to learn to juggle. Comparing the time 1 and 2 MRI scans between the two groups, physiologic changes, demonstrated by a significant increase in gray matter in the mid-temporal area and the left posterior intraparietal sulcus, were observed in the juggling group but not the control group, demonstrating positive neuroplasticity in the juggling group. However, the physiologic changes observed in the juggling group declined from time 2 to 3, when participants stopped learning to juggle and resumed engagement in less cognitively demanding tasks, demonstrating negative neuroplasticity.

Lampit et al. (2015) conducted a randomized, controlled trial to examine physiologic brain changes induced by computer-based cognitive training. Eighty healthy older adults were randomized into a computer-based cognitive training program (n = 41) or control group (n = 39). Those in the computer-based cognitive training group attended 36 one-hour sessions for 12 weeks. MRI scans were conducted with seven participants from the intervention group and five from the control group at three time points: time 1 (baseline), time 2 (after 9 training sessions), and time 3 (after 36 sessions). Compared to the control group, MRI scans of the computer-based cognitive training group showed physiologic changes, as evidenced by significantly increased gray matter density in the right postcentral gyrus at times 2 and 3, demonstrating positive neuroplasticity in the computer-based cognitive training group.
In summary, neuroplasticity can be positive or negative and can increase or inhibit cognitive reserve. The more cognitive reserve an individual has, the better his or her cognitive function. Using imaging, studies have demonstrated positive and negative neuroplasticity in healthy older adults (Boyke et al., 2008; Lampit et al., 2015).

### Healthy Older Adults and Computer-Based Cognitive Training

The Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study is the largest longitudinal study involving computer-based cognitive training (Ball et al., 2002; Rebok et al., 2014). ACTIVE participants, healthy older adults (N = 2,832) from six cities in the United States, were randomized to one of three intervention groups (computer-based speed of processing training [n = 712], memory training [n = 711], or reasoning training [n = 705]) or to a no-contact control group (n = 704). All three interventions consisted of 10 60- to 75-minute group sessions for five to six weeks. Computer-based speed of processing training focused on interactive computerized tasks that were aimed at improving speed of processing, memory training focused on learning mnemonic strategies, and reasoning training focused on learning problem-solving strategies. Neurocognitive testing was conducted at baseline, immediately postintervention, at a one-year follow-up, and at a two-year follow-up. Immediately postintervention, 87% of computer-based speed of processing training, 26% of memory training, and 74% of reasoning training participants demonstrated cognitive improvement in the cognitive domain in which they were focused (i.e., speed of processing, memory, or reasoning). In addition, at 11 months after the initial training, booster training was offered to randomly selected participants in all three intervention groups. Booster sessions consisted of four 75-minute sessions for two to three weeks. Booster training significantly enhanced training gains in computer-based speed of processing and reasoning interventions but not memory. These training gains were maintained at a two-year follow-up. In addition, the computer-based speed of processing (effect size = 0.66, 99% confidence interval [CI] [0.43, 0.88]) and reasoning (effect size = 0.23, 99% CI [0.09, 0.38]) interventions maintained their effects on their targeted cognitive domains at a 10-year follow-up, with the greatest effect seen in the computer-based speed of processing training group (Rebok et al., 2014).

Although the ACTIVE study was conducted in healthy older adults, its findings have led investigators to examine the use of computer-based cognitive training in other populations. These populations have included, but are not limited to, people with HIV (Cody, Fazeli, & Vance, 2015; Vance, Fazeli, Ross, Wadley, & Ball, 2012), stroke survivors (Park & Park, 2015; Yoo, Yong, Chung, & Yang, 2015), childhood cancer survivors (Conklin et al., 2015; Hardy, Willard, & Bonner, 2011), and BCS (Kesler et al., 2013; Von Ah et al., 2012). However, this article will focus on computer-based cognitive training interventions tested in BCS.

### Computer-Based Cognitive Training Interventions

A literature search was conducted using PubMed, CINAHL®, and PsycINFO® databases using the key words cognitive training and breast cancer survivors. This search yielded four unique articles, of which two were reviewed based on the following inclusion criteria: computer-based cognitive training intervention, BCS participants, and published in English.

