

# Predictors of Self-Reported Memory Problems in Patients With Ovarian Cancer Who Have Received Chemotherapy

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Changes in cognitive function, including memory problems, are recognized as a serious potential sequela to chemotherapy (Ahles & Saykin, 2001). Estimates of the frequency of chemotherapy-related cognitive impairment (CRCI) range from 75%–95% shortly following the completion of treatment and 17%–35% two or more years after completion of therapy (Ahles & Saykin, 2001). To date, most research on this topic has involved patients with breast cancer (Bender et al., 2006, 2007; Brezden, Phillips, Abdolell, Bunston, & Tannock, 2000; Castellon et al., 2004; Ferguson, McDonald, Saykin, & Ahles, 2007; Klemp, Stanton, Kimler, & Fabian, 2006; Kreukels et al., 2006; Schagen et al., 1999; Tchen et al., 2003; van Dam et al., 1998). Few studies have been conducted specifically to evaluate CRCI in patients with other solid tumors (Ahles et al., 2002; Malmstrom & Karlsson, 2003; Shapiro, 2005; Troy et al., 2000).

About 22,000 women in the United States are diagnosed with ovarian cancer each year (American Cancer Society, 2010). Treatment of ovarian cancer typically consists of combination therapy with a platinum-based regimen and a taxane. Second-line agents may include etoposide, liposomal anthracyclines, and iphosphamide (an analog of cyclophosphamide). These agents have been related to proinflammatory cytokine release and oxidative stress, both hypothesized causes of CRCI (Ahles & Saykin, 2007; Chen, Jungsuwadee, Vore, Butterfield, & St. Clair, 2007; Wood et al., 2006). Subtle cognitive changes may be associated with chemotherapy for patients with ovarian cancer (Malmstrom & Karlsson, 2003).

Results of previous research suggest that age and education are predictors of cognitive performance after chemotherapy (Jenkins et al., 2006) and that depression and fatigue are associated with cognitive function (Bender et al., 2006; Castellon et al., 2004). Contradictory results have been published related to CRCI and time since chemotherapy. No statistical difference related to time since chemotherapy and CRCI was noted by van Dam et al. (1998) for patients receiving chemotherapy

**Purpose/Objectives:** To examine the association between self-report of memory problems and the most commonly reported concurrent symptoms by women with ovarian cancer who have received chemotherapy.

**Design:** Secondary analysis.

**Setting:** Midwestern university-based school of nursing.

**Sample:** 638 women with ovarian cancer participating in a larger study who had received chemotherapy and 68 women with ovarian cancer who had not received chemotherapy.

**Methods:** Responses to a demographic questionnaire, disease and treatment history survey, and symptom severity index were analyzed using Pearson's correlations, hierarchical regression analysis, and Welch t tests for unequal sample size.

**Main Research Variables:** Self-rating of memory problems, time since chemotherapy, education level, and self-rating of commonly reported symptoms associated with ovarian cancer.

**Findings:** Nine symptoms accounted for 37% of the variance of memory problems (controlling for time since chemotherapy and education level). Significant predictors of memory problems included fatigue, mood swings, numbness or tingling, and sleep disturbance. Mean scores for self-reported memory problems were significantly different for participants who received chemotherapy compared to those who had not.

**Conclusions:** Findings suggest that memory problems were common following chemotherapy for ovarian cancer. Additional prospective study is warranted to evaluate potential mechanisms underlying these symptom interactions. Further qualitative study may be of value to describe the patient experience and identify effective coping strategies.

**Implications for Nursing:** Patient and family education should include information about the potential for memory problems following chemotherapy for ovarian cancer.

for breast cancer. However, Schagen et al. (1999) and Schagen, Muller, Boogerd, and van Dam (2002) found a decrease in changes in cognitive function between the time points of two and four years postchemotherapy,

