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Memory and Cancer: A Review of the Literature

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The mental health of cancer survivors has not always been the primary emphasis of treatment protocols since physical health outcomes have taken precedence. Older cancer survivors experience a double jeopardy since they are at risk for memory impairments and mild cognitive impairment and because they are greater than fifty-five years of age. Of the 9.6 million cancer survivors in the US who have completed active treatment, many report cognitive difficulties, with labels such as “chemo brain,” “not as sharp,” “woolly-headedness,” or the “mind does not work as quickly”. To date, most of our knowledge of cognitive impairment in cancer survivors comes from female breast cancer survivors. Studies indicate that these survivors have diminished executive function, verbal memory, and motor function. Cancer survivors want to live independently in the community for as long as possible however, these cognitive deficits may prevent this desired lifestyle. To broaden our understanding this paper reviews the literature on the cognitive impairment and memory deficits experienced by three groups of cancer survivors breast, colorectal, and prostate cancer, the latter make up 60% of all survivors nationally. Even though mental health declined after a cancer diagnosis, the long-term outcomes of cancer survivors did not differ from persons without cancer in depression or cognitive function.

An individual is a cancer survivor from the time of a cancer diagnosis through the remainder of his or her life (Office of Cancer Survivorship, National Cancer Institute; Pollack, Greer, Rowland, Miller, Doneski, Coughlin, et al. 2005). Because two-thirds of adults diagnosed with cancer will be alive in five years, the overall health of persons with a history of cancer beyond the acute diagnosis and treatment phase has become of interest to the medical and

scientific community (Blanchard, Stein, Baker, Dent, Denniston et al. 2004; Demark-Wahnefried, Aziz, Rowland, & Pinto, 2005; Hoffman, McCarthy, Recklitis, & Ng, 2009).

There are an estimated at 2.8 million rural cancer survivors in the US. As a group, these individuals are more likely than urban survivors to be non-Hispanic white, to have less education, and to lack health insurance (Weaver, Lu, Geiger, & Case, 2013). Cancer survivors from the 2006–2010 National Health Interview Survey were evaluated for health behaviors. This population-based sample of 1,642 rural county and 6,162 urban dwellers were adults eighteen years of age and older. Health behaviors, including leisure-time physical activity, alcohol use, smoking status, body weight, as well as the survivors' overall health (Weaver, Palmer, Lu, Case, & Geiger, 2013). The research found that rural cancer survivors could benefit from health promotion interventions. Other investigators, Schultz, & Winstead-Fry (2001) evaluated quality of life in cancer survivors (N=344) living in rural Maine and determined that these individuals reported higher scores than their urban counterparts.

More than 6 million people in the U.S. are at risk for memory impairments and mild cognitive impairment (MCI) because they are cancer survivors and are over 55 years of age (Schaie, 1989). In a nationally representative sample of the U.S. population (N=9,819), with equal numbers of males and females, participants answered a yes-or-no question, “Are you limited in any way because of difficulty remembering or because you experience periods of confusion?” (Jean-Pierre, Winters, Ahles, Antoni, Armstrong, et al., 2012). Of the respondents, 13%, or 1,305 individuals had a history of cancer, reported memory problems more often by adults who had a history of cancer than those without cancer (14% vs. 8%). Thus the cognitive impairment experienced by cancer survivors may be considered another comorbidity that directly affects prognosis, quality of life, and longer term outcomes (Bellizzi, Aziz, Rowland, Weaver, Arora et al., 2012; Gonzalez, Ferrante, Van Durme, Pal, & Roetzheim, 2001; Olin, 2001).

As a first step toward developing a longitudinal view, the review reported here critiqued and synthesized representative literature on memory and/or cognitive function in cancer survivors. The review was limited to published studies examining cognitive function, in survivors of one of three major cancers--breast, colorectal, and prostate because they make up 60% of cancer survivors.

