Symptom Clusters in Adults With Chronic Health Problems and Cancer as a Comorbidity

Catherine M. Bender, PhD, RN, Sandra J. Engberg, PhD, RN, Heidi S. Donovan, PhD, RN, Susan M. Cohen, PhD, FAAN, RN, Martin P. Houze, MS, Margaret Q. Rosenzweig, PhD, RN, Gail A. Mallory, PhD, RN, CNAA, Jacqueline Dunbar-Jacob, PhD, FAAN, RN, and Susan M. Sereika, PhD

Purpose/Objectives: To identify and compare symptom clusters in individuals with chronic health problems with cancer as a comorbidity versus individuals with chronic health problems who do not have cancer as a comorbidity and to explore the effect of symptoms on their quality of life.

Design: Secondary analysis of data from two studies. Study 1 was an investigation of the efficacy of an intervention to improve medication adherence in patients with rheumatoid arthritis (RA). Study 2 was an investigation of the efficacy of an intervention for urinary incontinence (UI) in older adults.

Setting: School of Nursing at the University of Pittsburgh.

Sample: The sample for study 1 was comprised of 639 adults with RA. The sample for study 2 was comprised of 407 adults with UI. A total of 154 (15%) subjects had a history of cancer, 56 (9%) of the subjects with RA and 98 (25%) of the subjects with UI.

Methods: Analysis of existing comorbidity and symptom data collected from both studies.

Main Research Variables: Symptom clusters, chronic disease, and cancer as a comorbidity.

Findings: Individuals with chronic health problems who have cancer may not have unique symptom clusters compared to individuals with chronic health problems who do not have cancer.

Conclusions: The symptom clusters experienced by the study participants may be more related to their primary chronic health problems and comorbidities.

Implications for Nursing: Additional studies are needed to examine symptom clusters in cancer survivors. As individuals are living longer with the disease, a comprehensive understanding of the symptom clusters that may be unique to cancer survivors with comorbidities is critical.

Patients with cancer frequently experience multiple symptoms concurrently. Because cancer survivors are living longer, they may develop other chronic health problems, and the symptom clusters they experience may be unique as a consequence of their history of cancer.

Key Points . . .

- Patients with cancer frequently experience multiple symptoms concurrently, or symptom clusters.
- Cancer survivors are living longer and may develop other chronic health problems over time.
- The symptom clusters experienced by individuals with other chronic health problems may be unique as a consequence of their history of cancer.
- Prospective studies are needed to examine the unique contributions of chronic health problems to the symptom experience of cancer survivors.

A symptom cluster is three or more concurrent symptoms that are related to one another (Dodd, Janson, et al., 2001). The symptoms often are found together given certain patient

Catherine M. Bender, PhD, RN, and Sandra J. Engberg, PhD, RN, are associate professors, Heidi S. Donovan, PhD, RN, is an assistant professor, Susan M. Cohen, PhD, FAAN, RN, is an associate professor, Martin P. Houze, MS, is a data analyst, and Margaret Q. Rosenzweig, PhD, RN, is an assistant professor, all in the School of Nursing at the University of Pittsburgh in Pennsylvania. Gail A. Mallory, PhD, RN, CNAA, is the director of research at the Oncology Nursing Society in Pittsburgh. Jacqueline Dunbar-Jacob, PhD, FAAN, RN, is a dean and professor and Susan M. Sereika, PhD, is an associate professor, both in the School of Nursing at the University of Pittsburgh. *This research was funded by the Oncology Nursing Society through the Health Research Formula Funds, Commonwealth of Pennsylvania. (The views expressed in this article are those of the authors and do not reflect the official policy or position of the Oncology Nursing Society.) (Submitted November 2006. Accepted for publication May 12, 2007.)*

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characteristics or clinical situations (Yarbro, Frogge, & Goodman, 2004). The symptoms in a cluster may not share the same etiology; however, symptoms in a cluster can influence one another (Dodd, Janson, et al.). Identifying the unique symptom clusters that patients with chronic health problems and cancer experience is important because the knowledge may direct interventions for the prevention and management of the symptom clusters.

Background

Symptom Clusters in Patients With Cancer

Most patients with cancer experience a high number of concurrent symptoms, ranging from 3–18, depending on the population being studied and the type of symptom questionnaire used (Carr et al., 2002; Cooley, 2000; Miaskowski et al., 2006; Sarna, 1998; Vainio & Auvinen, 1996). Increasingly, research is focusing on identifying specific symptom clusters, and a growing body of literature describes specific symptom clusters in patients with cancer (Barsevick, Dudley, & Beck, 2006; Broeckel, Jacobsen, Horton, Balducci, & Lyman, 1998; Fox & Lyon, 2006; Gaston-Johansson, Fall-Dickson, Bakos, & Kennedy, 1999; Gift, Jablonski, Stommel, & Given, 2004; Jacobsen et al., 1999).

Symptom Clusters in Patients With a Primary Cancer Diagnosis and Comorbid Conditions

Several studies have examined symptom clusters in individuals with cancer who have comorbid conditions (Deimling, Bowman, Sterns, Wagner, & Kahana, 2006; Dodd, Miaskowski, West, Paul, & Lee, 2002; Gift et al., 2004; Given, Given, Azzouz, & Stommel, 2001). Only Deimling et al. focused on survivors beyond the initial diagnosis and treatment period. They evaluated comorbidities and persistent cancer-related symptoms in a sample of 321 long-term (five or more years) older adult survivors of breast, prostate, or colorectal cancer. Survivors reported an average of 3.7 (SD = 2.4) comorbid health conditions, with 50% of the sample reporting four or more comorbidities. Survivors reported experiencing, on average, 3.5 (SD = 3.0) concurrent symptoms and attributed approximately one ($\bar{X}$ = 0.8; SD = 1.5) symptom to their experience of cancer. The most prevalent symptoms attributed to cancer were urinary incontinence (UI), hair loss, pain, diarrhea, numbness, bowel incontinence, and swelling (Deimling et al.).