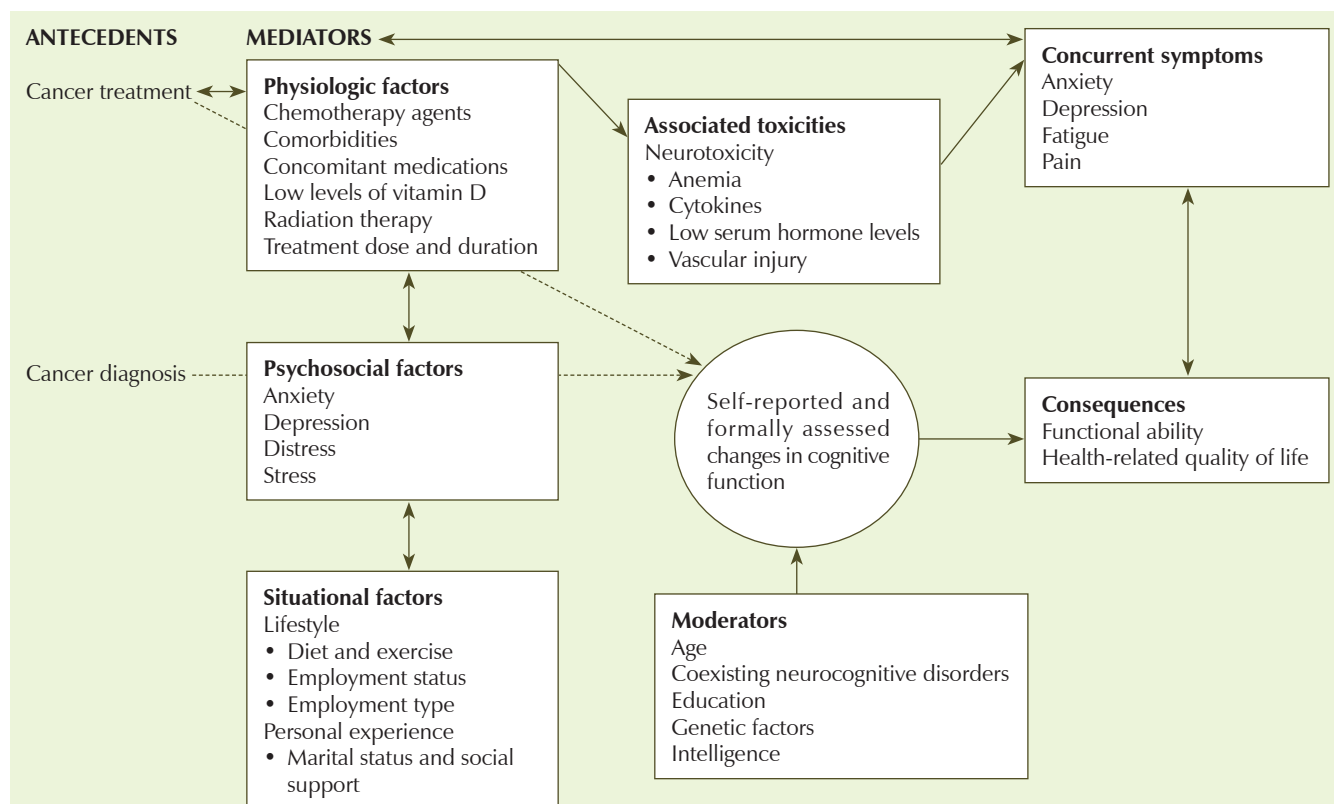
implying that changes in cognitive function may become less severe over time. The authors of this article hypothesized that active disease and treatment would be associated with memory problems and expected a negative correlation between memory problems and time since chemotherapy. The occurrence and relationship of multiple concurrent symptoms is particularly important for patients with cancer because this patient population rarely experiences one symptom at a time (Cleeland et al., 2000).

The blended (revised) model (Myers, 2009) of the Theory of Unpleasant Symptoms (Lenz, Pugh, Milligan, Gift, & Suppe, 1997; Lenz, Suppe, Gift, Pugh, & Milligan, 1995), the Conceptual Model of Chemotherapy-Related Changes in Cognitive Function (Hess & Insel, 2007), and the CRCI literature guided the conceptualization of this study. The model suggests a relationship between chemotherapy, concurrent symptoms, and self-reported changes in cognitive function. Age and education are depicted in the model as moderators between chemotherapy and changes in cognitive function. Depression is depicted in the model both as a potential mediator as well as a concurrent symptom along with fatigue. The model allows

the flexibility to study additional concurrent symptoms that may be identified with specific tumor types, such as ovarian cancer (see Figure 1).

The main purpose of this secondary analysis was to examine the association between potential predictors of self-report of memory problems for women with ovarian cancer who have received chemotherapy. The following research questions were posed for evaluation.

- Are age, education level, disease status, time since chemotherapy, and the most commonly reported symptoms (bowel disturbance, depression, drowsiness, fatigue, hot flashes, mood swings, numbness and tingling, pain, and sleep disturbance) associated with memory problems in women who have received chemotherapy for ovarian cancer?
- Do the most commonly reported symptoms continue to be associated with memory problems in women who have received chemotherapy for ovarian cancer after controlling for age, education level, disease status, and time since chemotherapy?
- Does a difference exist between complaints of memory problems for women with ovarian cancer who receive chemotherapy and those who do not?



Note. Dashed arrows depict relationships between cancer treatment and diagnosis, mediating factors, and self-reports of changes to cognitive function. Solid arrows show the contrast between unidirectional and bidirectional relationships for the other depicted variables.

**Figure 1. Revised Conceptual Model of Chemotherapy-Related Cognitive Changes in Cognitive Function Based on the Theory of Unpleasant Symptoms**

Note. From "Chemotherapy-Related Change in Cognitive Function: A Conceptual Model" by L.M. Hess and K.C. Insel, 2007, *Oncology Nursing Forum*, 34, p. 991. Copyright 2007 by the Oncology Nursing Society. Adapted with permission.

- Does a difference exist between complaints of memory problems for women with ovarian cancer who are currently receiving chemotherapy and those who have completed chemotherapy?

## Methods

### Design and Sample

A descriptive, correlational design was used to conduct this secondary analysis. The sample was drawn from a larger study conducted to explore the symptom experiences of women with ovarian cancer (Donovan, Ward, Sherwood, & Serlin, 2008). Participants in the larger study were recruited from the National Ovarian Cancer Coalition. This data set included responses from 713 women with a history of ovarian cancer. The overall sample was reduced to 710 because of missing data for three participants. Of these, 639 had reported receiving chemotherapy and 638 provided data on the dependent variable (memory problems). Of the remaining 74 participants, six were eliminated from the analysis because of missing data related to treatment history. The final sample for the main analysis was 638 participants who received chemotherapy and 68 who had not.