Cancer and Aging are Associated

Because 49% of the 10 million cancer survivors within the US are older than 65, a clearer understanding of cancer-related cognitive impairment is necessary to promote their successful independent living and survival (Ahles, Saykin, Furstenberg, Cole, Mott, et al., 2002; Anderson-Hanley, Sherman, Riggs, Agocha, & Compas, 2003; Beer, Bland, Bussiere, Neiss, Wersinger, et al., 2006; Goodwin, Smaet, & Hunt, 1998; Matsuda, Takayama, Tashiro, Nakamura, Ohashi, Shimozuma, 2005). Minisini, Atalay, Bottomley, Puglisi, Piccart, and Biganzoli (2004) evaluated eight studies of the effects of anticancer treatment on cognitive function. Their findings indicated that patients experienced cognitive changes because of treatment. Jansen, Miaskowski, Dodd, Dowling, and Kramer (2005) evaluated 16

studies and found significant chemotherapy-induced impairment in visual memories. Moreover, as compared with normative samples, significant negative effects were observed in four domains of cognitive function: executive function, information processing speed, verbal memory, and visual memory. These findings provide evidence that because of anti cancer treatment, cancer survivors suffer cognitive deficits that may interfere with their daily living.

Memory problems associated with aging have been negatively labeled as “Senior Moments,” but problems also are labeled “chemo brain,” not as sharp,“ and woolly-headedness” by 10–40% of cancer survivors (Cimprich, 1995; Cull, Hay, Love, Mackie, Smets, & Stewart, 1996; Matsuda, Takayama, Tashiro, Nakamura, Ohashi, & Shimozuma, 2005). The memory loss and concentration difficulty experienced in cancer patients and cancer survivors have often been attributed to anxiety, depression, and/or physical fatigue resulting from anticancer treatment in early studies that did not evaluate cognitive function (Cimprich, 1992; Van Oosterhout, Ganzevles, Wilmink, De Geus, Van Vonderen, & Twijnstra, 1996). However, though the risk of developing cognitive impairment is 3.3 to 3.5 times higher in patients treated with chemotherapy, the neuropsychological side effects of cancer treatment have not been sufficiently investigated (Stewart, Collins, Mackenzie, Tomiak, Verma, Bielajew, 2008; van Dam, Schagen, Muller, Boogerd, Wall et al., 1998). The implication of the labeling is that the cancer treatment precipitated the memory difficulties experienced by survivors and it may or may not be permanent. Whether these changes are transient or permanent will not be known without longitudinal studies to track the cognitive functioning of long-term cancer survivors (Ahles, Root, & Ryan, 2012; Saykin, Ahles, & McDonald, 2003).

Chemotherapy Induced Cognitive Impairment

Breast Cancer

Thirty-two women with a mean age of 54 (SD =14) who underwent surgery for localized (Stage I or II) breast cancer, showed deficits in attention within three days following mastectomy (Cimprich, 1992). Their attentional fatigue increased as the number of post-surgery days increased. In another study, recall of information related to treatments and associated risks was poor among 71 women diagnosed with breast cancer (mean age was 48.71 [SD = 11.02]) (Hughes, 1993).

A dose-effect relation between the chemotherapy delivered and the resulting cognitive impairment was observed and the investigators concluded that the incidence of cognitive impairment might be as high as 30% in breast cancer survivors (Ganz, 1998; 2001). In a study of 104 breast carcinoma patients with mean ages of 45.5 (SD = 6.2) and 48.1 (SD = 6.8) years, cognitive impairment was found in 32% of those treated with high-dose chemotherapy, 17% of those treated with standard-dose chemotherapy, and 9% of the control patients (van Dam, Schagen, Muller, Boogerd, Wall, Fortuyn, & Rodenhuis, 1998). After three years, breast carcinoma patients treated with high dose chemotherapy had significantly more problems with concentration and memory than patients who had not received this treatment (Schagen, van Dam, Muller, Boogerd, Lindeboom, & Bruning, 1999).

Five year breast cancer survivors who had received systemic chemotherapy scored in the lower quartile on the Neuropsychological Performance Index (39% v 14%) and self-reported greater problems with working memory than women treated with local therapy only (Ahles, Saykin, Furstenberg, Cole, Mott, Skalla, Whedon, Bivens, Mitchell, Greenberg, & Silberfarb, 2002). Bender, Sereika, Berga, Vogel, Brufsky, Paraska, and Ryan (2005) demonsrated that BCSs treated with chemotherapy and tamoxifen showed performance deficits in visual memory and verbal working memory, and reported more memory complaints. The women who only received chemotherapy had deficits in verbal working memory. Cognitive function scores improved over time in the women who received no anticancer therapy. Recently, in a Sweedish twin study, the cognitive function of 702 BCS aged 65 years of age and older was compared with their cancer-free twins. After controlling for genetics and environment, the cancer survivors were twice as likely to be diagnosed with dementia as their twins were; however, the odds ratio did not reach statistical significance (Heflin, Meyerowitz, Hall, Lichtenstein, Johansson, Pedersen, & Gatz, 2005). Adjuvant chemotherapy in women with breast cancer may be associated with deteriorations in memory, and this loss may persist over time.