The Influence of Cancer on Long-Term Health Outcomes

Large-sample, population-based studies have provided good evidence that individuals with a history of cancer have more negative health outcomes compared to individuals without such a history, regardless of number of years since cancer diagnosis (Hewitt, Rowland, & Yancik, 2003; Keating, Norredam, Landrum, Huskamp, & Meara, 2005; Yarbro et al., 2004). Specifically, individuals with a history of cancer have been shown to have greater loss of productivity, be less able to work, have poorer health status, and have greater need for assistance with activities of daily living than those without a history of cancer (Hewitt et al.; Keating et al.; Yarbro et al.).

In a population-based study using data from the 2002 wave of the Health and Retirement Study, Keating et al. (2005) highlighted the complex relationship among cancer, other chronic health problems, and physical and mental functioning. They compared 964 long-term (more than four years) cancer survivors with a cohort of 14,330 individuals with no history of cancer. They found that cancer survivors were significantly more likely to have been diagnosed with lung or heart disease, arthritis, or diabetes; were more likely to experience frequent pain and UI; and were more likely to have limitations in their daily activities. Using a logistic regression model, they found that approximately half of the reduction in perceived health between those with and without a history of cancer was associated with the presence of chronic health problems.

Influence of Cancer and Chronic Health Problems on Symptom Experiences

In addition to Keating et al.'s (2005) findings regarding the increased incidence of pain and UI in cancer survivors, five other studies have compared symptom experiences in patients with and without cancer. Only one of five studies (Reyes-Gibby, Aday, Anderson, Mendoza, & Cleeland, 2006) also systematically evaluated the influence of chronic health problems.

Broeckel, Thors, Jacobsen, Small, and Cox (2002) evaluated sexual functioning in 58 long-term ($\bar{X}$ = 7.65 years) breast cancer survivors who had received adjuvant chemotherapy compared to 61 age-matched women with no history of cancer. Compared to healthy controls, breast cancer survivors reported worse sexual functioning, fatigue, depression, hot flashes, and vaginal dryness.

Carpenter, Johnson, Wagner, and Andrykowski (2002) compared hot flashes, mood, affect, and hot flash interference with quality of life (QOL) of breast cancer survivors and age-matched healthy women. They found that survivors had more frequent, distressing, and longer hot flashes than age-matched women. They also reported more negative affect and greater hot flash interference with QOL. However, the researchers found no significant differences in mood between the two groups (Carpenter et al.).

In a study comparing symptoms experienced by older women with (n = 18) and without (n = 24) a history of breast cancer, Heidrich, Egan, Hengudomsub, and Randolph (2006) found that of 37 symptoms, only "aching" was reported more frequently by women with a history of breast cancer. In addition, women with a history of breast cancer were as likely to attribute their symptoms to aging and chronic health problems as were women without a history of breast cancer.

In a study comparing patients with cancer to depressed patients and nonpatient adults, Anderson et al. (2003) found that patients with cancer (n = 354) reported more severe fatigue, fatigue interference with life activities, and sleep disturbance than nonpatient community-dwelling adults (n = 290) but less than depressed patients (n = 72).

Finally, Reyes-Gibby et al. (2006) used a nationally representative sample of community-dwelling adults older than 50 and found a higher prevalence of pain, fatigue, and depression among those who had a history of cancer (n = 2,161) compared to those who did not (n = 15,049). In addition, they evaluated predictors of symptom clusters (two or more of the symptoms) and found that having a history of cancer increased risk (odds ratio [OR] = 1.31) of experiencing symptom clusters, even after controlling for gender, race, education, insurance status, and number of comorbid conditions. In the final model, they concluded that having a history of cancer, being female, having a lower level of education, and having more

comorbid conditions increased the risk for experiencing two or more of the symptoms in the cluster of fatigue, pain, and depression. Although Reyes-Gibby et al. examined symptom clusters in individuals with a history of cancer and examined the role of the number of comorbid conditions, they did not identify the types of comorbid conditions that influenced symptom clusters.

To date, no studies have evaluated the influence of cancer as a comorbidity on symptoms and symptom clusters for individuals with chronic health problems. As the number of cancer survivors increases, healthcare professionals will need to understand whether a history of cancer uniquely influences the symptoms experienced by individuals with other chronic health problems. This is an important area of research because patients with chronic health problems tend to experience multiple concurrent symptoms, which may have a negative effect on patient outcomes such as functional status and QOL (Beck, Dudley, & Barsevick, 2005; Dodd, Miaskowski, & Paul, 2001). Therefore, the purpose of this exploratory, secondary analysis was to identify and compare symptom clusters in individuals with chronic health problems with cancer versus individuals with chronic health problems who do not have cancer. The secondary aim was to compare the number and types of comorbid chronic health problems for individuals with and without a history of cancer and to explore the effect of symptoms on QOL.

Methods

This exploratory study was a secondary analysis of existing comorbidity and symptom data collected during baseline assessment for two independent studies of subjects with chronic health problems with and without cancer. Study 1 was an investigation of the efficacy of an intervention to improve medication adherence in patients with rheumatoid arthritis (RA) (National Institutes of Health, R01-NR04554). Study 2 was an investigation of the efficacy of an intervention to decrease relapse rates following pelvic floor muscle training for UI in older adults (National Institutes of Health, R01-NR04304). Only complete cases from each study were used for the secondary analysis. Cases with incomplete data were omitted.

Measures

Comorbidity was measured in studies 1 and 2 with the same self-report measure, the Comorbidity Questionnaire, which is modeled after the Charlson Comorbidity Index (Charlson, Pompei, Ales, & MacKenzie, 1987). The Comorbidity Questionnaire, developed in the Center for Research in Chronic Disorders (CRCD) in the School of Nursing at the University of Pittsburgh, is comprised of a self-report of comorbid conditions and symptom assessment. It covers 32 potential comorbid conditions. The conditions first are classified as present or absent. If present, they are classified further to examine whether the condition (a) was diagnosed by a healthcare provider, (b) was present in the past five years, (c) is being treated, (d) required hospitalization, or (e) decreased the subject's QOL. In addition to reporting detailed information with respect to each comorbid condition, subjects with cancer are asked to indicate (a) whether the cancer is controlled completely, (b) whether the cancer has spread from its original site, and (c) the primary site of the cancer.

The symptom assessment portion of the tool evaluates 32 symptoms. Presence or absence of each symptom is determined first, followed by a rating of whether each symptom has decreased QOL on a five-point Likert scale ranging from 0 (not at all) to 4 (extremely). Internal consistency of the measure using a Cronbach alpha was 0.93 in a sample of adults with diabetes. Work is ongoing to further develop the psychometric properties of the Comorbidity Questionnaire.