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**TABLE 1. Computer-Based Cognitive Intervention Studies for Chemotherapy-Related Cognitive Impairment in BCS**

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Design and Procedure</th>
<th>Findings</th>
<th>Strengths and Limitations</th>
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<tr>
<td>Kesler et al., 2013</td>
<td>41 chemotherapy-treated BCS; two randomized groups: home-based online cognitive training (n = 21, mean age = 55 years, mean months post-treatment = 72) and wait-list control (n = 20, mean age = 56 years, mean months post-treatment = 72)</td>
<td>BCS completed online exercises targeting executive functioning at home. Sessions lasted 20–30 minutes for 12 weeks. Outcome measures consisted of a neuropsychological test battery and self-report measures administered at baseline and within three days of intervention completion.</td>
<td>Compared to the control group, BCS in the intervention group showed improved cognitive flexibility, speed of processing, and verbal fluency, and self-reported improvement in executive behaviors.</td>
<td>Strengths: RCT, demonstrates efficacy of home-based training, neuropsychological test battery and self-report measures; limitations: small sample size, no extended follow-up, computer and Internet access required</td>
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<tr>
<td>Von Ah et al., 2012</td>
<td>82 chemotherapy-treated BCS; three randomized groups: computerized speed of processing training (n = 27, mean age = 57 years, 96% Caucasian, mean months post-treatment = 78), memory training (n = 26, mean age = 55 years, 81% Caucasian, mean months post-treatment = 59.5), and wait-list control (n = 29, mean age = 57 years, 90% Caucasian, mean months post-treatment = 59)</td>
<td>BCS in the computerized speed of processing training intervention attended 10 one-hour training sessions during a six- to eight-week period. Outcome measures consisted of a neuropsychological test battery and self-report measures administered at baseline, immediately post intervention, and at the two-month follow-up.</td>
<td>Compared to the control group, the memory training group showed significant improvement in memory at the two-month follow-up only. Compared to the control group, the speed of processing training group showed significant improvement in speed of processing and memory at both postintervention time points.</td>
<td>Strengths: RCT, neuropsychological test battery and self-report measures; limitations: small sample size, limited diversity of sample, no extended follow-up</td>
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</table>
Each of these studies is discussed and summarized in Table 1. Computer-based cognitive training interventions that have been examined in chemotherapy-treated BCS can be classified by the type of cognitive impairment aimed for improvement. These are speed of processing and executive function.

### Speed of Processing

Speed of processing refers to the rate at which cognitive operations are performed (Vance, McNees, & Meneses, 2009). Von Ah et al. (2012) randomized 82 chemotherapy-treated BCS into one of two intervention groups (computer-based speed of processing training or memory training) or a wait-list control group. In the computer-based speed of processing training intervention, BCS completed interactive computerized tasks that were aimed at improving speed of processing from Posit Science Corporation. In the memory training intervention, BCS learned mnemonic strategies for remembering word lists and sequences and completed memory exercises. Neurocognitive testing (i.e., Rey Auditory Verbal Learning Test, Rivermead Behavioral Paragraph Recall Test, and Useful Field of View test) was conducted at baseline, immediately postintervention, and at a two-month follow-up. The memory training group demonstrated significant improvement in memory compared to the control group, but only at a two-month follow-up. The computer-based speed of processing training group demonstrated significant improvement in speed of processing and memory compared to the control group immediately postintervention and at the two-month follow-up. Both interventions demonstrated improvements in perceived cognitive functioning, symptom distress, and quality of life. In addition, satisfaction was high for both interventions.

### Executive Function

Executive function refers to working memory, cognitive flexibility, multitasking, planning, and attention (Kesler et al., 2013). In a randomized, controlled trial, Kesler et al. (2013) tested a computer-based cognitive training program available online (www.lumosity.com), with the aim of improving executive function. Forty-one chemotherapy-treated BCS were randomized to the computer-based cognitive training group or wait-list control group. BCS in the intervention group completed 48 cognitive training sessions lasting 20–30 minutes for 12 weeks. Neurocognitive testing (i.e., Wisconsin Card Sorting Test, letter fluency test from the Delis-Kaplan Executive Function System, Hopkins Verbal Learning Test Revised for verbal memory, and digit span and symbol search subtests of the Wechsler Adult Intelligence Scale [4th ed.]) was conducted at baseline and immediately postintervention. Compared to the wait-list control group, BCS in the intervention group showed significant improvements in executive function, speed of processing, and self-reported executive function; although not significant, improvements in verbal memory also were seen.

### Discussion

Von Ah et al. (2012) and Kesler et al. (2013) used cognitive training programs that are commercially available online (www.lumosity.com and www.brainhq.com). Although Kesler et al. (2013) targeted executive function and Von Ah et al. (2012) targeted speed of processing, both interventions demonstrated that computer-based cognitive training enhanced cognitive function in BCS; however, young (aged younger than 40 years) BCS were excluded and minority BCS were underrepresented. Together, their findings among BCS are consistent with those of the ACTIVE study (Ball et al., 2002), which was conducted in healthy older adults.