Poppelreuter, Weis, Kulz, Tucha, Lange, and Bartsch (2004) evaluated the impact of ten anticancer treatments on the neuropsychological function of 119 patients (19% were breast cancer survivors). Cognitive impairment occurred in a clinically relevant percentage of cancer patients and could not be explained by depression or anxiety. Matsuda, Takayama, Tashiro, Nakamura, Ohashi et al (2005) reviewed ten studies of mild cognitive impairment (MCI) in breast cancer patients who had completed adjuvant chemotherapy. The cognitive symptoms identified included memory loss, lack of attention, and concentration difficulties. The authors concluded that while the MCI symptoms were transient, they nevertheless took several years to disappear. Anderson-Hanley et al (2003) included patients (N = 838) who were on average 49 years of age and 86 weeks (SD = 124.1) from either a diagnosis or treatment. Sex of the sample was not provided, although only 28% of the sample was breast cancer patients. Negative effects were most pronounced in the three cognitive domains of executive function, verbal memory, and motor function.

Jansen, Miaskowski, Dodd, Dowling, and Kramer (2005) reviewed 16 studies that included eight cognitive domains. The review included 996 patients who averaged 48 years of age (SD = 7.54). Most (84%) of the patients were female and 56% of the sample were in breast cancer studies. Even though all significant effect sizes were in the negative direction, visual memory was the sole cognitive domain that showed significant chemotherapy-induced impairment in all comparisons. Falleti, Sanfilippo, Maruff, Weih, and Phillips (2005) reviewed six studies that included six cognitive domains. They concluded that cognitive impairment occurred in women who had undergone adjuvant chemotherapy for breast cancer but the magnitude of this impairment found depended on the study design. Jim, Phillips, Chait, Paul, Popa et al. (2012) reviewed 17 studies of 807 patients previously treated with standard-dose chemotherapy for breast cancer. The individuals treated with chemotherapy performed worse than comparison subjects did in verbal and visuospatial ability. Hodgson, Hutchinson, Wilson, Nettelbeck (2013) reviewed 13 studies and found no relation between cognitive impairment and time since treatment cessation, but a significant

negative relation between cognitive impairment and treatment duration. The authors excluded patients who had mood or anxiety diagnoses (or psychiatric or substance abuse histories), had brain cancer or had received radiotherapy or hormone treatment. Age had no impact on treatment-related cognitive impairment.

Other studies have found that the cognitive effects from chemotherapy were variable. Six months after the completion of treatment for breast carcinoma, Donovan, Small, Andrykowski, Schmitt, Munster, and Jacobsen (2004) found no statistically significant differences between women (mean years = 55.4, *SD*=9.0) who received chemotherapy and those who did not with regard to performance on tests of episodic memory, attention, complex cognition, motor performance, or language.

Wefel, Lenzi, Theriault, Davis, and Meyers (2004) followed 18 women (*M* years=45.4, *SD*=6.7) with breast carcinoma for 18 months. At six months, 61% of the women had experienced a decline in one or more domains, including attention, learning, and processing speed. However, at the completion of the study, 50% of the women who had shown cognitive impairments demonstrated improvements and the remaining individuals were stable. Among these women, 35% had exhibited cognitive impairment before the start of systemic therapy.

These studies provide an inconclusive picture of cognitive impairment in breast cancer survivors and do not show clearly whether anticancer treatment causes cognitive impairment. Of the cognitive domains evaluated, scores were often lower for the cancer patients following treatments than for normative samples. However, the impact of chemotherapy on cognitive function may be delayed and may manifest later pointing to the need for longitudinal prospective study designs. In addition, the effects of these cognitive impairments on an individual's everyday function are not known (Garman, Pieper, Seo, & Cohen, 2003).