Demographic characteristics of participants from the two studies were assessed using the CRCD Sociodemographic Scale, which measures sociodemographic and socioeconomic attributes of subjects. The socioeconomic portion of the questionnaire was adapted from income and educational questions used in the 2000 U.S. Census.

Procedure

The study was approved by the University of Pittsburgh's institutional review board. With permission from the principal investigators of studies 1 and 2, an honest broker (who replaces study data identifiers with codes) was given password-protected access to the CRCD server to retrieve data from the CRCD Comorbidity Scale and the CRCD Sociodemographic Scale. The data were merged, and a de-identified dataset was created for the secondary analysis. No unique identifiers were available in the dataset; thus, identifying any subjects from the data used in the secondary analysis was impossible.

Statistical Analysis

Data were analyzed with SPSS® version 13 (SPSS Inc.) and Mplus® version 4.2 (Muthén & Muthén). Initially, the researchers performed exploratory data analysis to describe the total sample and the independent contributing studies and to screen the data for accuracy of response, outliers, missing data, and the statistical assumptions that underlie the methods applied to address objectives of the study. No aberrant data values were identified; the amount and pattern of missing data were assessed by participant and by variable and were found to be missing completely at random. No outliers were found in the sociodemographic variables; however, in some instances, univariate outliers were identified for the symptom indicators and the corresponding QOL ratings because of sparsely populated (< 10%) category levels. For categorical demographic variables (e.g., race) and symptom-specific QOL ratings, categories were meaningfully collapsed as necessary. Unless otherwise stated, a more conservative test-wise level of significance of 0.001 was used given the number of tests of hypotheses being performed. The Kruskal-Wallis test (using the H statistic) was used to compare groups based on the four combinations of the contributing studies and history of cancer on continuous type descriptors that were non-normally distributed (e.g., age), whereas chi-square type tests of independence were applied to compare the distribution of data for categorical descriptors across groups. Appropriate chi-square type tests of independence also were used to compare the prevalence of individual symptoms between studies (UI versus RA) as well as between history of cancer versus no history of cancer. If cell sizes were sparse, exact methods, such as the Fisher exact test, were used for group comparisons of categorical descriptors, symptoms, and collapsed QOL ratings.

To identify symptom clusters and descriptively compare them across the cancer combinations, exploratory factor analyses were undertaken on the binary symptom variables for the total sample and for each contributing study and by cancer history. Using Mplus, the researchers conducted binary-variable exploratory factor analyses with list-wise deletion of missing data using tetrachoric correlations. Because some of the cells in bivariate contingency tables for symptoms were sparse, the more robust estimation method of weighted least squares mean and variance adjusted was used, which yields robust mean- and variance-adjusted fit statistics that are less sensitive to departures of normality. For each of the subsamples, several symptom variables needed to be dropped from the analysis because of the presence of empty cells in multiple 2 x 2 contingency tables. Multiple criteria were used to decide the number of factors to retain, including eigenvalues (number greater than one and screeplot), the robust chi-square test of fit (p value greater than 0.05), the root mean square residual (RMSR) (less than 0.05), the root mean square error of approximation (RMSEA) (less than 0.06), estimated residual variances (no negative values), and the pattern of factor loadings (in terms of expectation and interpretability). Varimax rotation was used to simplify the factor structure and increase the interpretability of the factors. The symptom clusters were defined as factors having symptoms with factor loadings of 0.40 or higher from the final rotated solution. The percentage of the variance explained for the individual symptom variables was computed as the sum of the squares factor loading for each factor explained.

The symptom clusters were defined to be those factors having at least three symptoms with factor loadings of 0.40 or higher in the rotated solution. In the rare instance when a symptom loaded on more than one factor, the symptom was attributed to the factor with the highest loading value. The percentage of the symptom variance explained by a reported symptom cluster was based on the sum of the squared loadings for that symptom cluster from the orthogonal solution. The total percentage of symptom variance explained considered all factors retained, including the reported symptom clusters.

Results

The sample for study 1 (see Table 1) was comprised of 639 adults with RA aged 19–85 years ($\bar{X}$ = 59.5, SD = 11.9). Consistent with the overall RA population, the sample was predominantly female (81%, n = 516) and white (92%, n = 590.) Most were currently married (66%, n = 421) and either retired (29%, n = 186), employed part-time (21%, n = 137), or disabled and unable to work (19%, n = 123). All but one subject had some form of health insurance.

The sample for study 2 was comprised of 407 men and women aged 60 years or older ($\bar{X}$ = 76.9, SD = 8.2, range = 60–98) who self-reported UI at least twice a week for a minimum of three months. Nearly 40% were homebound. The sample was mostly white (95%, n = 385), widowed (49%, n = 201), and retired (91%, n = 370). Almost all had health insurance (99.8%, n = 406).

In general, subjects in study 2 were older than those in study 1. Although both samples were populated by more women than men, study 2 had more men than study 1. Furthermore, more subjects in study 2 had not completed high school and fewer of them had completed any education beyond high school. Finally, more subjects in study 1 indicated that they were multiracial than those in study 2.

Prevalence of Cancer

A total of 154 (15%) subjects had a history of cancer (excluding nonmelanoma skin cancer), 56 (9%) of those in study 1 and 98 (24%) of those in study 2. Subjects with UI were three times more likely to have a history of cancer than those with RA (OR = 3.3, 95% confidence interval [CI] = 2.30, 4.70). Breast cancer was the most common malignancy in both samples (n = 20, 3% in study 1; n = 32, 8% in study 2). Prostate cancer (n = 23, 6%) was the second most common malignancy in the UI sample, whereas melanoma (n = 11, 2%) was the second most common type in the RA sample (see Table 2). The only types of cancer with significantly different prevalence in the two samples were breast, colon, and cervical. Each of those three types of cancer was significantly more likely to be reported by study 1 subjects than by study 2 subjects. UI subjects were 1.6 times more likely to report having had breast cancer (95% CI = 1.10, 2.30; p = 0.001), 3.3 times more likely to have had colon cancer (95% CI 1.20, 9.10; p < 0.001), and 7.8 times more likely to report having had prostate cancer (95% CI = 2.10, 29.50; p < 0.001) than those with RA. Sixty-nine (45%) of the 154 subjects with cancer reported that it had been diagnosed in the past five years. Most subjects were not currently receiving cancer treatment (n = 108, 70%), reported that their cancer was completely controlled (n = 145, 97%), and had no known metastasis (n = 145, 94%). Most reported that cancer had no or only a slightly negative impact on their QOL (n = 127, 83%).

