

Cancer Symptom

Mark H Smith

Queens, New York 11418, USA
mark20082009@gmail.com

Abstract: Cancer is the cells that grow out of control. Cancer cells can also invade other tissues. Growing out of control and invading other tissues are what makes a cell a cancer cell. Involved in more than 100 diseases, cancers can cause serious illness and death. Normally, the cells become cancer cells because of DNA damage. This material is a literature collection of the researches on the cancer symptom.

[Smith MH. **Cancer Symptom.** *Cancer Biology* 2013;3(2):120-203]. (ISSN: 2150-1041). <http://www.cancerbio.net>.
4

Keywords: cancer; biology; life; disease; research; literature; symptom

1. Introduction

Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Literatures

Akechi, T., T. Ietsugu, et al. (2009). "Symptom indicator of severity of depression in cancer patients: a comparison of the DSM-IV criteria with alternative diagnostic criteria." *Gen Hosp Psychiatry* **31**(3): 225-32.

OBJECTIVE: The objective of this study was to explore the performances of several diagnostic criteria items for judging the severity of major depression among cancer patients. **METHOD:** Using modern item response theory, we examined the performances of the diagnostic criteria outlined by the DSM-IV and two sets of conceptual diagnostic criteria (the Endicott and the Cavanaugh criteria) in a series of 728 cancer patients who had been diagnosed with major depression using an inclusive approach. **RESULTS:** While all the DSM-IV diagnostic criteria, including feelings of worthlessness and suicidal ideation, had a low ability for discriminating the severity of depression, two proposed items (not participating in medical care and social withdrawal) appeared to be good markers of moderately severe major depressive disorder among cancer patients. In addition, the items "fearfulness or depressed appearance in face or body posture" and "brooding, self-pity or pessimism" may be good markers for mild major depressive disorders, while the item "cannot be

cheered up, doesn't smile, no response to good news or funny situations" may be a good marker for severe major depressive disorder. **CONCLUSIONS:** The findings of the present study suggest that alternative criteria may have utility in diagnosing depression severity in cancer patients.

Andrew, I. M., K. Waterfield, et al. (2009). "Quantifying the impact of standardized assessment and symptom management tools on symptoms associated with cancer-induced anorexia cachexia syndrome." *Palliat Med* **23**(8): 680-8.

The objective of this study was to quantify the impact of standardized assessment and management tools on patient symptom scores in cancer-induced anorexia cachexia syndrome (ACS) using a within-group study design. Baseline assessments included the Patient Generated Subjective Global Assessment (PG-SGA) tool and an amended Symptoms and Concerns Checklist (SCC). Symptom management strategies, written for this project, were instigated. Follow-up SCC scores were collected at 2 and 4 weeks. Forty out of 79 patients referred were recruited; 29/79 (36.7%) were too unwell or had died prior to consent. At baseline, the PG-SGA tool revealed 250 active symptoms associated with ACS. Total PG-SGA score was above 9 for all patients. Predominant interventions involved simple dietary advice and prescription of artificial saliva, mouthwash and prokinetic antiemetics. Median total SCC score improved sequentially from 11 at baseline, to 7 and 4 at first and second review, respectively (visit 1 to 2, $p = 0.001$; visit 1 to 3, $p < 0.001$; and visit 2 to 3, $p = 0.02$). We conclude that patients with ACS are recognised late in their disease and have a considerable burden of active symptoms. A structured approach to assessment and management has a significant impact on symptom burden.

Annakkaya, A. N., P. Arbak, et al. (2007). "Effect of symptom-to-treatment interval on prognosis in lung cancer." *Tumori* **93**(1): 61-7.

AIMS AND BACKGROUND: To evaluate the relationship between delayed diagnosis and the degree of invasion and survival in lung cancer. **METHODS:** One hundred and three patients (96 men) with lung cancer were included. Stages in the diagnosis of lung cancer were classified as follows: symptom-to-doctor interval, i.e., the interval from the first symptoms related to the presence of lung cancer to the first consultation with a medical professional; doctor-to-diagnosis interval, i.e., the interval between the first medical visit and confirmation of the diagnosis; and diagnosis-to-treatment interval, i.e., the interval between diagnosis and complete TNM staging and treatment. The symptom-to-treatment interval (STI) was the sum of the 3 intervals. The degree of invasion was determined by the TNM classification. **RESULTS:** The patients were followed up for a mean period (= SD) of 7.4+/-8.7 months. Seventy-six (74%) patients were diagnosed with non-small cell lung cancer (NSCLC) and 27 patients (26%) with small cell lung cancer (SCLC). The mean length of STI was 120+/-101 days (median, 90). The mean length of the symptom-to-doctor interval was 63+/-62 days (median, 45), while the doctor-to-diagnosis and diagnosis-to-treatment intervals were 41 +/-82 days (median, 10) and 16+/-12 days (median, 12), respectively. When the STIs of the patients were correlated with tumor stage, tumor invasion, lymph node involvement and metastasis, no significant differences were found. Patients with an STI longer than 60 days had a significantly longer survival. Regarding the type of lung cancer and STI, the median survival was shorter in patients with an STI of less than 60 days both in NSCLC and SCLC, although this was not statistically significant in SCLC. **CONCLUSIONS:** The shorter the diagnostic interval, the shorter was the median survival in our study. The reason for the apparent discrepancy between poor prognosis of lung cancer patients in spite of early diagnosis might be much faster progression of the disease itself.

Armer, J. M., M. H. Henggeler, et al. (2008). "The Health Deviation of Post-Breast Cancer Lymphedema: Symptom Assessment and Impact on Self-Care Agency." *Self Care Depend Care Nurs* **16**(1): 14-21.

Breast cancer is the leading cancer among women world-wide, affecting 1 of 8 women during their lifetimes. In the US alone, some 2 million breast cancer survivors comprise 20% of all cancer survivors. Conservatively, it is estimated that some 20-40% of all breast cancer survivors will develop the

health deviation of lymphedema or treatment-related limb swelling over their lifetimes. This chronic accumulation of protein-rich fluid predisposes to infection, leads to difficulties in fitting clothing and carrying out activities of daily living, and impacts self-esteem, self-concept, and quality of life. Lymphedema is associated with self-care deficits (SCD) and negatively impacts self-care agency (SCA) and physiological and psychosocial well-being. Objectives of this report are two-fold: (1) to explore four approaches of assessing and diagnosing breast cancer lymphedema, including self-report of symptoms and the impact of health deviations on SCA; and (2) to propose the development of a clinical research program for lymphedema based on the concepts of Self-Care Deficit Nursing Theory (SCDNT). Anthropometric and symptom data from a National-Institutes-of-Health-funded prospective longitudinal study were examined using survival analysis to compare four definitions of lymphedema over 24 months post-breast cancer surgery among 140 of 300 participants (all who had passed the 24-month measurement). The four definitions included differences of 200 ml, 10% volume, and 2 cm circumference between pre-op baseline and/or contralateral limbs, and symptom self-report of limb heaviness and swelling. Symptoms, SCA, and SCD were assessed by interviews using a validated tool. Estimates of lymphedema occurrence varied by definition and time since surgery. The 2 cm girth change provided the highest estimation of lymphedema (82% at 24 months), followed by 200 ml volume change (57% at 24 months). The 10% limb volume change converged with symptom report of heaviness and swelling at 24 months (38-39% lymphedema occurrence), with symptom report being the earliest predictor of lymphedema occurrence than any other measurement. Findings verify the importance of subjective assessment by symptom report of limb changes and SCD following breast cancer treatment as an essential tool in early detection and treatment of lymphedema. Findings also support the importance of pre-operative baseline measurements, symptom history, and SCA for later post-op comparisons. These preliminary findings underscore the importance of strengthening SCA by educating breast cancer survivors. Self assessment, early detection, and early treatment hold the best promise for optimal management of this chronic condition, limiting detrimental effects on SCA, and improving quality of life and physiological and psychosocial well-being. These findings lay the foundation for a clinical research program in breast cancer lymphedema based on SCDNT in which education in and awareness for self-report of lymphedema-associated symptoms is a first step in

screening. Increasing patient knowledge through education will increase SCA by identifying and providing information to meet self-care requisites (SCR) related to the health deviation of lymphedema. The nurse has the opportunity to assist patients in developing self-care actions as needed to meet universal and health deviation therapeutic requisites to address self-care demands following breast cancer treatment.

Badger, T., C. Segrin, et al. (2005). "Telephone interpersonal counseling with women with breast cancer: symptom management and quality of life." *Oncol Nurs Forum* **32**(2): 273-9.

PURPOSE/OBJECTIVES: To examine the effectiveness of a telephone interpersonal counseling (TIP-C) intervention compared to a usual care attentional control for symptom management (depression and fatigue) and quality of life (positive and negative affect, stress) for women with breast cancer. **DESIGN:** Experimental with repeated measures. **SETTING:** Academic cancer center and urban, private oncology offices. **SAMPLE:** 48 women with breast cancer who were in their mid-50s, married, and employed at the time of the study. **METHODS:** Women were assigned to either the six-week TIP-C or attentional usual care groups. Women were matched on stage and treatment. Data were collected at baseline, after the six interventions, and one month postintervention. Measures included the Center for Epidemiologic Studies Depression Scale, Positive and Negative Affect Schedule, Multidimensional Fatigue Inventory, and Index of Clinical Stress. **MAIN RESEARCH VARIABLES:** Depression, positive and negative affect, fatigue, and stress. **FINDINGS:** Women in the intervention group experienced decreases in depression, fatigue, and stress over time and increases in positive affect. **CONCLUSIONS:** The preliminary results partially supported the effectiveness of TIP-C for symptom management and quality of life. The authors hypothesized that decreased depression, reduced negative affect, decreased stress, decreased fatigue, and increased positive affect over time would be the resulting psychosocial effects, given the theoretical underpinnings of the intervention. **IMPLICATIONS FOR NURSING:** Nurses need to assess the quantity and quality of the social support network early in treatment; women with less social support need to be referred to counseling and support services. Because these women have limited participation in face-to-face interventions, they should be encouraged to participate in telephone or online support programs or in other programs or organizations (e.g., churches, social clubs) that would provide support.

Basch, E., A. Iasonos, et al. (2006). "Patient versus clinician symptom reporting using the National Cancer Institute Common Terminology Criteria for Adverse Events: results of a questionnaire-based study." *Lancet Oncol* **7**(11): 903-9.

BACKGROUND: The Common Terminology Criteria for Adverse Events (CTCAE) are used as standard practice in trials of cancer treatments by clinicians to elicit and report toxic effects. Alternatively, patients could report this information directly as patient-reported outcomes, but the accuracy of these reports compared with clinician reports remains unclear. We aimed to compare the reporting of symptom severity reported by patients and clinicians. **METHODS:** Between March and May, 2005, a questionnaire with 11 common CTCAE symptoms was given to consecutive outpatients and their clinicians (physicians and nurses) in lung and genitourinary cancer clinics in the Memorial Sloan-Kettering Cancer Center, New York, NY, USA. Patients completed a version that used language adapted from the CTCAE for patient self-reporting. The results from the questionnaire were compared with clinician reporting of the same symptoms. **FINDINGS:** Of 435 patients and their clinicians asked to take part in the study, 400 paired surveys were completed. For most symptoms, agreement between patient and clinician was high, and most discrepancies were within a grade difference of one point. Agreement was higher for symptoms that could be observable directly, such as vomiting and diarrhoea, than for more subjective symptoms, such as fatigue and dyspnoea. Differences in symptom reporting rarely would have changed treatment decisions or dosing, and patients assigned greater severity to symptoms more than did clinicians. No significant differences were recorded between the results when the questionnaire was completed by the patient before or after the clinician. **INTERPRETATION:** Patient reporting of symptoms could add to the current approach to symptom monitoring in cancer treatment trials. Future research should assess the effect of self reporting on clinical outcomes and efficiency, and the use of real-time collection of patient-reported outcomes for early detection of potentially serious adverse events.

Beck, S. L., W. N. Dudley, et al. (2005). "Pain, sleep disturbance, and fatigue in patients with cancer: using a mediation model to test a symptom cluster." *Oncol Nurs Forum* **32**(3): 542.

PURPOSE/OBJECTIVES: To test whether sleep disturbance mediates the effect of pain on fatigue. **DESIGN:** Cross-sectional. **SETTING:** Radiation therapy clinic, oncology ambulatory clinic, and inpatient oncology unit in an urban teaching

hospital. **SAMPLE:** 84 patients with cancer with multiple primary diagnoses who were experiencing pain. Fifty-three percent were female and 92% were Caucasian, with a mean age of 54 years. **METHODS:** All participants completed a symptom questionnaire that included the Brief Pain Inventory-Short Form, the Pittsburgh Sleep Quality Index, and the fatigue subscale of the Profile of Mood States questionnaire. Multistage linear regression was used to test a mediation model. **MAIN RESEARCH VARIABLES:** Fatigue, pain, and sleep disturbance. **FINDINGS:** Mediation analyses indicate that pain influences fatigue directly as well as indirectly by its effect on sleep. About 20% (adjusted $R^2 = 0.20$) of the variation in fatigue is explained by pain. Thirty-five percent of the variance in fatigue explained by pain was accounted for by the mediation pathway. **CONCLUSIONS:** Some of the effect of pain on fatigue is mediated by sleep disturbance, but pain has a direct effect on fatigue as well. **IMPLICATIONS FOR NURSING:** Although the relationship can be explained only partially by the commonsense point of view that people who are in pain lose sleep and naturally report more fatigue, this finding is important and leads to a potential intervention opportunity. Strategies to improve sleep by better pain management may contribute to decreased fatigue.

Beck, S. L., G. L. Towsley, et al. (2009). "Symptom experiences and quality of life of rural and urban older adult cancer survivors." *Cancer Nurs* 32(5): 359-69.

This study examined the symptom experience, health-related quality of life, and functional performance of elderly cancer survivors at 1 and 3 months after the completion of initial treatment. The study used a descriptive, comparative, repeated-measures design. A mixed-methods approach combined completion of survey instruments with qualitative interviews. Of the 52 participants, 22 resided in rural ($n = 12$) or semirural ($n = 10$) areas and 30 lived in urban settings. There were 23 women and 29 men ranging in age from 65 to 81 years (mean age, 71.53 years). Survivors experienced a significant number of symptoms (mean, 4.58), which were, on average, moderate in intensity and did not differ based on urban or rural residence. The Medical Outcomes Study SF-12 Physical Component Summary was less than the national norm for elderly individuals or those with a chronic disease. There was minimal improvement 3 months after treatment. Elderly survivors, regardless of whether they were rural or urban, experienced a significant number of unrelieved symptoms, including fatigue, pain, and difficulty sleeping. Eighty-eight percent had other chronic diseases. Comorbidities were associated with greater symptom intensity and less physical health status.

Survivorship care for elderly adults should include a comprehensive geriatric assessment and tailored strategies for symptom management.

Bekelman, D. B., J. S. Rumsfeld, et al. (2009). "Symptom burden, depression, and spiritual well-being: a comparison of heart failure and advanced cancer patients." *J Gen Intern Med* 24(5): 592-8.

BACKGROUND: A lower proportion of patients with chronic heart failure receive palliative care compared to patients with advanced cancer. **OBJECTIVE:** We examined the relative need for palliative care in the two conditions by comparing symptom burden, psychological well-being, and spiritual well-being in heart failure and cancer patients. **DESIGN:** This was a cross-sectional study. **PARTICIPANTS:** Sixty outpatients with symptomatic heart failure and 30 outpatients with advanced lung or pancreatic cancer. **MEASUREMENTS:** Symptom burden (Memorial Symptom Assessment Scale-Short Form), depression symptoms (Geriatric Depression Scale-Short Form), and spiritual well-being (Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being scale). **MAIN RESULTS:** Overall, the heart failure patients and the cancer patients had similar numbers of physical symptoms (9.1 vs. 8.6, $p = 0.79$), depression scores (3.9 vs. 3.2, $p = 0.53$), and spiritual well-being (35.9 vs. 39.0, $p = 0.31$) after adjustment for age, gender, marital status, education, and income. Symptom burden, depression symptoms, and spiritual well-being were also similar among heart failure patients with ejection fraction $< \text{or} = 30$, ejection fraction > 30 , and cancer patients. Heart failure patients with worse heart failure-related health status had a greater number of physical symptoms (13.2 vs. 8.6, $p = 0.03$), higher depression scores (6.7 vs. 3.2, $p = 0.001$), and lower spiritual well-being (29.0 vs. 38.9, $p < 0.01$) than patients with advanced cancer. **CONCLUSIONS:** Patients with symptomatic heart failure and advanced cancer have similar needs for palliative care as assessed by symptom burden, depression, and spiritual well-being. This implies that heart failure patients, particularly those with more severe heart failure, need the option of palliative care just as cancer patients do.

Bellizzi, K. M., D. M. Latini, et al. (2008). "Fear of recurrence, symptom burden, and health-related quality of life in men with prostate cancer." *Urology* 72(6): 1269-73.

OBJECTIVES: To examine the contributions of fear of recurrence and the more commonly examined treatment-related symptoms to the health-related quality of life (HRQOL) of men treated for localized prostate cancer. **METHODS:** A total of 730 men with localized disease were identified from the

Cancer of the Prostate Strategic Urologic Research Endeavor, a national, prospective study of men with prostate cancer. Pre- to post-treatment changes in fear of recurrence, treatment-specific symptoms and burden, comorbidities at diagnosis, number of new symptoms, and post-treatment HRQOL data were analyzed. RESULTS: Linear regression, adjusted for clinical and demographic characteristics, showed that improved fear of recurrence ($P < 0.01$), higher number of post-treatment symptoms ($P < 0.01$), and improved bowel function ($P < 0.01$) significantly predicted better mental health scores. For physical health, improved urinary bother ($P < 0.01$) and lower number of post-treatment symptoms ($P < 0.01$) were associated with better physical health. CONCLUSION: Understanding men's fears about cancer recurrence and how these fears influence physical and mental health are important components of providing care to this growing population.

Bender, C. M., S. J. Engberg, et al. (2008). "Symptom clusters in adults with chronic health problems and cancer as a comorbidity." *Oncol Nurs Forum* 35(1): E1-E11.

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.

Berger, A. M., D. E. Neumark, et al. (2007). "Enhancing recruitment and retention in randomized clinical trials of cancer symptom management." *Oncol Nurs Forum* 34(2): E17-22.

PURPOSE/OBJECTIVES: To describe techniques to overcome challenges of collaborating with multiple clinical sites and participants to enhance recruitment and retention for cancer symptom management randomized clinical trials (RCTs). DATA SOURCES: Personal experiences and publications related to recruitment and retention of sites and participants in RCTs, which were found by searching MEDLINE, CINAHL, and PsycINFO records. DATA SYNTHESIS: Techniques to overcome challenges related to multisite research, patient confidentiality guidelines, and work with an at-risk population were identified and applied successfully in an RCT designed to modify fatigue during and following adjuvant breast cancer chemotherapy. CONCLUSIONS: Successful recruitment and retention depended on the value that site personnel placed on symptom management research, identification of a designated contact person at each site, and flexibility in maintaining communication among the project director, contact individuals, and participants. IMPLICATIONS FOR NURSING: Initial and ongoing collaboration with participants and a contact person at each site, assurance of privacy of protected health information, and emotional support are critical to recruitment and retention throughout cancer symptom management RCTs.

Bezjak, A., D. Tu, et al. (2006). "Symptom improvement in lung cancer patients treated with erlotinib: quality of life analysis of the National Cancer Institute of Canada Clinical Trials Group Study BR.21." *J Clin Oncol* 24(24): 3831-7.

PURPOSE: This report describes the quality of life (QOL) findings of a randomized placebo controlled study of erlotinib, an epidermal growth factor receptor inhibitor, in patients with non-small-cell lung cancer (NSCLC). PATIENTS AND METHODS: This double-blind phase III trial randomly assigned 731 patients with NSCLC who had progressed after prior chemotherapy to erlotinib 150 mg daily or placebo, with survival as the primary study outcome. QOL was assessed by European Organisation for Research and Treatment of Cancer QLQ-C30 and the lung cancer module QLQ-LC13. The primary end points for QOL analysis were time to deterioration of three common lung cancer symptoms:

cough, dyspnea, and pain. RESULTS: Survival was significantly longer (hazard ratio, 0.70; $P < .0001$) in the erlotinib arm. Compliance with QOL was 87% at baseline and more than 70% during treatment. Patients receiving erlotinib had significantly longer median time to deterioration for all three symptoms (4.9 v 3.7 months for cough [$P = .04$]; 4.7 v 2.9 months for dyspnea [$P = .04$], and 2.8 v 1.9 months for pain [$P = .03$]). QOL response analyses showed that 44%, 34%, and 42% of patients receiving erlotinib had improvement in these three symptoms, respectively. This was accompanied by a significant improvement in the physical function (31% erlotinib v 19% placebo, $P = .01$), and global QOL (35% v 26%, $P < .0001$). Patients with complete or partial response were more likely to have improvement in the QOL response than patients with stable or progressive disease ($P < .01$). CONCLUSION: Erlotinib not only improves survival in previously treated patients with NSCLC, but also improves tumor-related symptoms and important aspects of QOL.

Bharucha, S., S. Hughes, et al. (2005). "Targets and elective colorectal cancer: outcome and symptom delay at surgical resection." *Colorectal Dis* 7(2): 169-71.

OBJECTIVE: To determine, for elective patients with colorectal cancer, if associations exist between the length of symptom history at surgical resection and Dukes stage, completeness of the surgical procedure and patient survival. PATIENTS AND METHODS: A prospective cohort study was undertaken. Five hundred and eighty-two patients with colorectal cancer, admitted for surgical resection after outpatient consultation, divided into four equal quartiles according to length of symptom history (short: $n = 131$, 0-103 days; medium: $n = 136$, 104-177 days; long: $n = 136$, 178-318 days; very long: $n = 137$, 319-1997 days). The main outcome measures used were the Extent of tumour (Dukes stage) at resection, completeness of resectional surgery (curative vs palliative), patient survival after resection. RESULTS: For patients undergoing elective surgical resection of colorectal cancer we did not find an association between Dukes stage and duration of patient history (Dukes stage C tumours were seen in 37% (CI: 26.2%-48.0%) of patients with a short symptomatic history as opposed to 34% (CI: 32%-62%) with a very long symptomatic history). Elective curative resection was not associated with a significantly different symptom duration than elective palliative resection (Palliative resections were performed in 24% (CI: 11.7%-36.4%) of patients with a short symptomatic history as opposed to 16% (CI: 2.4%-29.9%) with a very long symptomatic history). The median survival time for the four elective

colorectal patient groups defined by length of symptomatic history was not significantly different - (short: $n = 131$, 4.3 years; medium: $n = 136$, 5.9 years; long: $n = 136$, 7.1 years; very long: $n = 137$, 5.0 years). CONCLUSION: Tumour extent, completeness of resection and patient outcome after elective colorectal cancer resection was not found to have an association with length of patient history at the time of surgery.

Boehmke, M. M. and S. S. Dickerson (2005). "Symptom, symptom experiences, and symptom distress encountered by women with breast cancer undergoing current treatment modalities." *Cancer Nurs* 28(5): 382-9.

Adjuvant chemotherapy protocols used to treat women with breast cancer have evolved over the last decade and have dramatically altered the symptoms and symptom experiences of these women. The purpose of this study was to identify symptoms, symptom experiences, and resulting symptom distress encountered by women with breast cancer undergoing surgery and receiving current chemotherapy protocols. Convenience sampling was used to recruit 20 women for this study. Women were asked to tell their story and transcripts were analyzed using Colaizzi's procedural steps. Six themes emerged. The most important theme was that symptom experiences and symptom distress, similar among all 20 women, were congruent with the type of treatment. After surgery, women complained of numbness, pulling, and body image changes; while receiving Adriamycin and Cyclophosphamide, symptoms of intense nausea and hair loss caused distress; while receiving Paclitaxel, symptoms of intense bone pain and peripheral neuropathy caused distress. This study provides oncology nurses with a clear description of the symptoms, symptom experiences, and symptom distress women with breast cancer encounter during present-day treatment protocols. Knowing the symptoms and symptom experiences, as well as when they occur during treatment, provides oncology nurses with an opportunity to share with women about to start treatment for breast cancer the expected "normative" symptom experience. This in turn would allow women to anticipate symptoms, employ management strategies, and empower them to improve their cancer experience.

Bornhak, S., E. Heidemann, et al. (2007). "Symptom-oriented follow-up of early breast cancer is not inferior to conventional control. Results of a prospective multicentre study." *Onkologie* 30(8-9): 443-9.

BACKGROUND: The homogeneity of the schemes for follow-up care after curative surgical

treatment of early breast cancer is still a matter of debate in Germany. We investigated whether symptom-oriented follow-up is equivalent in terms of survival rates to conventional surveillance based on scheduled tests. **PATIENTS AND METHODS:** In a prospective, non-randomised, multicentre cohort study carried out between 1995 and 2000, 244 patients underwent a conventional follow-up (scheduled laboratory tests including CEA and CA 15-3, chest X-rays and liver ultrasound). 426 patients were monitored in a symptom-oriented manner (additional tests only in the case of symptoms indicating possible recurrence). Mammography, structured histories and physical examinations were done regularly in both branches. 1,108 patients did not participate in the project. They represent 'real world patients', unaffected by the implications of a study. **RESULTS:** The symptom-oriented follow-up group produced results not inferior to those of the intensive one ($p < 0.05$) in terms of overall and relapse-free survival. Furthermore, no difference was indicated in terms of overall survival between study participants and the 'real world patients' ($p = 0.316$). **CONCLUSION:** The results confirm that regular imaging and laboratory tests have no relevant effect on overall survival of patients after curative primary therapy of early breast cancer and support the implementation of a symptom-oriented routine follow-up.

Bottomley, A., C. Debruyne, et al. (2008). "Symptom and quality of life results of an international randomised phase III study of adjuvant vaccination with Bec2/BCG in responding patients with limited disease small-cell lung cancer." *Eur J Cancer* **44**(15): 2178-84.

AIMS: This study reports the symptom and HRQOL results in which standard treatment was compared to standard therapy plus Bec2, an anti-idiotypic antibody that mimics GD3, a ganglioside antigen. **METHODS:** Five hundred and fifteen LD SCLC patients were randomised to receive five vaccinations of Bec2 (2.5mg)/BCG vaccine arm (VA) or an observational arm (OA) administered over a 10-week period. Survival was the primary end-point; HRQOL was a secondary end-point, assessed using the EORTC QLQ-C30/LC 13. **RESULTS:** There was no improvement in survival or progression-free survival in the vaccination arm. At baseline patients in both arms demonstrated significantly impaired scores on the global QOL scale, when compared to a normative population. However, HRQOL and symptom scores between the two treatment arms were not statistically different at any time point. **CONCLUSION:** We found no benefits to patient HRQOL by additional vaccination with Bec2/BCG to

LD SCLC for patients who have been undergoing standard therapy.

Breen, S. J., C. M. Baravelli, et al. (2009). "Is symptom burden a predictor of anxiety and depression in patients with cancer about to commence chemotherapy?" *Med J Aust* **190**(7 Suppl): S99-104.

OBJECTIVES: To assess the prevalence, severity and distress from physical symptoms and the prevalence of anxiety and depression in patients about to undergo chemotherapy for potentially curable cancers; and to explore the presence of symptom clusters and investigate their relationships with anxiety and depression. **DESIGN, PARTICIPANTS AND SETTING:** Cross-sectional survey of 192 patients with breast or gastrointestinal cancers or lymphoma before first ever chemotherapy treatment with curative intent. **MAIN OUTCOME MEASURES:** Hospital Anxiety and Depression Scale to assess anxiety and depression and the Chemotherapy Symptom Assessment Scale to measure physical symptom prevalence, severity and distress ("bother"). **RESULTS:** Prevalence of anxiety was 45% and depression 25%. The most prevalent physical symptoms were pain (48%), feeling unusually tired (45%) and difficulty sleeping (45%). Physical symptoms rated as most severe were pain (28%), difficulty sleeping (26%) and feeling unusually tired (19%). Physical symptoms causing the most distress were pain (39%), constipation (18%) and nausea (16%). Factor analysis of symptom distress scores indicated that five factors explained 36.7% of the variance and included: gastrointestinal (nausea, vomiting, pain), general malaise (tiredness, feeling weak, headaches), emotional (feeling depressed, feeling anxious), nutritional (changes to appetite, weight loss or gain) and general physical (mouth/throat problems, shortness of breath). Regression analysis indicated that symptom distress for the malaise ($\beta = 1.46$; $P < 0.001$), nutritional ($\beta = 0.70$; $P < 0.05$) and gastrointestinal ($\beta = 0.73$; $P < 0.05$) factors were independent predictors of depression. **CONCLUSIONS:** Before commencing chemotherapy, patients are already experiencing distressing symptoms and have high scores for anxiety and depression, partially explained by physical symptom distress. Patients should be routinely screened for both emotional and physical needs and appropriate interventions should be developed. **TRIAL REGISTRATION:** Australian New Zealand Clinical Trials Registry ACTRN012606000178549.