Breast cancer patients with Stage 1–3, average age of 55 years were tested prior and after adjuvant treatment. Patient's score on reaction time were significantly lower than healthy controls. The patients were significantly more likely to have lower than expected overall cognitive performance (Ahles, Saykin, McDonald, Furstenberg, Cole et al., 2008). Essential for independent living and pursuing career goals, executive function encompasses several goal-directed behaviors such as planning, sequencing, and monitoring of one's behavior and is associated with cognitively demanding skills. Executive function is an umbrella term for cognitive processes that regulate, control, and manage other cognitive processes such as planning, working memory, attention, problem solving, verbal reasoning, inhibition, mental flexibility, task switching, and initiation and monitoring of actions (Dugbartey, Rosenbaum, Sanchez, & Townes, 1999). One study, Wefel, Saleeba, Buzdar, & Meyers (2010) found that before they received chemotherapy, 21% of breast cancer patients (9 of 42) had cognitive dysfunction. In the acute interval, 65% (24 of 37) demonstrated cognitive distraction. At long-term evaluation, after cessation of treatment 61% (17 of 28) cancer survivors evidenced cognitive dysfunction. In another study, women exposed to chemotherapy performed significantly worse than the reference group on cognitive tests of immediate and delayed verbal memory, processing speed, executive functioning, and psychomotor speed. They

experienced fewer symptoms of depression, but they had significantly more memory complaints that could not be explained by cognitive test performance (Koppelmans, Breteler, Boogerd, Seynaeve, Gundy et. al, 2012). Returning to work three years post treatment, BCS reported higher levels of fatigue, depressive symptoms, and work related cognitive limitations than a noncancer comparison group (Todd, Feuerstein, & Feuerstein, 2011).

In summary, breast cancer survivors have generously participated in research that has demonstrated a perplexing concern with cognitive impairments that may or may not become permanent after the active phase of cancer treatment. What is not as well known is the long-term effects of chemotherapy on women after menopause (Yancik, Wesley, Ries, Havlik, Edwards, & Yates, 2001)? Recently, Collins, Mackenzie, Stewart, Bielajew, & Verma (2009) found that in postmenopausal women survivors, the negative effects of chemotherapy dissipate after one year, but they suggest that these are tentative findings.

Colorectal Cancer

Over 2,000 cases and controls in Australia were innacurate in remembering their dietary intakes (Kune, Kune, & Watson, 1987). Seventeen patients with advanced colorectal cancer who received immunotherapy were tested on cognitive function (Walker, Wesnes, Heys, Walker, Lolley, & Eremin, 1996 and Walker, Walker, Heys, Lolley, & Wesnes, 1997). Compared with a control group who received chemotherapy alone, the immunotherapy group had greater impairment in executive function, memory, and digit symbol tests. Summer (2012) found that older male participants experience an increase in memory deficits in word generation and visual learning. Courneya and Friedenreich (1997) surveyed 130 colorectal survivors to determine exercise patterns and quality of life. Those whose exercise routines lapsed reported lowest quality of life scores. Five-year colorectal survivors (N=227) reported high quality of life, irrespective of stage at diagnosis and time from diagnosis; however, they had greater depressive symptoms (Ramsey, Berry, Moinpour, Giedzinska, Andersen, 2002). Female survivors (N=259) at nine years who had social networks reported better mental health (Sapp, Trentham-Dietz, Newcomb, Hampton, Moinpour, 2003). A study by Perkina, Poroshina, Kovalenko, and Berstein (2004) (article in Russian) found that short-term memory and concentration in endometrial carcinoma were significantly better than in colorectal cancer and or osteoporotic patients. Cognitive function of colorectal survivors is not well established because many of the studies were epidemological surveys interested in quality of life.

Prostate Cancer

In a national telephone survey of 421 men diagnosed with prostate cancer, their recall of diagnostic procedures was poor, with less than 20% remembering that they had had a biopsy (Miles, Giesler, & Kattan, 1999). In another survey of prediagnostic symptoms, men with prostate cancer were retested in six months (Legler, Potosky, Gilliland, Eley, Stanford, 2000). The researchers determined that 70% had high recall accuracy between baseline estimates of prediagnostic function and prospective and retrospective measures of change at follow up testing. Fear of recurrence is a major detriment to quality of life in prostate cancer

survivors (Freedland, Humphreys, Mangold, Eisenberger, Dorey et al. 2005; Knight, Chmiel, Sharp, Kuzel, Nadler et al. 2001).