Symptom Clusters in Individuals Who Have Cancer as a Comorbidity

Subjects were questioned about the presence of a variety of symptoms. They reported a mean of 7.8 (SD = 4.3) symptoms. The most common symptoms reported were joint pain (n = 829, 80%), fatigue (n = 622, 60%), mobility problems (n = 576, 55%), back pain (n = 527, 51%), and generalized pain (n = 481, 46%). Table 3 compares the prevalence of symptoms between the two study groups. Subjects with RA reported an average of 8.2 (SD = 4.6) symptoms compared to 7.1 (SD = 3.7) among UI subjects (p < 0.001). The following symptoms were significantly more likely to occur in subjects with RA than in those with UI: joint pain, fatigue, generalized pain, insomnia, arm or leg weakness, weight gain, itching, night sweats, skin rash, diarrhea, nausea, and weight loss. The only symptoms that were significantly less likely to occur in subjects with RA were frequent urination and problems with balance and hearing.

The researchers also compared the prevalence of the assessed symptoms among subjects who did and did not have a history of cancer. Subjects with and without a history of cancer reported the same number of symptoms ($\bar{X} = 7.8 \pm 4.2$ and $\bar{X} = 7.8 \pm 4.4$ symptoms, respectively). Subjects with a history of cancer were significantly more likely to report leaking urine (72%) than those without a history of cancer (48%, p < 0.001; OR = 2.76, 95% CI = 1.86, 4.02). No statistically significant differences (p < .001) were found in the prevalence of any other symptoms among subjects who did or did not have a history of cancer. However, a number of trends appeared (p = 0.03–0.002). More subjects with a history of cancer reported frequent urination (47%) than those without

Table 1. Sample Characteristics

Characteristic	Overall (N = 1,046)		Rheumatoid Arthritis (N = 639)				Urinary Incontinence (N = 407)				Statistic	
			With Cancer (n = 56)		Without Cancer (n = 583)		With Cancer (n = 98)		Without Cancer (n = 309)		Kruskal-Wallis	
Age (years)											H = 443.7 (0.000)	
$\bar{X}$	66.3		61.4		59.4		77.6		76.6			
SD	13.6		10.5		12.0		7.9		8.3			
Characteristic	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	χ^2	**p**
Gender											8.2	0.042
Male	203	19	11	20	112	19	29	30	51	17		
Female	843	81	45	80	471	81	69	70	258	84		
Race											13.1	0.000
White	975	93	54	97	536	92	95	97	290	94		
Black	40	4	2	3	22	4	2	2	14	5		
Asian	3	< 1	–	–	3	< 1	–	–	–	–		
Multiracial	24	2	–	–	20	3	–	–	4	1		
Other	4	< 1	–	–	2	< 1	1	1	1	< 1		
Education											19.0	0.004
Less than high school	140	13	8	14	57	10	20	20	55	18		
High school	502	48	23	41	287	49	41	42	151	49		
Beyond high school	404	39	25	45	239	41	37	38	103	33		

a history of cancer (38%, p = 0.03). The following symptoms were reported by fewer subjects with a history of cancer than by those without cancer: joint pain (72% versus 81%; p = 0.01), generalized pain (36% versus 48%, p = 0.006), and arm or leg weakness (23% versus 33%, p = 0.02).

Using binary exploratory factor analysis with varimax rotation and applying the criteria, the researchers identified four symptom clusters for (a) the total sample, (b) subjects with a history of cancer, (c) those without a history of cancer, and (d) those with UI. They identified three symptom clusters for subjects with RA (see Table 4). For the total sample, two symptoms (fainting and arm or leg paralysis) were excluded from the exploratory factor analysis because of empty cells in the bivariate contingency table. From the remaining 30 symptoms, six factors were extracted (χ^2 = 160.2, p = 0.07; RMSR = 0.05; RMSEA = 0.01) and explained 53.3% of the total variance in symptoms. Of those, four symptom clusters having at least three symptoms were identified, each explaining 7.3%–11.3% of the symptom variance.

Seven symptoms (fever, weight loss, vomiting, nonorthostatic dizziness, syncope, chest pain, and arm or leg paralysis) were excluded from the factor analysis for subjects with a history of cancer because of empty cells in the bivariate symptom contingency tables. From the remaining 25 symptoms, four factors were extracted (χ^2 = 60.00, p = 0.27; RMSR = 0.11; RMSEA = 0.03), explaining 49.7% of the total symptom variance. The four symptom clusters identified explained 9.2%–14.3% of the total symptom variance.

Three symptoms (vomiting, syncope, and arm or leg paralysis) were excluded from the factor analysis for subjects with a negative history for cancer. Seven factors were identified (χ^2 = 137.6, p = 0.23; RMSR = 0.04; RMSEA = 0.01) and explained 56% of the total variance of the 25 symptoms analyzed using exploratory factor analysis. About 7.1%–12.8% of the total symptom variance was explained for the four symptom clusters identified. No unique symptom clusters occurred among subjects with or without a history of cancer. The following symptoms, however, occurred in symptom clusters for subjects with a history of cancer but not for subjects who were not cancer survivors: skin rash, itching, constipation, orthostatic dizziness, urinary frequency, and UI. Night sweats was observed in the patients with and without cancer. Loss of appetite and arm or leg weakness were part of the clusters for patients without cancer but not for those with a history of cancer.