Bruner, D. W. (2007). "Outcomes research in cancer symptom management trials: the Radiation Therapy Oncology Group (RTOG) conceptual model." *J Natl Cancer Inst Monogr*(37): 12-5.

The Radiation Therapy Oncology Group (RTOG) Health Services Research and Outcomes (HSRO) Committee aims to guide the study of the interactions among clinical, humanistic, and economic variables that optimize patient outcomes on clinical trials. To guide this work, the RTOG Outcomes Model was developed. Within this framework, measurement focuses primarily on patient-reported outcomes (PROs). In the examples presented, these outcomes have served to better quantify the benefit of one therapy over alternative therapies, as in the example of multimodality therapy for lung cancer, and to add evidence to clinical outcomes when clinical outcomes alone have not been strong enough to change clinical practice, as in the example of palliative radiotherapy for painful bone metastasis. The unique contribution to the RTOG of the HSRO Committee is the selection and use of PRO measures that give "voice" to the patient in clinical trials as well as provide data to better manage symptoms.

Buchanan, D. R., A. M. O'Mara, et al. (2005). "Quality-of-life assessment in the symptom management trials of the National Cancer Institute-supported Community Clinical Oncology Program." *J Clin Oncol* **23**(3): 591-8.

PURPOSE: To examine how quality of life (QOL) is prospectively conceptualized, defined, and measured in the symptom management clinical trials supported by the National Cancer Institute Community Clinical Oncology Program (CCOP). **METHODS:** All QOL research objectives, rationales, assessment instruments, symptoms treated, and types of interventions from the CCOP symptom management portfolio of clinical trials were extracted and analyzed. **RESULTS:** QOL assessments were proposed in 68 (52%) of the 130 total CCOP symptom management trials initiated since 1987. A total of 22 global QOL instruments were identified. Both the frequency of symptom management trials and the frequency of QOL assessment have increased significantly over time. The Functional Assessment of Cancer Therapy and Uniscale instruments were the most widely used QOL instruments, included in 55% of trials assessing QOL. The conceptual framework for QOL inclusion was limited to univariate relationships between symptom relief and global improvements in QOL. No consistent associations were found between QOL assessment and either the symptoms targeted or types of interventions. **CONCLUSION:** To advance the state of the science, research protocols need to provide more explicit rationales for assessing QOL in symptom management trials and for the selection of the QOL instrument(s) to be used. Conceptual frameworks that specify the hypothesized links between the specific

symptom(s) being managed, interactions with other symptoms, different domains of QOL, and global QOL also need to be more precisely described. Methodologic and conceptual advances in QOL symptom management trials are critical to fulfill the promise of alleviating suffering and improving the QOL of cancer patients.

Buchanan, D. R., J. D. White, et al. (2005). "Research-design issues in cancer-symptom-management trials using complementary and alternative medicine: lessons from the National Cancer Institute Community Clinical Oncology Program experience." *J Clin Oncol* **23**(27): 6682-9.

PURPOSE: To identify major research-design issues in proposals submitted by investigators in the Community Clinical Oncology Program (CCOP) for clinical trials of complementary and alternative medicine (CAM) for cancer-symptom management. **METHODS:** We conducted content analysis of all scientific reviews of concepts and protocols submitted by the CCOP to the National Cancer Institute (NCI) to identify research challenges in conducting clinical trials designed to evaluate CAM interventions for cancer-symptom management. **RESULTS:** Since the inception of the NCI Office of Cancer Complementary and Alternative Medicine in 1998, a total of 46 symptom-management studies using CAM interventions have been proposed by CCOP investigators, with 20 studies now in progress comprising 22% of the current total CCOP symptom-management portfolio. Proposals fell into four categories: complex natural products; nutritional therapeutics; mind-body interventions; and alternative medical systems. The most significant research-design issues arose as a consequence of the lack of preclinical data for CAM interventions and the lack of quality-control standards comparable with those used in regulating new pharmaceutical agents. **CONCLUSION:** Across the different types of CAM interventions, the most common problems found in proposed research designs are related to unwarranted assumptions about the consistency and standardization of CAM interventions, the need for data-based justifications for the study hypotheses, and the need to implement appropriate quality control and monitoring procedures during the course of the trial. To advance the state of the science, future research must address these critical issues if CAM interventions are to be evaluated rigorously and have a consequent impact on clinical practice and general public awareness.

Burkett, V. S. and C. S. Cleeland (2007). "Symptom burden in cancer survivorship." *J Cancer Surviv* **1**(2): 167-75.

INTRODUCTION: The subjective experience of cancer survivorship can be assessed by various patient-reported outcome (PRO) methods, including measures of symptom burden and health-related quality of life (HRQOL). Symptom burden includes the presence and severity of multiple symptoms and the level of distress caused by symptoms that go untreated or unrelieved. The concept of symptom burden is more limited in scope than HRQOL but may provide information that better describes the status of various stages of survivorship. This paper contrasts symptom burden with general HRQOL and addresses the importance of including symptom burden as research tool throughout the trajectory of cancer survivorship. **METHODS:** We summarized studies that illustrate both HRQOL and symptoms as outcomes of treatment and of descriptive studies of cancer survivorship. Survivorship was operationally defined as beginning at the completion of primary anticancer treatment. **RESULTS:** HRQOL and symptom burden measures both provide meaningful but conceptually different data. Both types of measures are important in portraying aspects of cancer survivorship over time, although symptom burden may provide sufficient information to inform treatment decisions and identify long-term effects of cancer therapies. **CONCLUSIONS:** Cancer survivors are at risk for multiple severe and persistent symptoms, and assessing and monitoring the severity and impact of these multiple symptoms is critical to understanding the survivorship experience. The inclusion of multiple symptom measures along with the development of new and better methods of long-term symptom tracking in survivors is a critical step in improving the health status of survivors. **IMPLICATIONS FOR CANCER SURVIVORS:** Late and long-term effects seen in cancer survivors have historically been understudied. Symptom burden is an important area of assessment that can be used to specifically describe the symptoms that distress survivors. More descriptive data in this growing population may help identify biological processes in symptom production and maintenance, and facilitate in the development of better treatment and prevention to enhance cancer survivorship.

Cella, D., D. Eton, et al. (2008). "Relationship between symptom change, objective tumor measurements, and performance status during chemotherapy for advanced lung cancer." *Clin Lung Cancer* 9(1): 51-8.

PURPOSE: Our objective was to identify which symptoms of advanced lung cancer are most likely to change with objective tumor measurements (progressions and responses) or changes in performance status (PS). **PATIENTS AND**

METHODS: Eighty patients with advanced non-small-cell lung cancer were studied during the first 12 weeks of chemotherapy. Symptoms were assessed weekly through telephone administration of the Functional Assessment of Cancer Therapy-Lung Symptom Index-12. Data on PS were collected from patients every 3 weeks. Symptom reports were mapped onto clinical events (progression or response as determined by clinicians) and PS assessments. **RESULTS:** Disease progression and declining PS were associated with worsening of several symptoms. Pain, shortness of breath, cough, weight loss, and appetite loss worsened most from before to after progression. Patients with an objective response to chemotherapy reported more fatigue and difficulty breathing at response than before response. However, unlike patients who experienced progression, patients responding to chemotherapy never or rarely complained of clinically significant pain, weight loss, cough, chest tightness, nausea, or confusion before, during, or after response. With the exception of both with side effects of treatment, confusion, and difficulty breathing, symptoms tracked fairly closely over the 12 weeks with changes in PS. Declining PS was associated with considerably more symptom worsening than unchanged or improved PS, independent of treatment response. **CONCLUSION:** These data can help the clinician identify symptoms of lung cancer most reliably associated with objective responses and perceived changes in functional status during chemotherapy. Symptom self-reports could be used by clinicians to monitor patient status and possibly inform treatment modification.

Cella, D., S. R. Land, et al. (2008). "Symptom measurement in the Breast Cancer Prevention Trial (BCPT) (P-1): psychometric properties of a new measure of symptoms for midlife women." *Breast Cancer Res Treat* 109(3): 515-26.

PURPOSE: To evaluate scalability of a symptom scale administered to women enrolled in the Breast Cancer Prevention Trial (BCPT) (P-1) conducted by the National Surgical Adjuvant Breast and Bowel Project (NSABP). **PATIENTS AND METHODS:** Responses of 11,064 women recruited into a study of 20 mg daily tamoxifen versus placebo to prevent breast cancer in high-risk women were analyzed. Exploratory factor analyses of the 12 month data were conducted on a random subset of 4,000 women to estimate the factor structure. Baseline data on these same 4,000 women were analyzed to confirm the structure. The remaining sample was divided randomly into two data sets. Data on each set were then grouped by age (35-49, 50-59, or > or = 60 years) and treatment (tamoxifen or placebo) to corroborate these analyses. Correlations between the obtained

symptom clusters and two standard instruments (SF-36 and CES-D) were examined. Content analysis of open-ended responses was also conducted. RESULTS: Eight clinically-interpretable clusters of symptoms were identified and confirmed: Cognitive symptoms, musculoskeletal pain, vasomotor symptoms, nausea, sexual problems, bladder problems, body image, and vaginal symptoms. Scoring for each scale represented by these eight clusters is provided. Content analysis of open-ended responses suggested four items that are additional candidates: fatigue, back problems, abdominal pain, and leg/foot cramps or pain. CONCLUSIONS: Symptoms associated with hormone therapy for breast cancer can vary. Nevertheless, the BCPT Eight Symptom Scale (BESS) can be clustered into clinically relevant and reproducible factors that may be useful in future outcomes research.

Cella, D., L. Wagner, et al. (2007). "Should health-related quality of life be measured in cancer symptom management clinical trials? Lessons learned using the functional assessment of cancer therapy." *J Natl Cancer Inst Monogr*(37): 53-60.

There are several advantages to including comprehensive health-related quality of life (HRQL) in symptom trials in oncology. The most obvious is to test the hypothesis that HRQL will be improved in addition to the symptom benefit. We should not "require," however, that a successful symptom intervention also improve other dimensions of HRQL. On the other hand, we should expect that it will not make other dimensions worse through side effects or exacerbation of disease, even if it improves the symptom. HRQL assessment in the trial helps evaluate the competing risks of any therapy. Furthermore, assessment of HRQL is now accomplished with very brief assessment (usually 30 questions or less), and the knowledge gained is valuable. With HRQL, one can compare cancer patients with those with other conditions and can determine the contribution of symptoms and side effects to the more broadly defined HRQL. Examples using the Functional Assessment of Cancer Therapy measurement system will demonstrate how HRQL assessment has contributed to our understanding of common cancer symptoms and their place in the conceptualization of HRQL. The prevalence of clinically significant symptoms is greatest in poor performance status (PS) patients compared with patients with good PS. Symptom improvement trials specifically designed for these patients should be encouraged, particularly with interventions that can provide symptomatic relief and improve multidimensional HRQL.

Cella, D., S. Yount, et al. (2006). "Development and validation of the Functional Assessment of Cancer Therapy-Kidney Symptom Index (FKSI)." *J Support Oncol* 4(4): 191-9.

The Functional Assessment of Cancer Therapy (FACT)-Kidney Symptom Index (FKSI) was developed and validated to enhance treatment decision-making, practice guidelines, symptom management, and treatment efficacy for kidney cancer patients. Thirty-four symptoms related to the disease were identified and tested. An equal weighting of patient and clinician ratings of the relative importance of each of these items led to production of a 15-item index (FKSI-15) and a 10-item abbreviated option (FKSI-10). To assess psychometric properties, patients completed the FKSI, Functional Assessment of Cancer Therapy-General (FACT-G), Eastern Cooperative Oncology Group-Performance Status Rating (ECOG-PSR), and a Global Rating of Change Scale (GRCS). Patient responses to the FKSI were analyzed for internal consistency, test-retest reliability, convergent and discriminant validity, and responsiveness to change in clinical status. The FKSI-10 showed high internal consistency; correlations between both FKSI-10 and the physical and functional well being domains of the FACT-G were high. The FKSI-10 differentiated patients grouped by ECOG-PSR (all $P < 0.001$) and discriminated patients based on their GRCS rating. The minimally important difference (MID) range estimate for the FKSI-10 was 2-4 points; the psychometric properties of the FKSI-15 were very similar (MID range, 3-5 points). Thus, the FKSI-15 and FKSI-10 are reliable and valid symptom indices for evaluating kidney cancer patients.

Chan, C. W., A. Richardson, et al. (2005). "A study to assess the existence of the symptom cluster of breathlessness, fatigue and anxiety in patients with advanced lung cancer." *Eur J Oncol Nurs* 9(4): 325-33.

The purpose of this small-scale study was to assess the existence of a symptom cluster involving breathlessness, fatigue and anxiety in patients with advanced lung cancer undergoing palliative radiation. A convenience sample of 27 patients were asked to complete a set of 100mm horizontal visual analogue scales (VAS) measuring the intensity of anxiety, breathlessness and fatigue at 3 points in time: 1 day prior to palliative radiotherapy (RT) (baseline, T0), and at week 3 (T1) and week 6 (T2) after the commencement of the RT. The prevalence of the 3 symptoms ranged from 59% to 96%. At baseline the median intensity of symptoms was mild, becoming progressively worse at T1 and T2. The correlations between the 3 symptoms were moderately strong at

T1 and T2 ($r=0.49-0.75$). The proposed symptom cluster had high internal consistency across T0-T2. These data support the notion that the symptoms--breathlessness, fatigue, and anxiety--may be viewed as a symptom cluster. The high prevalence and moderate intensity of the symptom cluster demonstrates a need for an intervention to manage these symptoms simultaneously.

Chen, L., L. Antras, et al. (2007). "Psychometric validation of the Patient Symptom Assessment in Lung Cancer instrument for small cell lung cancer." *Curr Med Res Opin* 23(11): 2741-52.

OBJECTIVE: Patient Symptom Assessment in Lung Cancer (PSALC) is a symptom scale developed for use in patients with small cell lung cancer (SCLC) to assess nine lung cancer symptoms (shortness of breath, cough, chest pain, hemoptysis, appetite loss, sleep interference, hoarseness, fatigue, interference with daily activities) scored from 1 (not at all) to 4 (very much). This study aims to retrospectively evaluate the psychometric properties of PSALC using clinical trial data. **METHODS:** Data were analyzed from a randomized, open-label, multicenter trial with 211 patients with SCLC receiving i.v. topotecan versus cyclophosphamide, doxorubicin, and vincristine. PSALC was evaluated at baseline and at 3-week intervals. Internal consistency, reliability, construct validity, and responsiveness were evaluated. **RESULTS:** Factor analysis indicated that one factor could represent all symptom items, so a PSALC total score (PSALC-TS) was used for psychometric validation. Internal consistency was supported by Cronbach's alpha of 0.74. Reliability of PSALC was supported by an intraclass correlation coefficient of 0.61 and concordance correlation coefficient of 0.72. Construct validity was supported by associations of lower PSALC-TS (less severe symptoms) with better ECOG performance status ($p < 0.0001$), and of PSALC-TS changes with clinical response. PSALC-TS was responsive to tumor progression (responsiveness statistic = 0.64). **LIMITATIONS:** The validation was performed retrospectively and was limited by small sample sizes at later assessment timepoints due to disease progression. **CONCLUSIONS:** A retrospective analysis suggests that the PSALC is a reliable, valid, and responsive instrument for measuring SCLC symptoms. If feasible in this population, a prospective validation study could be used to further evaluate these findings.

Chen, L., L. Antras, et al. (2008). "Symptom assessment in relapsed small cell lung cancer: cross-validation of the patient symptom assessment in lung cancer instrument." *J Thorac Oncol* 3(10): 1137-45.

INTRODUCTION: Lung cancer symptoms can be burdensome for patients with small cell lung cancer (SCLC). Patient Symptom Assessment in Lung Cancer (PSALC), a self-report scale for assessing SCLC symptom burden, was developed and validated previously using intravenous topotecan clinical trial data. This study cross-validates the PSALC using oral topotecan (OT) trial data. **METHODS:** Data were analyzed from a randomized, open-label, multicenter trial including 71 patients with relapsed SCLC receiving OT with best supportive care and 70 patients receiving best supportive care alone. PSALC and EQ-5D were administered at baseline and at 3-week intervals. Internal consistency, reliability, construct validity, and responsiveness were evaluated. **RESULTS:** Only one factor was indicated in factor analysis, hence PSALC total score (PSALC-TS) was used for psychometric analysis. Internal consistency was supported by Cronbach's alpha of 0.78. Construct validity was supported by significant associations of higher PSALC-TS (higher symptom burden) with worse Eastern Cooperative Oncology Group performance status and by correlations of PSALC-TS with EQ-5D utility index and visual analog scale score (all $p < 0.001$). Reliability was supported by intraclass correlation coefficient of 0.68 (using PSALC-TS before clinical status change) and concordance correlation coefficient of 0.69 (using PSALC-TS at baseline and before first visit). PSALC-TS was responsive to clinical status change from baseline to tumor response (responsiveness statistic = -0.99) and to tumor progression (responsiveness statistic = 0.94). **CONCLUSIONS:** Consistent with prior psychometric results, this cross-validation study using OT trial data showed acceptable validity, reliability, and responsiveness of the PSALC scale, further supporting its use to measure symptom burden in previously treated SCLC.

Chen, M. L. and C. C. Lin (2007). "Cancer symptom clusters: a validation study." *J Pain Symptom Manage* 34(6): 590-9.

Cancer patients often experience multiple symptoms concurrently, a phenomenon called symptom clustering. Different symptom clusters have been identified by various symptom assessment tools, as well as by different research methods, but no study has reported whether these identified symptom clusters can be replicated in a new sample. The severity of nine symptoms in 321 cancer patients was assessed using a Taiwanese version of the M.D. Anderson Symptom Inventory. The fit between these data and a model with three symptom factors (sickness, gastrointestinal, and emotional) was evaluated using confirmatory factor analysis. Most fitness indices demonstrated a satisfactory fit between

the data and a prespecified three-factor model except one; the root mean square error of approximation was <0.06. A modified model with one symptom (lack of appetite) double loaded in the sickness and gastrointestinal factors demonstrated a significantly better fit between the data and the model. Higher scores in each of the three symptom factors were associated with poorer functional status. Metastatic disease and receiving both chemotherapy and radiation therapy were associated with higher scores in sickness and gastrointestinal factors, but not in the emotional factor. Only hospitalization affected patients' scores in emotional factors. Our findings confirmed the prespecified structure of symptom clusters. A modified model showed a better fit. Patients' complex symptom experience may be better represented by subscale scores based on meaningful clusters rather than on an overall score across all symptoms.

Chen, M. L. and H. C. Tseng (2006). "Symptom clusters in cancer patients." *Support Care Cancer* **14**(8): 825-30.

GOALS OF WORK: Cancer patients often experience multiple symptoms, many of which have been reported to correlate with each other. The goals of this study were to understand which cancer-related symptoms cluster together and to test the conceptual meanings of the revealed symptom clusters. **PATIENTS AND METHODS:** Patients with various cancer diagnoses (N=151) were recruited from a medical center in northern Taiwan. The 13-item M.D. Anderson symptom inventory was used to assess patients' symptom severity. Selected symptoms were factored using principal-axis factoring with oblique rotation. The known-group technique was used to validate the conceptual meanings of revealed factors. **MAIN RESULTS:** Patients' symptom severity ratings fit a three-factor solution that explained 55% of the variance. These three factors (symptom clusters) were named sickness symptom cluster, gastrointestinal symptom cluster, and emotional symptom cluster. Patients with pain and with advanced diseases had significantly higher mean scores in the sickness symptom cluster than patients without pain and with earlier-stage diseases. The patients' functional status was negatively correlated with mean scores in the sickness symptom cluster. Patients under chemotherapy demonstrated significantly higher mean scores in the gastrointestinal symptom cluster than patients under other treatments. Patients with anxiety or depression also had significantly higher mean scores in the emotional symptom cluster than patients without anxiety or depression. **CONCLUSIONS:** This study identified three underlying symptom clusters and verified their conceptual meaning in cancer

patients. Knowing these symptom clusters may help healthcare professionals understand plausible mechanisms for the aggregation of symptoms.

Cheng, K. K., E. M. Wong, et al. (2009). "Measuring the symptom experience of Chinese cancer patients: a validation of the Chinese version of the memorial symptom assessment scale." *J Pain Symptom Manage* **37**(1): 44-57.

The purpose of this study was to translate the Memorial Symptom Assessment Scale (MSAS) into Chinese and evaluate the psychometric properties of this version. The original MSAS is a 32-item, patient-rated measure that was developed to assess common cancer-related physical and psychological symptoms with respect to frequency, intensity, and distress. In this study, a two-phase design was used. Phase I involved iterative forward-backward translation, testing of content validity (CVI) and a pretest. Phase II established the psychometric properties of the Chinese version MSAS (MSAS-Ch). Results showed that the MSAS-Ch achieved content relevancy CVI of 0.94 and semantic equivalence CVI of 0.94. Pretesting was performed in 10 cancer patients, and the results revealed adequate content coverage and comprehensibility of the MSAS-Ch. A convenience sample of 370 patients undergoing cancer therapy or at the early post-treatment stage was recruited for psychometric evaluation. Confirmatory factor analysis confirmed the construct validity of the MSAS-Ch, with a good fit between the factor structure of the original version and our present sample data (goodness-of-fit indices all above 0.95). The internal consistency reliability of subscales and total MSAS-Ch was moderately high, with Cronbach alpha coefficients ranging from 0.79 to 0.87. The test-retest intraclass correlation results for the subscale and total MSAS-Ch ranged from 0.68 to 0.79. The subscale scores of MSAS-Ch were moderately correlated with the scores on various validation measurements that assessed psychological distress, pain, and health-related quality of life ($r = 0.46-0.65$, $P < 0.01$), confirming that they were measurements of similar constructs. The validity of the construct validity was also supported by comparing the MSAS-Ch scores for subpopulations that varied clinically. Inpatients and patients with poorer performance status scored higher on the MSAS-Ch subscale and total scores than outpatients and patients with higher performance status ($P < 0.05$). Our study shows that the MSAS-Ch has adequate psychometric properties of validity and reliability, and can be used to assess symptoms during cancer therapy and at the early post-treatment stage in Chinese-speaking patients.

Cheung, W. Y., N. Barmala, et al. (2009). "The association of physical and psychological symptom burden with time to death among palliative cancer outpatients." *J Pain Symptom Manage* **37**(3): 297-304.

Previous studies have reported on the symptom burden of cancer inpatients, but outpatient studies have been few and have not examined the association of symptoms with time to death (TTD). Cancer patients seen in an oncology palliative care clinic from January 2005 to June 2006 and who subsequently died were identified from a palliative care database. Data from the last outpatient Edmonton Symptom Assessment Scale (ESAS) score completed in clinic were analyzed among patients who were followed during the last four months of life. Multiple linear regression analyses with Bonferroni adjustment were used to determine the association of ESAS total symptom distress score (TSDS), physical subscore (PHS), psychological subscore (PSS), and individual symptom scores with demographic parameters, disease characteristics, and TTD. Data from 198 patients were analyzed. All had stage IV cancer, the median age was 65, and 55% were men. There was no significant association between symptom burden and age, gender, or cancer site. TTD was significantly associated with TSDS ($P=0.001$) and PHS ($P=0.001$) but not with PSS ($P=1.0$). Individual symptoms most strongly associated with TTD were lack of appetite ($P=0.001$), drowsiness ($P=0.006$), dyspnea ($P=0.009$), and fatigue ($P=0.01$). There was no significant association between TTD and anxiety ($P=1.0$) or depression ($P=1.0$). Lack of appetite, drowsiness, dyspnea and fatigue represent a cluster of symptoms that tend to intensify at the end of life. The lack of intensification of psychological symptoms in relation to time to death is striking and needs to be further investigated using specific validated measures for depression and anxiety.

Chow, E., G. Fan, et al. (2007). "Symptom clusters in cancer patients with bone metastases." *Support Care Cancer* **15**(9): 1035-43.

PURPOSE: The purpose of this study is to explore whether bone pain "clusters" with other symptoms in patients with bone metastases. **MATERIALS AND METHODS:** Patients with bone metastases referred to a palliative radiotherapy clinic were asked to rate their symptom distress using the Edmonton Symptom Assessment Scale (ESAS). Analgesic consumption during the previous 24 h was captured at initial consultation. To determine interrelationships between symptoms, a principal component analysis (PCA) with "varimax rotation" was performed on the nine ESAS symptoms. This study defined a "symptom cluster" as two or more symptoms that occur together, are stable, and are

relatively independent of other clusters. Patients were followed 1, 2, 4, 8, and 12 weeks post-radiation treatment by telephone. Statistical analysis was performed at each time point for both responders and nonresponders to radiation (response was defined in accordance to the International Bone Metastases Consensus Working Party). **RESULTS:** Five hundred eighteen patients with bone metastases provided complete baseline data using the ESAS. The four most prevalent symptoms were poor sense of well-being (93.5%), fatigue (92.3%), pain (84.1%), and drowsiness (81.8%). Three clusters were identified and accounted for 66% of the total variance at baseline. Cronbach's alpha coefficient demonstrated high internal reliability in the clusters, with a coefficient ranging from 0.61 to 0.81. It was observed that the clusters changed post-radiation in both responders and nonresponders and that pain clustered with different symptoms (or remained a separate symptom in responders). In nonresponders, three symptom clusters were consistently present, except in week 8. **CONCLUSION:** Radiotherapy influenced the structure of symptom clusters in both responders and nonresponders. There was evidence that pain clustered out in responders of radiation to pain. It was found that pain clustered with fatigue, drowsiness, and poor sense of well-being at baseline. However, these findings must be heeded with caution, as more work is needed to clearly define symptom clusters and to understand the effects of radiation in the symptom experience of patients with bone metastases.

Chow, E., G. Fan, et al. (2008). "Symptom clusters in cancer patients with brain metastases." *Clin Oncol (R Coll Radiol)* **20**(1): 76-82.

AIM: To explore the presence of symptom clusters in patients with brain metastases. **MATERIALS AND METHODS:** Patients with brain metastases referred to an outpatient palliative radiotherapy clinic were asked to rate their symptom distress using the Edmonton Symptom Assessment Scale (ESAS). Baseline demographic data were obtained. To determine interrelationships between symptoms, a principal component analysis with 'varimax rotation' was carried out on the nine ESAS items. Follow-up was carried out by telephone 1, 2, 4, 8 and 12 weeks after radiation. **RESULTS:** Between January 1999 and January 2002, 170 patients with brain metastases provided complete baseline data on the ESAS. The most common primary cancer sites were lung, breast and gastrointestinal. Fatigue was the highest scored symptom, followed by a poor sense of well-being, anxiety, drowsiness and poor appetite. The four most prevalent symptoms were fatigue (91.7%), a poor sense of well-being (88.1%), drowsiness (82.2%) and anxiety (82.1%). Three

symptom clusters were found at baseline. Cluster 1 included fatigue, drowsiness, shortness of breath and pain. Cluster 2 included anxiety and depression. Cluster 3 included poor appetite, nausea and a poor sense of well-being. Fatigue, nausea, drowsiness and poor appetite showed an overall increase in symptom severity over time; whereas fatigue, drowsiness and poor appetite were experienced to some extent by a greater proportion of patients at week 12 compared with baseline. Symptom clusters emerged in all weeks of follow-up, but consisted of different symptoms in each week. **CONCLUSION:** Symptom clusters seemed to exist in patients with brain metastases before and after whole brain radiotherapy. However, different symptoms clustered at various time points. The effectiveness of whole brain radiotherapy in providing palliative relief to patients with brain metastases needs to be explored with regards to symptom clusters.

Cirillo, M., M. Venturini, et al. (2009). "Clinician versus nurse symptom reporting using the National Cancer Institute-Common Terminology Criteria for Adverse Events during chemotherapy: results of a comparison based on patient's self-reported questionnaire." *Ann Oncol* **20**(12): 1929-35.

BACKGROUND: Monitoring adverse events during chemotherapy by clinicians is a standard practice but clinicians may report fewer side-effects or lower symptom severity than patients. Our aim was to compare symptoms self-reported by patients with symptoms registered by clinicians and nurses, to assess validity of a nurse reporting. **METHODS:** From April to August 2007, a double-blind questionnaire with 13 common items graduated according to the National Cancer Institute's Common Terminology Criteria for Adverse Events was completed by clinicians and nurses for outpatients undergoing chemotherapy at our Medical Oncology Day Hospital Unit. Patients completed a modified questionnaire with simplified terms. They were requested to specify seriousness of symptoms with a subjective scale varying from 1 to 4. Every patient-nurse-clinician questionnaire was registered for the statistical analysis. Agreement was evaluated by Cohen's kappa coefficient. **RESULTS:** Eighty-five paired questionnaires were completed. Patients, nurses and clinicians agreed on most symptoms and toxicity grade. Agreements between patients and nurses were stronger than those between patients and physicians for the six most common symptoms: asthenia (kappa 75% versus 37%), constipation (83% versus 45%), neuropathy (82% versus 55%), mucositis (78% versus 46%) and diarrhoea (90% versus 77%). These differences mainly reflected differences in the proportion of positive agreement: nurses were more

able to detect symptoms self-reported by patients than physicians. The only exception was nausea, as kappa coefficient was very good for both health professionals (91% versus 89%). When considering the different grade of toxicity by the weighted kappa coefficient, we scored again the highest agreement between patient and nurse, with weighted kappa ranging from 55% (asthenia) to 86% (diarrhoea), and the lowest agreement between patient and physician, with weighted kappa ranging from 32% (asthenia) to 74% (nausea). The agreement between physician and nurse slightly improved, with weighted kappa ranging from 41% (constipation) to 77% (nausea). **CONCLUSION:** Our results support the validity of nurse toxicity reporting and that the nurse staff could be successfully employed in collecting toxicity data because of a greater ability to elicit information from patients than the medical staff.