Treatment for prostate cancer often includes treatment with hormones, and males who receive androgens may or may not have cognitive deficits; however, the age of the males often confounds the ability to make an association (Beer, Bland, Bussiere, Neiss, Wersinger, Garzotto, Ryan, & Janowsky, 2006; Cherrier, 2005; Kenny, Fabregas, Song, Biskup, & Bellantonio, 2004; Shahinian, Kuo, Freeman, & Goodwin, 2006; Taxel, Stevens, Trahiotis, Zimmerman, Kaplan, 2004). In one study, males who received androgen suppression monotherapy over a six-month period, performed worse on memory and executive function both at baseline and six months later (Green, Pakenham, Headley, Yaxley, Nicol, Mactaggart, Swanson, Watson, & Gardiner, 2002). Whereas, Cherrier, Rose, and Higano (2003) found that the males had a beneficial effect on verbal memory, but a decrease in spatial ability at nine months. Bennett, Bishop, Zadik, and Lincon (2004) found no difference in memory complaints between males who were treated with a transurethral resection of the prostate or of the bladder in the previous 10 months. Mohile, Lacy, Rodin, Bylow, Dale et al. (2010) tested males before and six months after androgen deprivation therapy (ADT). Among the older males, 71 years of age, 38% demonstrated a decline in measures of executive functioning and 48% showed improvement on measures of visuospatial abilities.

A prospective observational study by Choa, Uchio Zhang et al. (2012) combined neuropsychological testing with functional magnetic resonance imaging (fMRI) of 30 prostate cancer participants and found a statistically significant association between ADT use and decreased medical prefrontal cortical activation during cognitive control and functional brain connectivity impairment on fMRI. The authors suggested further studies to identify the long-term implications of these findings.

A review of eleven studies examining the effects of ADT on standardized tests found that spatial memory was negatively affected by the ADT (Jamadar, Winters, & Maki, 2012). Because the studies did not contain a comparison group of older cancer free males, differences from normative groups in cognitive function are unknown. Engstrom (2008) proposed studying hot flashes in males with prostate cancer. Jensen et al 2006 and Kayl, Wefel, and Meyers (2006) who examined the mechanisms of chemotherapy, indicated that 16 agents produce impairments in attention and concentration, executive function, memory, and visuospatial skills. Their results are included in Table 1.

Summary of Cognitive Effects

Breast, colorectal, and prostate cancer account for 60% of the cancers in the US. Even though the treatment regimes are different, survivors of these three cancers have similar cognitive impairments. Seventeen cognitive domains have been identified as impaired (15 in breast cancer, seven in colorectal, and five in prostate, with four domains overlapping among the 3 cancers). The four overlapping domains identified in all three cancers are executive function, memory, verbal memory, and recall. Table 2 includes the cognitive

domains that have been identified in the published literature as affected by either breast, colorectal, or prostate cancer.

Castellon, Ganz, Bower, Petersen, Abraham, and Greendale (2004) found that breast cancer survivors who had also received adjuvant chemotherapy, performed worse on verbal learning, visuospatial functioning, and visual memory between 2 and 5 years after surgery than did BCS treated with surgery only. There was no relation between subjective cognitive complaints and objective performance, though complaints were related to psychological distress and fatigue. Similarly, Cherrier, Aubin and Higano (2009) found similar findings in a non-metastatic prostate cancer study that included both a treatment and control group. The treatment group received Androgen deprivation therapy and was tested at baseline, and after three and nine months. There was evidence to suggest that a significant decline in spatial reasoning, spatial abilities and working memory during treatment compared with baseline. No significant changes noted in the control group cognitive test. However, Tan and Colleagues (2013) found no decline in cognition or memory function among 49 participants diagnosed with prostate cancer that were between 59–89 years of age. The Mini Mental State Examination was used to assess at baseline and follow up visits.