For subjects with RA, four symptoms were excluded from the factor analysis (vomiting, fainting, leg or arm paralysis, and joint pain). Six factors were retained (χ^2 = 132.2, p = 0.17; RMSR = 0.05; RMSEA = 0.01) and explained 54.6% of the total variance in the 28 symptoms considered. The four individual symptom clusters identified explained 8.1%–12% of the total symptom variance. Seven symptoms were excluded from the factor analysis for subjects with UI because of empty cells in multiple 2 x 2 symptom tables (fever, weight loss, nausea, nonorthostatic dizziness, arm or leg weakness, joint pain, and balance problems). From the remaining 25 symptoms, seven factors were revealed (χ^2 = 75.6, p = 0.52; RMSR = 0.06; RMSEA < 0.01), which explained 51.6% of the total symptom variance. The three symptom clusters identified explained 6.6%–12.4% of the variance. One unique symptom cluster in the RA sample was not identified in the UI sample. Based on the symptoms included in the factor analysis for both groups, the cluster included loss of appetite, which had a positive loading value of 0.75, and weight gain and overeating, with negative loading values of –0.68 and –0.82, respectively. In addition to this unique cluster, the following symptoms occurred in RA but not UI clusters: night sweats, fatigue, nausea, back pain, leaking urine, and frequent urination. The only symptom that occurred in the UI clusters that did not appear in the RA clusters was orthostatic dizziness.

Table 2. Prevalence of Specific Cancers in Subjects

	Overall (N = 1,046)		Rheumatoid Arthritis (N = 639)		Urinary Incontinence (N = 407)			
Cancer	n	%	n	%	n	%	χ^2	p
Breast	52	5.0	20	3.1	32	7.9	11.8	0.001
Prostate	25	2.4	2	0.3	23	5.7	30.4	< 0.001
Melanoma	19	1.8	11	1.7	8	2.0	–	–
Colon	16	1.5	3	0.5	13	3.2	12.3	< 0.001
Cervical	10	0.9	6	0.9	4	1.0	–	–
Uterine	10	0.9	3	0.5	7	1.7	–	–
Ovarian	7	0.7	5	0.8	2	0.5	–	–
Bladder	3	0.3	2	0.3	1	0.2	–	–
Brain	2	0.2	2	0.3	–	–	–	–
Lung	2	0.2	–	–	2	0.5	–	–
Lymphoma	8	0.8	3	0.5	5	1.2	–	–
Leukemia	1	0.1	–	–	1	0.2	–	–
Oral	1	0.1	–	–	1	0.2	–	–
Neck and throat	1	0.1	1	0.1	–	–	–	–
Rectal	1	0.1	–	–	1	0.2	–	–
Thyroid	2	0.2	1	0.1	1	0.2	–	–
Other	9	0.9	2	0.3	7	1.7	–	–

Impact of Symptoms on Quality of Life

The researchers compared differences in the effects of symptoms on QOL reported by subjects with and without cancer; no significant differences were found between the two groups. They also explored differences in the effects of symptoms on QOL between subjects in study 1 and study 2. Most symptoms were reported by fewer than 25% of the subjects in the two studies. Responses to the effect-on-QOL questions were collapsed into two categories: (a) little or no effect and (b) a moderate, great, or extreme effect. The only significant differences in self-reported QOL effects between the two samples were for joint pain, involuntary urine loss, and night sweats. A significantly higher proportion of RA subjects reported that joint pain had a moderate to severe effect on their QOL than UI subjects (n = 384, 68% versus n = 117, 48%; $p < 0.001$). Likewise, significantly more RA subjects reported that night sweats had a moderate to extreme effect on QOL (n = 37, 29%) than UI subjects (n = 1, 3%; p = 0.001). In contrast, significantly more UI subjects (n = 160, 43%) reported that involuntary urine loss had a moderate to extreme effect on QOL than those with RA (n = 41, 27%; p = 0.001)

Prevalence of Comorbidities

Subjects were asked about the presence of a number of comorbid conditions. They reported an average of 5.4 comorbid conditions (SD = 2.9). Subjects with UI reported an average of 6.2 ± 2.8 conditions, whereas subjects with RA reported a mean of 4.8 ± 2.9 comorbidities ($p \leq 0.001$). Comorbidities reported by 5% or more of the subjects are listed in Table 5. For the total sample, the most common comorbidity was hypertension, reported by 41% (n = 430) of the subjects.

Table 5 also compares the prevalence of the comorbid conditions among subjects with UI or RA. When a significant difference ($p \leq 0.001$) in prevalence was found between the two groups, most conditions were more prevalent among UI subjects than among RA subjects. The following conditions were significantly more likely to be reported by UI than RA subjects: coronary artery disease, irregular heart beat, hypertension, cerebral vascular disease, diabetes mellitus, digestive disease, and osteoarthritis. Only anemia and headaches were significantly less likely to occur in subjects with UI than in those with RA.

Subjects with a history of cancer reported an average of 6.8 ± 2.9 comorbid conditions compared to 5.1 ± 2.9 among those without a history of cancer ($p < 0.001$). The prevalence of comorbid conditions was compared among subjects with and without a history of cancer (see Table 6). Subjects with a history of cancer were significantly more likely to report having osteoarthritis (OR = 1.4, 95% CI = 1.1, 1.7) than those without a history of cancer and significantly less likely to have RA (OR = 0.57, 95% CI = 0.48, 0.66). Hypertension also was more prevalent among subjects with cancer (n = 80, 52.6%) than among those without a history of cancer (n = 350, 39.4%; p = 0.002).

Discussion

The findings of the study suggest similar symptom clusters among individuals with chronic health problems who have cancer as a comorbid condition versus individuals with chronic health problems who do not have cancer as a comorbid condition. This is particularly evident when comparing the clusters including fatigue, nausea, diarrhea, generalized pain, or sleeping problems. Other clusters that were similar between the two groups include (a) weight gain and overeating and (b) walking and balance problems. In fact, few symptoms were unique to the individuals who have cancer as a comorbid condition, and those symptoms (i.e., skin rash, itching, constipation, dizziness, frequent urination, and UI) are not commonly associated with the diagnosis or treatment of cancer. The fact that the findings do not point to clear differences in the symptom clusters between the two groups suggests that the symptom clusters experienced may be more related to the primary chronic health problems and other comorbid conditions in the subjects.