A power analysis was conducted to verify adequacy of the sample size. Based on correlation and regression analysis, anticipating an effect size of 0.15, an  $\alpha$  level of 0.05, desired power of 0.8, and 11 predictor variables, a sample size of 122 was required (Cohen, 1992). The sample size in the data set was more than sufficient, therefore, the study was potentially overpowered.

### Variables and Measures

**Demographic questionnaire:** The questionnaire was incorporated in the survey of the larger study. Participants' responses to demographic questions included age and education level. Additional demographic information was collected to describe the sample.

**Disease and treatment history survey:** The survey was developed for the larger study to gather information from participants regarding the date of diagnosis, initial stage of disease (I–IV), and history of surgeries for ovarian cancer (total number and date of most recent procedures). Participants were asked questions related to the current status of their disease (e.g., "Does your cancer show up on x-rays, scans, or pelvic examinations?" "Do you have elevated CA-125 levels?" "Do you have metastases?" and "Do you consider yourself to have active ovarian cancer?"). Participants acknowledging receipt of chemotherapy also were asked about the number of new regimens received, type of current therapy (if any), and date of the last therapy. Similar information was gathered related to radiation therapy. Participants were asked to list any other health issues they were experiencing that were unrelated to cancer and to rate their present health.

**Symptom Severity Index:** The Symptom Severity Index (SSI) subscale to the Symptom Representation Questionnaire was developed by Donovan et al. (2008) based on a list of 22 symptoms from the M.D. Anderson Symptom Inventory (Cleeland et al., 2000) with input from four gynecologic oncologists, two oncology certified nurses with expertise in gynecologic oncology, and two doctorally prepared experts in symptom assessment. The SSI measures severity of symptoms experienced during the prior week. The SSI consists of 22 symptoms (including memory problems) rated on a scale ranging from 0 (did not have the symptoms) to 10 (as bad as I can imagine). Respondents are given the opportunity to add any other symptom not listed in the SSI. Subsequent psychometric testing of the Symptom Representation Questionnaire indicated internal consistency ( $\alpha$  ranged from 0.63–0.88) and construct validity in the evaluation of multiple concurrent cancer-related symptoms ( $p < 0.01$ ).

The most commonly reported concurrent symptoms (those reported to be experienced during the prior week by more than 50% of participants) were selected as independent predictor variables to explore potential relationships with memory problems. These symptoms included bowel disturbances, depression, drowsiness, fatigue, hot flashes, mood swings, numbness and tingling (neuropathy), pain, and sleep disturbance.

Responses to the question "Do you consider yourself to have active ovarian cancer?" were used to reflect the presence or absence of active disease. Responses to this item were confirmed with questions regarding radiographic evidence of disease, current chemotherapy, and current CA-125 levels. Time since chemotherapy was calculated based on participants' response to the question, "What was the date of your last chemotherapy?" and the date the questionnaire was received. The date of last chemotherapy was subtracted from the date the questionnaire was received to obtain the number of days since the patient last received treatment. These values were divided by 30 to yield the approximate number of months since treatment and were added to the data set.

### Research Procedure

Human subjects committee approval was obtained from the University of Kansas for this secondary analysis. The original larger study received institutional review board approval from the University of Wisconsin. De-identified data were obtained from the principal investigator (PI) of the larger study.

### Data Analysis

SPSS® [v.17.0] was used to analyze the data. Descriptive statistics were used to describe the characteristics of the sample and the study variables. Pearson's correlation was used to determine the direction and strength of the

**Table 1. Sample Characteristics**

Characteristic	Received Chemotherapy (N = 639)		No Chemotherapy (N = 68)	
	n	%	n	%
<b>Years since diagnosis</b>				
0–5	416	65	43	63
6–10	169	26	14	21
11–15	39	6	7	10
More than 15	15	3	4	6
<b>Stage at diagnosis</b>				
I	139	22	51	75
II	85	13	3	4
III	358	56	10	15
IV	42	7	1	2
Do not know or no response	15	2	3	4
<b>Income (\$)</b>				
Less than 30,000	100	16	12	18
30,000–60,000	214	34	20	29
61,000–90,000	151	24	18	27
More than 90,000	129	20	15	22
No response	45	7	3	4
<b>Ethnicity</b>				
Caucasian	608	95	63	93
Hispanic	11	2	–	–
Mixed heritage	6	1	1	2
African American	5	1	1	2
Asian or Pacific Islander	3	1	–	–
Japanese	1	< 1	–	–
Ashkenazi Jew	1	< 1	1	2
Native American or Caucasian	1	< 1	–	–
No response	3	1	2	3
<b>Marital status</b>				
Married or life partner	455	71	43	63
Divorced or separated	66	10	11	16
Single or never married	61	10	11	16
Widowed	42	7	1	2
Other or no response	15	2	2	3
<b>Employment status</b>				
Full-time	207	32	42	62
Retired	148	23	8	12
On leave or on disability	107	17	3	4
Part-time	89	14	9	13
Homemaker	55	9	3	4
Unemployed	13	2	1	2
Student	3	1	–	–
Self-employed	2	< 1	–	–
Volunteer	1	< 1	–	–
Other or no response	14	2	2	3
<b>Age (years)</b>				
15–29	14	2	3	4
30–39	49	8	17	25
40–49	131	21	23	34
50–59	249	39	14	21
60–69	136	21	5	7
70 or older	57	9	4	6
No response	3	< 1	2	3
<b>Education level</b>				
Less than high school	11	2	1	2
High school graduate	90	14	3	4
Some college	208	33	19	28
College graduate	160	25	17	25
Postgraduate	166	26	26	38
No response	4	1	2	3
<b>Active disease</b>	238	37	3	4
<b>Memory problems</b>	466	73	36	53

Note. Because of rounding, not all percentages total 100.

bivariate relationship between the study variables. Multiple regression analysis was used to examine the association between the independent variables and the dependent variable. Welch t tests for independent samples of unequal size were performed to compare the mean value of self-reported memory problems between participants who received chemotherapy (n = 638) and those that did not (n = 68), as well as between those who had received chemotherapy (n = 478) with those who were currently receiving chemotherapy (n = 160). Variables were coded, as appropriate, and assumptions of correlation and regression were examined. Violation of assumptions was not a concern.