Cohen, M. Z., C. F. Musgrave, et al. (2005). "The cancer pain experience of Israeli adults 65 years and older: the influence of pain interference, symptom severity, and knowledge and attitudes on pain and pain control." *Support Care Cancer* **13**(9): 708-14.

GOALS: Little is known about Israeli elders' cancer pain experience. The purpose of this study was to explore the cancer pain experience, including pain intensity, pain management index, pain interference, symptom severity, and knowledge and attitudes toward pain and pain control. **PATIENTS AND METHODS:** Descriptive cross-sectional methods were used to obtain data with four instruments. The patients were 39 Israelis 65 years and older who were receiving outpatient treatment for cancer in a major hospital center in Israel. **RESULTS:** Results showed that over half (56.7%) reported severe worst pain and had negative pain management indexes (56.4%). In addition, knowledge and attitudes toward pain and pain control were poor (54.55%). There were no significant relationships between pain intensity and other variables. However, pain interference demonstrated a significant positive relationship with symptom severity. Post hoc analysis revealed that Ashkenazi Jewish and more educated patients reported significantly less pain interference than Sephardic Jewish patients. **CONCLUSION:** Larger samples representative of the cultural differences in Israel are needed to more definitively identify elements of the cancer pain experience in Israeli elders that can be addressed to improve pain management.

Cruciani, R. A., E. Dvorkin, et al. (2006). "Safety, tolerability and symptom outcomes associated with L-carnitine supplementation in patients with cancer,

fatigue, and carnitine deficiency: a phase I/II study." *J Pain Symptom Manage* **32**(6): 551-9.

Carnitine deficiency is among the many metabolic disturbances that may contribute to fatigue in patients with cancer. Administration of exogenous L-carnitine may hold promise as a treatment for this common symptom. Little is known about L-carnitine safety, tolerability, and dose-response in patients with cancer. We conducted a Phase I/II open-label trial to assess the safety and tolerability of exogenous L-carnitine and clarify the safe dose range associated with symptom effects for future controlled trials. Adult patients with advanced cancer, carnitine deficiency (free carnitine <35 for males or <25 microM/L for females, or acyl/free carnitine ratio >0.4), moderate to severe fatigue, and a Karnofsky Performance Status (KPS) score > or =50 were entered by groups of at least three into a standard maximum tolerated dose design. Each successive group received a higher dose of L-carnitine (250, 750, 1250, 1750, 2250, 2750, 3000 mg/day, respectively), administered in two daily doses for 7 days. To compare symptom outcomes before and after supplementation, patients completed validated measures of fatigue (Brief Fatigue Inventory [BFI]), depressed mood (Center for Epidemiologic Studies Depression Scale [CES-D]), quality of sleep (Epworth Sleeplessness Scale [ESS]), and KPS at baseline and 1 week later. Of the 38 patients screened for carnitine levels, 29 were deficient (76%). Twenty-seven patients participated ("intention to treat, ITT") (17 males, 10 females), and 21 completed the study ("completers"); 17 of these patients ("responders," mean±[SD] age=57.9±15) had increased carnitine levels at the end of the supplementation period. The highest dose achieved was 3000 mg/day. No patient experienced significant side effects and no toxicities were noted. Analysis of all the patients accrued (ITT, n=27) showed a total carnitine increase from 32.8±10 to 54.3±23 microM/L (P<0.001) and free carnitine increase from 26.8±8 to 44.1±17 microM/L (P<0.001). BFI decreased significantly, from 66±12 to 39.7±26 (P<0.001); ESS decreased from 12.9±12 to 9±6 (P=0.001); and CES-D decreased from 29.2±12 to 19±12 (P<0.001). A separate analysis of the 17 "responders" showed a dose-response relationship for total- (r=0.54, P=0.03), free-carnitine (r=0.56, P=0.02) levels, and fatigue (BFI) scores (r=-0.61, P=0.01). These findings suggest that l-carnitine may be safely administered at doses up to 3000 mg/day and that positive effects may be more likely at relatively higher doses in this range. This study provides the basis for the design of future placebo-controlled studies of l-carnitine supplementation for cancer-related fatigue.

Daly, B. J., S. L. Douglas, et al. (2007). "Psychosocial registry for persons with cancer: a method of facilitating quality of life and symptom research." *Psychooncology* **16**(4): 358-64.

Research focused on the psychosocial aspects of the experience of persons with cancer and their family caregivers is hampered by the methodological challenges inherent in quality of life research. A data registry offers a potential solution to many of these problems in providing a large, comprehensive database, using standardized instruments. We report here our preliminary experience with establishing a Psychosocial Registry designed to advance research in the psychological, social, and spiritual aspects of quality of life of newly diagnosed cancer patients and their family caregivers. The first six months of enrollment demonstrated that the majority of newly diagnosed patients approached for consent (68%) and their primary family caregiver (92%) were willing to participate in the registry; of these, 80% also agreed to be contacted in the future for additional studies. Face-to-face interview was the preferred method of data collection. Our preliminary experience suggests that continuation of the registry with the current modest level of resources would generate a sample of approximately 1000 patients in three years. The long-range goal is to establish a national psychosocial data registry that will enroll patients at diagnosis and follow them through the entire cancer experience, including end of life or survivorship.

Davis, K., S. Yount, et al. (2007). "An innovative symptom monitoring tool for people with advanced lung cancer: a pilot demonstration." *J Support Oncol* **5**(8): 381-7.

Treatment for advanced lung cancer is not curative; therefore, the primary goals of its care are to maximize symptom management and minimize treatment toxicity. Increasingly, patient-reported symptoms and health-related quality of life (HRQL) outcomes have been accepted as important endpoints; several validated measures have gained wide acceptance in research, but their use in practice has been limited. Computer technology increasingly is used to reduce patient and administrative burden in conducting assessments to produce a real-time presentation of symptom and HRQL data. This paper describes a technology-based monitoring system developed for patients with advanced lung cancer who were starting chemotherapy. Among the 90 participants, compliance with the weekly symptom survey was 92%. Patient acceptability of the system was high, as evidenced by 30 patients who elected to complete an additional monitoring interval beyond the 12-week study period. Of patients who reported discussing their responses with a provider (95%), a

majority (69%) stated that the questionnaire helped them to focus on issues to be discussed with their physicians. The system also was favorably reviewed by physicians, who indicated that the report helped them to compare patients' responses over time. Next steps will include a randomized trial to test the system's efficacy in improving symptom management.

Davis, M. P., D. Walsh, et al. (2006). "Early satiety in cancer patients: a common and important but underrecognized symptom." Support Care Cancer **14**(7): 693-8.

INTRODUCTION: The severity of anorexia correlates with the presence of early satiety. The sense of fullness limits nutritional intake. The symptom is poorly understood because most assessment questionnaires do not include early satiety. **METHODS:** Patients rarely volunteer early satiety. Central and peripheral mechanisms may be involved in the genesis of early satiety. These would include central sensory specific satiety, food aversions, diurnal changes in intake, gastric motility and accommodation and as gastrointestinal hormones. **CONCLUSIONS:** Prokinetic medications, such as metoclopramide are used to treat early satiety. However, other medications which influence gastric accommodation such as clonidine, sumatriptan, or sildenafil, or diminish enteric afferent output such as kappa opioid receptor agonists, may favorably influence early satiety and should be subject to future research. Translational research is needed to understand the relationship of early satiety to gastric motility and accommodation.

de Marinis, F., J. R. Pereira, et al. (2008). "Lung Cancer Symptom Scale outcomes in relation to standard efficacy measures: an analysis of the phase III study of pemetrexed versus docetaxel in advanced non-small cell lung cancer." J Thorac Oncol **3**(1): 30-6.

BACKGROUND: Patients with advanced non-small cell lung cancer (NSCLC) require care that emphasizes symptom palliation in addition to extending survival. The low response rates and minimal survival gains observed in second-line studies underscore the need to assess treatment efficacy with symptomatic end points. **METHODS:** To characterize the relationship between patient-reported health-related quality of life outcomes and efficacy end points (tumor response, overall survival [OS], progression-free survival [PFS]), retrospective analyses were performed on Lung Cancer Symptom Scale (LCSS) data (n = 488) from the phase III study of pemetrexed (500 mg/m² once every 3 weeks) versus docetaxel (75 mg/m² once every 3 weeks) in advanced NSCLC. The LCSS data consisted of patient

ratings of six symptoms and three summary items using 100-mm visual analogue scales. The mean maximum improvement for each item was categorized according to best tumor response, with statistical analyses based on a two-factor interaction model (with treatment arm and response group as fixed factors). Additional analyses pooled data between treatment arms and examined correlation (nonparametric and Pearson's) of time to first worsening of symptoms (TWS) with PFS and OS. **RESULTS:** All LCSS items, except hemoptysis, showed mean maximum improvement over baseline for responders and patients with stable disease (p < 0.01), with greater improvement associated with response. Median TWS for each LCSS item ranged between 2.3 months (fatigue) and 7.0 months (cough), with correlation between TWS and PFS and OS (all p values <=0.017). **CONCLUSIONS:** For most NSCLC patients, second-line chemotherapy provides symptomatic improvement that is linked to standard efficacy outcomes. Health-related quality of life data provides complementary efficacy information that can guide routine clinical practice.

Delgado-Guay, M., H. A. Parsons, et al. (2009). "Symptom distress in advanced cancer patients with anxiety and depression in the palliative care setting." Support Care Cancer **17**(5): 573-9.

BACKGROUND: Mood disorders are among the most distressing psychiatric conditions experienced by patients with advanced cancer; however, studies have not shown a direct association of physical symptoms with depression and anxiety. **PURPOSE:** The purpose of this study is to determine the relationship between the frequency and intensity of patients' physical symptoms and their expressions of depression and anxiety. **PATIENTS AND METHODS:** We retrospectively reviewed the records of 216 patients who had participated in three previous clinical trials conducted by our group. We assessed patients' demographic data using descriptive statistics. We analyzed physical symptom frequency and intensity using the Edmonton Symptom Assessment System (ESAS) and anxiety and depression using the respective subscales of the Hospital Anxiety and Depression Scale (HADS-A and HADS-D). **RESULTS:** Sixty-two percent were male; the median age was 59 years (range 20-91 years). Seventy nine (37%) of the patients had depressive mood (HADS-D > or = 8), and 94 (44%) had anxiety (HADS-A > or = 8). Patients with depressive mood expressed higher frequency of drowsiness (68/78, 64%; p = 0.0002), nausea (52/79, 66%; p = 0.0003), pain (74/79, 94%; p = 0.0101), dyspnea (68/79, 86%; p = 0.0196), worse appetite (72/79, 91%; p = 0.0051), and worse well-being (78/79, 99%; p = 0.0014) and expressed higher

intensity of symptoms (ESAS \geq 1) [median (Q1-Q3)] including drowsiness [4 (3-7), $p = 0.0174$], fatigue [7 (5-8), $p < 0.0001$], and worse well-being [6 (5-7), $p < 0.0001$]. Patients with anxiety expressed higher frequency of nausea (59/94, 57%; $p = 0.0006$), pain (88/94, 89%; $p = 0.0031$), and dyspnea (84/94, 96%, $p = 0.0002$) and expressed a higher intensity of pain [6 (3-8), $p = 0.0082$], fatigue [6 (5-8), $p = 0.0011$], worse appetite [6 (4-8), $p = 0.005$], and worse well-being [5 (3-7), $p = 0.0007$]. Spearman's correlation showed a significant association between HADS-A and HADS-D and other symptoms in the ESAS. Spearman's correlations of HADS with ESAS-Anxiety and ESAS-Depression were 0.56 and 0.39, respectively ($p < 0.001$). CONCLUSION: Expression of physical symptoms may vary in frequency and intensity among advanced cancer patients with anxiety and depression. Patients expressing high frequency and intensity of physical symptoms should be screened for mood disorders in order to provide treatment for these conditions. More research is needed.

Delgado-Guay, M. O., H. A. Parsons, et al. (2009). "Symptom distress, interventions, and outcomes of intensive care unit cancer patients referred to a palliative care consult team." *Cancer* **115**(2): 437-45.

BACKGROUND: The symptom burden of intensive care unit (ICU) patients who are referred to a palliative care team (PCT) has not been characterized to the authors' knowledge, and the response of these symptoms to the palliative care intervention has not been reported. METHODS: The authors retrospectively reviewed PCT consults for ICU patients who were seen between July 2006 and October 2007. To characterize symptom distress and outcomes in ICU patients who were referred to PCT in a cancer center, information and descriptive statistics about patients' demographics, comorbidities, PCT findings, interventions, and outcomes were obtained. The chi-square test was used to analyze ICU and PCT mortality, and the signed-rank test was used to analyze PCT interventions. RESULTS: Of 1637 PCT consults, 88 consults (5%) were from the ICU. The median patient age was 60 years (range, 22-87 years), and 41 patients (46%) were women. The types of cancers were hematologic (19 patients; 22%), gastrointestinal (19 patients; 22%), lung (18 patients; 20%), and others (24 patients; 26%). Nineteen patients were on mechanical ventilation (MV), and 24 patients were on bilevel positive airway pressure (BIPAP). The findings were delirium (71 patients; 81%), dyspnea (67 patients; 76%), pain (74 patients; 84%), fatigue (84 patients; 95%), and anxiety (57 patients; 65%). The interventions used were opioid management (99%), steroids (70%), antipsychotics

(76%), and counseling (100%), do not resuscitate conversion (62 of 88 patients; 70%), withdrawal of MV (15 of 19 patients; 79%), and withdrawal of BIPAP (26 of 26 patients; 100%). Improvement was reported in pain (67 patients; 90%), dyspnea (60 patients; 90%), anxiety (51 patients; 80%), and delirium (31 patients; 44%). Thirty-five patients (40%) were transferred to the palliative care unit (PCU). Fifty-one ICU/PCT patients (58%) died during admission versus 130 of 1549 (8%) non-ICU PCT patients ($P < 0.0001$). Twenty-three of 35 patients who were transferred to the PCU (66%) died there versus 212 of 629 patients (34%) who were admitted to the PCU from another service ($P < 0.0001$). Thirty-seven of 88 ICU/PCT patients (42%) were discharged alive. CONCLUSIONS: ICU patients who are referred to the PCT have severe symptom distress. The PCT was able to identify multiple problems and make numerous pharmacologic and nonpharmacologic recommendations that improved these symptoms, including the participation in do not resuscitate conversion and withdrawal of MV and BIPAP. Although many patients in this population died, a significant subset, including those who were transferred to the PCU, survived to discharge.

Donovan, H. S., S. Ward, et al. (2008). "Evaluation of the Symptom Representation Questionnaire (SRQ) for assessing cancer-related symptoms." *J Pain Symptom Manage* **35**(3): 242-57.

Multidimensional, multisymptom approaches to cancer symptom assessment and management have been emphasized across health disciplines. However, each dimension that is assessed significantly increases patient/subject burden. Efficient, reliable, and valid assessment of the critical dimensions of patients' most salient symptoms is important in clinical and research settings. The Symptom Representation Questionnaire (SRQ), derived from information processing theory, assesses critical cognitive and emotional factors that are known to influence coping and outcomes. The SRQ was developed and evaluated in a three-phase process: (1) item selection, modification, and review by theoretical and clinical experts; (2) pilot evaluation of feasibility and psychometric properties; and (3) large sample psychometric evaluation. In Phase 3, members ($n=713$) of the National Ovarian Cancer Coalition participated via mailed surveys. Internal consistency was good for all subscales ($\alpha=0.63-0.88$). The internal structure of the SRQ was theoretically consistent except that emotional representation, identity, and consequence items all loaded onto a single factor. Between-group comparisons supported construct validity: Representations differed between long-term survivors and women with active disease. Finally, there were

significant correlations between SRQ subscales and Symptom Interference and Life Satisfaction. The SRQ appears to be a psychometrically sound instrument for assessing representations of cancer-related symptoms. This instrument could play an essential role in advancing knowledge of the relationships among representations of symptoms, symptom management processes, and symptom-related outcomes. It could also be used in intervention research when changes in symptom representations are hypothesized to mediate changes in outcomes as a result of psychoeducational interventions.

Donovan, K. A. and P. B. Jacobsen (2007). "Fatigue, depression, and insomnia: evidence for a symptom cluster in cancer." *Semin Oncol Nurs* **23**(2): 127-35.

OBJECTIVES: To review the evidence for considering fatigue, depression, and insomnia as a symptom cluster in cancer. **DATA SOURCES:** Empirical studies, clinical articles, and review articles. **CONCLUSION:** The single- and multi-symptom measurement approaches are of limited usefulness in distinguishing fatigue, depression, and insomnia. Studies in which these symptoms have been measured concurrently in patients with cancer yield consistent evidence of high positive correlations. Results do not appear to be solely a function of overlap in measurement approaches. **IMPLICATIONS FOR NURSING PRACTICE:** Successful management of fatigue, depression, and insomnia in cancer patients are likely to combine pharmacologic and nonpharmacologic therapies.

Dooms, C. A., K. E. Pat, et al. (2006). "The effect of chemotherapy on symptom control and quality of life in patients with advanced non-small cell lung cancer." *Expert Rev Anticancer Ther* **6**(4): 531-44.

Differences in survival outcomes with various treatments for advanced non-small cell lung cancer are very modest. Despite this, end points looking at the patients' subjective benefit, such as symptom control, quality of life or clinical benefit, have only been sparsely implemented into clinical trials as primary points of interest. This review focuses on available evidence regarding these patients' subjective end points in recent clinical trials. Compared with best supportive care, chemotherapy offers symptom control, not only in patients with objective response to chemotherapy, but also in a proportion of patients with disease stabilization. However, interpretation of quality-of-life objectives is more difficult, owing to several methodological problems, but improvement in various domains of quality of life is also reported. Different treatment options, such as older platinum-based schedules, modern platinum-based doublets, single-agent

treatment with a new drug or nonplatinum-based doublets, are comprehensively reviewed. Future randomized studies should take up the challenge of looking at the patients' benefit as a primary end point.

Doorenbos, A. Z., C. W. Given, et al. (2006). "Symptom experience in the last year of life among individuals with cancer." *J Pain Symptom Manage* **32**(5): 403-12.

Individuals with cancer often experience many symptoms that impair their quality of life at the end of life. This study examines symptom experience at end of life among individuals with cancer, and determines if symptom experience changes with proximity to death, or differs by depressive symptomatology, sex, site of cancer, or age. A secondary analysis of data from three prospective, descriptive, longitudinal studies (n=174) was performed, using a three-level hierarchical linear model. Fatigue, weakness, pain, shortness of breath, and cough were the five most prevalent symptoms in the last year of life. The symptom experience in the last year of life was significantly associated with site of cancer, depressive symptomatology, dependencies in activities of daily living, and independent activities of daily living at the start of the study. These findings shed light on the symptom experience in the last year of life for individuals with cancer. With greater understanding of the symptom experience, intervention strategies can be targeted to achieve the desired outcome of increased quality of life at the end of life.

Doorenbos, A. Z., N. Verbitsky, et al. (2005). "An analytic strategy for modeling multiple-item responses: a breast cancer symptom example." *Nurs Res* **54**(4): 229-34.

BACKGROUND: Item Response Theory (IRT) is increasingly applied in health research to combine information from multiple-item responses. IRT posits that a person's susceptibility to a symptom is driven by the interaction of the characteristics of the symptom and person. This article describes the statistical background of incorporating IRT into a multilevel framework and extends this approach to longitudinal health outcomes, where the self-report method is used to construct a multi-item scale. **METHODS:** A secondary analysis of data from 2 descriptive longitudinal studies is performed. The data include 21 symptoms reported across time by 350 women with breast cancer. A 3-level hierarchical linear model (HLM) was used for the analysis. Level 1 models the item responses, consisting of symptom presence or absence. Level 2 models the trajectory of each individual, representing change over time of the IRT-created latent variable symptom experience.

Level 3 explains that trajectory using person-specific characteristics such as age and location of care. The purpose of the analysis is to examine if older and younger women with breast cancer differ in their symptom experience trajectory after controlling for location of care. RESULTS: Fatigue and pain were the most prevalent symptoms. The symptom experience of women with breast cancer was found to improve over time. Neither age nor location of care was significantly associated with the symptom experience trajectory. DISCUSSION: Embedding IRT into an HLM framework produces several benefits. The example provided demonstrates benefits through the creation of a latent symptom experience variable that can be used either as an outcome or as a covariate in another model, examining the latent symptom experience trajectory and its relationship with covariates at the individual level, and managing symptom nonresponse.

Duncan, J. G., M. J. Bott, et al. (2009). "Symptom occurrence and associated clinical factors in nursing home residents with cancer." *Res Nurs Health* 32(4): 453-64.

Little is known about the factors that contribute to symptoms in nursing home residents with cancer. We compared rates of symptoms in residents with (n = 1,022) and without cancer (n = 9,910) and examined physiologic, psychologic and situational factors potentially related to symptoms in residents with cancer. Pain, shortness of breath, vomiting, weight loss, and diarrhea were significantly (p < .05) more prevalent in residents with cancer. Cancer treatments, comorbid illnesses, and situational factors were not consistently correlated with symptoms. Improved symptom control was especially needed for the 30% of residents with cancer who clinically deteriorated within 3 months of admission; physical dependence and deteriorating clinical status were associated with pain, shortness of breath, and weight loss.

Duncan, J. G., S. Forbes-Thompson, et al. (2008). "Unmet symptom management needs of nursing home residents with cancer." *Cancer Nurs* 31(4): 265-73.

Nursing home residents living with cancer have unacceptably high percentages of unrelieved pain and other symptoms. However, residents with cancer have received relatively little attention in the literature to date. This article provides an overview of previous symptom research for residents with cancer, explores clinical and organizational factors that impede effective symptom management, and proposes an agenda for future research and clinical practice. Residents with cancer have numerous symptoms that tend to be different from the symptoms of other

nursing home residents. Symptom management for residents with cancer is often complicated by cognitive impairment, declining physical functioning, and comorbid illnesses. Barriers to symptom management include underuse of analgesics and hospice, nursing home staffing patterns, and lack of resources. Additional research is necessary to provide a more comprehensive understanding of residents with cancer, explore how organizational factors affect the care of residents with cancer, and evaluate interventions for effective symptom assessment and management. Collaboration of oncology nurses with clinicians and researchers in nursing home settings is needed to improve care for residents with cancer.

Erridge, S. C., M. N. Gaze, et al. (2005). "Symptom control and quality of life in people with lung cancer: a randomised trial of two palliative radiotherapy fractionation schedules." *Clin Oncol (R Coll Radiol)* 17(1): 61-7.

AIMS: To determine whether palliation of chest symptoms from a 10 Gy single fraction (regimen 1) was equivalent to that from 30 Gy in 10 fractions (regimen 2). MATERIALS AND METHODS: Patients with cytologically proven, symptomatic lung cancer not amenable to curative therapy, with performance status 0-3, were randomised to receive either 30 Gy in 10 fractions or a 10 Gy single fraction. Local symptoms were scored on a physician-assessed, five-point categorical scale and summed to produce a total symptom score (TSS). This, performance status, Hospital Anxiety and Depression (HAD) score and Spitzer's quality-of-life index were noted before treatment, at 1 month after treatment and every 2 months thereafter. Palliation was defined as an improvement of one point or more in the categorical scale. Equivalence was defined as less than 20% difference in the number achieving an improvement in the TSS. RESULTS: We randomised 149 patients and analysed 74 in each arm. According to the design criteria, palliation was equivalent between the two arms. TSS improved in 49 patients (77%) on regimen 1, and in 57 (92%) patients on regimen 2, a difference of 15% (95% confidence interval [CI] 3-28) in the proportion improving between the two regimens. A complete resolution of all symptoms was achieved in three (5%) on regimen 1, and in 14 (23%) patients on regimen 2 (P < 0.001), a difference in the proportion between the two regimens of 21% (95% CI 10-33). A significantly higher proportion of patients experienced palliation and complete resolution of chest pain and dyspnoea with regimen 2. No differences were observed in toxicity. The median survival was 22.7 weeks for regimen 1 and 28.3 weeks for regimen 2 (P = 0.197). CONCLUSIONS: Although this trial met the pre-determined criteria for equivalence between

the two palliative regimens, significantly more patients achieved complete resolution of symptoms and palliation of chest pain and dyspnoea with the fractionated regimen.

Eton, D. T., D. Cella, et al. (2007). "Validation of the functional assessment of cancer therapy--lung symptom index-12 (FLSI-12)." *Lung Cancer* **57**(3): 339-47.

We tested the reliability and validity of a brief symptom index for use with patients in the advanced stages of lung cancer. The Functional Assessment of Cancer Therapy--Lung Symptom Index-12 (FLSI-12) is a brief self-report measure that combines seven items addressing symptoms common in advanced-stage lung cancer with five symptoms or concerns that are relevant to most people with advanced-stage cancer. The index was administered prospectively to 92 advanced-stage lung cancer patients beginning at the initiation of chemotherapy and for 12 consecutive weeks. Reliability, convergent and concurrent validities, and responsiveness to change were determined and a minimally important difference (MID) was estimated. The index had good internal consistency (all Cronbach's alpha's > 0.70), moderate to high item-to-total correlations (93% rho's > or = 0.30), and correlated highly with a measure of overall quality of life (rho's > or = 0.50). Baseline scores differentiated patients with better versus worse clinical features (p's < .05). Prospective changes in index scores were sensitive to changes in performance status ratings (p's < .05). An MID of 3-4 points was estimated by combining guideline-, distribution-, and anchor-based methods. The results show that the FLSI-12 is a psychometrically sound measure and support its use as an endpoint in clinical trials of advanced-stage lung cancer.

Fadol, A., T. Mendoza, et al. (2008). "Psychometric testing of the MDASI-HF: a symptom assessment instrument for patients with cancer and concurrent heart failure." *J Card Fail* **14**(6): 497-507.

BACKGROUND: The debilitating symptoms of cancer and heart failure (HF) can adversely affect the patient's quality of life. This study evaluated the psychometric properties of the MD Anderson Symptom Inventory--Heart Failure (MDASI-HF), a 27-item self-report assessment instrument for patients with cancer and concurrent HF. **METHODS AND RESULTS:** Psychometric testing used data from 156 patients (age 63.3 +/- 13.2 years, 56% male) with a diagnosis of cancer and HF receiving care in a major cancer center. Reliability of the MDASI-HF for the 13 symptoms (alpha = 0.89), 8 HF-specific items (alpha = 0.83), and interference items (alpha = 0.92) was high. Criterion-related

validity with the Eastern Cooperative Oncology Group performance scale (r = 0.63) and the New York Heart Association classification (r = 0.65) were statistically significant, P = .01. Construct validity supported two constructs for the additional HF specific items: covert HF factor and overt HF factor. **CONCLUSION:** The MDASI-HF is a valid and reliable instrument for symptom assessment in patients with cancer and HF. This instrument can be used to identify symptom occurrence and enhance the provider's understanding of the prevalence and severity of symptoms from the patient's perspective.

Fan, G., L. Filipczak, et al. (2007). "Symptom clusters in cancer patients: a review of the literature." *Curr Oncol* **14**(5): 173-9.

Cancer patients often experience multiple symptoms, and those symptoms can independently predict changes in patient function, treatment failures, and post-therapeutic outcomes. Symptom clusters are defined as two or more concurrent symptoms that are related and may or may not have a common cause. The purpose of the present study was to review, in cancer patients, common symptom clusters and their predictors. Using MEDLINE, EMBASE, Cochrane Central, and CINAHL, we conducted a literature search on symptom clusters in cancer patients. Studies that investigated predetermined clusters were not included. We identified seven individual studies and one group of five studies validating the M.D. Anderson Symptom Inventory. These studies had been published between 1997 and 2006. Two of the seven individual studies and the group of five studies that had validated the M.D. Anderson Symptom Inventory included patients with any cancer type; three studies included breast cancer patients only; and two studies included lung cancer patients only. A gastrointestinal cluster consisting of nausea and vomiting was the single cluster common to two of the studies. The severity of this cluster increased when patients were treated with chemotherapy. No common clusters were found in the lung and breast cancer patient populations. However, breast cancer patients experienced more symptom cluster involvement while undergoing chemotherapy. We noted methodology disparities among the papers with regard to assessment tools used, statistical analyses, and populations. Research on symptom clusters is still in an early stage. Multiple symptoms clearly affect prognosis, quality of life, and functional status. The study of symptom clusters is important for its implications regarding patient management, and a consensus on appropriate research methodology is vital.