Table 3. Symptom Prevalence

	Overall (N = 1,046)		Rheumatoid Arthritis (N = 639)		Urinary Incontinence (N = 407)		If Significant at p ≤ 0.001			
Symptom	**n**	**%**	**n**	**%**	**n**	**%**	**χ^2**	**p**	**OR[a]**	**95% CI**
Joint pain	829	80	584	92	245	61	144.8	< 0.001	0.14	0.10, 0.20
Fatigue	622	60	470	73	152	38	130.2	< 0.001	0.22	0.17, 0.29
Mobility problems	576	55	348	55	228	56	–	–	–	–
Back pain	527	51	320	51	207	51	–	–	–	–
Generalized pain	481	47	389	62	92	23	147.6	< 0.001	0.18	0.14, 0.25
Insomnia	423	41	295	46	128	32	20.8	< 0.001	0.55	0.42, 0,71
Frequent urination	404	39	186	29	218	54	65.9	< 0.001	2.90	2.20, 3.80
Visual problems	377	37	229	36	148	39	–	–	–	–
Balance problems	340	33	178	28	162	40	16.0	< 0.001	1.70	1.30, 2.20
Arm or leg weakness	328	32	240	38	88	22	28.4	< 0.001	0.46	0.35, 0.62
Weight gain	298	29	238	38	60	15	60.7	< 0.001	0.29	0.21, 0.40
Hearing problems	269	25	130	20	130	32	17.7	< 0.001	1.80	1.40, 2.40
Dyspnea	254	24	161	25	93	23	–	–	–	–
Itching	219	21	156	25	63	16	11.5	0.001	0.58	0.42, 0.79
Orthostatic dizziness	188	18	115	18	72	18	–	–	–	–
Constipation	176	17	100	16	76	19	–	–	–	–
Night sweats	167	16	128	20	39	10	19.4	< 0.001	0.42	0.29, 0.63
Overeating	165	16	120	19	45	11	10.7	0.001	0.54	0.38, 0.79
Skin rash	164	16	114	18	50	13	–	–	–	–
Diarrhea	133	13	108	17	25	6	25.4	< 0.001	0.33	0.21, 0.51
Palpitations	122	12	83	13	39	10	–	–	–	–
Nonorthostatic dizziness	95	9	63	10	32	8	–	–	–	–
Anorexia	92	9	62	10	30	8	–	–	–	–
Nausea	86	8	80	13	6	2	39.7	< 0.001	0.11	0.05, 0.24
Abdominal pain	82	8	58	9	24	6	–	–	–	–
Chest pain	71	7	43	7	28	7	–	–	–	–
Weight loss	65	6	52	40	13	3	10.2	0.001	0.38	0.20, 070
Arm or leg paralysis	20	2	9	1	11	3	–	–	–	–
Fever	19	2	17	3	2	<1	–	–	–	–
Vomiting	13	1	13	2	–	–	–	–	–	–
Syncope	9	1	6	1	3	1	–	–	–	–

[a] Urinary incontinence versus rheumatoid arthritis

CI—confidence interval; OR—odds ratio

When comparing the symptom clusters experienced by individuals with RA versus UI, less similarity existed in terms of the symptoms that comprised the clusters. Shortness of breath, chest palpitations, and chest pain populated a cluster in both groups. Many more symptoms were unique to individuals with RA. The findings also suggest that symptom clusters are comprised of symptoms that are related to an individual's current, primary chronic health condition.

In the sample, subjects reported an average of five comorbid conditions, with RA subjects reporting 5.2 and UI subjects reporting 6.2. Participants with UI were significantly more likely to experience comorbid conditions than those with RA. The vast majority of individuals in both studies reported that their cancer was completely controlled and that it did not or only slightly influenced their QOL. The findings suggest that having a history of cancer does not impart a unique set of symptoms and that the symptoms that individuals do experience are more likely to be driven by their current chronic and comorbid conditions.

The findings are different from those of Dodd et al. (2002), who found eight "symptom groupings" in a cross-sectional study of 100 patients with cancer who also had comorbid conditions. They reported the prevalence of eight symptom groupings, including no symptoms (42%), only pain (10%), only fatigue (6%), only sleep disturbance (8%), pain and fatigue (4%), pain and sleep disturbance (9%), fatigue and sleep disturbance (6%), and pain, fatigue, and sleep disturbance (13%). The comorbidities in their sample included back problems (65%), allergies (59%), headaches (51%), hemorrhoids (46%), arthritis (33%), and hypertension (30%). However, Dodd et al. (2002) examined the prevalence of a predetermined symptom cluster (pain, fatigue, and sleep disturbances), rather than a comprehensive symptom assessment. Thus, what additional symptoms were experienced and what symptom clusters may have emerged from an analysis of a more comprehensive symptom assessment are not clear. Moreover, the subjects in the study were actively receiving cancer treatment and, thus, were at a very different point in the disease trajectory than most of the subjects with cancer in the current study. The divergent timing of symptom assessment also may contribute to the differences in symptoms experienced.

The approach used to identify symptom clusters in the current study (i.e., factor analysis of a comprehensive set of symptoms) is different from the approach of some other

Table 4. Symptom Clusters From Binary Exploratory Factor Analyses With Weighted Least Squares Estimation and Varimax Rotation