## Results

### Characteristics of the Sample and Study Variables

The demographic and clinical characteristics of study participants are presented in Tables 1 and 2. Demographics between the two groups were very similar. Participants who received chemotherapy ranged in age from 15–91 years. The majority were educated at the college level or higher (84%), married or had a life partner (71%), Caucasian (95%), and able to maintain employment or role as a homemaker (55%). Mean time since diagnosis was 57.5 months, and most of the participants were diagnosed with stage III disease (56%). Only 37% of participants reported active disease and 25% of these were currently receiving chemotherapy. A majority of the participants reported memory problems (73%).

### Relationships Among Demographics, Commonly Reported Symptoms, and Memory Problems

As shown in Table 3, a small but significant negative correlation was seen between the time since chemotherapy and the symptoms related to active disease and treatment, such as bowel disturbance ( $r = -0.14$ ,  $p < 0.01$ ), depression ( $r = -0.11$ ,  $p < 0.01$ ), neuropathy ( $r = -0.09$ ,  $p < 0.05$ ), and fatigue ( $r = -0.24$ ,  $p < 0.01$ ). Memory problems were significantly negatively correlated with education level ( $r = -0.14$ ,  $p < 0.01$ ). No significant correlations were seen between age or active disease and memory problems; therefore, these two variables were not included in the regression analyses.

### Association Between Commonly Reported Symptoms and Memory Problems

Hierarchical regression analysis results are shown in Table 4. The linear combination of the nine most commonly reported concurrent symptoms ex-

**Table 2. Common Symptoms and Active Disease Status of Study Participants**

Variable	Received Chemotherapy (N = 639)						No Chemotherapy (N = 68)					
	n	%	$\bar{X}$	SD	SK	KT	n	%	$\bar{X}$	SD	SK	KT
<b>Most commonly reported symptoms</b>												
Bowel disturbance	438	69	3.26	3.14	0.58	-0.93	47	69	2.89	3.01	1.01	0.06
Depression	382	59	2.22	2.55	1.05	0.25	44	65	2.64	2.7	0.76	-0.39
Drowsiness	396	62	2.54	2.74	0.81	-0.49	36	53	2.35	2.79	0.94	-0.34
Fatigue	547	86	4.16	2.99	0.24	-0.11	57	84	3.79	2.72	0.3	-0.82
Hot flashes	350	55	2.52	3.06	1.03	-0.14	33	49	2.11	2.81	1.27	0.66
Mood swings	397	62	2.32	2.6	1.03	0.23	43	63	2.6	2.78	0.86	-0.35
Numbness and tingling	373	58	2.76	3.01	-0.62	-0.62	20	29	1.14	2.33	2.58	6.67
Pain	350	55	2.53	3.03	-0.27	-0.27	33	49	2.15	2.74	1.11	0.19
Sleep disturbance	446	70	3.47	3.2	-1.04	-1.04	44	65	3.3	3.29	0.58	-1.21
<b>Active disease</b>	238	37	0.38	0.49	0.5	-1.76	3	4	0.04	0.21	4.54	19.2

KT—kurtosis; SK—skewness

plained 37% of the variance of memory problems after controlling for time since chemotherapy and education level ( $R^2 = 0.37$ , adjusted  $R^2 = 0.36$ ,  $R^2$  change = 0.34,  $F_{9,595} = 35.98$ ,  $p < 0.01$ ). Significant predictors of memory problems included the following symptoms: fatigue ( $\beta = 0.18$ ,  $p < 0.01$ ), mood swings ( $\beta = 0.23$ ,  $p < 0.01$ ), numbness and tingling ( $\beta = 0.07$ ,  $p < 0.05$ ), and sleep disturbance ( $\beta = 0.16$ ,  $p < 0.01$ ). Neither education level nor time since chemotherapy contributed significantly to the regression model.

### Differences in Memory Problems Related to Chemotherapy

Results from the Welch t test for independent samples of unequal size indicated a statistically significant difference between mean scores for self-reported memory problems for participants who received chemotherapy ( $\bar{X} = 3.04$ ,  $SD = 2.86$ ,  $n = 638$ ) and those who had not ( $\bar{X} = 2$ ,  $SD = 2.55$ ,  $n = 68$ ;  $t[82.7] = -3.12$ ,  $p < 0.01$ ,  $\bar{X}$  difference =  $-1.04$ , 95% confidence interval from  $-1.7$  to  $-0.38$ ). No significant difference in the severity of memory problems was seen between participants who had ever received chemotherapy and those currently receiving chemotherapy ( $p = 0.7$ ).