Intervention Studies to Improve Cognitive Function

While the mechanisms causing cognitive impairment in older cancer survivors remains unclear, some interventions have been found helpful in improving cognitive function, especially memory. Using a pre- post quasi-experimental design, McDougall (1999; 2001) tested the effectiveness of the Cognitive Behavioral Model of Everyday Memory (CBMEM), an efficacy-based memory curriculum, in a retirement community in NE Ohio. Of the 78 participants (58Fs, 20Ms), the average age was 82 years, and the average MMSE score was 28. The benefits of the training for the 11 cancer survivors in the sample (Fs=8, Ms=3) was evaluated. They were significantly older M=84.12 years, scored significantly lower at the pretest on metamemory capacity (M = 2.5, SD = 0.5), and performed fewer self-reported instrumental activities of daily living (IADLs). On the Rivermead Behavioral Memory Test (RBMT), five individuals improved from pre-to post test, three declined, and one maintained; data were missing for two individuals. The prospective memory aspect of belonging (M1 = .88, M2 = 1.25) significantly improved. In addition, short term memory scores improved on immediate ($M1$ = 1.13, $M2$ = 1.34) and delayed ($M1$ = 1.13, $M2$ = 1.50) story recall.

McDougall et al (2010) also tested a memory-training intervention with known efficacy, SeniorWISE in a randomized control trial. In the subgroup of cancer survivors, memory performance scores improved, as did memory self-efficacy and use of memory strategies (McDougall, & Becker, Vaughan, Acee, & Delville, 2011). The final sample included 22 cancer survivors who completed the four data collections, 8 in the intervention and 14 in the comparison group. At T2 posttest, data were available for 25 on memory performance. Moderate increases were found on the RBMT, Brief Visual Memory Test (BVMT), and Hopkins Verbal Learning Test (HVLT) scores. There were also moderate improvements on the Center for Epidemiological Studies Depression Scale (CESD), and the Capacity, Change, Locus, and Task subscales of the metamemory measure. Because of the small

sample, some moderate effects were not statistically significant; however, the findings suggest that meaningful differences were occurring.

Ferguson, Ahles, Saykin, McDonald, Furstenberg et al. (2007) tested the effectiveness of a cognitive-behavioral intervention following chemotherapy for well educated, middle-aged, women newly diagnosed with Stage I or II breast cancer. Twenty-nine women participated in four in-office monthly visits (30–50 minutes each) with three contacts between visits, for seven contacts. The participants showed significant improvements over baseline in verbal and executive function, self-reported cognitive function, and quality of life, but there was no control group.

In a recent study, 82 BCS completed a three-group randomized, controlled trial (Von Ah. Carpenter, Saykin, Monahan, Wu et al. 2012). Cognitive and affective outcomes included memory and speed of processing, perceived cognitive functioning, symptom distress (mood disturbance, anxiety, and fatigue), and quality of life. Data were collected at baseline, post-intervention, and 2-month follow-up; in particular, speed of processing improved at post-intervention and 2-month follow-up. The intervention was also associated with improvements in perceived cognitive functioning, symptom distress, and quality of life. Ratings of satisfaction/acceptability were high. Another cognitive behavioral treatment (Ferguson et al 2012) tested with 40 breast cancer survivors found improvements in verbal memory and spiritual well being, but the subjective evaluation of cognitive complaints was unchanged. In summary, the treatment interventions to remediate memory impairment in BCS, or any cancer survivors are in the nascent stages of development.

Synthesis of Research

In addition to the problems with memory that arise from the aging process (and thus may precede a cancer diagnosis), memory dysfunction is associated with cancer and cancer treatment. Treatment for breast cancer often includes chemotherapy and cancer treatment, particularly chemotherapy, seems to induce cognitive changes (Hurria, Rosen, Hudis, Zuckerman, Panageas et al, 2006; Minisini, Atalay, Bottomley, Puglisi, Piccart, & Biganzoli, 2004; Tannock, Ahles, Ganz, & van Dam, 2004). Further, the co-morbidities of cancer may include cognitive impairment. Older patients with hematological disease or cancer of the intestinal tract have experienced negative outcomes (Eberhardt Dilger Musial, Wedding, Weiss, & Miltner, 2006).