### Implications for Practice and Research

Oncology nurses can support BCS with chemotherapy-related cognitive impairment. Foremost, oncology nurses can validate the existence of cognitive impairment and apply the NCCN guidelines (Denlinger et al., 2015), which first describe that BCS should be screened for depression, pain, fatigue, and sleep disturbances. Next, current medications should be reviewed and any aspect of medication that interferes with cognition should be discussed. Third, strategies for healthy living (e.g., exercise, sleep, stress reduction) should be provided.

Computer-based cognitive training programs have been tested in BCS and are commercially available and easily accessible. Therefore, oncology nurses can provide evidence about the studies and discuss the feasibility of using this approach with BCS. This use of computer-based cognitive training to manage cognitive impairment may potentially empower BCS and, therefore, aid in addressing BCS’ perceived or subjective cognitive impairment, which significantly affects their quality of life and everyday functioning.

Chemotherapy-related cognitive impairment in BCS is a complex issue, and management may need to be specifically tailored. Additional interventions to improve positive neuroplasticity (e.g., exercise, nutrition, good sleep hygiene), used in combination with computer-based cognitive training, may result in a greater increase in cognitive reserve and, thereby, better cognitive function (Eggenberger, Schumacher, Angst, Theill, & de Bruin, 2015). Therefore, oncology nurses can suggest that BCS incorporate a combination of exercise, nutrition, good sleep hygiene, and computer-based cognitive training into their daily routines (Vance, Eagerton, Harnish, McKie, & Fazeli, 2011).

### Implications for Practice

- Apply the National Comprehensive Cancer Network guidelines by validating breast cancer survivors’ concerns, screening for co-occurring conditions, reviewing medications, and providing healthy living strategies.
- Educate breast cancer survivors about underlying mechanisms of cognitive impairment and how computer-based cognitive training creates physiologic changes in the brain.
- Suggest a combination of computer-based cognitive training and healthy living strategies for self-management of cognitive impairment.
With only two studies having examined the use of computer-based cognitive training in chemotherapy-treated BCS, a great need exists for further investigation. For example, given that cognitive impairment is multifactorial and the specific cause is unknown, additional studies should include all BCS, not just those who were treated with chemotherapy. Inclusion of all BCS may improve understanding of intervention response by allowing for comparison by treatment type. In addition, although MRI scans revealed physiologic changes (positive neuroplasticity) in the brains of healthy older adults who have undergone computer-based cognitive training (Lampit et al., 2015), whether BCS experience these same changes is unknown. Inclusion of MRI scans in additional studies may improve understanding of neuroplasticity in BCS after treatment. In addition, larger studies that included extended postintervention follow-up assessments are needed to determine the sustainability of computer-based cognitive training effects after training has ended. Larger studies with a diverse sample of BCS also would aid in understanding individual responses to computer-based cognitive training, which may lead to developing tailored computer-based cognitive training interventions.

**Conclusion**

This article suggests that computer-based cognitive training may enhance cognitive function in BCS with chemotherapy-related cognitive impairment, addressing an urgent and currently unmet need in BCS. Studies among healthy older adults demonstrated that computer-based cognitive training produces physiologic changes in the brain (Lampit et al., 2015) and enhances cognitive function (Ball et al., 2002), and that enhancement is sustainable (Rebok et al., 2014). Although limited, studies support the use of computer-based cognitive training in BCS with chemotherapy-related cognitive impairment (Kesler et al., 2013; Von Ah et al., 2012). Oncology nurses are in a unique position to support BCS experiencing chemotherapy-related cognitive impairment. In addition to acknowledging BCS’ concerns, screening for other potential factors, reviewing medications, and providing education on healthy living, nurses can provide evidence about computer-based cognitive training studies and discuss the feasibility of using this approach with BCS. In addition, to address the complexity of chemotherapy-related cognitive impairment, nurses can suggest that BCS incorporate a combination of exercise, nutrition, good sleep hygiene, and computer-based cognitive training into their daily routine. Although literature supports the use of computer-based cognitive training in enhancing cognitive function in healthy older adults (Ball et al., 2002; Kesler et al., 2013; Lampit et al., 2015; Rebok et al., 2014), larger studies, a diverse sample, extended postintervention follow-up assessments, inclusion of non–chemotherapy-treated BCS, and imaging are needed to better understand its effects in BCS.

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