### Discussion

In this secondary analysis, the authors explored the relationship between age, disease state, and time since chemotherapy with self-report of memory problems by women with ovarian cancer who had received chemotherapy. The authors also examined the relationships between commonly reported symptoms of patients with ovarian cancer and memory problems. The severity of memory problems was compared between women with ovarian cancer who had received chemotherapy and those who had not.

Seventy-three percent of women who received chemotherapy for ovarian cancer reported memory problems. The mean scores for self-reported memory problems were significantly higher for participants who had received chemotherapy compared to those who had not. This finding is supported by previous research reporting memory problems being associated with chemotherapy (Ahles et al., 2002; Bender et al., 2006; Brezden et al., 2000; Schagen et al., 1999; Wieneke & Dienst, 1995); however, this information must be cautiously interpreted because the sample sizes of the two groups were unequal. No differences in mean scores were seen between participants who were currently receiving chemotherapy and those that had received chemotherapy in the past. This result contradicts the idea that memory problems are more significant during treatment. The authors recommend studies to further explore and test the timing of memory problems.

Four of the independent variables (fatigue, mood swings, numbness and tingling, and sleep disturbance) explained 37% of the variance for memory problems after controlling for time since chemotherapy and education level. These findings may support the hypothesis that fatigue, mood swings, and sleep disturbances may affect the ability to concentrate. Proinflammatory cytokine release may be associated both with neuropathy and a more general neurotoxicity affecting cognitive function as a result of chemotherapy agents that cross the blood-brain barrier at standard doses (Lee et al., 2004). The finding that pain was not a significant predictor of memory problems was inconsistent with previous findings where pain has been reported to have the potential to affect concentration (Hart, Wade, & Martelli, 2003).

Although depression was significantly correlated with memory problems in Pearson's correlation analysis, a significant contribution to the regression model was not demonstrated. One potential explanation may be that depression and mood swings may reflect aspects of the

**Table 3. Bivariate Correlations Between the Study Variables**

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Memory	1													
2. Age	-0.06	1												
3. Active disease	0.05	0.12**	1											
4. Time since chemotherapy	-0.13**	-0.03	-0.49**	1										
5. Education level	-0.14**	-0.09*	-0.06	0.02	1									
6. Bowel disturbance	0.28**	-0.01	0.26**	-0.14**	-0.09	1								
7. Depression	0.44**	-0.12**	0.14**	-0.11**	-0.08	0.34	1							
8. Drowsiness	0.37**	-0.08*	0.14**	-0.1*	-0.07	0.33**	0.39**	1						
9. Fatigue	0.49**	-0.07	0.29**	-0.24**	-0.13	0.43**	0.51**	0.66*	1					
10. Hot flashes	0.29**	-0.21**	0.06	-0.09*	-0.09	0.22**	0.24**	0.19**	0.27**	1				
11. Mood swings	0.5**	-0.25**	0.11**	-0.1**	-0.1	-0.31**	0.66**	0.36**	0.49**	0.39**	1			
12. Numbness and tingling	0.27**	0.09*	0.11**	-0.09*	-0.07	0.16**	0.2**	0.27**	0.34**	0.17**	0.2**	1		
13. Pain	0.33**	-0.08	0.11**	-0.07	-0.08	0.41**	0.36**	0.34**	0.44**	0.27**	0.38**	0.35**	1	
14. Sleep disturbance	0.43**	-0.1*	0.11**	-0.11**	-0.07	0.25**	0.44**	0.34**	0.49**	0.32**	0.45**	0.29**	0.39**	1

N = 638

\* p < 0.05; \*\* p < 0.01

same construct. Bivariate correlation between depression and mood swings was strong, as was the bivariate correlation between fatigue and sleep, suggesting the potential for measurement of overlapping constructs.

Age and education have been examined in relationship to chemotherapy-related changes with conflicting results. Results of some studies have shown age and education to be predictors of cognitive performance after chemotherapy (Jenkins et al., 2006), whereas other studies have shown no correlation (Brezden et al., 2000; Schagen et al., 1999). A relationship between cognitive changes and aging in general is supported in the literature (Barnes et al., 2007; Hillman et al., 2006); however, no significant association between age and cognitive changes was seen in this study. Older women may be more susceptible to CRCI as evidenced by studies conducted to assess baseline cognitive function and symptom distress (Cimprich, So, Ronis, & Trask, 2005), although studies have indicated that younger women with breast cancer may experience more distress related to cognitive changes than older women (Cimprich et al., 2005). This distress is hypothesized to be related to high baseline performance and a more significant impact on quality of life at this point in the life cycle (Cimprich et al., 2005).

The small but significant negative correlation ( $r = -0.13$ ,  $p < 0.01$ ) between time since chemotherapy and report of memory problems was encouraging because this may indicate additional support for improvement in cognitive function over time after completion of therapy (Ahles & Saykin, 2001). The negative correlation between education level and memory problems was small but significant ( $r = 0.14$ ,  $p < 0.01$ ), indicating that higher levels of education were associated with less difficulty with memory. However, neither time since chemotherapy nor education level contributed significantly to the regression model. Education levels previously have been demonstrated to be negatively associated with scores on verbal and nonverbal memory tests (Jacobs, Jacobsen, Booth-Jones, Wagner, & Anasetti, 2007). Cognitive reserve has been described in high (cognitive) functioning adults in studies evaluating the affect of age on cognitive ability (Barnes et al., 2007; Daffner et al., 2006). All small but statistically significant correlations observed in this current study should be interpreted with caution as the study was potentially overpowered because of a large sample size.