Indeed, the risk of developing cognitive impairment was 3.5 times higher in patients treated with high-dose chemotherapy (van Dam, Schagen, Muller, Boogerd, vd Wall E et al., 1998). Survivors of ovarian cancer who received chemotherapy also self-reported memory problems (Myers, Sousa, & Donovan, 2010). However, the relevance of specific cognitive impairments on an individuals' everyday function is unknown. Further, anxiety, depression, sleep disturbance and fatigue, all side effects of cancer treatment, have documented impacts on cognitive performance. To determine the differential effects of anticancer treatment on various cognitive function domains, future studies should include executive function, verbal memory, and motor function. Whether cognitive impairment was present before the initiation of chemotherapy and/or other anticancer treatments will require a comparison

group of individuals who have not been treated for cancer. Finally, future studies can examine the relation between subjective cognitive function and objective performance. Empirical evidence that many older cancer survivors suffer cognitive and affective problems that limit their quality of life, it is not known how these cognitive deficits, whether permanent or temporary, interfere with daily living.

Perceived impairment in cognitive function is a frequent complaint of cancer patients both during and after chemotherapy. Questions still exist regarding the prevalence of genuine organic impairment versus, for example, subjective complaints that are not demonstrated on cognitive testing, sequelae of depression/fatigue that are not related to chemotherapy, or natural age-related deterioration. Regardless of the source of patient complaints, interventions that might improve cognitive functioning have clear potential to improve quality of life for that subset of patients affected. If a practical intervention were available to improve memory performance and self efficacy for memory and related daily functions amongst cancer survivors, this would be highly significant.

Whether chemotherapy and other anticancer treatments cause cognitive impairments is unknown. According to Saykin, Ahles, and McDonald (2003) they believe there is a knowledge gap of the mechanisms responsible for the chemotherapy-related cognitive changes. The researchers hypothesize that the neurotoxic effects may result from immune responses that lead to causing inflammation and microvascular injury. In addition, altered neurotransmitter levels and metabolites could constitute an additional mechanism related to neurotoxic effects. Clearly, however, decreasing cognitive and functional ability lead to poorer quality of life and may determine which cancer survivors will remain independent and which will require care and formal services (Greiner, Snowdon, & Schmitt, 1996; Liu, Wall, Wissoker, 1997; Snowdon, Ostwald, & Kane, 1989). Cancer survivors and gerontological researchers are thus extremely interested in the maintenance of cognitive function and quality of life.

Tannock, Ahles, Ganz, and van Dam (2004) concluded that anticancer treatment could have a negative impact on cognitive functioning. They therefore recommended large scale clinical studies with longitudinal designs, identification of neuropsychological tests that are sensitive to chemotherapy-induced cognitive changes, exploration of discrepancies between subjective reports of cognitive function and the objective results of cognitive testing, and studies of cognitive function in those receiving treatment for diseases other than breast cancer, and in both men and women.

Decreasing cognitive performance and functional ability lead to poorer quality of life and may determine which cancer survivors will be able to remain independent and which will require care and formal services (Earle, Burstein,Winer, & Weeks, 2003; Greiner, Snowdon, & Schmitt, 1996; Liu, Wall, Wissoker, 1997). Impaired executive functioning has been found to be the best predictor of functional decline. As memory problems increase, problems with instrumental activities of daily living (IADLs) begin to emerge. In cancer survivors, the presence of this comorbidity, rather than the cancer per se, is associated with impaired functional ability. Functional ability is of the utmost importance, particularly activities demanding cognitive capacity such as using the telephone, remembering to take

medications, managing financial matters, and remembering to turn off the stove after cooking. Loss of control and independence are highly valued tasks to maintain independence.

Implications for Geropsychiatric Nurses

Cancer survivors are living longer. Estimates from 2006 indicate that sixty percent of all cancer survivors are age 65 or older. Since two-thirds of adults diagnosed with cancer will be alive in 5 years, the health and life of a person with a history of cancer beyond the acute diagnosis and treatment phase has become of interest to the medical and scientific community. Elderly cancer survivors report difficulty with attention, concentration, and memory. More than 6.8 million people in the US are at high-risk for memory impairments and mild cognitive impairment (MCI), both because they are cancer survivors and because they are over 65 years of age (Office of Cancer Survivorship, National Cancer Institute, 2010).