Fan, G., S. Hadi, et al. (2007). "Symptom clusters in patients with advanced-stage cancer referred for palliative radiation therapy in an outpatient setting." Support Cancer Ther 4(3): 157-62.

Purpose: The aim of this study was to explore the presence of symptom clusters in patients with advanced cancer. **Patients and Methods:** Patients with metastatic cancer referred to an outpatient palliative radiation therapy clinic were asked to rate their symptom distress using the Edmonton Symptom Assessment Scale (ESAS). Baseline demographic data were obtained. To determine interrelationships between symptoms, a principal component analysis with "varimax rotation" was performed on the 9 ESAS symptoms. **Results:** Between January 1999 and January 2002, a total of 1296 patients with metastases provided complete baseline data on the ESAS. The most common primary cancer sites were lung, breast, and prostate. Fatigue was the highest scored symptom, followed by poor sense of well-being, pain, lack of appetite, and drowsiness. The 4 most prevalent symptoms were poor sense of well-being (92.7%), fatigue (92.2%), drowsiness (79.7%), and anxiety (78.7%). Three symptom clusters were found. Cluster 1 included lack of appetite, nausea, poor sense of well-being, and pain. Cluster 2 included fatigue, drowsiness, and shortness of breath. Cluster 3 included anxiety and depression. **Conclusion:** More work needs to be done on symptom cluster research, especially in setting a consensus in methodology.

Farah, R. and N. Makhoul (2009). "Pneumomediastinum as a presenting symptom of perforated sigmoid cancer: a case report." Cases J 2: 7356.

We report a rare case of spontaneous pneumomediastinum due to perforation of sigmoid cancer in a patient suffering from Vogt-Koyanagi-Harada syndrome and temporal arteritis, two rare diseases. This patient, who generally receives corticosteroid and methotrexate therapy, was admitted to hospital with vague abdominal and left flank pain, urinary disorders and low grade fever one day prior to admission. Initial evaluation including X-ray and laboratory tests was normal. Several hours later a repeat chest X-ray showed pneumomediastinum. Chest and abdominal Computed Tomography were performed because of worsening abdominal pain, and revealed a perforated sigma due to carcinoma.

Fellowes, D., K. Barnes, et al. (2008). "WITHDRAWN: Aromatherapy and massage for symptom relief in patients with cancer." Cochrane Database Syst Rev(4): CD002287.

BACKGROUND: Aromatherapy massage is a commonly used complementary therapy, and is

employed in cancer and palliative care largely to improve quality of life and reduce psychological distress. **OBJECTIVES:** To investigate whether aromatherapy or massage, or both, decreases psychological morbidity, lessens symptom distress and/or improves the quality of life in patients with a diagnosis of cancer. **SEARCH STRATEGY:** We searched CENTRAL (The Cochrane Library, Issue 1, 2002), MEDLINE (1966 to May week 3 2002), CINAHL (1982 to April 2002), British Nursing Index (1994 to April 2002), EMBASE (1980 to Week 25 2002), AMED (1985 to April 2002), PsycINFO (1887 to April week 4 2002), SIGLE (1980 to March 2002), CancerLit (1975 to April 2002) and Dissertation Abstracts International (1861 to March 2002). Reference lists of relevant articles were searched for additional studies. **SELECTION CRITERIA:** We sought randomised controlled trials (RCTs); controlled before and after studies; and interrupted time series studies of aromatherapy or massage, or both, for patients with cancer, that measured changes in patient-reported levels of physical or psychological distress or quality of life using reliable and valid tools. **DATA COLLECTION AND ANALYSIS:** Two review authors independently assessed trials for inclusion in the review, assessed study quality and extracted data. Study authors were contacted where information was unclear. **MAIN RESULTS:** The search strategy retrieved 1322 studies. Ten studies met the inclusion criteria and these represented eight RCTs (357 participants). The most consistently found effect of massage or aromatherapy massage was on anxiety. Four trials (207 participants) measuring anxiety detected a reduction post intervention, with benefits of 19 to 32% reported. Contradictory evidence exists as to any additional benefit on anxiety conferred by the addition of aromatherapy. The evidence for the impact of massage/aromatherapy on depression was variable. Of the three trials (120 participants) that assessed depression in cancer patients, only one found any significant differences in this symptom. Three studies (117 participants) found a reduction in pain following intervention, and two (71 participants) found a reduction in nausea. Although several of the trials measured changes in other symptoms such as fatigue, anger, hostility, communication and digestive problems, none of these assessments was replicated. **AUTHORS' CONCLUSIONS:** Massage and aromatherapy massage confer short term benefits on psychological well being, with the effect on anxiety supported by limited evidence. Effects on physical symptoms may also occur. Evidence is mixed as to whether aromatherapy enhances the effects of massage. Replication, longer follow up, and larger trials are need to accrue the necessary evidence.

Ferreira, K. A., M. Kimura, et al. (2008). "Impact of cancer-related symptom synergisms on health-related quality of life and performance status." *J Pain Symptom Manage* **35**(6): 604-16.

To identify the impact of multiple symptoms and their co-occurrence on health-related quality of life (HRQOL) dimensions and performance status (PS), 115 outpatients with cancer, who were not receiving active cancer treatment and were recruited from a university hospital in Sao Paulo, Brazil completed the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30, the Beck Depression Inventory, and the Brief Pain Inventory. Karnofsky Performance Status scores also were completed. Application of TwoStep Cluster analysis resulted in two distinct patient subgroups based on 113 patient experiences with pain, depression, fatigue, insomnia, constipation, lack of appetite, dyspnea, nausea, vomiting, and diarrhea. One group had multiple and severe symptom subgroup and another had less symptoms and with lower severity. Multiple and severe symptoms had worse PS, role functioning, and physical, emotional, cognitive, social, and overall HRQOL. Multiple and severe symptom subgroup was also six times as likely as lower severity to have poor role functioning; five times more likely to have poor emotional; four times more likely to have poor PS, physical, and overall HRQOL; and three times as likely to have poor cognitive and social HRQOL, independent of gender, age, level of education, and economic condition. Classification and Regression Tree analyses were undertaken to identify which co-occurring symptoms would best determine reduction in HRQOL and PS. Pain and fatigue were identified as indicators of reduction on physical HRQOL and PS. Fatigue and insomnia were associated with reduction in cognitive; depression and pain in social; and fatigue and constipation in role functioning. Only depression was associated with reduction in overall HRQOL. These data demonstrate that there is a synergic effect among distinct cancer symptoms that result in reduction in HRQOL dimensions and PS.

Fortner, B. V., L. S. Schwartzberg, et al. (2007). "Symptom Burden for Patients with Metastatic Colorectal Cancer Treated with First-Line FOLFOX or FOLFIRI with and Without Bevacizumab in the Community Setting." *Support Cancer Ther* **4**(4): 233-40.

Background: FOLFOX (oxaliplatin/leucovorin/5-fluorouracil) and FOLFIRI (irinotecan/leucovorin/5-fluorouracil) with or without bevacizumab have become standard-of-care regimens in first-line treatment of metastatic colorectal cancer.

However, there is a paucity of symptom burden information regarding these regimens from the patient perspective in community oncology. Patients and Methods: This retrospective chart review and telephone interview study examined patients with first-line metastatic colorectal cancer from 5 community oncology centers treated with FOLFOX or FOLFIRI with and without bevacizumab. Patient-reported outcomes were taken from the Patient Care Monitor 1.0 Revised, a validated tablet computer-based questionnaire that measures symptom burden and several scales of functioning and quality of life. A subset of patients completed structured telephone interviews about the impact of treatment on practical activities and income. Results: Eighty-eight patients with an average age of 62 years were included. Patients completed a median of 8 cycles of treatment. The most common moderate to severe symptom complaint was fatigue. Gastrointestinal symptoms were common but did not cluster in one regimen versus another. Neuropathy-related symptoms were also common across all regimens except FOLFIRI without bevacizumab. Nausea and neutropenia were common indications for concomitant medications. One third reported work and other activity interference, and care produced out-of-pocket expenditures in excess of \$1000. Conclusion: Although sample size was small in the FOLFIRI-based regimens, patient reports and chart records suggested that there was not a systematic difference between FOLFOX and FOLFIRI regimens in type of symptom. The addition of bevacizumab did not appear to increase symptom burden.

Fox, S. W. and D. Lyon (2007). "Symptom clusters and quality of life in survivors of ovarian cancer." *Cancer Nurs* **30**(5): 354-61.

Ovarian cancer has nonspecific symptoms, and no screening tool is available for early diagnosis; therefore, only 19% of ovarian cancers are found at an early stage. Given the late diagnosis, women with ovarian cancer often have a prolonged course of treatment and significant morbidity that lasts into survivorship. However, distressing symptoms and their effects on quality of life have been relatively understudied, particularly in survivors of the disease. The purpose of this study was to describe a symptom cluster and its relationship to quality of life in women with ovarian cancer who were recruited from an online cancer support group. Descriptive statistics and hierarchical regression techniques were used to analyze the data obtained from a larger study testing the psychometric properties of a quality-of-life instrument. Most participants had stage III ovarian cancer, and nearly all (97%) had undergone treatment before the study. A symptom cluster composed of

depression and fatigue was identified using work by Kim and colleagues [Symptom clusters: concept analysis and clinical implications for cancer nursing. *Cancer Nurs.* 2005;28(4):270-282]. The symptom cluster explained 41% ($P = .000$) of the variance in quality of life. These results suggest that fatigue and depression are significant problems for survivors of ovarian cancer.

Fox, S. W. and D. E. Lyon (2006). "Symptom clusters and quality of life in survivors of lung cancer." *Oncol Nurs Forum* 33(5): 931-6.

PURPOSE/OBJECTIVES: To explore the prevalence and intensity of depression, fatigue, and pain in survivors of lung cancer; to examine the relationship of symptoms in a cluster; and to examine the relationship of the symptom cluster to quality of life (QOL). **DESIGN:** Secondary data analysis. **SETTING:** Online lung cancer support group. **SAMPLE:** 51 patients diagnosed with lung cancer. **METHODS:** Mailed survey with self-report of depression, fatigue, and pain measured by subscales of the Short-Form 36 Health Status Survey and QOL measured by the Fox Simple QOL Scale. Pearson's correlation and multiple regression analyses were used to examine the possible symptom cluster. **MAIN RESEARCH VARIABLES:** Depression, fatigue, pain, and QOL. **FINDINGS:** Depression, fatigue, and pain were found in a majority of survivors, with pain being the least common symptom. Fatigue was the most intense of the three symptoms. Two significantly correlated symptoms were depression and fatigue. The cluster explained 29% (p less than 0.01) of the variance in QOL in the lung cancer survivors. **CONCLUSIONS:** The data provided preliminary support for the presence of a symptom cluster in patients with lung cancer consisting of depression and fatigue. The cluster had a negative relationship with QOL. Survivors of lung cancer have depression and fatigue that affect QOL. **IMPLICATIONS FOR NURSING:** Healthcare providers must assess the potential for symptoms to cluster, adversely affecting key patient outcomes such as QOL. Through increased knowledge of symptom clusters, clinicians will be able to more effectively target the most distressing set of symptoms for intervention.

Francoeur, R. B. (2005). "The relationship of cancer symptom clusters to depressive affect in the initial phase of palliative radiation." *J Pain Symptom Manage* 29(2): 130-55.

Research on comorbidity across cancer symptoms, including pain, fatigue, and depression, could suggest if crossover effects from symptom-specific interventions are plausible. Secondary analyses were conducted on a survey of 268 cancer

patients with recurrent disease from a northeastern U.S. city who were initiating palliative radiation for bone pain. Moderator regression analyses predicted variation in depressive affect that could be attributed to symptom clusters. Patients self-reported difficulty controlling each physical symptom over the past month on a Likert scale and depressive symptoms on a validated depression measure (Center for Epidemiologic Studies-Depression [CES-D]) over the past week on a four-category scale. An index of depressive affect was based on items of negative and positive affect from the CES-D. In predicting depressive affect, synergistic interactions of pain with fever, fatigue, and weight loss suggest separate pathways involving pain. A similar interaction with fever occurs when nausea was tested in place of pain. Further, the interaction between pain and fatigue is similar in form to the interaction between difficulty breathing and fatigue (when sleep is not a problem). Follow-up to the latter interaction reveals: 1) additional moderation by hypertension and palliative radiation to the hip/pelvis; and 2) a similar cluster not involving hypertension when appetite problems and weight loss were tested in place of fatigue. The significance and form of these interactions are remarkably consistent. Similar sickness mechanisms could be generating: 1) pain and nausea during fever; 2) pain and fatigue during weight loss; and 3) pain and breathing difficulty when fatigue is pronounced. Crossover effects from symptom-specific interventions appear promising.

Friedlander, M., P. Butow, et al. (2009). "Symptom control in patients with recurrent ovarian cancer: measuring the benefit of palliative chemotherapy in women with platinum refractory/resistant ovarian cancer." *Int J Gynecol Cancer* 19 Suppl 2: S44-8.

Most women with advanced ovarian cancer will relapse and subsequently develop platinum-resistant/refractory ovarian cancer. The benefit of treatment is currently based on objective response rates, which are a crude measure of benefit. It would be clinically meaningful if we were better able to measure the benefit of palliative therapy and, in particular, ascertain whether cancer-related symptoms improve with treatment and how this impacts on quality of life. This paper reviews the management of patients with platinum-resistant/refractory ovarian cancer and highlights the gaps in our knowledge and shortcomings with the current approaches to measure the benefit of treatment. The ultimate objective is to describe and encourage recruitment to the Gynecologic Cancer Intergroup study that has recently opened. This study will recruit a large number of patients from around the world in an effort to develop more robust instruments to measure the benefit of

chemotherapy and to understand the impact of chemotherapy on symptom control and quality of life. In addition, this study will give us an insight into how all patients are managed rather than a select minority who are treated in clinical trials.

Frostad, A. (2008). "Association between respiratory symptom score and 30-year cause-specific mortality and lung cancer incidence." *Clin Respir J* 2 Suppl 1: 53-8.

INTRODUCTION: Respiratory symptoms are among the main reasons why patients make contact with healthcare professionals and they are associated with several diseases. **OBJECTIVE:** The aim of this study was to investigate the relationship between respiratory symptoms reported at one time and 30 years cause-specific mortality and incidence of lung cancer in an urban Norwegian population. **MATERIALS AND METHODS:** A total of 19 998 men and women, aged 15-70 years, were in 1972 selected from the general population of Oslo. They received a postal respiratory questionnaire (response rate 89%). All were followed for 30 years for end-point mortality and for lung cancer. The association between respiratory symptoms, given as a symptom load, and end point of interest were investigated separately for men and women by multivariable analyses, with adjustment for age, occupational exposure to air pollution and smoking habits. **RESULTS:** A total of 6710 individuals died during follow-up. Obstructive lung diseases (OLDs) and pneumonia accounted for 250 and 293 of the total deaths, respectively. Ischaemic heart disease (IHD) accounted for 1572; stroke accounted for 653 of all deaths. Lung cancer developed in 352 persons during follow-up. The adjusted hazard ratio for mortality from OLD and pneumonia, IHD and stroke increased in a dose-response manner with symptom score, more strongly for OLD and IHD than for pneumonia and stroke. **CONCLUSIONS:** Respiratory symptoms were positively associated with mortality from OLD, pneumonia, IHD and stroke, and incidence of lung cancer. This association was significant for mortality from OLD and IHD.

Fu, O. S., K. D. Crew, et al. (2009). "Ethnicity and persistent symptom burden in breast cancer survivors." *J Cancer Surviv* 3(4): 241-50.

INTRODUCTION: Relatively few studies of breast cancer survivors have included nonwhite women or women who do not speak English. **METHODS:** We administered a survey to patients who were ≥ 3 months post-completion of their adjuvant treatment for stage 0-III breast cancer at Columbia University Medical Center in order to assess the prevalence of 16 physical and emotional

symptoms and identify sociodemographic factors associated with these symptoms. Univariate analysis, factor analysis, ANOVA, and multiple linear regression analysis were performed. **RESULTS:** Of 139 patients surveyed, 58 were white, 63 Hispanic, and 18 black. The symptom most commonly reported was fatigue(76%), and the most common severe symptom was muscle aches(40%). Most patients(70%) complained of ≥ 6 symptoms. Hispanic women were more likely to report >10 symptoms ($p < 0.05$). Factor analysis reduced the 16 symptoms to 4 underlying symptom clusters that we categorized as 'depression', 'chemotherapy', 'hormone', and 'pain'-related. In the multiple linear regression models, Hispanic women were more likely to report chemotherapy-related symptoms ($p < 0.05$) and pain-related symptoms ($p < 0.05$). Unemployed women were more likely to report chemotherapy-related symptoms ($p < 0.05$). Women <45 years old were less likely to report chemotherapy ($p < 0.05$) and pain-related symptoms ($p < 0.05$). **CONCLUSIONS:** The majority of women in this study, particularly those who were Hispanic, elderly, or unemployed, experienced persistent symptoms, most commonly fatigue and muscle aches. **IMPLICATIONS FOR CANCER SURVIVORS:** Because Hispanic, elderly, or unemployed women experience greater symptom burden, efforts should be made to address their unique needs.

Gning, I., P. C. Trask, et al. (2009). "Development and initial validation of the thyroid cancer module of the M. D. Anderson Symptom Inventory." *Oncology* 76(1): 59-68.

OBJECTIVE: The M. D. Anderson Symptom Inventory (MDASI) and its modules measure common symptoms related to cancer and its treatment. We report the development and initial validation of the MDASI-Thyroid Cancer module (MDASI-THY). **METHODS:** A list of thyroid-cancer-specific symptoms was generated through focus groups and interviews with thyroid cancer patients, clinicians and researchers. These MDASI-THY items were added to the original MDASI and administered to 60 patients with thyroid cancer. Symptom prevalence and severity were evaluated, along with the reliability and content, construct and known-group validity of the MDASI-THY. **RESULTS:** Cognitive debriefing performed on a subset of patients indicated that the MDASI-THY items were clear, concise, relevant and easy to understand. Fatigue, drowsiness, sleep disturbance, distress and difficulty remembering were the 5 most prevalent and severe symptoms. Twenty-eight percent of patients had moderate to severe fatigue (≥ 5 on a 0-10 scale). Average severity was 1.28 and 1.29 for the symptom and

interference subscales, respectively. MDASI-THY symptoms were severer for patients with poorer performance status. Cronbach alpha-values were 0.76, 0.85 and 0.92 for the thyroid-specific symptom items, core symptom subscale and interference subscale, respectively. CONCLUSIONS: This study demonstrates preliminary evidence for the validity and reliability of the MDASI-THY.

Goff, B. A., L. S. Mandel, et al. (2007). "Development of an ovarian cancer symptom index: possibilities for earlier detection." Cancer **109**(2): 221-7.

BACKGROUND: Currently, screening for ovarian cancer is not recommended for the general population. Targeting women with specific symptoms for screening has been evaluated only recently, because it was believed that symptoms had limited specificity. METHODS: A case-control study of 149 women with ovarian cancer, including 255 women who were in a screening program and 233 women who were referred for pelvic/abdominal ultrasound, was conducted by inviting women to complete a survey of symptoms. Patients were divided randomly into an exploratory group and a confirmatory group. Symptom types, frequency, severity, and duration were compared between cases and controls. Logistic regression analyses were used to determine which factors independently predicted cancer in the exploratory group and then were used to develop a symptom index, which was tested for sensitivity and specificity in the confirmatory group. RESULTS: Symptoms that were associated significantly with ovarian cancer were pelvic/abdominal pain, urinary urgency/frequency, increased abdominal size/bloating, and difficulty eating/feeling full when they were present for <1 year and occurred >12 days per month. In a logistic regression analysis, symptoms that were associated independently with cancer were pelvic/abdominal pain ($P < .001$), increased abdominal size/bloating ($P < .001$), and difficulty eating/feeling full ($P = .010$). A symptom index was considered positive if any of those 6 symptoms occurred >12 times per month but were present for <1 year. In the confirmatory sample, the index had a sensitivity of 56.7 for early-stage disease and 79.5% for advanced-stage disease. Specificity was 90% for women age >50 years and 86.7% for women age <50 years. CONCLUSIONS: Specific symptoms in conjunction with their frequency and duration were useful in identifying women with ovarian cancer. A symptom index may be useful for identifying women who are at risk.

Goodell, T. T. and L. M. Nail (2005). "Operationalizing symptom distress in adults with

cancer: a literature synthesis." Oncol Nurs Forum **32**(2): E42-7.

PURPOSE/OBJECTIVES: To address inconsistencies in the definition and operationalization of symptom distress by synthesizing the literature on cancer-related symptom distress in adults. DATA SOURCES: Electronic nursing, psychology, and medicine databases; online meeting abstracts; and various print sources. DATA SYNTHESIS: Eight distinct methods of operationalizing the concept were identified. Gender, ethnic, developmental, cultural, and individual differences in symptom distress have not been identified. Relationships among symptom frequency, intensity, and distress are unclear. CONCLUSIONS: Lack of clarity and consensus in defining and operationalizing symptom distress hinder meta-analysis, research synthesis, and research utilization. Symptom distress may be emerging as a component of the multidimensional symptom experience. IMPLICATIONS FOR NURSING: Defining and operationalizing symptom distress consistently will enhance research synthesis and assist clinicians with more effectively meeting the needs of people with cancer. Research is needed to identify the meanings of symptom distress to patients with cancer and to differentiate symptom distress from symptom frequency and intensity.

Goyal, S., J. Roscoe, et al. (2004). "Symptom interval in young people with bone cancer." Eur J Cancer **40**(15): 2280-6.

Symptom interval (SI), the time from first symptom/sign to diagnosis and initiation of treatment, appears to be principally influenced by tumour biology. Whether the age of the patient, patient delay, professional delay and access to health professionals influences the SI in bone tumours was investigated in this study. 115 patients with newly diagnosed osteosarcoma and Ewing's sarcoma were retrospectively reviewed. The median total SI for all bone tumours was 3.8 months (range 1-46 months). Patients older than 12 years had a longer SI ($P = 0.05$) and more patient delays ($P = 0.02$). Total SI and professional delays were longer if the General Practitioner was first seen compared with an Accident and Emergency Consultant ($P = 0.02$ and 0.02 , respectively). However, SI did not influence overall and event-free survival in this series. Bone tumour patients have long SIs that are significantly affected by age and local health-care support systems. Early referral to specialists would help to alleviate anxiety and distress to the patient and family, even if currently delay does not influence outcome.

Gralla, R. J. (2004). "Quality-of-life considerations in patients with advanced lung cancer: effect of

topotecan on symptom palliation and quality of life." *Oncologist* **9 Suppl 6**: 14-24.

Key goals in the treatment of lung cancer are to improve both survival and quality of life (QOL). While formal techniques are frequently used to evaluate survival and response, such rigor is used less often in assessing the impact of treatment on quality of life. Many patients with lung cancer are elderly and have complex medical histories and a myriad of comorbidities. In these patients, with limited survival expectations, symptom palliation, quality of life, and convenience of therapy are especially important end points. Indeed, clinical trials are now incorporating symptom scores and QOL outcomes in their designs (now combined as "patient reported outcomes" or PROs). Moreover, symptom palliation correlates well with QOL and survival duration, providing further rationale for therapy selection based on these parameters. The potential palliative and QOL benefits of chemotherapy have been investigated for several agents in lung cancer trials. Of these, topotecan (Hycamtin; GlaxoSmithKline; Philadelphia, PA) is the best characterized in relapsed small cell lung cancer (SCLC). In a phase III trial of topotecan versus cyclophosphamide, doxorubicin (Adriamycin; Bedford Laboratories; Bedford, OH), and vincristine (Oncovin; Eli Lilly and Company; Indianapolis, IN) (CAV) in patients with recurrent SCLC, topotecan was associated with statistically significant ($p < 0.05$) improvements in general symptoms (e.g., fatigue and interference with daily activity) and disease-specific symptoms (e.g., dyspnea and hoarseness). Moreover, the introduction of oral therapies, such as oral topotecan, may increase the convenience of therapy by reducing the time needed for therapy and the need for frequent venipuncture. This review summarizes the role of chemotherapy in symptom palliation, with an emphasis on the impact of topotecan therapy on symptom parameters in patients with relapsed SCLC and the emerging role of oral therapy in this setting.

Gralla, R. J., M. J. Edelman, et al. (2009). "Assessing quality of life following neoadjuvant therapy for early stage non-small cell lung cancer (NSCLC): results from a prospective analysis using the Lung Cancer Symptom Scale (LCSS)." *Support Care Cancer* **17**(3): 307-13.

BACKGROUND: The assessment of the impact of neoadjuvant therapy on quality of life (QL) has rarely been prospectively planned and evaluated, although validated QL instruments are available—such as the Lung Cancer Symptom Scale (LCSS) used in this study. The modest but significant survival gains reported with neoadjuvant and adjuvant approaches need to be viewed in terms of the added risks and toxicities associated with two or three modalities of

treatment. **MATERIALS AND METHODS:** The objective was to compare patient-determined QL ratings from baseline (prior to neoadjuvant chemotherapy) with those in subsequent months of follow-up. All patients had clinical stage I or II non-small cell lung cancer (NSCLC) and participated in one of two similar randomized protocols. Patients received preoperative chemotherapy (three cycles) of gemcitabine plus carboplatin or paclitaxel in one trial or gemcitabine plus carboplatin or cisplatin in the second. Patients completed the LCSS at baseline, every 3 weeks preoperatively, and every 3 months postoperatively up to 12 months. **RESULTS:** Full QL data are available for 43 patients with at least one postsurgical evaluation and for 23 patients with evaluation at 1-year postsurgery. In patients with at least one postsurgical evaluation, 84% had an ECOG performance status of 0, 93% had a complete resection, and 67% (95% CI = 52, 81) of patients experienced improved or stable symptoms. A subgroup of patients (14 of 43) reported worsening of QL (33%). These patients experienced a mean worsening of 66% in individual symptom parameters, with an average of seven of nine LCSS symptom parameters declining. **CONCLUSIONS:** Most patients reported improved or stable QL. Prospectively planned QL assessment is feasible with neoadjuvant trials and adds useful information not otherwise attainable.

Hadi, S., G. Fan, et al. (2008). "Symptom clusters in patients with cancer with metastatic bone pain." *J Palliat Med* **11**(4): 591-600.

PURPOSE: The primary objective was to explore how patients' worst pain clustered together with functional interference items. Secondary objectives were to determine whether symptom clusters change with palliative radiotherapy (RT) and to compare the difference between responders and nonresponders to radiation. **MATERIALS/METHODS:** Worst pain at the site of treatment and functional interference scores were assessed using the Brief Pain Inventory (BPI). Patients provided their scores at baseline, 4, 8, and 12 weeks post-RT. A principal component analysis was performed on the 8 items (worst pain and 7 functional interference items) at all time points to determine interrelationships between symptoms. Principal components with an eigenvalue higher than 0.90 and explaining more than 10% of the variance were selected. The Cronbach alpha statistic was used to estimate the internal consistency and reliability of the derived clusters at baseline and at subsequent follow-ups. Robust relationship and correlation among symptoms were displayed with a biplot graphic. **RESULTS:** From May 2003 to January 2007, 348

patients with bone metastases that were referred for palliative RT were accrued into the study. There were 206 males (59%) and 142 females (41%), with a median age of 68 years (range, 30-91). Lung (26%), breast (25%) and prostate (24%) were the most common primary cancer sites. Treatment ranged from single to multiple fractions, with the majority of patients receiving a single 8 Gy (58%) and 20 Gy/5 (35%). The most prevalent sites of RT were spine (31%), pelvis (16%), and hips (15%). Two symptom clusters were identified. Cluster 1 included walking ability, general activity, normal work, enjoyment of life and worst pain. Cluster 2 included relations with others, mood and sleep. The two clusters at baseline accounted for 67% of the total variance with a Cronbach alpha of 0.87 and 0.70, respectively. In responders to radiation treatment, the two symptom clusters disintegrated at 4, 8, and 12 weeks post-RT. All symptom severity items improved over time ($p < 0.0001$). In nonresponders, two clusters had disappeared at week 4, reemerged at week 8, and disintegrated at week 12. **CONCLUSION:** Symptom clustering has proved to be therapeutically important because treatment of one symptom may affect others within the same cluster. The significant correlations between worst pain and the functional interference items reaffirm the importance of pain reduction as a treatment goal for palliative radiotherapy. By treating a patient's symptom of worst pain, it would subsequently ease their response burden on their daily functional activities by decreasing symptom severity, increasing function, and improving overall quality of life.