The study results were somewhat different than those achieved for the evaluation of symptom clusters in patients with cancer. Depression, fatigue, and pain have been linked as concurrent symptoms (Fleishman, 2004), as have pain, sleep disturbance, and fatigue (Beck, Dudley, & Barsevick, 2005).

Most studies conducted to evaluate chemotherapy-related cognitive impairment have been conducted with patients with breast cancer (Castellon et al., 2004; Kreukels et al., 2006; O'Shaughnessy, 2003; Schagen et al.,

**Table 4. Association Between Commonly Reported Symptoms and Memory Problems After Controlling for Time Since Chemotherapy and Education Level**

Predictor	Beta	Standard Error	$\beta$
<b>Step 1<sup>a</sup></b>			
Time since chemotherapy	-0.08	—	-0.12**
Education	-0.32	-0.11	-0.12**
<b>Step 2<sup>b</sup></b>			
Time since chemotherapy	—	—	—
Education	-0.09	0.09	-0.03
Bowel disturbances	0.01	0.03	0.01
Depression	0.08	0.05	0.07
Drowsiness	0.03	0.05	0.03
Fatigue	0.17	0.05	0.18**
Hot flashes	0.05	0.03	0.06
Mood swings	0.25	0.05	0.23**
Numbness and tingling	0.07	0.03	0.07*
Pain	0.03	0.04	0.04
Sleep disturbance	0.14	0.04	0.16**

N = 638

\*  $p < 0.05$ ; \*\*  $p < 0.01$

<sup>a</sup>  $R^2 = 0.03$ , adjusted  $R^2 = 0.03$ , and  $F_{2,604} = 9.74^{**}$

<sup>b</sup>  $R^2 = 0.37$ , adjusted  $R^2 = 0.36$ ,  $R^2$  change = 0.34, and  $F_{9,595} = 35.98^{**}$

2002). Few studies have explored lymphoma, testicular cancer, or prostate cancer (Ahles et al., 2002; Shapiro, 2005; Troy et al., 2000). To date, only one abstract was found that specifically focused on CRCI in ovarian cancer (Malmstrom & Karlsson, 2003). A sample of 40 women with advanced disease was compared to 15 healthy age-matched controls. Measures of memory performance were significantly different after three and seven courses of treatment in the chemotherapy group. No association was seen between memory performance and anemia, fatigue, or mood.

The current study results suggest a significant association between memory problems and four commonly reported concurrent symptoms noted by women with ovarian cancer treated with chemotherapy. These symptoms included fatigue, mood swings, neuropathy, and sleep disturbance. Small but significant associations were seen between memory problems and education level, as well as time since chemotherapy. Fatigue, mood swings, and sleep disturbance all are symptoms associated with postmenopausal status and decreased levels of estrogen. Some literature supports a relationship between reduced estrogen and changes in cognitive func-

tion, although estrogen replacement therapy remains controversial (Jenkins, Shilling, Fallowfield, Howell, & Hutton, 2004; Yaffe et al., 2007).

## Limitations

The purpose of the original larger study was to explore the experiences of women with ovarian cancer. Therefore, the assessment tool was not specifically designed to capture data related to changes in cognitive function. The data were collected cross-sectionally, so no baseline comparison can be made related to participants' reports of memory problems prior to the initiation of therapy. The present study did not include any objective measures of cognitive performance. The composition of the study sample was primarily Caucasian; however, this demographic matches the epidemiology for ovarian cancer in that the majority of patients at risk for this disease are non-Hispanic Caucasian women (Tortolero-Luna & Mitchell, 2004).

## Implications for Nursing

Results from this study indicate that patients with ovarian cancer who have received chemotherapy do report memory problems. Prospective evaluation to assess baseline cognitive function prior to the initiation of chemotherapy in patients with ovarian cancer also would be of value so that comparisons following the completion of treatment can be made. Fatigue, mood swings, neuropathy, and sleep disturbance were associated with memory problems. Additional prospective study is warranted to evaluate potential mechanisms underlying the symptoms' interactions. The majority of the sample who received chemotherapy (73%) reported experiencing memory problems. Patient and family education should include provision of information about the potential for memory problems following chemotherapy for ovarian cancer. Additional qualitative study may be of value to describe the patient experience and identify effective coping strategies.

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## References

- Ahles, T.A., & Saykin, A.J. (2001). Cognitive effects of standard-dose chemotherapy in patients with cancer. *Cancer Investigation*, 19, 812-820. doi: 10.1081/CNV-100107743
- Ahles, T.A., & Saykin, A.J. (2007). Candidate mechanisms for chemotherapy-induced cognitive changes. *Nature Reviews Cancer*, 7, 192-201. doi: 10.1038/nrc2073
- Ahles, T.A., Saykin, A.J., Furstenberg, C.T., Cole, B., Mott, L.A., Skalla, K., . . . Siberfarb, P.M. (2002). Neuropsychologic impact of standard-dose systemic chemotherapy in long-term survivors of breast cancer and lymphoma. *Journal of Clinical Oncology*, 20, 485-493.
- American Cancer Society. (2010). *Cancer facts and figures, 2010*. Atlanta, GA: Author.