Cancer survivors also experience high levels of depression, stress and anxiety associated with the fear that the cancer may return and uncertainty about how to interpret and appropriately handle symptoms (Caplette-Gingras, & Savard, 2008; Segar, Katch, Roth, Garcia, Portner et al, 1998). Psychological needs are the most frequently reported and discussed in the literature. Some studies have demonstrated that cancer survivors experience significantly higher levels of psychological morbidity than healthy women (Fann, Thomas-Rich, Katon, Cowley, & Pepping et al., 2008). However, while much has been written about psychological morbidity among cancer patients, there are very few publications describing interventions for helping cancer survivors, particularly older adult survivors with psychological and emotional issues (Perkins, Small, Balducci, Extermann, Robb et al., 2007).

Deficits in cognitive function have been documented before and after adjuvant therapy and may be related to affect or stress as much as neurological factors. How this information will be interpreted to patients is frustrating to clinicians. An intervention may be intended to improve memory skill or capacity, memory function in day-to-day living, or participant perception of or efficacy for memory functions, or all of the above. The concerns about cognitive difficulties and perceived impairments in daily living related to cognitive deficits such as diminished memory skills is a primary concern of survivors and is a component of symptom management.

Complaints of cognitive impairment following breast cancer treatment are well known and have been frequently studied, although questions still exist regarding the prevalence of genuine organic impairment versus, for example, subjective complaints that are not demonstrated on cognitive testing, squeal of depression and/or fatigue that are not related to chemotherapy, or natural age-related deterioration. Regardless of the source of patient complaints, interventions that might improve cognitive functioning have clear potential to improve quality of life for that subset of patients affected.

In the booklet, Life After Cancer Treatment (National Institutes of Health, 2004; No. 04-2424), Chapter 3 (Your Mind and Your Feelings after Cancer Treatment) provides tips

for improving memory and concentration and validates the experience of many cancer survivors. However, evidenced-based interventions for this aspect of symptom management are almost non-existent. Clinicians are often at a loss on how to intervene with survivors for cognitive problems experienced post treatment. Adult cancer survivors experiencing memory problems want to improve their everyday memory in specific domains that are of concern, such as remembering faces and names, dates and telephone numbers, household objects, recent and past events, meetings and appointments, information and facts, and directions. Whether cognitive stimulation or memory interventions will alleviate the cognitive difficulties experienced by cancer survivors remains unknown.

The mental health of cancer survivors has not always been the primary emphasis of treatment protocols since physical health outcomes have taken precedence (Keating, Norredam, Landrum, Haskump, & Meara, 2005; Costanzo, Ryff, & Singer, 2009). Even though mental health declined after a cancer diagnosis, the long-term outcomes of cancer survivors did not differ from persons without cancer in depression or cognitive function. The older survivors manifested resiliency whereas the younger survivors may have more adjustments.

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Table 1

Cognitive Domains Impaired from Chemotherapy

	Attention & Concentration	Executive function	Memory	Visuospatial Skill
Asparaginase	X	X	X	X
Capecitabine	X	X	X	
Carboplatin	X	X	X	
Cisplatin	X	X	X	X
Cyclophosphamide	X	X	X	X
Cytarabine	X	X	X	X
Docetaxel	X	X	X	
Doxorubicin	X	X	X	X
5-Fluorouracil	X	X	X	X
Gemcitabine	X	X	X	
Ifosfamide	X	X	X	X
Methotrexate	X	X	X	X
Nitrosureas	X	X	X	X
Paclitaxel	X	X	X	X
Vincristine	X	X	X	X
Vinorelbine	X	X	X	

Table 2

Cognitive Domains Impaired in Cancer Diagnoses

Impaired Function	Breast	Colorectal	Prostate
Attention	x		
Cognition	x		
Concentration	x	x	
Dementia	x		
Digit Symbol		x	
Executive Function	x	x	x
Learning	x		
Memory complaints	x		
Memory	x	x	x
Memory (verbal)	x	x	x
Memory (visual)	x		
Memory (working)	x		
Mild Cognitive Imp.	x		
Motor Function	x	x	
Processing Speed	x		
Recall	x	x	x
Spatial Ability			x