Hedgepeth, R. C., J. Labo, et al. (2009). "Expanded Prostate Cancer Index Composite versus Incontinence Symptom Index and Sexual Health Inventory for Men to measure functional outcomes after prostatectomy." *J Urol* **182**(1): 221-7; discussion 227-8.

PURPOSE: Evaluating quality of life outcomes following prostate cancer treatment is important because different treatments provide similar survival outcomes. A wide variety of quality of life surveys are used with an unknown correlation between domain specific and broad domain instruments. We compared the urinary and sexual outcome measures of the Expanded Prostate Cancer Index Composite, a broad domain instrument, to those of the Incontinence Symptom Index and the Sexual Health Inventory for Men, which are domain specific instruments. **MATERIALS AND METHODS:** A total of 640 patients undergoing radical prostatectomy at our institution completed a combination of the Expanded Prostate Cancer Index Composite, Incontinence Symptom Index and Sexual Health Inventory for Men questionnaires. Matching

functional domains were compared and correlation coefficients were calculated. Subgroup analysis was performed to compare specific information pertinent to recovery from prostatectomy. **RESULTS:** Correlations between measures of incontinence were 0.26 to 0.84, while indicators of sexual function were 0.70 to 0.84. Subgroup analysis comparing measures of irritative symptoms demonstrated weaker correlations. Analysis in patients reporting no sexual activity also showed a significantly lower correlation of scores than that in patients reporting sexual activity. **CONCLUSIONS:** Expanded Prostate Cancer Index Composite scores generally demonstrate strong correlations with corresponding Incontinence Symptom Index and Sexual Health Inventory for Men scores, indicating similar measurements of information. Divergent correlations between irritative scores as well as scores in men who are not sexually active may indicate that the Expanded Prostate Cancer Index Composite has more descriptive validity in this population. Wider use of a single broad domain instrument such as the Expanded Prostate Cancer Index Composite to assess outcomes after prostate cancer treatment may improve clinical efficiency and allow comparative quality of life research across treatment types in the future.

Heidrich, S. M., R. L. Brown, et al. (2009). "An individualized representational intervention to improve symptom management (IRIS) in older breast cancer survivors: three pilot studies." *Oncol Nurs Forum* **36**(3): E133-43.

PURPOSE/OBJECTIVES: To test the feasibility and acceptability of an individualized representational intervention to improve symptom management (IRIS) in older breast cancer survivors and test the short-term effects of an IRIS on symptom distress. **DESIGN:** Two small randomized clinical trials and one pre-experimental study. **SETTING:** Oncology clinic and community. **SAMPLE:** 41 women with breast cancer (aged 65 years and older) in pilot study 1, 20 in pilot study 2, and 21 in pilot study 3. **METHODS:** In pilot study 1, women were randomized to the IRIS or usual care control. In pilot study 2, women were randomized to the IRIS or delayed IRIS (wait list) control. In pilot study 3, all women received the IRIS by telephone. Measures were collected at baseline, postintervention, and follow-up (up to four months). **MAIN RESEARCH VARIABLES:** Feasibility, acceptability, symptom distress, symptom management behaviors, symptom management barriers, and quality of life. **FINDINGS:** Across three pilot studies, 76% of eligible women participated, 95% completed the study, 88% reported the study was helpful, and 91% were satisfied with the study. Some measures of symptom distress decreased

significantly after the IRIS, but quality of life was stable. Women in the IRIS group changed their symptom management behaviors more than controls. CONCLUSIONS: Preliminary evidence supports the need for and feasibility of an IRIS. IMPLICATIONS FOR NURSING: Nurses may help older breast cancer survivors manage their numerous chronic symptoms more effectively by assessing women's beliefs about their symptoms and their current symptom management strategies.

Heidrich, S. M., J. J. Egan, et al. (2006). "Symptoms, symptom beliefs, and quality of life of older breast cancer survivors: a comparative study." Oncol Nurs Forum **33**(2): 315-22.

PURPOSE/OBJECTIVES: To compare symptoms, symptom beliefs, and quality of life (QOL) of older breast cancer survivors to those of older women without breast cancer. DESIGN: Descriptive, correlational study. SETTING: Urban and rural communities in the Midwest United States. SAMPLE: 18 breast cancer survivors and 24 women without breast cancer, older than age 64 (X age = 76 years). METHODS: In-home interviews using structured instruments. MAIN RESEARCH VARIABLES: Symptom distress (number of and distress from symptoms), symptom beliefs, chronic health problems, and QOL. FINDINGS: No group differences existed in demographic characteristics, symptom number, symptom bother, chronic health conditions, or QOL. Women in both groups most often attributed the cause of their symptoms to aging, chronic illness, or unknown, but rarely to breast cancer. Attributing symptoms to chronic illness or breast cancer was significantly related to more pain, depression, role impairment, and poorer mental health. Not knowing the cause of symptoms was significantly related to poorer social functioning, mental health, and purpose in life; less energy; and higher levels of depression and anxiety. CONCLUSIONS: The symptom experience and QOL of older breast cancer survivors are similar to those of older women with other chronic health problems. Beliefs about symptoms influence QOL in older women. IMPLICATIONS FOR NURSING: A broader assessment of symptoms is needed to assist older breast cancer survivors with symptom management. Symptom interventions in older women should address patients' beliefs about symptoms if QOL is to be enhanced.

Hendrix, C. and C. Ray (2006). "Informal caregiver training on home care and cancer symptom management prior to hospital discharge: a feasibility study." Oncol Nurs Forum **33**(4): 793-8.

PURPOSE/OBJECTIVES: To determine the feasibility of individualized caregiver training for home care and symptom management conducted at the bedside of older patients with cancer prior to hospital discharge. DESIGN: Pilot study. SETTING: The Extended Care Rehabilitation Center at the Durham Veterans Affairs Medical Center in North Carolina. SAMPLE: 7 female informal caregivers with a mean age of 56 (range = 26-76). More than half were African American. Most commonly, caregivers were spouses of the patients with cancer. METHODS: Individualized and experiential training on home care and cancer symptom management was conducted at the bedside of patients before hospital discharge. Caregiver demographic data were collected. An informal interview at the end of the training asked about the usefulness of the training in preparing for home caregiving. MAIN RESEARCH VARIABLES: Feasibility of the training. FINDINGS: Individualized bedside training to caregivers prior to hospital discharge is feasible. All caregivers noted the relevance of the content as well as the approach to the training. CONCLUSIONS: When given an opportunity for training on symptom management and home care, informal caregivers were very interested in participating. The individualized approach gave caregivers an opportunity to have their particular needs met. The flexibility of when to conduct the training proved to be crucial when soliciting attendance. The biggest challenge was in recruiting caregiver subjects through patients with cancer. IMPLICATIONS FOR NURSING: The impetus now is to look at the effects of the training on caregiver-patient variables as well as the cost-effectiveness and sustainability of such an approach to caregiver training.

Hendrix, C. C., A. Abernethy, et al. (2009). "A pilot study on the influence of an individualized and experiential training on cancer caregiver's self-efficacy in home care and symptom management." Home Healthc Nurse **27**(5): 271-8.

The aim of this pilot study was to investigate if an individualized and experiential training can promote family caregiver's confidence (self-efficacy) in home care and symptom management. The study was conducted in a hematology/oncology unit in a southeastern regional medical center. Twenty informal cancer caregivers participated in the study. The individualized and experiential training was conducted at the bedside prior to patient's hospital discharge. Self-efficacy in home care and cancer symptom management was measured using the Cancer Caregiver Self-Efficacy Measure before and after training, and at 1 week after hospital discharge of cancer patients. Results of the study showed mean

Cancer Caregiver Self-Efficacy Measure increased by 41.1 points immediately after the training ($z = 4.49$, $p < 0.001$) and was 31.7 points higher at 1-week follow-up ($z = 3.22$, $p < 0.01$). The findings of this study suggest that individualized and experiential training may be another avenue for nurses, including home care nurses, to support family home caregiving. By helping family members in home care, favorable patient outcomes may be achieved, enabling older patients with cancer to stay longer in the comfort of their homes.

Henoch, I., A. Ploner, et al. (2009). "Increasing stringency in symptom cluster research: a methodological exploration of symptom clusters in patients with inoperable lung cancer." *Oncol Nurs Forum* 36(6): E282-92.

PURPOSE/OBJECTIVES: To inductively explore the existence of symptom clusters among a homogenous group of patients with inoperable lung cancer close to diagnosis and to explore if the symptom clusters are consistent when examined with different instruments and analytical methods. **DESIGN:** Cross-sectional. **SETTING:** Lung medicine department at two university hospitals in Sweden. **SAMPLE:** 400 patients (52% men, 48% women) newly diagnosed with lung cancer with a mean age of 64.5 years. **METHODS:** Data were analyzed from various questionnaires, including the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30, the EORTC LC13, and the Symptom Distress Scale. Items in the instruments were adapted to increase their correspondence. Symptom clusters were analyzed with Pearson correlations, cluster analysis, factor analysis, and Cronbach alphas. **MAIN RESEARCH VARIABLES:** Symptom clusters. **FINDINGS:** Three clusters were found to be notably consistent across instruments and analyses: first, a pain cluster consisting of pain, nausea, bowel issues, appetite loss, and fatigue; second, a mood cluster consisting of mood, outlook, concentration, and insomnia; and third, a respiratory cluster consisting of breathing and cough, with fatigue and appetite loss closely related to more than one cluster in several analysis. **CONCLUSIONS:** The authors found consistent symptom clusters for a large cohort of patients with lung cancer at a comparable point in their cancer trajectory, across different measurement tools and statistical methods. **IMPLICATIONS FOR NURSING:** The symptom cluster consistency for patients with lung cancer is an important finding because the relevance of symptom cluster research is questionable if consistency is lacking across data collection and analysis approaches. Achieving consistency is possible in

symptom cluster research across instruments and analysis methods if instrument items are comparable.

Hermansen-Kobulnicky, C. J. (2009). "Symptom-monitoring behaviors of rural cancer patients and survivors." *Support Care Cancer* 17(6): 617-26.

GOALS OF WORK: Symptom monitoring is described among rural cancer patients and survivors with comparison across study variables. **MATERIALS AND METHODS:** An anonymous survey was mailed to adult cancer patients and survivors. Sampling was via a cancer center serving a region of a US rural-frontier state. Symptom monitoring was measured as keeping written track of symptoms, side effects, trends in how one is feeling, and/or limits to what one can do. **MAIN RESULTS:** Useable response rate was 60.4% (134/222). Respondents were on average 62.3 years old, 53.0% were female, and 52.3% had earned less than a college degree. Breast (30.6%) and prostate (28.4%) cancers were most common. Symptom monitoring was reported and confirmed via tracking means, by 32.1% of respondents. Symptom monitoring was associated with "shared" or "passive" symptom management decisions, keeping written track of questions to ask providers and answers received, report of fatigue, and having received the suggestion or advice on how to monitor. Symptom monitoring was not associated with age, education, sex, number of symptoms, or being given something with which to monitor. **CONCLUSIONS:** Symptom monitoring apart from intervention appears common among rural cancer patients and survivors. Findings support using multi-dimensional ways to inquire of, and refer to, such behavior. Data show symptom monitoring is more common among those suffering cancer-related fatigue, indicating opportunities for intervention to optimize monitoring for improved outcomes. Findings also suggest symptom-monitoring patients may rely on, or interact more with, providers regarding symptom management.

Hockenberry, M. and M. C. Hooke (2007). "Symptom clusters in children with cancer." *Semin Oncol Nurs* 23(2): 152-7.

OBJECTIVES: To discuss the symptoms of fatigue, sleep disturbance, and pain in children undergoing cancer treatment, and a framework for the clustering of these symptoms. **DATA SOURCES:** Published articles, research studies, and clinical experience. **CONCLUSION:** Symptoms experienced by children undergoing cancer treatment are distressing, prevalent, and rarely occur in isolation. Multiple symptoms may share underlying mechanisms, influence the severity of the distress experienced, and interfere with a child's ongoing

development. Developing knowledge of the relationships among symptoms may be important for improving quality of life during cancer treatment while supporting the child's development. **IMPLICATIONS FOR NURSING PRACTICE:** Nurses must be aware of the symptom distress occurring in children with cancer to manage its symptoms and its treatments.

Hoekstra, J., P. J. Bindels, et al. (2004). "The symptom monitor. A diary for monitoring physical symptoms for cancer patients in palliative care: feasibility, reliability and compliance." *J Pain Symptom Manage* 27(1): 24-35.

The aim of this study was to evaluate the feasibility, reliability and compliance of a new instrument, a diary to monitor physical symptoms for patients with cancer in the palliative phase of their illness. The development of the diary took place in three phases: two pilot studies and one intervention study. In Pilot I, reliability was tested within 13 pairs of patients and their proxy in a patient-proxy comparison. Pilot II was performed to test the feasibility of the instrument among 47 frail elderly. In the intervention study among patients with cancer in the palliative phase, the feasibility as well as the compliance has been tested. The phases have been completed with good results: reliability (ICC) of prevalent symptoms was above 0.75, good feasibility and good compliance. The Symptom Monitor can be used by patients and doctors as an instrument to monitor physical symptoms. The effectiveness of the use of this diary for improvement in treatment of symptoms in the palliative phase of cancer is being tested in a randomized clinical trial.

Hoekstra, J., M. J. Vernooij-Dassen, et al. (2007). "The added value of assessing the 'most troublesome' symptom among patients with cancer in the palliative phase." *Patient Educ Couns* 65(2): 223-9.

OBJECTIVE: In this study among patients with cancer in the palliative phase, we analysed whether assessing the symptom, which is causing the most trouble in the patient's every day life ('most troublesome' symptom) had added value apart from the presence and severity of symptoms, which are most commonly assessed in clinical practice. **METHODS:** Patients with cancer (lung, gastro-intestinal, breast cancer) in the palliative phase from two non-academic hospitals were included in the study. Using the Symptom Monitor tool, 10 physical symptoms were assessed with regard to presence and severity. The Symptom Monitor has an extra added item indicating as the 'most troublesome' symptom. This item was monitored to determine whether it had added value apart from the presence of symptoms and

'most severe' symptom. The severity score on the indicated 'most troublesome' symptom was subtracted from the severity score of the 'most severe' symptom. The generated delta score of 0 indicated no added value, whereas a score of one or more indicated that the 'most troublesome' symptom would have been missed if not specifically asked for by the physician, because its severity was lower than the 'most severe' symptom. **RESULTS:** One hundred and forty-six patients reported 590 symptoms to be present. In total, 227 symptoms were reported as 'most severe' symptom (n = 138 patients). Among these, fatigue (n = 52) and pain (n = 24) were reported most frequently as 'most severe' symptom. In total, 134 patients indicated a symptom as 'most troublesome'. Fatigue (n = 33; 25%) and pain (n = 22; 16%) were also indicated by most of these patients as the 'most troublesome' symptom. One hundred and fifty-two comparisons could be made between the 'most severe' and the 'most troublesome' symptom. In 102 (67%) of the comparisons assessing the 'most troublesome' symptom had no added value: the score for 'most severe' symptom did not differ from the score for the 'most troublesome' symptom revealing a delta score of 0. In 23 times (15%) of the 152 comparisons made, the delta score was 1 and in 27 (18%) of the comparisons the delta score was 2 or more indicating that assessing the 'most troublesome' symptom substantially had added value. **CONCLUSION:** In patients in the palliative phase of their disease, extra attention for the 'most troublesome' symptom is needed. In our study, in almost 1/3 of the cases, this symptom would have been missed the physicians attention if not specifically asked for. **PRACTICE IMPLICATIONS:** We recommend not only to assess the presence and severity of symptoms, but furthermore to assess the patient's 'most troublesome' symptom in addition.

Hollen, P. J., R. J. Gralla, et al. (2005). "A comparison of visual analogue and numerical rating scale formats for the Lung Cancer Symptom Scale (LCSS): does format affect patient ratings of symptoms and quality of life?" *Qual Life Res* 14(3): 837-47.

PROBLEM AND PURPOSE: The Lung Cancer Symptom Scale (LCSS), a site-specific health-related quality of life measure for patients with lung cancer, was originally developed using a Visual Analogue Scale (VAS) format. However, the VAS format is not readily compatible with data management and software programs using scanning. The primary aim of this study was to evaluate the convergence of ratings obtained with a Numerical Rating Scale (NRS), with an 11-pt response category format, to those obtained with a VAS format. The intent was to determine the degree of agreement

between two formats to generalize the existing psychometric properties for the original measure to the new presentation. DESIGN/SETTING: This methodological study evaluated the feasibility, reliability, and validity of a NRS format for the LCSS. The study was conducted at two cancer centers in New York City. PATIENTS/PROCEDURES: Sixty-eight patients with non-small cell lung cancer (NSCLC) completed both versions of the LCSS along with demographic and feasibility questions on a single occasion. The VAS form was administered first, followed by the NRS form to prevent bias. The intraclass correlation coefficient (ICC), Lin's concordance correlation coefficient (CCC), and Bland-Altman plots were used to evaluate agreement and to characterize bias. RESULTS: Cronbach's alpha for the NRS format total score was 0.89 for the 68 patients with NSCLC. Agreement was excellent, with both the ICC and CCC ≥ 0.90 for the two summary scores (total score and average symptom burden index) for the LCSS. Only five of the nine individual items showed this level of strict agreement. An agreement criterion of ≥ 0.80 (representing excellent) was observed for seven of the nine individual items (all but appetite loss and hemoptysis). Mean differences tended to be slightly lower for the VAS format compared to the NRS format (more so for the appetite and hemoptysis items), with evidence of scale shift for the same two items. The summary measures showed good concordance as measured by the ICC and CCC, but did display mean differences (VAS - NRS) of -2.7 and -3.1, respectively. CONCLUSIONS: Overall, the NRS format for the LCSS suitable for scanning has good feasibility, reliability (internal consistency), and convergent validity. The complete set of concordance evaluation measures supports the reproducibility of VAS scores by NRS scores, particularly for the two summary scores.

Hollen, P. J., R. J. Gralla, et al. (2004). "Adapting the Lung Cancer Symptom Scale (LCSS) to mesothelioma: using the LCSS-Meso conceptual model for validation." *Cancer* **101**(3): 587-95.

BACKGROUND: The underpinning conceptual model for the Lung Cancer Symptom Scale (LCSS), an instrument used to assess health-related quality of life in patients with lung cancer, has been described elsewhere. The patient-rated scale of the LCSS was modified slightly for patients with mesothelioma (LCSS-Meso), because no other mesothelioma-specific instrument was available. METHODS: In the current methodologic study, the authors tested the conceptual model for the LCSS-Meso. Chemotherapy-naïve patients with unresectable malignant pleural mesothelioma who were

participating in two clinical trials of pemetrexed (ALIMTA; Eli Lilly, Indianapolis, IN) completed the scale twice before the start of therapy and once weekly during the trials. Three time points were analyzed: baseline, Day 40, and Day 82. Poisson regression was used to determine the contribution of predictive factors (i.e., symptoms) to the summary items (symptom distress, activity level, and global quality of life). RESULTS: The model was tested in 495 patients who had malignant pleural mesothelioma. More than 85% of patients reported pain, dyspnea, fatigue, and appetite loss. Pain, dyspnea, and fatigue were significant and stable predictors for all summary items; however, pain had a significant effect on global quality of life only through Day 40. Appetite loss was a significant and stable predictor of activity level and global quality of life. The explained variance for the model was 39-55%. CONCLUSIONS: Further support for the content validity of the LCSS-Meso was obtained, as nearly all patients validated that the symptoms described in the scale captured their disease experience. The only exception was the hemoptysis item, which was removed based on the current large normative data set. Support for the construct validity of the LCSS-Meso also was obtained. For both mesothelioma and lung cancer, the majority of factors within the LCSS model are relevant and have the expected amount of variability. These findings support the use of the LCSS as a sensitive instrument for serial measurement during clinical trials involving patients with lung malignancies.

Hollen, P. J., R. J. Gralla, et al. (2006). "Measuring quality of life in patients with pleural mesothelioma using a modified version of the Lung Cancer Symptom Scale (LCSS): psychometric properties of the LCSS-Meso." *Support Care Cancer* **14**(1): 11-21.

Health-related quality of life (QOL) assessment is a key component in patient assessment and the development of therapies for malignant pleural mesothelioma. However, no mesothelioma-specific instrument was available. The Lung Cancer Symptom Scale (LCSS), a site-specific instrument used to assess QOL in patients with lung cancer, was identified as an instrument that could be appropriate. A modified nine-item patient-reported and six-item observer-reported LCSS was incorporated into two clinical trials of pemetrexed in patients with pleural mesothelioma. Basic psychometric properties of feasibility, reliability, and validity were tested. Properties were stable or enhanced by deletion of the hemoptysis item. Feasibility was demonstrated with a high completion rate of 90% by 512 patients. Reliability was acceptable, with good internal consistency for the eight-item measure (alpha

coefficient=0.86) and reasonably good for the five-item observer measure (alpha coefficient=0.66); there was also good stability for the patient measure using test-retest ($r=0.87$). Content validity was supported by a literature review and patient self-report of presenting symptoms (>90% of patients had three or more symptoms). Construct validity was well supported by finding better scores in the higher performance status groups and greater symptom improvement in patients with tumor response, good concordance with the LCSS conceptual model and good explanation of variance for summation items, and a high degree of convergence between the patient and observer forms ($r=0.57$). Criterion-related validity was supported by predicting survival time, time to progression, and tumor response rate; all three summary items and the total LCSS-Meso score were statistically significant predictors ($p<0.005$). The LCSS-Meso is a feasible, reliable, and valid instrument to assess health-related QOL in patients with pleural mesothelioma. One item, hemoptysis, was dropped from the original LCSS based on these findings.

Hopfgarten, T., J. Adolfsson, et al. (2006). "The choice between a therapy-induced long-term symptom and shortened survival due to prostate cancer." *Eur Urol* **50**(2): 280-9.

OBJECTIVES: A patient with newly diagnosed localized prostate cancer can choose from an array of therapies. A patient's willingness to trade life for freedom from therapy-induced long-term symptoms is poorly investigated. **METHODS:** In October 2002, we attempted to collect information from the 591 men who had been diagnosed and registered with prostate cancer in 1999 in Stockholm County. In a postal questionnaire, men were asked to balance absence or presence of certain therapy-induced long-term symptoms against varying lengths of survival gain as a consequence of the therapy. **RESULTS:** Information was provided by 511 (86%) of the 591 men. A large majority of the men participating in this study ended up in one of two extreme categories: either they accepted the therapy-induced symptom to gain survival or they did not. For fecal leakage, 78% of the men chose one of two extreme categories compared with 74% for urinary leakage, 71% for tender enlarged breasts, 73% for erectile dysfunction, and 78% for restricted diet. Thirty-seven percent of the men in the study were willing to accept fecal leakage if there was only the slightest chance to gain survival, comparing percentages for urinary leakage, tender enlarged breasts, restricted diet, and erectile dysfunction and were 48%, 53%, 55%, and 64%, respectively. **CONCLUSION:** Willingness to accept therapy-induced long-term symptoms to avoid a shortened

survival due to prostate cancer varies dramatically among men with localized prostate cancer and a large majority of men are in one of two extreme categories. Among symptoms, long-term fecal leakage was the one fewest men were willing to accept to gain survival.

Hsiao, C. P., L. J. Loescher, et al. (2007). "Symptoms and symptom distress in localized prostate cancer." *Cancer Nurs* **30**(6): E19-32.

For over a decade, symptom distress has been a key concept in several studies of cancer. However, the definition of symptom distress is still unclear, and there are few measures targeting symptom distress, in general, and specific cancers, in particular. Prostate cancer is the sixth most common cancer worldwide and the second leading cause of death in American men. Many men with clinically localized prostate cancer may experience unique and multidimensional symptoms that occur from diagnosis through treatment, and thereafter. These symptoms associated with the disease and its treatments are in the form of physical and psychological sequelae such as urinary and bowel problems and sexual dysfunction. The purposes of this article are to (1) systematically review literature on symptoms and symptom distress in localized prostate cancer and (2) synthesize evidence of symptom distress applications and measurement in this group. A comprehensive, systematic review was conducted to identify original, data-based studies of symptoms and symptom distress in localized prostate cancer. Clarification of symptom distress and more comprehensive information about symptoms and symptom distress will provide nurses with a better foundation for developing self-management interventions aimed at ameliorating symptom distress and, ultimately, enhancing the quality of life of patients with localized prostate cancer.

Hwang, S. S., C. B. Scott, et al. (2004). "Prediction of survival for advanced cancer patients by recursive partitioning analysis: role of Karnofsky performance status, quality of life, and symptom distress." *Cancer Invest* **22**(5): 678-87.

We performed an exploratory recursive partitioning analysis (RPA) in 429 metastatic cancer patients who had completed a Functional Assessment of Cancer Therapy-General (FACT-G) and a Memorial Symptom Assessment Scale-Short Form (MSAS-SF) to define survival prognostic groups. The Cox model analysis also was performed. Both RPA and Cox models included Karnofsky performance status (KPS), age, FACT-G subscales, and MSAS-SF subscales as survival predictors. Of 429 patients, 348 patients (81.1%) had expired at time of analysis. The

median age was 67 years (27-89), with median length of survival of 147 days. The RPA identified four distinct survival groups ($p < .0001$) with three variables: KPS, physical well-being, and physical symptom distress. The most significant split was KPS of 50%, followed by physical well-being score of 25 and physical symptom distress score of 0.6. The median survival time was 29 days for patients with KPS $< 50\%$; 146 days for patients with KPS $\geq 50\%$ and physical well-being < 25 ; 292 days for patients with KPS $> 50\%$, physical well-being ≥ 25 , and physical symptom distress score > 0.6 ; and 610 days for patients with KPS $\geq 50\%$, physical well-being ≥ 25 , and physical symptom distress score ≤ 0.6 . The Cox model found, in addition to KPS ($p < .0001$) and physical well-being ($p = .08$), different predictors: psychological symptom distress ($p = .0007$), global distress index ($p = .02$), and age ($p < .0001$). We concluded that the KPS, quality of life, and symptom distress scores can be combined to define prognostic groups. Such models may be helpful for clinical decision making.

Ivanova, M. O., T. I. Ionova, et al. (2005). "Cancer-related symptom assessment in Russia: validation and utility of the Russian M. D. Anderson Symptom Inventory." *J Pain Symptom Manage* **30**(5): 443-53.

This multicenter cross-sectional study ($n=226$) validated the Russian-language M. D. Anderson Symptom Inventory (MDASI-R) in Russian cancer patients with hematological malignancies or solid tumors. The Russian-language Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36-R) also was used for validation. Factor analysis found three underlying constructs for symptom items--general, treatment-related, and affective symptoms--with Cronbach alphas of 0.86, 0.68, and 0.90, respectively. Convergent validity was established by comparing MDASI-R items with SF-36-R subscales. The MDASI-R detected significant differences in symptom severity and interference levels by performance status, supporting known-group validity. The most prevalent symptoms were fatigue, sleep disturbance, pain, sadness, and poor appetite; 53% of the sample reported one to four moderate-to-severe symptoms (≥ 5 on 0-10 scale). Symptoms interfered most with work and general activity. Medical professionals underestimated the severity of pain, fatigue, and distress. The MDASI-R is valid and reliable for measuring symptom severity and interference in Russian cancer patients.

Janz, N. K., M. Mujahid, et al. (2007). "Symptom experience and quality of life of women following breast cancer treatment." *J Womens Health (Larchmt)* **16**(9): 1348-61.

BACKGROUND: Few studies have examined the correlates of breast cancer-related symptoms that persist posttreatment and determined the relationship between symptoms and quality of life (QOL). **METHODS:** A population-based sample of women in the United States with stage 0-II breast cancer ($n = 1372$) completed a survey including the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire and the Breast Cancer-Specific Quality of Life Questionnaire. Described are the presence and frequency of 13 symptom scales and their associations with 10 QOL dimensions. **RESULTS:** All study participants had completed primary treatment (surgery and radiation and/or chemotherapy, if applicable). Mean time from initial surgical treatment to completion of the questionnaire was 7.2 months (range 0.5-14.9 months). Mean number of symptoms reported was 6.8, with the 5 most common symptom scales being systemic therapy side effects (87.7%), fatigue (81.7%), breast symptoms (72.1%), sleep disturbance (57.1%), and arm symptoms (55.6%). Younger age and poorer health status at diagnosis were associated with worse symptoms. Fatigue had the greatest impact on QOL, with significant differences between those with high and low fatigue across 7 QOL dimensions. Sociodemographic, prior health status, clinical, and treatment/diagnostic factors explained only 9%-27% of the variance in QOL outcomes. Adding symptom experience increased the variance explained to 18%-60%. **CONCLUSIONS:** More attention to the reduction and management of disease and treatment-related symptoms could improve QOL among women with breast cancer.

Jena, A., S. Taneja, et al. (2008). "Magnetic resonance (MR) patterns of brain metastasis in lung cancer patients: correlation of imaging findings with symptom." *J Thorac Oncol* **3**(2): 140-4.