- Barnes, D.E., Cauley, J.A., Lui, L.Y., Fink, H.A., McCulloch, C., Stone, K.L., & Yaffe, K. (2007). Women who maintain optimal cognitive function into old age. *Journal of the American Geriatric Society*, 55, 259–264. doi: 10.1111/j.1532-5415.2007.01040.x
- Beck, S., Dudley, W.N., & Barsevick, A.M. (2005). Pain, sleep disturbance, and fatigue in patients with cancer: Using a mediation model to test a symptom cluster [Online exclusive]. *Oncology Nursing Forum*, 32, E48–E55. doi: 10.1188/05.ONFE48-E55
- Bender, C.M., Sereika, S.M., Berga, S.L., Vogel, V.G., Brufsky, A.M., Paraska, K.K., & Ryan, C.M. (2006). Cognitive impairment associated with adjuvant therapy in breast cancer. *Psycho-Oncology*, 15, 422–430. doi: 10.1002/pon.964
- Bender, C.M., Sereika, S.M., Brufsky, A.M., Ryan, C.M., Vogel, V.G., Rastorgi, P., . . . Berga, S.L. (2007). Memory impairments with adjuvant anastrozole versus tamoxifen in women with early-stage breast cancer. *Menopause*, 14, 995–998. doi: 10.1097/gme.0b013e318148b28b
- Brezden, C.B., Phillips, K.A., Abdoell, M., Bunston, T., & Tannock, I.F. (2000). Cognitive function in breast cancer patients receiving adjuvant chemotherapy. *Journal of Clinical Oncology*, 18, 4175–4183.
- Castellon, S.A., Ganz, P.A., Bower, J.E., Peterson, L., Abraham, L., & Greendale, G.A. (2004). Neurocognitive performance in breast cancer survivors exposed to adjuvant chemotherapy and tamoxifen. *Journal of Clinical and Experimental Neuropsychology*, 26, 955–969. doi: 10.1080/13803390490510905
- Chen, Y., Jungsuwadee, P., Vore, M., Butterfield, D.A., & St. Clair, D.K. (2007). Collateral damage in cancer chemotherapy: Oxidative stress in nontargeted tissues. *Molecular Interventions*, 7, 147–155. doi: 10.1124/mi.7.3.6
- Cimprich, B., So, H., Ronis, D.L., & Trask, C. (2005). Pretreatment factors related to cognitive functioning in women newly diagnosed with breast cancer. *Psycho-Oncology*, 14, 70–78. doi: 10.1002/pon.821
- Cleeland, C.S., Mendoza, T.R., Wang, X.S., Chou, C., Harle, M.T., Morrissey, M., & Engstrom, M.C. (2000). Assessing symptom distress in cancer patients: The M.D. Anderson Symptom Inventory. *Cancer*, 89, 1634–1646.
- Cohen, J. (1992). A power primer. *Psychological Bulletin*, 112, 155–159.
- Daffner, K.R., Ryan, K.K., Williams, D.M., Budson, A.E., Rentz, D.M., Wolk, D.A., & Holcomb, P.J. (2006). Increased responsiveness to novelty is associated with successful cognitive aging. *Journal of Cognitive Neuroscience*, 18, 1759–1773. doi: 10.1162/jocn.2006.18.10.1759
- Donovan, H.S., Ward, S., Sherwood, P., & Serlin, R. (2008). Evaluation of the Symptom Representation Questionnaire (SRQ) for assessing cancer-related symptoms. *Journal of Pain and Symptom Management*, 35, 242–257. doi: 10.1016/j.jpainsymman.2007.04.017
- Ferguson, R.J., McDonald, B.C., Saykin, A.J., & Ahles, T.A. (2007). Brain structure and function differences in monozygotic twins: Possible effects of breast cancer chemotherapy. *Journal of Clinical Oncology*, 25, 3866–3870. doi: 10.1200/JCO.2007.10.8639
- Fleishman, S.B. (2004). Treatment of symptom clusters: Pain, depression, and fatigue. *Journal of the National Cancer Institute. Monographs*, 32, 119–123. doi: 10.1093/jncimonographs/lgh028
- Hart, R.P., Wade, J.B., & Martelli, M.F. (2003). Cognitive impairment in patients with chronic pain: The significance of stress. *Current Pain and Headache Reports*, 7, 116–126. doi: 10.1007/s11916-003-0021-5
- Hess, L.M., & Insel, K.C. (2007). Chemotherapy-related change in cognitive function: A conceptual model. *Oncology Nursing Forum*, 24, 981–994. doi: 10.1188/07.ONFE981-994
- Hillman, C.H., Moti, R.W., Pontifex, M.B., Posthuma, D., Stubbe, J.H., Boomsma, D.I., & de Geus, E.J. (2006). Physical activity and cognitive function in a cross-section of younger and older community-dwelling individuals. *Health Psychology*, 25, 678–687.
- Jacobs, S.R., Jacobsen, P.B., Booth-Jones, M., Wagner, L.I., & Anasetti, C. (2007). Evaluation of the functional assessment of cancer therapy cognitive scale with hematopoietic stem cell transplant patients. *Journal of Pain and Symptom Management*, 33, 13–23.
- Jenkins, V., Shilling, V., Deutsch, G., Bloomfield, D., Allan, S., Bishop, H., . . . Winstanley, J. (2006). A 3-year prospective study of the effects of adjuvant treatments on cognition in women with early stage breast cancer. *British Journal of Cancer*, 94, 828–834.