Sample	Symptom Cluster 1	Symptom Cluster 2	Symptom Cluster 3	Symptom Cluster 4	Statistics
Total sample (N = 995)	Shortness of breath (0.56) Chest palpitations (0.62) Chest pain (0.76) Abdominal pain (0.43) Back pain (0.42)	Night sweats (0.54) Fatigue (0.56) Nausea (0.83) Vomiting (0.61)	Leg or arm weakness (0.50) Generalized pain (0.51) Joint pain (0.48) Walking problems (0.81) Balance problems (0.45)	Weight loss (–0.75) Weight gain (0.68) Loss of appetite (–0.58) Overeating (0.81)	χ^2= 160.218 df = 135 p = 0.068 RMSR = 0.048 RMSEA = 0.014
Cancer history (n = 149)	Skin rash (0.52) Itching (0.53) Night sweats (0.85) Constipation (0.63) Dizziness standing (0.65) Abdominal pain (0.57) Back pain (0.50)	Fatigue (0.73) Nausea (0.66) Diarrhea (0.72) Generalized pain (0.66) Sleeping problems (0.50)	Leaking urine (–0.80) Frequent urination (–0.58) Walking problems (–0.60) Balance problems (–0.48)	Weight gain (0.81) Overeating (0.90) Shortness of breath (0.41) Chest palpitations (0.47) Joint pain (0.61)	χ^2 = 60.005 df = 54 p = 0.267 RMSR = 0.106 RMSEA = 0.027
No cancer history (n = 846)	Shortness of breath (0.54) Chest palpitations (0.61) Chest pain (0.68) Back pain (0.51)	Night sweats (0.60) Fatigue (0.64) Nausea (0.75) Diarrhea (0.63) Generalized pain (0.46) Abdominal pain (0.54) Sleep problems (0.41)	Weight loss (–0.77) Weight gain (0.64) Loss of appetite (–0.63) Overeating (0.80)	Leg or arm weakness (0.47) Walking problems (0.83) Balance problems (0.52)	χ^2 = 137.607 df = 126 p = 0.226 RMSR = 0.044 RMSEA = 0.010
Rheumatoid arthritis (n = 597)	Hearing problems (0.41) Shortness of breath (0.54) Chest palpitations (0.44) Chest pain (0.57) Back pain (0.41) Leaking urine (0.45) Frequent urination (0.46)	Night sweats (0.59) Fatigue (0.65) Nausea (0.66) Diarrhea (0.59) Abdominal pain (0.50) Sleep problems (0.41)	Weight loss (0.78) Weight gain (–0.68) Loss of appetite (0.75) Overeating (–0.82)	Leg or arm weakness (0.45) Generalized pain (0.48) Walking problems (0.90) Balance problems (0.58)	χ^2 = 132.249 df = 118 p = 0.175 RMSR = 0.050 RMSEA = 0.014
Urinary incontinence (n = 399)	Diarrhea (0.63) Hearing problems (0.65) Dizziness standing (0.48)	Fainting (0.64) Sleep problems (0.65) Walking problems (0.57)	Leg or arm paralysis (0.50) Shortness of breath (0.75) Chest palpitations (0.50) Generalized pain (0.90) Chest pain (0.51) Abdominal pain (0.44)	–	χ^2 = 75.581 df = 77 p = 0.524 RMSR = 0.060 RMSEA < 0.001

df—degrees of freedom; RMSEA—root mean square error of approximation; RMSR—root mean square residual

Note. Smaller sample sizes compared to original sample were caused by some missing symptom data.

investigators who used a priori designated symptom clusters. The current researchers found interpreting the pattern of symptom clustering within and between groups very difficult. However, they believed that evaluating a comprehensive list of symptoms using exploratory factor analysis was important when little evidence supported exploration of any particular set of symptoms that may cluster with one another.

The findings indicating that cancer survivors were more likely to experience UI are similar to those of Keating et al. (2005), who also reported that more cancer survivors (n = 960) had UI (p = 0.001) than individuals with no cancer history (n = 14,330). Similarly, Deimling et al. (2006) reported UI among other symptoms in their examination of comorbidities and persistent cancer-related symptoms in older adults who were long-term cancer survivors. The characteristics of Keating et al.'s and Deimling et al.'s samples were similar to the current sample, with cancer survivors being older and more commonly female. The risk of developing cancer increases with advancing age. Therefore, advancing age and female gender may be factors that contribute to the likelihood of experiencing UI. UI is a syndrome that occurs commonly with advancing age, particularly in postmenopausal women. Radical prostatectomy also is associated with increased risk for UI (Augustin et al., 2002; Kao et al., 2000), and significantly more men had been diagnosed with prostate cancer in the UI study than in the RA study.

Consistent with the current findings, breast cancer was the most common malignancy in the cancer survivors in Keating et al.'s (2005) and Deimling et al.'s (2006) studies. Treatments for breast cancer can result in premature menopause in women who are pre- and perimenopausal at the time of diagnosis (Reyno, Levine, Skingley, Arnold, & Abu Zahra, 1992), and levels of reproductive hormones are significantly reduced in women with breast cancer who receive adjuvant therapy regardless of menopausal status (Bender, Paraska, Sereika, Ryan, & Berga, 2001). Cancer and cancer therapy may have an influence on some symptoms experienced by long-term cancer survivors. However, more research is needed to elicit information about the effects of treatment on symptoms in long-term cancer survivors.

Table 5. Prevalence of Comorbidities

	Overall (N = 1,046)		Rheumatoid Arthritis (N = 639)		Urinary Incontinence (N = 407)		If Significant at p ≤ 0.001			
Comorbidity	**n**	**%**	**n**	**%**	**n**	**%**	**χ^2**	**p**	**OR[c]**	**95% CI**
Cancer	154	15	56	9	98	24	46.4	< 0.001	3.30	2.30, 4.70
Coronary artery disease[a]	140	13	53	8	87	21	36.7	< 0.001	2.60	1.90, 3.50
Irregular heart beat	151	15	65	10	86	21	24.2	< 0.001	2.10	1.50, 2.80
Valvular heart disease	71	7	37	6	34	8	–	–	–	–
Heart failure	89	9	42	7	47	12	–	–	–	–
Hypertension	430	41	210	33	220	54	46.3	< 0.001	1.60	1.40, 1.90
Anemia	173	17	124	20	49	12	10.3	0.001	0.61	0.49, 0.83
Asthma	114	11	69	11	45	11	–	–	–	–
Chronic bronchitis	73	7	51	8	22	5	–	–	–	–
Emphysema	50	5	23	4	27	7	–	–	–	–
Headache	249	24	199	31	50	12	49.2	< 0.001	0.39	0.30, 0.52
Cerebral vascular disease[b]	101	10	25	4	76	19	62.6	< 0.001	4.80	3.10, 7.40
Thyroid disease	192	18	105	17	87	21	–	–	–	–
Diabetes mellitus	125	12	44	7	81	20	39.5	< 0.001	–	–
Urinary incontinence	505	49	98	15	407	100	710.2	< 0.001	2.90	2.00, 4.10
Kidney diseases	52	5	27	4	25	6	–	–	6.50	5.40, 7.80
Peptic ulcer	118	11	82	13	36	9	–	–	–	–
Digestive disease	121	12	57	9	64	16	11.2	0.001	–	–
Osteoarthritis	455	44	160	25	295	73	227.7	< 0.001	1.80	1.30, 2.50
Osteoporosis	284	27	189	30	95	24	–	–	2.90	2.50, 3.40
Skin disorders	150	14	90	14	60	15	–	–	–	–
Depression	228	22	132	21	96	24	–	–	–	–
Anxiety	160	15	103	16	57	14	–	–	–	–

[a] Based on history of myocardial infarction or coronary artery disease

[b] Based on history of stroke or transient ischemia attack

[c] Urinary incontinence versus rheumatoid arthritis

CI—confidence interval; OR—odds ratio

Individuals with UI reported more comorbidities than those with RA. By contrast, individuals with RA reported more symptoms than those with UI. RA is a disease affecting multiple body systems, resulting in a constellation of symptoms that have been well documented (Burton & Lloyd, 2006). The pathology of RA coupled with the medical management of the disease likely influenced the symptoms experienced by individuals comprising that sample.