INTRODUCTION: Asymptomatic brain metastasis in lung cancer patients, if detected early have been reported to show survival benefit with treatment. These asymptomatic metastasis have been found to be smaller and less in number than those with symptoms. We however observed that many lung cancer patients bear a significant metastatic load in the brain irrespective of the stage or neurologic symptoms at the time of initial presentation. **MATERIAL AND METHODS:** A retrospective study was conducted on 175 patients of proven non-small cell lung cancer to assess the patterns of brain metastasis in the two groups of patients, with and without neurologic symptoms. All patients had undergone screening magnetic resonance imaging for brain metastasis as an initial staging protocol. The patients with brain metastasis were divided into two groups:

asymptomatic (group I) and symptomatic (group II). The lesions were studied with regards to the number, size, site, nature (solid with and without necrosis), and presence of perilesional edema and intralesional hemorrhage in both the groups in various stages of disease. RESULTS: Brain metastasis was seen in 62 (31.3%) patients of whom 46.7% were neurologically asymptomatic. Patients (90.3%) with brain metastasis were in stage IV at the time of presentation. No statistically significant correlation was found between the two groups regarding the number of lesions ($p = 0.554$), size of lesion ($p = 0.282$), site of lesion ($p = 0.344$), nature of lesion ($p = 0.280$), presence of perilesional edema ($p = 0.404$), and presence or absence of intralesional hemorrhage ($p = 0.09$). In our study, brain metastases were present only in stages III and IV disease with no statistically significant difference in the lesion patterns. CONCLUSION: The study reveals almost equal number of patients with brain metastasis in the symptomatic and asymptomatic groups with no significant difference in lesion patterns. We therefore conclude that although imaging surveillance of the brain for metastasis will detect asymptomatic metastasis early for early institution of appropriate therapy the prognosis in these patients would not solely depend on the presence or absence of symptoms and the pattern of lesion may have an influence on the patients' response to therapy and survival benefit specially for those asymptomatic patients with equally large metastatic load.

Jensen, K., A. Bonde Jensen, et al. (2006). "The relationship between observer-based toxicity scoring and patient assessed symptom severity after treatment for head and neck cancer. A correlative cross sectional study of the DAHANCA toxicity scoring system and the EORTC quality of life questionnaires." *Radiother Oncol* **78**(3): 298-305.

BACKGROUND AND PURPOSE: Morbidity is an important issue in cancer research. The observer-based toxicity scoring system used by DAHANCA (the Danish head and neck cancer study group) has proved itself sensitive to differences in toxicity in a large randomised study, but like other toxicity scoring systems it has not been formally validated. Conversely, the EORTC quality of life questionnaire (QLQ) has been validated as a tool for collecting information about the consequences of disease and treatment on the well being of cancer patients. The purpose of this study was to examine the relationship between the two methods of side effect recording. **PATIENTS AND METHODS:** One hundred and sixteen recurrence free patients with laryngeal ($n=44$), pharyngeal ($n=34$) and oral cavity ($n=38$) cancer attending follow-up after radiotherapy ($n=83$) or surgery ($n=33$) completed EORTC C30, the

core questionnaire concerning general symptoms and function and EORTC H&N35 the head and neck specific questionnaire. The attending physicians in the follow-up clinic evaluated and recorded DAHANCA toxicity scores on the same patients. RESULTS: The DAHANCA toxicity scoring system and the EORTC QLQ correlated with several clinical endpoints. The conceptually similar endpoints of the two methods correlated significantly. The objective endpoints of the DAHANCA scoring system were only correlated with quality of life endpoints to a very low degree. The DAHANCA toxicity scores had a low sensitivity (0.48-0.74) in detecting equivalent subjective complaints from the questionnaires and the observer-based scoring system severely underestimated patient complaints. A specific patient group where the DAHANCA score had a higher tendency to fail could not be detected. CONCLUSION: The DAHANCA toxicity score is an effective instrument in assessing objective treatment induced toxicity in head and neck cancer patients but insensitive and non-specific with regard to patient assessed subjective endpoints. This weakness seems inherent in an observer-based scoring system, and will probably also apply to newer ones like CTCAE 3.0.

Jeon, S., C. W. Given, et al. (2009). "The utility of screening in the design of trials for symptom management in cancer." *J Pain Symptom Manage* **38**(4): 606-14.

Clinical trials that test interventions for symptom management must target patients whose symptoms are severe and can benefit from participation. Screening symptoms for their severity prior to trial entry may be an important element of trial design. This research describes the utility of screening for severity of symptoms prior to entry into clinical trials for symptom management in cancer. To accomplish this, 601 cancer patients undergoing chemotherapy were assessed at screening and at the initial intervention contact, using the 0-10 rating scale for severity of nine symptoms. Post-test probabilities and likelihood ratios (LRs) were estimated across cut-offs in screening severity scores. Areas under receiver operating characteristic curves for reaching threshold of four at the initial intervention contact were estimated by a nonparametric method. It was found that screening severity scores were good predictors for identifying patients who would not reach threshold but did not always accurately predict patients who would. The cut-offs between 2 and 4 on a 0-10 scale could be used to identify patients that might benefit from receipt of interventions. For all symptoms, the LRs were greater than one across possible screening cut-offs. The findings indicate that decision rules based on screening prior to entry into cancer symptom

management trials can provide reasonable discriminative accuracy by differentiating among patients who are likely to reach higher levels of severity later in the trial from those who are not. Optimal severity cut-offs can be established based on LRs and desired sensitivity and specificity.

Johansson, E., A. Bill-Axelsson, et al. (2009). "Time, symptom burden, androgen deprivation, and self-assessed quality of life after radical prostatectomy or watchful waiting: the Randomized Scandinavian Prostate Cancer Group Study Number 4 (SPCG-4) clinical trial." *Eur Urol* **55**(2): 422-30.

BACKGROUND: Quality-of-life outcomes are important in the choice of treatment strategy for men with localized prostate cancer. **OBJECTIVE:** To evaluate how follow-up time, number of physical symptoms, and presence of androgen deprivation affected quality of life among men randomized to radical prostatectomy or watchful waiting. **DESIGN, SETTING, AND PARTICIPANTS:** The study group was composed of all 376 living men included in the Swedish part of the Scandinavian Prostate Cancer Group Study Number 4 (SPCG-4) between January 1, 1989, and February 29, 1996. Quality-of-life data were collected after a mean follow-up time of 4.1 yr. **INTERVENTION:** All patients were randomly assigned to radical prostatectomy or watchful waiting. Forty-five men were androgen deprived. **MEASUREMENTS:** Data of specific symptoms, symptom-induced stress, sense of well-being, and self-assessed quality of life were obtained by means of a questionnaire. Psychological symptoms were assessed using seven-point visual digital scales. **RESULTS AND LIMITATIONS:** In analyses stratified on the basis of the numbers of physical symptoms, anxiety and depressed mood were less common, and sense of well-being and self-assessed quality of life were better throughout in the radical prostatectomy group than in the watchful waiting group. As the number of physical symptoms increased, all psychological variables became worse and more prominent in the watchful waiting group. After a follow-up time of 6-8 yr, a significant decrease in quality of life ($p=0.03$) was seen in the watchful waiting group. Twenty-four percent of androgen-deprived patients assigned to watchful waiting reported high self-assessed quality of life compared with 60% in the radical prostatectomy group. Eighty-eight percent of patients had clinically detected tumors. **CONCLUSIONS:** Androgen deprivation negatively affected self-assessed quality of life in men assigned to watchful waiting. The number of physical symptoms was associated with the level of quality of life. Quality of life was lower with longer follow-up

time in both groups and was statistically significant in the watchful waiting group ($p=0.03$).

Joly, F., J. Vardy, et al. (2007). "Quality of life and/or symptom control in randomized clinical trials for patients with advanced cancer." *Ann Oncol* **18**(12): 1935-42.

BACKGROUND: Measures reflecting quality of life (QoL) or symptom control should be included as major endpoints in most phase III trials for patients with advanced cancer. Here we review the use of such endpoints. **METHODS:** We evaluated methodological aspects relating to QoL or symptom control in randomized controlled trials (RCTs) that included ≥ 150 patients, published from 1994 to 2004, using a 10-point checklist. **RESULTS:** Of 112 RCTs that met our criteria, few were rated as high quality: 22% defined QoL or symptom control as a primary endpoint; 19% established an a priori hypothesis relevant to palliation and 21% defined minimal differences in QoL or symptom scores that were clinically meaningful. Most trials (81%) analyzed differences between mean or median scores across groups and only 21% defined the proportion of individual patients who met criteria for palliative response. Only 15% of the studies met more than 5/10 criteria from our checklist. There was improvement over time in methodology and reporting. **CONCLUSIONS:** Current standards for analyzing QoL and symptom control in RCTs are poor. Definition of a palliative endpoint, with an a priori hypothesis, is essential; defining the proportion of patients with palliative response is preferred. The proposed checklist could raise standards of reporting in future RCTs.

Kenefick, A. L. (2006). "Patterns of symptom distress in older women after surgical treatment for breast cancer." *Oncol Nurs Forum* **33**(2): 327-35.

PURPOSE/OBJECTIVES: To describe patterns of symptom distress over time in older women receiving surgical treatment for breast cancer and to examine the relationship of selected patient and clinical characteristics to symptom distress. **DESIGN:** Secondary analysis of breast cancer data from a prospective, longitudinal study of older patients with several types of cancer. **SETTING:** Large mid-Atlantic teaching hospital. **SAMPLE:** 57 patients with breast cancer participated. Subjects had a mean age of 68 and were predominantly white, not Hispanic, married, Protestant, retired, and in stage I or II. A total of 55 subjects completed the study. **METHODS:** The Symptom Distress Scale was used. Data were collected on discharge and at three and six months postdischarge. Descriptive statistics, t test, analysis of variance, correlation coefficients, and stepwise

multiple regression were analyzed. MAIN RESEARCH VARIABLES: Total symptom distress and 13 individual symptom scores. FINDINGS: Fatigue, frequency of pain, outlook, and insomnia consistently were most prevalent and severe. Symptoms decreased gradually. Younger, more educated, and married women experienced more distress. CONCLUSIONS: Interactions among symptoms are complex. Later symptom distress may be predicted by early experience and demographic characteristics. IMPLICATIONS FOR NURSING: Clinicians should inquire about symptom distress at each encounter, expect multiple symptoms, and anticipate greater symptom distress in patients who are younger, more educated, or married or living with a partner. In women with more severe, earlier symptom distress, nurses should intervene promptly. Research should determine interrelationships of symptoms and how they might be affected by contextual variables, describe critical attributes of the nurse-patient interaction that might mitigate symptom distress, characterize the relationship of symptom intensity and distress, clarify the mechanism of the relationship between marital status and symptom distress, and identify the effect of symptoms, individually and collectively, on survival and quality of life.

Khattak, I., N. J. Eardley, et al. (2006). "Colorectal cancer—a prospective evaluation of symptom duration and GP referral patterns in an inner city teaching hospital." *Colorectal Dis* 8(6): 518-21.

OBJECTIVE: A high percentage of colorectal cancer patients (CRC) present as an emergency. Our aim was to evaluate delays in referral based on patient and general practitioner (GP) factors to see if there was any difference between elective and emergency patients. METHOD: Symptom questionnaires were prospectively collected from 101 consecutive patients presenting to a single colorectal unit (58 male, 43 female; median age 72 years) and entered into a database. Questionnaires assessed time from symptom onset until first GP visit, time for GP to refer, and type of admission. Symptoms and Dukes stage were noted. RESULTS: Fifty-eight (57%) patients presented electively and 43 (43%) as an emergency. Eighty-eight patients (87%) saw their GP of which 34 (39%) later presented as emergency; 13 (13%) did not see their GP. The median time before patients first sought medical advice was 30 days (0-1095 days). Median delay until treatment was 90 days (range 0-1460 days). Emergency patients waited a median of 11.5 days before visiting the GP, and elective a median of 49.5 days ($P = 0.04$) (Mann-Whitney U). Nine of 13 patients who did not see their GP presented as an emergency (median wait 44 days).

The median time taken for a GP to refer to a hospital specialist was 28 days in elective patients and 14 days in the emergency group. ($P = ns$) Thirty (38%) patients took longer than six weeks to be referred (33% as an emergency). Thirty-six patients had Dukes A or B and took a median of 30 days to first presentation. Sixty-five had Dukes C or D and took a median of 32 days to first presentation. ($P = ns$) CONCLUSION: Emergency patients have symptoms for less time before seeking medical advice compared to elective patients. The duration of these symptoms is unrelated to the histological stage at diagnosis. Although the majority of GPs referred CRC patients within six weeks, there was no association between time taken to refer and mode of presentation. The factors that relate to disease stage occur before symptoms are acted on.

Kim, H. J. and I. L. Abraham (2008). "Statistical approaches to modeling symptom clusters in cancer patients." *Cancer Nurs* 31(5): E1-10.

This study examined statistical methods to identify and quantify symptom clusters in diverse disciplines, discussed methodological issues in symptom cluster research in oncology, and provided guidance to researchers and clinicians as to the choice and conceptual implications of particular methods. Correlation and related measures of association show the mathematical evidence of a concurrent tendency for 2 or more symptoms. Graphical modeling reveals a more concrete image of possible symptom clusters and provides an idea as to how and why they are correlated. Structural equation modeling can be used to identify symptom clusters with a large number of symptoms, complex relationships, and/or directional relationships. Factor analysis can identify groups of symptoms which are interrelated due to a common underlying cause. Cluster analysis can group symptoms which have similar patterns across patients and find clinical subgroups based on symptom experience. The best strategy to study symptom clusters is to combine various methods while recognizing the strengths and limitations inherent in each method. A tight partnership of clinicians, clinical oncology researchers, and statisticians is essential. Designing a research to identify symptom clusters involves practical issues related to levels of measurement, dimensionality, confounding variables, symptom selection, and heuristic versus deterministic search.

Kim, H. J., A. M. Barsevick, et al. (2008). "Treatment-related symptom clusters in breast cancer: a secondary analysis." *J Pain Symptom Manage* 36(5): 468-79.

This study investigated treatment-related symptom clusters and the influence of selected demographic/clinical variables on symptom clustering in breast cancer patients across a treatment trajectory. A secondary analysis of 282 breast cancer patients receiving chemotherapy or radiotherapy was done to determine the clustering of oncologic treatment-related symptoms at selected time points of treatment. Two distinct clusters were identified: a psychoneurological cluster and an upper gastrointestinal cluster. The clustering of symptoms was generally stable across the treatment trajectory. The clustering, however, was weaker when the time lapse after the completion of treatment became longer. Demographic and clinical variables did not significantly influence symptom clustering. Psychoneurological symptoms had a tendency to occur together across the treatment trajectory, as did upper gastrointestinal symptoms. Effective symptom assessment/management strategies need to take into account this co-occurrence of symptoms. The findings from this study underscore the need for further investigation of the common biological basis of symptoms to attain more effective management of multiple symptoms.

Kim, H. J., D. B. McGuire, et al. (2005). "Symptom clusters: concept analysis and clinical implications for cancer nursing." *Cancer Nurs* **28**(4): 270-82; quiz 283-4.

The purpose of this article is to analyze the concept of symptom clusters and to discuss its application to cancer nursing to promote communication and enhance scientific knowledge. Rodgers' evolutionary method of concept analysis served as the framework for reviewing literature from psychology/psychiatry, general medicine, and nursing. Attributes of symptom clusters were relationships of symptoms and relationships of clusters, concurrence, underlying dimensions, stability, and common etiology. The major antecedent was the presence of 2 or more symptoms. Consequences were poorer physical health status, interference with activities of daily living, emotional distress, and increased financial burden. A symptom cluster is defined as consisting of 2 or more symptoms that are related to each other and that occur together. Symptom clusters are composed of stable groups of symptoms, are relatively independent of other clusters, and may reveal specific underlying dimensions of symptoms. Relationships among symptoms within a cluster should be stronger than relationships among symptoms across different clusters. Symptoms in a cluster may or may not share the same etiology. Symptom should be broadened to include both subjective (self-reported) symptoms and objective

(observed) signs. Implications for researchers include the need to use a clear definition, determine the optimal methods of identifying etiology and nature of symptom clusters in various populations, assess the clinical utility of symptom clusters, and test interventions. Implications for practitioners include the need to comprehensively assess symptoms over the entire cancer trajectory, select interventions that target single and multiple symptoms, and evaluate outcomes that include quality of life and economic variables.

Kim, M. K., K. Kim, et al. (2009). "A hospital-based case-control study of identifying ovarian cancer using symptom index." *J Gynecol Oncol* **20**(4): 238-42.

OBJECTIVE: Recently, a symptom index for identification of ovarian cancer, based on specific symptoms along with their frequency and duration, was proposed. The current study aimed at validation of this index in Korean population. **METHODS:** A case-control study of 116 women with epithelial ovarian cancer and 209 control women was conducted using questionnaires on eight symptoms. These included pelvic/abdominal pain, urinary urgency/frequency, increased abdominal size/bloating, difficulty eating/feeling full. The symptom index was considered positive if any of the 8 symptoms present for <1 year that occurred >12 times per month. The symptoms were compared between ovarian cancer group and control group using chi-square test. Logistic regression analysis was used to determine whether the index predicted cancer. Sensitivity and specificity of the symptom index were also determined. **RESULTS:** The symptom index was positive in 65.5% of women with ovarian cancer, in 31.1% of women with benign cysts, and in 6.7% of women on routine screening (ps<0.001). Significantly higher proportion of ovarian cancer patients were positive for each symptom as compared with control group (ps<0.001). Results from the logistic regression indicated that the symptom index independently predicted cancer (p<0.001; OR, 10.51; 95% CI, 6.14 to 17.98). Overall, the sensitivity and specificity of the symptom index were 65.5% and 84.7%, respectively. Analyses of sensitivity by stage showed that the index was positive in 44.8% of patients with stage I/II disease and in 72.9% of patients with stage III/IV disease. **CONCLUSION:** The current study supported previous studies suggesting that specific symptoms were useful in identifying women with ovarian cancer.

Kirkova, J., M. P. Davis, et al. (2006). "Cancer symptom assessment instruments: a systematic review." *J Clin Oncol* **24**(9): 1459-73.

PURPOSE: A variety of assessment instruments have been created to identify cancer

symptoms. We reviewed systematically cancer symptom assessment instruments published in English. **METHODS:** A systematic search of the MEDLINE database, Cochrane Library, Cumulative Index of Nursing and Allied Health Literature (CINAHL), and EMBASE was performed. Non-peer-reviewed articles were identified through BIOSIS. Articles were accessed through the related article links in PubMed and references were searched by hand. Studies were included if the instrument had symptom assessment as the primary outcome. Quality-of-life instruments were excluded. **RESULTS:** We identified 21 instruments; some had undergone modification or validation. An additional 28 studies examined symptom prevalence and interrelations; many involved symptom checklists. Studies varied in design, patient characteristics, symptoms, and outcome. Meta-analysis was not possible due to heterogeneity in design, study outcomes, and validation. Seventy-six articles and two conference abstracts (derived from MEDLINE, Cochrane, CINAHL, EMBASE, BIOSIS, related articles link in PubMed, and search by hand) met inclusion/exclusion criteria. The electronic search (without related links) yielded only 26% of those articles and conference abstracts that met inclusion criteria. Searches by hand of related articles identified 59% of studies. **CONCLUSION:** Twenty-one instruments were identified as appropriate for clinical use. The instruments vary in symptom content and extent of psychometric validation. Both comprehensive and shorter instruments have been developed, and some instruments are intended for specific symptom assessment or symptoms related to treatment. There is no ideal instrument, and the wide variety of instruments reflects the different settings for symptom assessment. Additional research is necessary.

Kurtz, M. E., J. C. Kurtz, et al. (2006). "Effects of a symptom control intervention on utilization of health care services among cancer patients." *Med Sci Monit* **12**(7): CR319-24.

BACKGROUND: In this study we investigated the effects of a clinical nursing symptom control intervention on utilization of physician, hospital and emergency room services. **MATERIAL/METHODS:** Two hundred twenty-two patients currently undergoing chemotherapy were recruited for the study, and were randomized into either the 10-contact, 20-week experimental intervention group (110), where the intervention focused on assisting the patient in managing their symptoms, or to a conventional care control group (112). **RESULTS:** A random effects regression model revealed that patients in the intervention group reported fewer emergency room visits than patients in

the control group ($p=0.050$). Greater symptom severity and more comorbid conditions were also predictive of more emergency room visits. The intervention was effective in reducing the number of hospital visits for the subgroup of patients who at baseline reported above average symptom severity ($p=0.023$). **CONCLUSIONS:** These findings suggest that a nursing intervention focusing on educating patients regarding specific strategies to be applied for controlling symptoms may be worthwhile, as the patients may regain some control in managing their symptoms and thus ultimately require fewer emergency room services and hospital visits. Such a straightforward approach may empower patients, enhance their quality of life and reduce overall costs of cancer care.

Labori, K. J., M. J. Hjerstad, et al. (2006). "Symptom profiles and palliative care in advanced pancreatic cancer: a prospective study." *Support Care Cancer* **14**(11): 1126-33.

OBJECTIVES: To describe prospectively the prevalence and severity of disease-related symptoms, quality of life (QOL) and need for palliative care in patients with advanced pancreatic cancer. **PATIENTS AND METHODS:** Fifty-one patients treated for advanced pancreatic cancer filled in the Edmonton Symptom Assessment Scale (ESAS) for symptom registration and the EORTC QLQ-C30 and QLQ-PAN26 quality of life questionnaires at first contact (baseline) and the ESAS in the following consultations. Need for palliative interventions were registered. **RESULTS:** Of the 22 women and 29 men (mean age, 62 years), 20 had locally unresectable cancer, 19 had metastatic disease, and 12 had recurrent disease after curative resection. Forty-six patients died during follow-up (median survival, 99 days). At baseline, patients reported significantly impaired QOL on nine of 15 scales/items ($p<0.01$) relative to the general population. Fatigue, loss of appetite, and impaired sense of well-being were the most troublesome symptoms on the ESAS, measured to $4.4(+/-2.8)/5.3(+/-2.3)$, $4.4(+/-3.2)/5.9(+/-2.7)$, and $4.0(+/-2.9)/4.6(+/-2.7)$ (mean \pm SD) at baseline and 8 weeks before death, respectively. Forty-four of the 51 (86%) initial consultations and 107 (58%) of the 185 follow-ups (124 clinical and 61 phone-calls) resulted in palliative care interventions, most frequently changes in opioid or laxative medication and dietary advice. **CONCLUSIONS:** Patients with advanced pancreatic cancer develop several distressing symptoms. ESAS was useful for assessment of symptom prevalence and intensity and is a clinically adequate method for symptom control. A multidisciplinary approach is necessary for the best

palliation of symptoms at the time of diagnosis and during follow-up.

Ladas, E. J., J. Post-White, et al. (2006). "Evidence for symptom management in the child with cancer." *J Pediatr Hematol Oncol* **28**(9): 601-15.

The use of complementary/alternative medicine (CAM) has been well documented among children with cancer. This report summarizes the research evidence on the role of CAM therapies for prevention and treatment of the most commonly reported cancer-related symptoms and late effects among children with cancer. Small clinical trials document evidence of effectiveness for select therapies, such as acupuncture or ginger for nausea and vomiting, TRAUMEEL S for mucositis, and hypnosis and imagery for pain and anxiety. Several relatively small clinical trials of varying quality have been conducted on these CAM therapies in children with cancer. Some herbs have demonstrated efficacy in adults, but few studies of herbs have been conducted in children. Larger randomized clinical trials are warranted for each of these promising therapies. Until the evidence is more conclusive, the providers' role is to assess and document the child's use of CAM, critically evaluate the evidence or lack of evidence, balance the potential risks with possible benefits, and assist the family in their choices and decisions regarding use of CAM for their child with cancer.

Lasheen, W., D. Walsh, et al. (2009). "Symptom variability during repeated measurement among hospice patients with advanced cancer." *Am J Hosp Palliat Care* **26**(5): 368-75.

AIM: In this prospective study, we explored symptom variability in patients with cancer during repeated measurements. METHODS: Patients with cancer admitted to an inpatient hospice completed a daily questionnaire throughout their admission. The questionnaire consisted of 5 visual analogue scales (VAS) for anxiety, depression, nausea, pain, and sedation and 3 verbal rating scales (VRS) for depression, pain, and vomiting. Data from those who completed 5 consecutive days were used for the primary analysis. We used all available data points to compare VAS and VRS. An index was developed to assess for daily symptom variability. RESULTS/DISCUSSION: A total of 125 hospice inpatients were enrolled; 46 (38%) completed 3 consecutive daily questionnaires and 30 (24%), 5 days. We found (1) a statistically significant decrease in severity of symptoms present on admission, (2) new symptoms developed, (3) consequently overall symptom prevalence on days 1 and 5 appeared unchanged, (4) high daily symptom variability as

demonstrated by the variability index and also changing daily symptom interrelationships, (5) demographic characteristics influenced symptom patterns on admission and subsequently, (6) severe pain predicted more frequent and severe symptom burden only on admission, (7) severe depression predicted more frequent and severe symptom burden on admission and thereafter, (8) VAS scores for depression and pain did not correspond with discrete VRS categories (mild, moderate, severe). CONCLUSIONS: (1) Symptom studies in advanced disease while difficult to conduct yield valuable information, (2) symptom relationships changed daily; strict timing of data collection is crucial for data analysis, (3) symptom monitoring following admission is an overlooked measure of risk assessment, (4) symptom prevalence studies alone for treatment follow-up may be misleading, (5) depression is an important predictor of symptoms and need to be more aggressively assessed and treated, (6) demographic characteristics may help identify symptom patterns and better direct treatment, (7) VRS rather than VAS was more reliable for assessing symptoms in hospice cancer patients.

Leak, A., J. Hu, et al. (2008). "Symptom distress, spirituality, and quality of life in African American breast cancer survivors." *Cancer Nurs* **31**(1): E15-21.

This study examined the relationships among the demographic characteristics, symptom distress, spirituality, and quality of life (QOL) of African American breast cancer survivors. A convenience sample of 30 survivors with a mean age of 56 years and a mean survival of 6 years was recruited from African American breast cancer support groups and churches in the Southeastern United States. Data were collected through face-to-face interviews using a demographic questionnaire, the Quality of Life Index-Cancer Version, the Symptom Distress Scale, and the Spiritual Perspective Scale. Statistically significant relationships were found between symptoms and QOL ($r = -0.62$, $P < .05$) and between spirituality and QOL ($r = 0.70$, $P < .05$). No statistically significant relationships were found between age at diagnosis, income, or education and QOL. This research suggests that symptoms and spirituality are associated with QOL. Culturally appropriate care should be provided to these women to reduce health disparities and to improve their QOL.

Lee, E. H. (2005). "Relationships of mood disturbance, symptom experience, and attentional function in women with breast cancer based upon the theory of unpleasant symptoms." *Taehan Kanho Hakhoe Chi* **35**(4): 728-36.

PURPOSE: The purpose of this study was to identify direct, mediating, and moderating relationships of mood disturbance, symptom experience, and attentional function in Korean women with breast cancer based upon a middle-range theory of unpleasant symptoms. **METHODS:** This study used a cross-sectional, correlational design. A convenience sample of 125 women receiving chemotherapy for breast cancer was recruited from a university hospital in South Korea. The women completed questionnaires on mood disturbance, symptom experience, and attentional function using the Linear Analogue Self-Assessment Scale, the Symptom Experience Scale, and the Attentional Function Index, respectively. **RESULTS:** Each mood disturbance and symptom experience showed a significant relationship with attentional function. Symptom experience did not act as a mediator between mood disturbance and attentional function, but it did act as a moderator: patients with a higher level of mood disturbance exhibited a lower level of attentional function when their symptoms were at the level of medium, but not when their symptoms were either high or low. **CONCLUSION:** This suggests that clinical interventions for attenuating the influence of mood disturbance on attentional function may be effective only in women experiencing medium level of symptoms.

Lee, E. H., B. Yae Chung, et al. (2004). "Relationships of mood disturbance and social support to symptom experience in Korean women with breast cancer." *J Pain Symptom Manage* 27(5): 425-33.

The purpose of this study was to identify how mood disturbance and social support were related to the symptoms experienced by Korean women with breast cancer. A cross-sectional, correlational design was used for the study. A convenience sample of 134 Korean women receiving chemotherapy for breast cancer was recruited. The participants completed questionnaires on symptom experience using the Symptom Experience Scale, mood disturbance using the Linear Analogue Self-Assessment Scale, and social support using the Social Support Scale. Mood disturbance and social support had a significant interaction effect on symptom experience. A higher level of mood disturbance led to a higher level of symptoms when the level of social support was average or low, which implies that clinical interventions for attenuating the impact of mood disturbance on symptom experience might be effective only for women perceiving average or low levels of social support.

Lehrer, S., J. Cesaretti, et al. (2006). "Urinary symptom flare after brachytherapy for prostate cancer

is associated with erectile dysfunction and more urinary symptoms before implantation." *BJU Int* 98(5): 979-81.