- Jenkins, V., Shilling, V., Fallowfield, L., Howell, A., & Hutton, S. (2004). Does hormone therapy for the treatment of breast cancer have a detrimental effect on memory and cognition? A pilot study. *Psycho-Oncology*, 13, 61–66. doi: 10.1002/pon.709
- Klemp, J.R., Stanton, A.L., Kimler, B.F., & Fabian, C.J. (2006). *Evaluating the effects of chemotherapy on cognitive function and quality of life in premenopausal women with breast cancer*. Paper presented at the San Antonio Breast Cancer Symposium, San Antonio, TX.
- Kreukels, B.P., Schagen, S.B., Ridderinkhof, K.R., Boogerd, W., Hamburger, H.L., Muller, M.J., & van Dam, F.S. (2006). Effects of high-dose and conventional-dose adjuvant chemotherapy on long-term cognitive sequelae in patients with breast cancer: An electrophysiologic study. *Clinical Breast Cancer*, 7, 67–78. doi: 10.3816/CBC.2006.n.015
- Lee, B., Dantzer, R., Langley, K.E., Bennett, G.J., Dougherty, P.M., Dunn, A.J., . . . Cleeland, C.S. (2004). A cytokine-based neuroimmunologic mechanism of cancer-related symptoms. *Neuroimmunomodulation*, 11, 279–282. doi: 10.1159/000079408
- Lenz, E.R., Pugh, L.C., Milligan, R.A., Gift, A.G., & Suppe, F. (1997). The middle-range theory of unpleasant symptoms: An update. *Advances in Nursing Science*, 19(3), 14–27.
- Lenz, E.R., Suppe, F., Gift, A.G., Pugh, L.C., & Milligan, R.A. (1995). Collaborative development of middle-range nursing theories: Toward a theory of unpleasant symptoms. *Advances in Nursing Science*, 17(3), 1–13.
- Malmstrom, H., & Karlsson, T. (2003). Cognitive functions in patients with ovarian cancer receiving chemotherapy [Abstract 1855]. *Proceedings of the American Society of Clinical Oncologists*, 22, 462.
- Myers, J.S. (2009). A comparison of the theory of unpleasant symptoms and the conceptual model of chemotherapy-related changes in cognitive function [Online exclusive]. *Oncology Nursing Forum*, 12, E1–E10. doi: 10.1188/09.ONFE1-E10
- O'Shaughnessy, J. (2003). Chemotherapy-related cognitive dysfunction in breast cancer. *Seminars in Oncology Nursing*, 19(Suppl. 2), 17–24.
- Schagen, S.B., Muller, M.J., Boogerd, W., & van Dam, F.S. (2002). Cognitive dysfunction and chemotherapy: Neuropsychological findings in perspective. *Clinical Breast Cancer*, 3(Suppl. 3), S100–S1008. doi: 10.3816/CBC.2002.s.020
- Schagen, S.B., van Dam, F.S., Muller, M.J., Boogerd, W., Lindeboom, J., & Bruning, P.F. (1999). Cognitive deficits after postoperative adjuvant chemotherapy for breast carcinoma. *Cancer*, 85, 640–650.
- Shapiro, P.J. (2005). Neurocognitive function (NCF) in long-term survivors of testicular cancer (TC) [Abstract 8034]. Retrieved from [http://meeting.ascpubs.org/cgi/content/abstract/23/16\\_suppl/8034](http://meeting.ascpubs.org/cgi/content/abstract/23/16_suppl/8034)
- Tehen, N., Juffs, H.G., Downie, F.P., Yi, Q.L., Hu, H., Chemerynsky, I., & Tannock, I.F. (2003). Cognitive function, fatigue, and menopausal symptoms in women receiving adjuvant chemotherapy for breast cancer. *Journal of Clinical Oncology*, 21, 4175–4183.
- Tortolero-Luna, G., & Mitchell, M.F. (2004). The epidemiology of ovarian cancer. *Journal of Cellular Biochemistry*, 59(S23), 200–207.
- Troy, L., McFarland, K., Littman-Power, S., Kelly, B.J., Walpole, E.T., Wyld, D., & Thomson, D. (2000). Cisplatin-based therapy: A neurological and neuropsychological review. *Psycho-Oncology*, 9, 29–39.
- van Dam, F.S., Schagen, S.B., Muller, M.J., Boogerd, W., Wall, E., Droogelever Fortuyn, M.E., & Rodenhuis, S. (1998). Impairment of cognitive function in women receiving adjuvant treatment for high-risk breast cancer: High-dose versus standard-dose chemotherapy. *Journal of the National Cancer Institute*, 90, 210–218.
- Wieneke, M.H., & Dienst, E.R. (1995). Neuropsychological assessment of cognitive functioning following chemotherapy for breast cancer. *Psycho-Oncology*, 4, 61–66. doi: 10.1002/pon.2960040108
- Wood, L.J., Nail, L.M., Perrin, N.A., Elsea, C.R., Fischer, A., & Druker, B.J. (2006). The cancer chemotherapy drug etoposide (VP-16) induces proinflammatory cytokine production and sickness behavior-like symptoms in a mouse model of cancer chemotherapy-related symptoms. *Biological Research for Nursing*, 8, 157–169.
- Yaffe, K., Barnes, D.E., Lindquist, K., Cauley, J.A., Simonsick, E.M., Penninx, B., . . . Health ABC Investigators. (2007). Endogenous sex hormone levels and risk of cognitive decline in an older biracial cohort. *Neurobiology of Aging*, 28, 171–178.