The researchers also explored the effect of symptoms on subjects' QOL. More RA subjects reported that joint pain and night sweats had a moderate to severe effect on QOL than did UI subjects. Conversely, more UI subjects reported that involuntary urine loss had a moderate to extreme effect on QOL than did RA subjects. No differences were found in the effects of symptoms on QOL between subjects with or without cancer as a comorbidity. The results must be interpreted with caution because most symptoms were reported by fewer than 25% of the subjects in both studies. However, at least with respect to joint pain and involuntary urine loss, the symptoms that had a significant effect on subjects' QOL were those most closely related to their primary chronic health problems.

Subjects with RA were significantly younger than those with UI, which may have been a factor in their symptom experiences. Some evidence suggests that younger individuals with cancer experience more symptoms, poorer QOL, and more psychological distress than older individuals with the disease (Baucom, Porter, Kirby, Gremore, & Keefe, 2005–2006; Mosher & Danoff-Burg, 2005; Viklund, Wengstrom, Rouvelas, Lindblad, & Lagergren, 2006). Multiple factors likely are associated with the symptom experience of younger individuals, including the effect of cancer therapies on reproductive status and less expectancy of disease and concomitant symptoms. Conversely, older individuals may accept that disease and concomitant symptoms are a natural part of aging and may have had more time to adapt and cope with symptoms. Heidrich et al. (2006) found that the symptom experiences and QOL of older women with breast cancer did not differ from those of older women with other chronic health problems.

This secondary analysis has limitations. The information assessed regarding subjects' cancer diagnoses was limited to the primary site of the disease, whether the cancer was completely controlled, and whether the cancer had spread from its original site. Furthermore, it used a self-report measure but no confirmation of the validity of the responses. Missing was information about the time of diagnosis, the type of cancer therapy received, and the time since the conclusion of cancer therapy.

Significant differences in age and education existed between the two groups in the study. The differences in education between groups may be related to the fact that subjects in study 2 were significantly older than those in study 1. The current results differ from those of Reyes-Gibby et al. (2006), who found that having a lower level of education, among other

Table 6. Prevalence of Comorbidities in Subjects With and Without a History of Cancer

	History of Cancer (N = 154)		No History of Cancer (N = 892)	
Comorbidity	**n**	**%**	**n**	**%**
Coronary artery disease	27	18	113	12
Irregular heart beat	25	16	125	14
Valvular heart disease	6	4	63	7
Heart failure	19	12	70	8
Hypertension	80	53	350	39
Anemia	24	16	149	17
Asthma	12	8	101	11
Chronic bronchitis	13	9	60	7
Emphysema	11	7	39	4
Headache	32	21	216	24
Cerebral vascular disease	18	12	83	9
Thyroid disease	34	22	158	18
Diabetes mellitus	22	14	103	12
Kidney disease	12	8	40	5
Peptic ulcer disease	16	14	101	11
Digestive disease	24	18	96	11
Osteoarthritis	**88**	**58**	**366**	**41**
Rheumatoid arthritis	**62**	**41**	**592**	**66**
Osteoporosis	44	29	239	27
Skin disorder	24	16	125	14
Depression	31	20	196	22
Anxiety	26	23	133	15

Note. The bolded rows represent the only two comorbidities that were significant: osteoarthritis ($\chi^2 = 14.4$, $p < 0.001$; odds ratio [OR] = 1.4, 95% confidence interval [CI] = 1.10, 1.70) and rheumatoid arthritis ($\chi^2 = 37.3$, $p < 0.001$; OR = 0.57, 95% CI = 0.48, 0.66).

factors, increased the risk for experiencing two or more of the symptoms in the cluster of fatigue, pain, and depression. Future studies should be designed in such a way to examine whether age and education contribute to symptoms.

The assessment used in both studies was not specifically designed to evaluate symptoms commonly experienced by patients with cancer. Furthermore, the assessment was limited to the presence or absence of symptoms, provided no information about symptom frequency or severity, and did not offer the opportunity for participants to indicate whether they attributed individual symptoms to their cancer diagnoses or to other comorbid conditions. Future prospective studies of symptom clusters in cancer survivors are needed and should include comprehensive symptom assessment that yields information about symptom frequency and severity and the effects of symptoms on QOL.

To tease out the relative contribution of a history of cancer to the symptoms experienced by individuals with a chronic health problem, a future study might compare individuals with a single chronic health problem who are cancer survivors to individuals with the same chronic health problem who are not cancer survivors. However, the generalizability of such a study may be questioned. Subjects in the current sample actually may be more representative of individuals with chronic health problems who commonly have comorbidities. In fact, Keating et al. (2005) found that cancer survivors were significantly more likely to have been diagnosed with arthritis, diabetes, lung disease, or heart disease than those who were not cancer survivors. Ideally, future studies should be designed to examine symptoms in individuals with a history of cancer and no other comorbidities. But, in reality, such studies may be difficult to implement because cancer occurs more commonly in older adults, as does the likelihood that individuals will have other chronic health problems (Gosney, 2005).

Conclusion

Additional prospective studies are needed to examine symptom clusters in survivors of cancer. As individuals are living longer with the disease, a comprehensive understanding of the symptom clusters that may be unique to cancer survivors with comorbid conditions is critical. Assessments should evaluate the frequency and severity of symptoms as well as whether cancer survivors attribute their symptoms to cancer or to other conditions. The review of previous research and this secondary analysis demonstrate the importance of developing and utilizing consistent measurements of symptoms across studies. Understanding the unique contributions of chronic health problems to the symptom experiences of cancer survivors is important. The information will guide the development of interventions to manage symptoms.

Author Contact: Catherine M. Bender, PhD, RN, can be reached at cbe100@pitt.edu, with copy to editor at ONFEditor@ons.org.

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