OBJECTIVE: To examine the relationship of 'symptom flare' with sexual function and lower urinary tract symptoms (LUTS) before brachytherapy, as we noted that after brachytherapy for prostate cancer, some patients had recurrent LUTS after an asymptomatic period; this secondary exacerbation of symptoms ('symptom flare') occurred at approximately 2 years after implantation and was transient in most patients. **PATIENTS AND METHODS:** In all, 854 patients with organ-confined prostate carcinoma had transrectal ultrasonography-guided transperineal 125I interstitial brachytherapy of the prostate gland between June 1991 and September 2002, and were considered candidates for this study. Detailed information on urinary function was self-administered and prospectively collected before treatment and at intervals using the International Prostate Symptom Score (IPSS). Sexual function was evaluated with the Sexual Health Inventory for Men (SHIM), a five-question, self-administered diagnostic test that can help to indicate the presence or absence of erectile dysfunction (ED). We used previously established criteria to estimate the risk of prostate-specific antigen (PSA) failure by dividing the men into three risk groups, i.e. low-risk, with a PSA level of ≤ 10 ng/mL, stage \leq T2a, Gleason ≤ 6 ; medium-risk, with a PSA level of ≤ 15 ng/mL, Gleason 7 or stage T2b; and high-risk, with a PSA level of > 15 ng/mL, stage $>$ T2b, or Gleason ≥ 8 . **RESULTS:** There was a significant association of flare with ED; men with flare reported significantly more ED than men without ($P = 0.020$). Men with high-risk disease reported more ED because they received more intensive treatment (hormones and increased radiation dose) than men with medium- or low-risk disease. To correct for this confounding factor, multivariate linear regression was used; the regression was significant overall ($P < 0.001$), and the effects of risk group ($P < 0.001$) and flare ($P < 0.026$) on SHIM score were significant and independent of each other. Flare was also significantly associated with a higher pre-implant IPSS; the probability of flare was 62% for a pre-implant IPSS of zero, to 94% for an IPSS of 30. **CONCLUSIONS:** Radiation reaction and radiation sensitivity contribute to ED and greater LUTS in men who have had brachytherapy for prostate cancer. This contribution is evident, e.g. in men with ataxia-telangiectasia (ATM) gene mutations. Sequence variants in the ATM gene, particularly those that encode for an amino-acid substitution, are associated with adverse radiotherapy responses among patients treated with 125I prostate brachytherapy. Our finding of the association of urinary symptom flare

with ED suggests it would be worthwhile to determine whether sildenafil is as effective in men with flare, and if not, whether higher sildenafil doses would be of value. Alternatively, alpha1-selective adrenoceptor-blocking agents, e.g. terazosin, combined with sildenafil, might be of benefit. Also, patients with a high IPSS before brachytherapy can be warned that they have a greater risk of flare and ED.

Lin, C. C., A. P. Chang, et al. (2007). "Taiwanese version of the M. D. Anderson symptom inventory: symptom assessment in cancer patients." J Pain Symptom Manage **33**(2): 180-8.

The purpose of this study was to validate the Taiwanese version of the M. D. Anderson Symptom Inventory (MDASI-T) in a sample of 556 Taiwanese patients with multiple diagnoses of cancer. The internal consistency Cronbach alpha was 0.89 for symptom severity items and 0.94 for interference items. The test-retest reliability was 0.97 for the severity composite score and 0.96 for the interference composite score over a 3-day interval in a sample of 12 patients. Construct validity was established by factor analysis, which revealed a two-factor structure. Concurrent validity was examined by correlating the MDASI-T scores and scores of the Medical Outcome Study 36-Item Short-Form Health Survey. Known-group validity was established by comparing MDASI-T scores between patients having low functional status and those having high functional status (Karnofsky Performance Status scores ≤ 50 or > 50 , respectively) and between inpatients and outpatients. The MDASI-T's sensitivity (its ability to detect small differences in reporting variations) was examined by comparing the MDASI-T composite symptom scores and composite interference scores before, during, and one week after treatment in a sample of 20 breast cancer patients receiving chemotherapy. The MDASI-T is a reliable, valid, and sensitive instrument for measuring the severity and interference with daily life of cancer-related symptoms among Taiwanese cancer patients.

Liu, L., L. Fiorentino, et al. (2009). "Pre-treatment symptom cluster in breast cancer patients is associated with worse sleep, fatigue and depression during chemotherapy." Psychooncology **18**(2): 187-94.

OBJECTIVE: The concept of symptom clusters is relatively new in cancer patients' symptom management. This study, which spanned four cycles of chemotherapy, combined three commonly seen pre-treatment symptoms in cancer patients (i.e. sleep disturbances, fatigue and depression) into one symptom cluster, to explore the associations between pre-treatment cluster categories and longitudinal profiles of these same symptoms during

chemotherapy. **METHODS:** This was a prospective study. Seventy-six women with newly diagnosed stage I-III breast cancer, scheduled to receive at least four cycles of adjuvant or neoadjuvant anthracycline-based chemotherapy participated. Data were collected at seven time points before and during treatment. Sleep quality was measured with the Pittsburgh Sleep Quality Index. Fatigue was measured with the Multidimensional Fatigue Symptom Inventory--Short Form. Depressive symptoms were measured with the Center of Epidemiological Studies--Depression. Patients were divided into three groups based on the number of symptoms they experienced before the start of chemotherapy (i.e. no symptoms, 1-2 symptoms or all three symptoms) and a symptom cluster index (SCI) was computed. **RESULTS:** All women reported worse sleep, more fatigue and more depressive symptoms during treatment compared with baseline (all p 's < 0.01); however, those women with a higher SCI (i.e. more symptoms pre-treatment) continued to experience worse symptoms during treatment compared with those who began with fewer symptoms (all p 's < 0.01). **CONCLUSIONS:** A higher clinically relevant-based pre-treatment symptom cluster was associated with more sleep disturbances, greater fatigue and more depressive symptoms during chemotherapy. Specific interventions for these pre-treatment symptoms may improve the frequency and severity of these same symptoms during chemotherapy, when they are most severe and most disruptive to quality of life.

Lobchuk, M. M., L. F. Degner, et al. (2006). "Promoting enhanced patient and family caregiver congruence on lung cancer symptom experiences." Oncol Nurs Forum **33**(2): 273-82.

PURPOSE/OBJECTIVES: To test the effects of different perspective-taking instructional sets, gender, caregivers' personal histories with cancer, and caregiving relationship factors on family caregiver and patient perceptual agreement of symptom experiences of patients with lung cancer. **DESIGN:** Counterbalanced. **SETTING:** Thoracic oncology outpatient clinical setting in Canada. **SAMPLE:** 98 dyads consisting of patients with lung cancer and their family caregivers. **METHODS:** Data were collected on a one-time basis by employing an abbreviated version of the Memorial Symptom Assessment Scale targeting lack of energy and worrying. Caregivers were randomized to one of six counterbalanced conditions of perspective-taking instructions. **MAIN RESEARCH VARIABLES:** Caregiver discrepancy scores, instructional sets (i.e., neutral, self-report, and imagine-self and imagine-patient perspective-taking), order effects, gender, caregivers' personal history with cancer, and caregiving relationship factors.

FINDINGS: No order effects were found for the instructional sets. Instructions to imagine the patient's perspective over imagining how the caregiver would feel if he or she had cancer were most effective in enhancing the caregiver's ability to estimate the patient's lack of energy and worrying. Gender had no significant effects. The amount of patient-caregiver communication had a positive impact on the accuracy of caregivers' perspectives. **CONCLUSIONS:** The patient-oriented instructions had a limited impact on enhancing patient-caregiver congruence on patient symptoms. This likely is related to the study's convenience sample of caregivers who appear to naturally engage in empathic processes of patient-oriented perspective-taking when they assessed and reported on patient symptom conditions. **IMPLICATIONS FOR NURSING:** Further exploratory work should identify interpersonal conditions that negatively hamper the effects of caregiver perspective-taking on their reasonable understanding of patient symptoms.

Loprinzi, C. L., S. L. Wolf, et al. (2008). "Symptom management in premenopausal patients with breast cancer." *Lancet Oncol* 9(10): 993-1001.

Women with breast cancer have many adverse symptoms, of which some are specific to premenopausal patients. Management of these common symptoms include non-hormonal drugs, such as antidepressants and antiseizure compounds to alleviate hot flashes. Non-oestrogenic vaginal lubricants seem to moderately decrease occurrence of vaginal dryness and dyspareunia. Transdermal testosterone alone has not been shown to improve libido in these women. Options for fertility preservation include cryopreservation of embryos or oocytes before chemotherapy. Exercise is the one evidenced-based intervention shown to positively affect cancer-related fatigue. However, effective prevention and treatments for peripheral neuropathy and paclitaxel acute pain syndrome remain elusive. Weight-bearing exercise helps to maintain bone strength with adequate intake of calcium and vitamin D. Use of bisphosphonates in women taking aromatase inhibitors (combined with ovarian suppression in premenopausal women) to prevent bone fractures has not been substantiated, although it should be considered in women with osteoporosis. No specific drug has been shown to prevent radiation-induced dermatitis alone. Although some effective treatments can counteract symptoms related to cancer or treatments, research is needed to expand evidence-based care in premenopausal survivors of breast cancer.

Lovgren, M., H. Levealahti, et al. (2008). "Time spans from first symptom to treatment in patients with lung cancer--the influence of symptoms and demographic characteristics." *Acta Oncol* 47(3): 397-405.

BACKGROUND: Cancer stage at diagnosis is the most important prognostic factor for lung cancer (LC), but most patients are diagnosed with advanced disease with many and intense symptoms. This study explores relationships between LC patients' first symptoms, symptoms triggering health care system (HCS) contact, demographic/clinical characteristics, and time spans in the care trajectory from first symptom(s) to treatment start. **MATERIALS AND METHODS:** Medical records were examined from all 314 patients diagnosed with primary LC in 2003 at a Department of Respiratory Medicine, in Stockholm Sweden. Descriptive analysis was used to examine symptoms and time spans in the care trajectory. Cox regression analysis was conducted to explore the influence of symptoms and demographic/clinical characteristics on the time spans. **RESULTS:** Tumor-specific symptoms led to HCS visits to a greater extent than did systemic symptoms, despite reports of weight loss, fatigue and appetite loss as common first symptoms. Minor differences between women and men were found regarding specific symptoms. The study confirms that the time spans from first symptoms reported to treatment start are extensive, exceeding Swedish national recommendations. A lump/resistance, neurological symptoms, appetite loss, hemoptysis and non-thoracic related pain were associated with significantly shorter time spans in the care trajectory. People >74 years old risked longer time span from first HCS visit to treatment start. **CONCLUSION:** This study indicates a need for a more efficient LC care trajectory. Elderly patients could be particularly vulnerable for longer time spans.

Lowe, K. A., M. R. Andersen, et al. (2009). "The temporal stability of the Symptom Index among women at high-risk for ovarian cancer." *Gynecol Oncol* 114(2): 225-30.

OBJECTIVE: To evaluate the temporal stability of self-reported symptoms known to be associated with ovarian cancer. **METHODS:** This report is a longitudinal analysis of symptom reporting from 123 women who participated in the Seattle-based Ovarian Cancer Early Detection Study (OCEDS). The OCEDS population includes women at increased risk of ovarian cancer based on a family history of cancer or a BRCA I/II mutation. Data on symptoms were collected at two time points using a Symptoms Index that included abdominal pain, pelvic pain, feeling full quickly, inability to eat normally, abdominal bloating, and increased abdominal size. **RESULTS:** There was a median of 101 days between

the two time points, with a range of 72-332 days. The median age of the women was 51, with a range of 32-79 years. Abdominal bloating was the most commonly reported symptom at both time points. The symptom least commonly reported at the two time points was inability to eat normally. The Symptoms Index was negative at both time points for 86% of all women and positive at both time points for 2% of all women. There were no statistically significant patterns of change for symptom reporting between time points. **CONCLUSIONS:** The Symptoms Index and women's report of abdominal pain, pelvic pain, feeling full quickly, unable to eat normally, abdominal bloating, increased abdominal size were stable between two time points in this sample. These findings provide evidence that longitudinal measurements of symptoms reporting by women in a screening study are likely to be reliable.

Luo, X., J. C. Cappelleri, et al. (2009). "Using the Rasch model to validate and enhance the interpretation of the Functional Assessment of Cancer Therapy-Kidney Symptom Index--Disease-Related Symptoms scale." *Value Health* **12**(4): 580-6.

OBJECTIVES: The Functional Assessment of Cancer Therapy-Kidney Symptom Index-Disease-Related Symptoms (FKSI-DRS) was developed to assess patients' kidney-cancer-related symptoms. The Rasch rating scale, a one-parameter logistic item response model, may enhance FKSI-DRS interpretation and validate its measurement properties. **METHODS:** We applied the Rasch model to FKSI-DRS data from a randomized phase 3 trial in which first-line sunitinib therapy showed superiority to interferon-alfa in patients with metastatic renal cell carcinoma. Of 750 enrolled patients, 668 patients completed the questionnaire on cycle 1, day 28 and were evaluated in the current study. The nine FKSI-DRS items were analyzed to enhance interpretation of the summary score by using an item characteristic curve that related score to probability of reporting specific symptoms. **RESULTS:** The Rasch model fitted the FKSI-DRS well: 8 of 9 items had acceptable infit and outfit statistics (<1.5 , >0.5); item difficulty spanned a wide range (-3.23 to 1.64 logits); and the five response categories performed adequately. The item characteristic curve offered enhanced interpretation of FKSI-DRS: For example, an FKSI-DRS score of 27 (mean baseline score for total sample) indicated a 47% chance of reporting "no" to "lack of energy," although a two-point difference between sunitinib and interferon-alfa, averaged across all assessments (29 vs. 27), corresponded to sunitinib achieving a 28% increase (13% absolute difference) in the probability of reporting "no" to "lack of energy" (60% vs. 47%). **CONCLUSIONS:** Data suggest that

the FKSI-DRS is an adequate measure of symptom status in patients with metastatic renal cell carcinoma. The Rasch model supports its validation and enhances its interpretation.

Maliski, S. L., L. Kwan, et al. (2008). "Symptom clusters related to treatment for prostate cancer." *Oncol Nurs Forum* **35**(5): 786-93.

PURPOSE/OBJECTIVES: To identify symptom clusters that include urinary and erectile dysfunction among men treated for prostate cancer. **DESIGN:** Secondary data analysis. **SETTING:** University-affiliated urology clinic. **SAMPLE:** Data collected on 402 men for a longitudinal prostate cancer quality-of-life study. **METHODS:** Data were collected from an eight-month time point. Four analytic approaches were applied to determine whether consistent clusters of symptoms were identifiable. **MAIN RESEARCH VARIABLES:** Pain, fatigue, emotional distress, and urinary, sexual, and bowel dysfunction. **FINDINGS:** Thirty-three percent of patients reported scores on three or more quality-of-life measures falling in the lowest quartile for that measure. Although composition of the clusters was not consistent, poor mental health or poor energy was a component of any cluster made up of three or more symptoms. **CONCLUSIONS:** Using a four-way analytic approach enabled the authors to explore how symptom clusters measuring general and disease-specific quality of life occurred in patients who have been treated for prostate cancer. When clusters occur, fatigue and emotional distress often are included. **IMPLICATIONS FOR NURSING:** Fatigue and emotional distress may be seen together or in combination with prostate cancer-specific symptoms. Nurses should be more alert to the possibility of additional treatment-related symptoms when fatigue or emotional distress is present.

Mallick, I., S. C. Sharma, et al. (2007). "Endobronchial brachytherapy for symptom palliation in non-small cell lung cancer--analysis of symptom response, endoscopic improvement and quality of life." *Lung Cancer* **55**(3): 313-8.

AIMS: Endobronchial brachytherapy (EBBT) is a useful modality for the palliation of endobronchial symptoms in advanced non-small cell lung cancer (NSCLC). We report our experience with a special emphasis on duration of symptom palliation and the impact on quality of life (QOL). **MATERIALS AND METHODS:** The records of 95 previously untreated patients with locally advanced NSCLC were treated with palliative radiation using EBBT with or without palliative external radiation (XRT) were analysed. Eighty patients received EBBT and palliative XRT. EBBT was delivered in two

sessions of EBBT 8Gy each or a single session of 10Gy. Fifteen patients received EBBT alone to 15Gy in a single session. Symptomatic response rates, duration of symptom palliation, obstruction scores and complications were assessed and compared. Quality of life outcomes, measured using the EORTC QLQ C30 and LC13 questionnaires, were analysed. RESULTS: The overall symptomatic response rates were 93% for dyspnea, 81% for cough, 97% for haemoptysis and 91% for obstructive pneumonia. The median time to symptom relapse was 4-8 months for all symptoms, and the median time to symptom progression was 6-11 months. Quality of life showed significant improvement in symptom scores, functional scales and overall QOL. Complication rates were low. Only one patient died of fatal haemoptysis. CONCLUSION: EBBT is thus a safe and effective palliative tool in advanced non-small cell lung cancer, with a relatively long duration of symptom palliation and a considerable improvement in the quality of life. There is significant reduction of endobronchial obstruction.

Manning-Walsh, J. (2005). "Social support as a mediator between symptom distress and quality of life in women with breast cancer." J Obstet Gynecol Neonatal Nurs **34**(4): 482-93.

OBJECTIVE: To examine relationships between symptom distress and quality of life when religious support and personal support were introduced as mediating variables. DESIGN: Cross-sectional, correlational. SETTING: Internet recruitment following university institutional review board approval. PARTICIPANTS: Mailed questionnaires from 100 women with breast cancer, mean age 46, length of time since surgery 1 to 24 months, predominantly White. INSTRUMENTS: Symptom Distress Scale, Religious Support Scale, FACT-B, and Facit-Sp-12. RESULTS: Personal support was positively related to quality of life and partially mediated the effects of symptom distress. Religious support did not mediate symptom distress and was not directly related to quality of life. CONCLUSIONS: Social support from family members and friends helped to decrease the negative effects of symptoms on quality of life. This study underscores the need to continue to assess for symptom distress and adequacy of personal support throughout the cancer trajectory and to facilitate the garnering of support resources when needed.

Manning-Walsh, J. K. (2005). "Psychospiritual well-being and symptom distress in women with breast cancer." Oncol Nurs Forum **32**(3): 543.

PURPOSE/OBJECTIVES: To examine the relationship between symptom distress and

psychospiritual well-being in women with breast cancer. DESIGN: Descriptive, cross-sectional, correlational study. SETTING: Secondary analysis of data collected in 2000 from the Breast Cancer Support Web site at <http://pages.prodigy.net/replyasap/bc>. SAMPLE: 100 women were invited to participate in the study after posting an entry in the Web site guest book. Most had stage I or II breast cancer, were nearly 46 years old, and were 10.25 months postdiagnosis. METHODS: Mailed questionnaires. Women were required to meet the following inclusion criteria: a confirmed breast cancer diagnosis, first cancer experience, fewer than two years postsurgery for breast cancer, 18 years of age or older, and the ability to read and write in English. Symptom distress was measured using the Symptom Distress Scale. Psychospiritual well-being was measured by combining scores from the psychological subscale of the breast-cancer specific version of the Functional Assessment of Cancer Therapy Scale and the Functional Assessment of Chronic Illness Therapy (Spiritual) Measurement System 12 for a composite score. MAIN RESEARCH VARIABLES: Symptom distress, psychospiritual well-being. FINDINGS: Symptom distress and psychospiritual well-being were inversely related. No relationship was found between age and symptom distress; however, age was inversely related to psychospiritual well-being. Age and symptom distress accounted for 23.1% of the variance in psychospiritual well-being. CONCLUSIONS: Participants experienced a small amount of symptom distress, which was inversely related to psychospiritual well-being. Although their symptom distress was similar to other studies, patients in this study reported lower psychospiritual well-being than participants in other studies. IMPLICATIONS FOR NURSING: Psychospiritual well-being is an important concept for nurses seeking a holistic approach to practice because it connects the mind and spirit with the body.

Mansky, P. J. and D. B. Wallerstedt (2006). "Complementary medicine in palliative care and cancer symptom management." Cancer J **12**(5): 425-31.

Complementary and alternative medicine (CAM) use among cancer patients varies according to geographical area, gender, and disease diagnosis. The prevalence of CAM use among cancer patients in the United States has been estimated to be between 7% and 54%. Most cancer patients use CAM with the hope of boosting the immune system, relieving pain, and controlling side effects related to disease or treatment. Only a minority of patients include CAM in the treatment plan with curative intent. This review article focuses on practices belonging to the CAM

domains of mind-body medicine, CAM botanicals, manipulative practices, and energy medicine, because they are widely used as complementary approaches to palliative cancer care and cancer symptom management. In the area of cancer symptom management, auricular acupuncture, therapeutic touch, and hypnosis may help to manage cancer pain. Music therapy, massage, and hypnosis may have an effect on anxiety, and both acupuncture and massage may have a therapeutic role in cancer fatigue. Acupuncture and selected botanicals may reduce chemotherapy-induced nausea and emesis, and hypnosis and guided imagery may be beneficial in anticipatory nausea and vomiting. Transcendental meditation and the mindfulness-based stress reduction can play a role in the management of depressed mood and anxiety. Black cohosh and phytoestrogen-rich foods may reduce vasomotor symptoms in postmenopausal women. Most CAM approaches to the treatment of cancer are safe when used by a CAM practitioner experienced in the treatment of cancer patients. The potential for many commonly used botanical to interact with prescription drugs continues to be a concern. Botanicals should be used with caution by cancer patients and only under the guidance of an oncologist knowledgeable in their use.

Mao, J. J., K. Armstrong, et al. (2007). "Symptom burden among cancer survivors: impact of age and comorbidity." *J Am Board Fam Med* **20**(5): 434-43.

BACKGROUND: Previous research among specific cancer populations has shown high but variable symptom burden; however, very little is known about its extent and pattern among the entire population of US cancer survivors, which is more clinically relevant to primary care physicians. **METHODS:** To determine the prevalence of ongoing symptom burden among cancer survivors and compare it with the general population without cancer, we analyzed data from the 2002 National Health Interview Survey, which included 1,904 cancer survivors and 29,092 controls. Main outcome measures included self-reported ongoing pain, psychological distress, and insomnia. Multivariate logistic regression models were used to adjust for confounders and test for interactions. **RESULTS:** The rates of ongoing pain, psychological distress, and insomnia among cancer survivors were 34%, 26%, and 30%, respectively, and were significantly higher (all $P < .001$) than controls without a history of cancer (18%, 16%, and 17%). Compared with controls in the same age groups, younger survivors (younger than 50) were much more likely to report ongoing symptoms than older survivors (older than 64); adjusted odds ratios were 2.96 and 1.36 for pain in the respective age groups ($P < .001$). Comorbidities also interact with

cancer status and contribute to a marked increase in reports of ongoing symptom burden among cancer survivors, with a greater number of comorbidities leading to greater degree of symptom burden in a dose-dependent manner ($P < .001$). **CONCLUSIONS:** The symptom burden among cancer survivors on a population level is substantial and can be impacted by other comorbidities. Thus, engaging primary care physicians in the design, testing, and implementation of effective interventions is important to reduce the symptom burden among cancer survivors.

Mehling, W. E., B. Jacobs, et al. (2007). "Symptom management with massage and acupuncture in postoperative cancer patients: a randomized controlled trial." *J Pain Symptom Manage* **33**(3): 258-66.

The level of evidence for the use of acupuncture and massage for the management of perioperative symptoms in cancer patients is encouraging but inconclusive. We conducted a randomized, controlled trial assessing the effect of massage and acupuncture added to usual care vs. usual care alone in postoperative cancer patients. Cancer patients undergoing surgery were randomly assigned to receive either massage and acupuncture on postoperative Days 1 and 2 in addition to usual care, or usual care alone, and were followed over three days. Patients' pain, nausea, vomiting, and mood were assessed at four time points. Data on health care utilization were collected. Analyses were done by mixed-effects regression analyses for repeated measures. One hundred fifty of 180 consecutively approached cancer patients were eligible and consented before surgery. Twelve patients rescheduled or declined after surgery, and 138 patients were randomly assigned in a 2:1 scheme to receive massage and acupuncture ($n=93$) or to receive usual care only ($n=45$). Participants in the intervention group experienced a decrease of 1.4 points on a 0-10 pain scale, compared to 0.6 in the control group ($P=0.038$), and a decrease in depressive mood of 0.4 (on a scale of 1-5) compared to +/-0 in the control group ($P=0.003$). Providing massage and acupuncture in addition to usual care resulted in decreased pain and depressive mood among postoperative cancer patients when compared with usual care alone. These findings merit independent confirmation using larger sample sizes and attention control.

Mehnert, A., C. Lehmann, et al. (2007). "Presence of symptom distress and prostate cancer-related anxiety in patients at the beginning of cancer rehabilitation." *Onkologie* **30**(11): 551-6.

BACKGROUND: A growing body of research points towards a substantial number of prostate cancer patients experiencing distress and

anxiety. This study examines the frequency and character of cancer- and treatment-related problems and its association with symptom distress and prostate cancer-related anxiety in patients at the beginning of an oncological rehabilitation program. **PATIENTS AND METHODS:** 197 prostate cancer patients who had undergone prostatectomy (92.5% participation rate) completed the Memorial Anxiety Scale for Prostate Cancer (MAX-PC), the NCCN Distress Thermometer and EORTC QLQ-C30 subscales emotional function and global quality of life. **RESULTS:** 88% of patients report cancer- or treatment-related problems with a mean of 5 problems, and 104 patients (53%) experience distress and/or prostate cancer-related anxiety. The most prevalent symptoms are changes in urination, sexual problems, difficulties getting around, pain, fatigue and sleep problems. Emotional problems such as nervousness, worries, fears and sadness are prevalent in at least 53% of patients. Patients with distress and anxiety are confronted with a higher number and a wider range of problems and experience significantly lower levels of quality of life. **CONCLUSION:** Findings emphasize the role of cancer rehabilitation and underline the importance of psychosocial screening measures and the provision of psychosocial support in prostate cancer patients.

Menczer, J., A. Chetrit, et al. (2009). "The effect of symptom duration in epithelial ovarian cancer on prognostic factors." *Arch Gynecol Obstet* **279**(6): 797-801.

PURPOSE: To assess the association between duration of symptoms and main prognostic factors of invasive epithelial ovarian cancer (EOC). **METHODS:** The data of all histologically confirmed EOC patients diagnosed in Israel during the period 1994-1999 (n = 1,005) were retrieved from discharge summaries and admission records. Of the 371 (36.9%) patients with known presenting symptoms, the durations of 187 (50.4%) were recorded. **RESULTS:** The most common presenting symptoms were abdominal pain (65.2%). The percentage of patients with three or more symptoms increased significantly with stage (P = 0.001). No statistically significant association between duration of symptoms and prognostic factors was found. **CONCLUSION:** Our findings did not show an association between duration of symptoms and prognostic factors in EOC patients and may indicate that prognosis is not a function of delay in diagnosis.

Miaskowski, C., B. E. Aouizerat, et al. (2007). "Conceptual issues in symptom clusters research and their implications for quality-of-life assessment in

patients with cancer." *J Natl Cancer Inst Monogr*(37): 39-46.

The majority of the research on the various aspects of symptom management has focused on individual symptoms. However, patients with cancer often experience multiple symptoms simultaneously as a result of their disease and treatment. In 2001, symptom management researchers began to study the impact of symptom clusters on patient outcomes. Over the past 6 years, a number of conceptual reviews as well as several research studies have been published on symptom clusters in oncology patients. This paper summarizes the conceptual basis for symptom cluster research, describes two conceptual approaches to symptom cluster research, and discusses the implications of symptom clusters for quality-of-life research. The paper concludes with an enumeration of the critical considerations that need to be addressed if this area of scientific inquiry is to move forward.

Miaskowski, C., B. A. Cooper, et al. (2006). "Subgroups of patients with cancer with different symptom experiences and quality-of-life outcomes: a cluster analysis." *Oncol Nurs Forum* **33**(5): E79-89.

PURPOSE/OBJECTIVES: To identify subgroups of outpatients with cancer based on their experiences with the symptoms of fatigue, sleep disturbance, depression, and pain; to explore whether patients in the subgroups differed on selected demographic, disease, and treatment characteristics; and to determine whether patients in the subgroups differed on two important patient outcomes: functional status and quality of life (QOL). **DESIGN:** Descriptive, correlational study. **SETTING:** Four outpatient oncology practices in northern California. **SAMPLE:** 191 outpatients with cancer receiving active treatment. **METHODS:** Patients completed a demographic questionnaire, Karnofsky Performance Status scale, Lee Fatigue Scale, General Sleep Disturbance Scale, Center for Epidemiological Studies Depression Scale, Multidimensional Quality-of-Life Scale Cancer, and a numeric rating scale of worst pain intensity. Medical records were reviewed for disease and treatment information. Cluster analysis was used to identify patient subgroups based on patients symptom experiences. Differences in demographic, disease, and treatment characteristics as well as in outcomes were evaluated using analysis of variance and chi square analysis. **MAIN RESEARCH VARIABLES:** Subgroup membership, fatigue, sleep disturbance, depression, pain, functional status, and QOL. **FINDINGS:** Four relatively distinct patient subgroups were identified based on patients experiences with four highly prevalent and related symptoms. **CONCLUSIONS:** The subgroup of patients who reported low levels of all four symptoms

reported the best functional status and QOL. IMPLICATIONS FOR NURSING: The findings from this study need to be replicated before definitive clinical practice recommendations can be made. Until that time, clinicians need to assess patients for the occurrence of multiple symptoms that may place them at increased risk for poorer outcomes.

Miner, T. J., M. F. Brennan, et al. (2004). "A prospective, symptom related, outcomes analysis of 1022 palliative procedures for advanced cancer." *Ann Surg* **240**(4): 719-26; discussion 726-7.

OBJECTIVE: To prospectively evaluate surgical procedures performed with palliative intent. SUMMARY BACKGROUND DATA: There is a paucity of outcomes data necessary to allow sound surgical decision-making and informed consent for palliative procedures. METHODS: Procedures to palliate symptoms of advanced cancer were identified prospectively from all operations performed. Patients were observed for >90 days or until death. RESULTS: There were 1022 palliative procedures performed in 823 patients from July 2002 to June 2003. Operative (713/1022) or endoscopic (309/1022) procedures were performed for gastrointestinal obstruction (34%), neurologic symptoms (23%), pain (12%), dyspnea (9%), jaundice (7%) or other symptoms (15%). Symptom improvement or resolution within 30 days was achieved in 80% (659/823). Median duration of symptom control was 135 days. Recurrence of the primary symptom occurred in 25% (165/659) while treatment of debilitating additional symptoms was required in 29% (191/659). Palliative procedures were associated with 30-day postoperative morbidity (29%) and mortality (11%). A major postoperative complication reduced the probability of symptom improvement to 17%. Median survival was 194 days from the time of the palliative procedure and was adversely associated with poor performance status (ECOG > or = 2 [P < 0.001] or NCI fatigue score of > or =1 [P < 0.001]), poor nutrition (albumin <3.5 [P = 0.005] or significant weight loss [P = 0.003]), and no previous cancer therapy (P = 0.002). CONCLUSIONS: In carefully selected patients, relief of symptoms following palliative procedures can be expected, but new or recurrent symptoms limit durability. Potential benefits are minimized by postoperative complications and are less predictable for patients with poor performance status, malnutrition and no prior cancer therapy.

Molassiotis, A., S. Brearley, et al. (2009). "Effectiveness of a home care nursing program in the symptom management of patients with colorectal and breast cancer receiving oral chemotherapy: a

randomized, controlled trial." *J Clin Oncol* **27**(36): 6191-8.

PURPOSE: To assess the effectiveness of a symptom-focused home care program in patients with cancer who were receiving oral chemotherapy in relation to toxicity levels, anxiety, depression, quality of life, and service utilization. PATIENTS AND METHODS: A randomized, controlled trial was carried out with 164 patients with a diagnosis of colorectal (n = 110) and breast (n = 54) cancers who were receiving oral capecitabine. Patients were randomly assigned to receive either a home care program by a nurse or standard care for 18 weeks (ie, six cycles of chemotherapy). Toxicity assessments were carried out weekly for the duration of the patients' participation in the trial, and validated self-report tools assessed anxiety, depression, and quality of life. RESULTS: Significant improvements were observed in the home care group in relation to the symptoms of oral mucositis, diarrhea, constipation, nausea, pain, fatigue (first four cycles), and insomnia (all P < .05). This improvement was most significant during the initial two cycles. Unplanned service utilization, particularly the number of inpatient days (57 v 167 days; P = .02), also was lower in the home care group. CONCLUSION: A symptom-focused home care program was able to assist patients to manage their treatment adverse effects more effectively than standard care. It is imperative that patients receiving oral chemotherapy are supported with such programs, particularly during initial treatment cycles, to improve their treatment and symptom experiences.

Murakami, N., J. Itami, et al. (2008). "Urethral dose and increment of international prostate symptom score (IPSS) in transperineal permanent interstitial implant (TPI) of prostate cancer." *Strahlenther Onkol* **184**(10): 515-9.

PURPOSE: To find the factors which influence the acute increment of International Prostate Symptom Score (IPSS) after transperineal permanent interstitial implant (TPI) using (125)I seeds. PATIENTS AND METHODS: From April 2004 through September 2006, 104 patients with nonmetastatic prostate cancer underwent TPI without external-beam irradiation. Median patient age was 70 years with a median follow-up of 13.0 months. 73 patients (70%) received neoadjuvant hormone therapy. The increment of IPSS was defined as the difference between pre- and postimplant maximal IPSS. Clinical, treatment, and dosimetric parameters evaluated included age, initial prostate-specific antigen, Gleason Score, neoadjuvant hormone therapy, initial IPSS, post-TPI prostatic volume, number of implanted seeds, prostate V(100), V(150),

D(90), urethral D(max), and urethral D(90). In order to further evaluate detailed urethral doses, the base and apical urethra were defined and the dosimetric parameters were calculated. RESULTS: The IPSS peaked 3 months after TPI and returned to baseline at 12-15 months. Multivariate analysis demonstrated a statistically significant correlation of post-TPI prostatic volume, number of implanted seeds, and the dosimetric parameters of the base urethra with IPSS increment. CONCLUSION: The base urethra appears to be susceptible to radiation and the increased dose to this region deteriorates IPSS. It remains unclear whether the base urethral dose relates to the incidence of late urinary morbidities.

Murphy, B. A. (2009). "Advances in quality of life and symptom management for head and neck cancer patients." *Curr Opin Oncol* **21**(3): 242-7.

PURPOSE OF REVIEW: Head and neck cancer and its therapy are associated with marked symptom burden, functional impairment and decreased quality of life. This review will encompass the recent studies addressing supportive care issues facing head and neck cancer patients. RECENT FINDINGS: Although it has long been recognized that head and neck cancer therapy results in significant acute toxicity, it is now becoming recognized that the late effects of therapy are equally problematic. In addition, it is clear that many acute and late effects of therapy, including oral health issues, nutritional deficiencies and the role of physical therapy and rehabilitation, are under recognized and under studied. Although supporting data are scant, allied health professions play a critical role in managing acute and late effects of therapy. SUMMARY: Healthcare providers must take an active role in the evaluation and management of the acute and late effects of therapy. Referral for appropriate supportive care and rehabilitative services is critical in order to minimize the acute and late effects of therapy and to maximize long-term function.

Mystakidou, K., C. Cleeland, et al. (2004). "Greek M.D. Anderson Symptom Inventory: validation and utility in cancer patients." *Oncology* **67**(3-4): 203-10.

OBJECTIVE: The M.D. Anderson Symptom Inventory (MDASI) is a brief assessment of the severity and impact of cancer-related symptoms. The purpose of this study was the translation and validation of the questionnaire in Greek (G-MDASI). METHODS: The translation and validation of the assessment took place at a Pain Relief and Palliative Care Unit. The final validation sample included 150 cancer patients (61 males, 89 females, age range 31-88 years, mean age 63.32). The patients completed the

questionnaires at the outpatient clinic. Assessing the validity and reliability constituted the actual validation of the G-MDASI. RESULTS: The item 'diarrhea' had a score of 0 in 139 patients and, thus was omitted from the 'core' list. Consequently, the core questionnaire consisted of 14 items. Factor analysis resulted in a 3-factor model, in both validation and cross-validation samples. The examination of the sensitivity of the MDASI revealed that there were differences between patients with poor-to-good performance status but no differences were found between patients in different treatment groups. CONCLUSIONS: The results showed that the G-MDASI is a reliable and valid measure in Greek cancer patients. It has proved to be a comprehensive symptom assessment tool.

Mystakidou, K., E. Parpa, et al. (2009). "How is sleep quality affected by the psychological and symptom distress of advanced cancer patients?" *Palliat Med* **23**(1): 46-53.

The aim of this study was to assess the relationship between sleep quality, pain, psychological distress, cognitive status and post-traumatic experience in advanced cancer patients. Participants were 82 advanced cancer patients referred to a palliative care unit for control of pain and other symptoms. A variety of assessment tools were used to examine the prevalence of sleep disturbance, the severity of pain and depression, hopelessness, cognitive function and quality of life. Using the Pittsburgh Sleep Quality Index (PSQI) 96% of patients were 'poor sleepers'. Statistically significant associations were found between PSQI and the SF-12 (Short Form-12) Quality of Life Instrument (MCS, $P < 0.0005$, PCS, $P < 0.0005$), depression (Greek Depression Inventory) ($P < 0.0005$) and hopelessness (Beck Hopelessness Scale) ($P = 0.003$). Strong associations were also found between PSQI and IES-R (Impact of Event Scale-Revised) ($P = 0.004$). The strongest predictors of poor sleep quality in this model were MCS ($P < 0.0005$), PCS ($P < 0.0005$) and IES-R ($P = 0.010$). Post-traumatic experience and quality of life seemed to be the strongest predictors of sleep quality in a sample of advanced cancer patients referred for palliative care.

Natale, R. B. (2004). "Epidermal growth factor receptor-targeted therapy with ZD1839: symptom improvement in non-small-cell lung cancer." *Int J Radiat Oncol Biol Phys* **59**(2 Suppl): 39-43.

Non-small-cell lung cancer (NSCLC) is a common and frequently incurable disease. Patients with advanced Stage IIIB and Stage IV disease, although not candidates for curative resection, can benefit from receiving treatment (chemotherapy and

radiation therapy) that prolongs survival, alleviates symptoms, and/or reduces complications. However, these therapies are often associated with significant adverse events. Treatments have recently been developed to selectively target cancer-specific molecules and signaling pathways. By acting preferentially on tumor cells, these drugs leave normal cells relatively undisturbed, thereby limiting toxic effects and preserving the patient's quality of life. ZD1839 is one of a new class of targeted anticancer agents known as tyrosine kinase inhibitors that has demonstrated activity in the treatment of NSCLC. In clinical trials, ZD1839 produced responses in patients with relapsed or refractory NSCLC, reduced disease-related symptoms, and was associated with an improvement in quality of life. Results from pivotal trials with single-agent ZD1839 are reviewed in this article, with an emphasis on its effects on quality of life and symptom improvement.

Natale, R. B. (2004). "Inhibition of epidermal growth factor receptor and symptom improvement in advanced non-small cell lung cancer." *Semin Respir Crit Care Med* **25 Suppl 1**: 29-32.

The majority of patients with non-small cell lung cancer (NSCLC) are not candidates for curative resection because of advanced disease at the time of diagnosis. Systemic chemotherapy has been employed with modest success to provide symptom relief and prolonged survival for patients with this incurable disease. Any benefit derived from chemotherapy in this palliative setting must be balanced against the substantial toxicity associated with cytotoxic drugs. A novel approach to anticancer treatment based on specific targeting molecular processes has recently demonstrated efficacy. ZD1839 is a low-molecular-weight molecule that is capable of inhibiting epidermal growth factor receptor (EGFR)-associated tyrosine kinase activity. Consequently, ZD1839 interrupts EGFR-mediated activities such as tumor cellular proliferation, motility, survival, and invasiveness. In vitro and in vivo studies have shown that ZD1839 has activity against NSCLC. The results of ZD1839 in randomized clinical trials of patients with advanced NSCLC are reported in this review. In addition to evaluating response rates and clinical endpoints, these trials prospectively evaluated symptom improvement and quality of life.

Nedstrand, E., Y. Wyon, et al. (2006). "Psychological well-being improves in women with breast cancer after treatment with applied relaxation or electro-acupuncture for vasomotor symptom." *J Psychosom Obstet Gynaecol* **27(4)**: 193-9.

The aim of this study was to evaluate the effect of applied relaxation and electro-acupuncture

(EA) on psychological well-being in breast cancer-treated women with vasomotor symptoms. Thirty-eight breast cancer-treated postmenopausal women with vasomotor symptoms were included in the study. They were randomized to either treatment with electro-acupuncture (EA) (n = 19, three of them with tamoxifen) or applied relaxation (AR) (n = 19, five of them with tamoxifen) over a 12-week study period with six months follow-up. Vasomotor symptoms were registered daily. A visual analog scale was used to assess climacteric symptom, estimation of general well-being was made using the Symptom Checklist, and mood using the Mood Scale. These were applied during treatment and at follow-up. In total 31 women completed 12 weeks of treatment and six months of follow-up. Hot flushes were reduced by more than 50%. Climacteric symptoms significantly decreased during treatment and remained so six months after treatment in both groups. Psychological well-being significantly improved during therapy and at follow-up visits in both groups. Mood improved significantly in the electro-acupuncture treated group. In conclusion psychological well-being improved in women with breast cancer randomized to treatment with either AR or EA for vasomotor symptoms and we therefore suggest that further studies should be performed in order to evaluate and develop these alternative therapies.

Nunobe, S., M. Sasako, et al. (2007). "Symptom evaluation of long-term postoperative outcomes after pylorus-preserving gastrectomy for early gastric cancer." *Gastric Cancer* **10(3)**: 167-72.

BACKGROUND: Since the early 1990s, pylorus-preserving gastrectomy (PPG) has been used in the treatment of patients with early gastric cancer in order to reduce postprandial symptoms. To date, there have been few reports of long-term symptom evaluation following this procedure. The aim of this study was to evaluate long-term postoperative outcomes after PPG. **METHODS:** Three hundred and ninety-seven patients with early gastric cancer were enrolled in this study: 194 patients who underwent PPG and 203 who underwent distal gastrectomy with Billroth-I reconstruction (DGBI). We compared the symptoms for the two groups in a questionnaire on postoperative functional outcomes, endoscopy findings and the appearance of gallstones after surgery. **RESULTS:** The incidence of symptoms suggesting early dumping syndrome was significantly lower in the PPG group compared with the DGBI group (P < 0.05). The incidences of disturbed bowel habit and frequent flatus were significantly lower in the PPG than in the DGBI group. The average relative body weight (actual BW/ BW immediately before the surgery) was significantly better in the PPG than in

the DGBI group ($P < 0.001$). **CONCLUSION:** The long-term results show that PPG has clear advantages over DGBI in terms of postoperative symptoms and functional outcomes. These results imply that PPG should be the recommended procedure for early gastric cancers located in the middle third of the stomach.

Oh, E. G. (2004). "Symptom experience in Korean adults with lung cancer." *J Pain Symptom Manage* **28**(2): 133-9.

This study aimed to examine how symptoms vary in relation to demographic characteristics (age and sex), stage of disease, histology of lung cancer, and treatment type in Korean adults with lung cancer. Symptoms were measured with the Symptom Distress Scale. A total 106 patients with a mean age of 60.9 (SD = 10.38) years participated. The results indicated that 1) overall symptom distress was more severe (mean 32.74, SD 10.75) compared to the studies reported in Western countries, and 2) among the variables, only the stage of lung cancer showed a significant relationship with total symptom distress ($P < 0.05$). In analyses of the individual symptoms, bowel-related symptoms showed significant relationships with sex, age, and type of treatment. The results highlight the importance of symptom management as well as the need to tailor clinical interventions according to related factors in order to maximize effective symptom management in Korean patients with lung cancer.

Oi-Ling, K., D. T. Man-Wah, et al. (2005). "Symptom distress as rated by advanced cancer patients, caregivers and physicians in the last week of life." *Palliat Med* **19**(3): 228-33.

OBJECTIVES: To study the symptom distress as rated by patients with advanced cancer during their last week of life, and to compare patients' ratings with those perceived by caregivers and physicians. **METHOD:** This was a prospective study on all patients admitted to the Hospice Unit of the Caritas Medical Centre with an estimated life expectancy of two weeks or less from May 2002 to September 2002. A questionnaire with a list of 13 symptoms, including pain, dyspnoea, nausea, vomiting, dry mouth, cough, fatigue, cachexia, anorexia, constipation, diarrhoea, insomnia and haemoptysis, was administered to assess the distress. Distress was rated by a verbal rating scale consisting of five grades (grade 0 to grade 4). Patients, caregivers and physicians completed the questionnaire weekly until the patient died. Only the questionnaires completed in the last week of life were included for analysis. **RESULTS:** Of 82 patients who were recruited in the study, 30 patients were able to

complete the questionnaire within the last week of life. Their median age was 69 years and the gender ratio was 1:1. Lung cancer was the most common primary tumour. Fatigue, cachexia and anorexia caused distress of all grades in nearly all 30 patients and caused significant distress of grade 3 and above in two-thirds of patients. Neither the caregivers nor the physicians gave congruent distress scores for these three symptoms ($\kappa < 0.4$). Caregivers' ratings agreed well with those of patients for five symptoms ($\kappa > 0.4$, $P < 0.005$), including dyspnoea, cough, dry mouth, constipation and insomnia. For physicians, good agreement was found for three symptoms only, including pain, dyspnoea and cough. Moreover, physicians tended to underrate the distress. **CONCLUSION:** Fatigue, cachexia and anorexia were the three most distressful symptoms in the last week of life in this group of patients, but caregivers and physicians failed to rate them in agreement with patients.

Olson, K., L. Hayduk, et al. (2008). "The changing causal foundations of cancer-related symptom clustering during the final month of palliative care: a longitudinal study." *BMC Med Res Methodol* **8**: 36.

BACKGROUND: Symptoms tend to occur in what have been called symptom clusters. Early symptom cluster research was imprecise regarding the causal foundations of the coordinations between specific symptoms, and was silent on whether the relationships between symptoms remained stable over time. This study develops a causal model of the relationships between symptoms in cancer palliative care patients as they approach death, and investigates the changing associations among the symptoms and between those symptoms and well-being. **METHODS:** Complete symptom assessment scores were obtained for 82 individuals from an existing palliative care database. The data included assessments of pain, anxiety, nausea, shortness of breath, drowsiness, loss of appetite, tiredness, depression and well-being, all collected using the Edmonton Symptom Assessment System (ESAS). Relationships between the symptoms and well-being were investigated using a structural equation model. **RESULTS:** The model fit acceptably and explained between 26% and 83% of the variation in appetite, tiredness, depression, and well-being. Drowsiness displayed consistent effects on appetite, tiredness and well-being. In contrast, anxiety's effect on well-being shifted importantly, with a direct effect and an indirect effect through tiredness at one month, being replaced by an effect working exclusively through depression at one week. **CONCLUSION:** Some of the causal forces explaining the variations in, and relationships among, palliative care patients' symptoms changed over the final month of life. This

illustrates how investigating the causal foundations of symptom correlation or clustering can provide more detailed understandings that may contribute to improved control of patient comfort, quality of life, and quality of death.

Olsson, L., L. Bergkvist, et al. (2004). "Symptom duration versus survival in non-emergency colorectal cancer." *Scand J Gastroenterol* **39**(3): 252-8.

BACKGROUND: Morbidity and mortality from colorectal cancer remain as major public health problems. Previous studies have demonstrated a lack of association between symptom duration and stage. Emergency cases are, however, known to present with a more advanced disease stage. This study was set up to define the effect of symptom duration on stage and survival separately in the elective population. **METHODS:** Between 1998 and 1999, 228/235 (97%) eligible patients with recently diagnosed colorectal cancer in Vastmanland County, Sweden were included in the study. A questionnaire was designed to collect information on the nature and date of first symptoms within two weeks' accuracy. Symptom duration could be categorized as more or less than 26 weeks for 164 (70%) patients. Data on type of admittance (elective or emergent), date of surgery, site and stage were retrieved from the surgical records. Survival was checked in November 2003 and Kaplan-Meier survival estimates were calculated. **RESULTS:** Median symptom duration was 17 weeks, 20 in the elective and 13 in the emergency population ($P < 0.01$). In the elective population, median symptom duration for Dukes' A and B cancer was 19 compared with 21 weeks for Dukes' C and D cancer (mean difference in symptom duration 0.04 (95% CI-0.31; 0.23). Symptom duration did not influence overall survival in the non-emergency group (log rank 2.8; $P = 0.09$). **CONCLUSION:** To diminish the impact of colorectal cancer on public health, strategies other than a shortening of symptom duration are needed.

Ostlund, U., A. Wennman-Larsen, et al. (2007). "What symptom and functional dimensions can be predictors for global ratings of overall quality of life in lung cancer patients?" *Support Care Cancer* **15**(10): 1199-205.

PURPOSE: This study explores what dimensions of a health-related quality of life (HRQOL) questionnaire predict global ratings of overall quality of life (QOL) in lung cancer patients in assessments by patients and significant others, respectively. **MATERIAL AND METHODS:** The analyses were based on dyadic assessments from lung cancer patients and their significant others. A subset of scales and items from the Swedish version of the European Organization for Research and Treatment of

Cancer (EORTC) QLQ C30 and the lung-cancer-specific module, LC-13, was selected. Using multiple regression procedures, the relative importance of different symptoms and of functional impairments in predicting overall QOL was examined. **RESULTS:** The multiple regressions revealed that emotional functioning and fatigue were the only significant predictors of overall QOL for both the patients and the significant others' assessments. In addition, physical functioning was found to be another predictor in the significant others' assessments. **CONCLUSION:** The results emphasize that it is essential to consider both emotional functioning and fatigue as important areas for overall QOL in lung cancer patients.

Ott, J. J., A. Ullrich, et al. (2009). "The importance of early symptom recognition in the context of early detection and cancer survival." *Eur J Cancer* **45**(16): 2743-8.

Since there is evidence that stage is an important prognostic factor in cancer, interventions aimed at 'down-staging' are part of a comprehensive cancer control approach. Besides organised screening programmes, raising awareness of detectable signs and symptoms is recommended. A precise definition of early cancer signs and symptoms, however, is lacking and there has also been no systematic review regarding the impact of awareness raising interventions on cancer outcomes. We reviewed the scientific medical literature to assess the consistency and availability of a definition for early cancer symptoms as well as to assess the impact of early cancer diagnosis on survival. Although early diagnosis is an important factor for cancer survival, other considerations such as the cancer profile of a country, the characteristics of cancer types and the availability of devices for diagnosis should be taken into account in promoting early cancer detection. There is a clear need for research to categorize cancer types according to early symptoms in order to increase comparability of studies in this field and to provide guidance for health personnel in primary care settings in low income regions.

Ozlu, T., Y. Bulbul, et al. (2004). "Time course from first symptom to the treatment of lung cancer in the Eastern Black Sea Region of Turkey." *Med Princ Pract* **13**(4): 211-4.

OBJECTIVES: To determine the delay between the onset and the diagnosis and treatment of patients with lung cancer in two cancer centres in the Eastern Black Sea Region of Turkey. **SUBJECTS AND METHODS:** The records of 226 patients (217 males, 9 females) were evaluated retrospectively for the dates noted for the onset of symptoms, first presentation to a physician, histopathological

diagnosis and start of treatment. The median time intervals from the appearance of the first symptom to definitive diagnosis and treatment were calculated. RESULTS: The patients presented to their physicians 30 (range 2-365) days after their complaints began. The time that elapsed between admission and histopathological diagnosis and between the diagnosis and initiation of therapy were 8 (range 1-210) and 17.5 days (range 0-206), respectively. The median time span from presentation to treatment was 30 days (range 1-253). There were no significant time interval differences between onset of symptoms and first presentation and the subsequent diagnostic and therapeutic processes for histopathology, stage of the tumour and treatment procedures ($p > 0.05$). CONCLUSION: Reasons for the delayed treatment of lung cancer patients were late presentation to the physician and the long time interval between tissue diagnosis and treatment. This delay was mostly associated with a large number of patients and delayed appointments for imaging procedures--the result of organisational problems within the health services of Turkey.

Paice, J. A. (2004). "Assessment of symptom clusters in people with cancer." J Natl Cancer Inst Monogr(32): 98-102.

The control, and ideally prevention, of symptoms such as pain, depression, and fatigue is dependent on a comprehensive clinical assessment. Furthermore, to advance the science of this field, symptom research requires the use of multidimensional instruments with proven validity and reliability in a cancer population across the lifespan. Studies demonstrate a significant correlation among pain, depression, fatigue, and other symptoms commonly seen throughout the course of cancer. Therefore, multidimensional scales incorporating the most common symptoms would ensure systematic assessment. Optimally, valid and reliable tools that measure symptom clusters would be feasible for use in both clinical and research settings. Currently available instruments that measure symptom clusters include the Edmonton Symptom Assessment Scale, the M.D. Anderson Symptom Inventory, the Memorial Symptom Assessment Scale, the Rotterdam Symptom Checklist, the Symptom Distress Scale, and others. Special populations include cancer patients with advanced disease, where symptom prevalence is expected to increase. Newer tools that attempt to address these populations are the Brief Hospice Inventory and the Hospice Quality of Life Index, appropriate for cancer patients with more advanced disease. Each of these tools has demonstrated utility in measuring symptom severity and quality of life. Few scales have been validated in the measurement of

symptom clusters in children, in cognitively impaired adults, or in non-English speaking patients from various cultural backgrounds. The strengths and limitations presented in the clinical and research uses of each these instruments will be presented, as will be areas for future investigation.

Palmer, J. L. and M. J. Fisch (2005). "Association between symptom distress and survival in outpatients seen in a palliative care cancer center." J Pain Symptom Manage 29(6): 565-71.

Clinical observation and preliminary reports suggest that higher scores for symptoms such as pain may be associated with shorter survival. We undertook a survival analysis to determine whether symptom expression in outpatients with complex cancer is related to the duration of their survival. Participants were 225 outpatients with cancer evaluated in our comprehensive cancer center for pain management or palliative care over a 10-week period ending June 2000. In addition to age and other clinical and demographic information, the patients completed the Anderson Symptom Assessment System (ASAS), which assesses pain, fatigue, nausea, depression, anxiety, drowsiness, shortness of breath (dyspnea), appetite, sleep, and feeling of well-being on a 0-10 scale. Univariate analyses showed that higher symptoms of dyspnea, drowsiness, problems with appetite, and nausea were significantly associated with shorter survival whereas pain, depression and other ASAS items were not. In multivariate analyses, only higher levels of dyspnea and drowsiness showed a significant association ($P=0.01$ and $P=0.02$, respectively) with shorter survival. Knowledge about these symptoms may be important in formulating adaptive randomization techniques for clinical trials and for research concerning estimates of survival.

Papagoras, C., J. Kountouras, et al. (2007). "Rheumatic-like syndrome as a symptom of underlying gastric cancer." Clin Rheumatol 26(6): 1029-31.

Several observations imply that atypical rheumatic manifestations may be associated with occult neoplasia. A 71-year-old woman was admitted to the hospital three times in 2 years. Initially, she was admitted for investigation of an iron-deficient anemia associated with upper intestinal tract symptoms. Endoscopy revealed hiatus hernia, esophagitis, and duodenal ulcer with a *Helicobacter pylori* infection, but there were no signs of malignancy, and the patient received appropriate drug treatment. Two years later, she presented with arthralgias concerning the upper and lower limbs in an asymmetrical distribution, low fever, and persistence of the anemia, despite the treatment she had received and the fact that her

gastrointestinal symptoms had long ceased. Immunological assays showed no specific rheumatic disorder, and the patient was discharged after showing significant improvement with the use of COX-2 selective NSAIDs. Finally, 4 months later, she was readmitted with worsening of the arthralgias, arthritis in the right radiocarpal joint, and severe anemia. Hematemesis that occurred during her hospital stay led to an emergency endoscopy and the diagnosis of gastric adenocarcinoma. Only a few cases have been reported so far concerning rheumatic manifestations as signs of an occult gastric cancer. Thus, there must be some degree of suspicion when dealing with patients with anemia and rheumatic symptoms that cannot be classified into a particular rheumatologic entity, because they might conceal a gastrointestinal malignancy not yet evident.

Parsons, H. A., M. O. Delgado-Guay, et al. (2008). "Alcoholism screening in patients with advanced cancer: impact on symptom burden and opioid use." *J Palliat Med* **11**(7): 964-8.

PURPOSE: Alcoholism is a devastating disease that can cause patient and family suffering and is frequently underdiagnosed. Preliminary studies suggest that it is associated with increased symptom expression and opioid dose escalation. The CAGE questionnaire is a widely used tool for alcoholism screening. The purpose of this study was to determine the frequency and characteristics of patients who screen positive for alcoholism in a palliative care outpatient clinic (PCOC). **METHODS:** We reviewed 665 consecutive charts of patients referred to the PCOC and collected data regarding age, gender, and type of cancer. For the first 100 consecutive CAGE positive (CAGE+) and 100 consecutive CAGE negative (CAGE-) patients, time from advanced cancer diagnosis (AC) to PCOC was calculated, and symptoms (Edmonton Symptom Assessment Scale, ESAS) and Morphine Equivalent Daily Dose (MEDD) were collected. **RESULTS:** CAGE was available for 598 of 665 (90%) patients. Of 598 patients, 100 (17%) were CAGE+. CAGE+ patients were younger (58 versus 60 years, $p < 0.05$), predominantly male (68% versus 47%, $p < 0.0001$), and with head/neck malignancies (24% versus 9%, $p < 0.05$). CAGE+ patients were referred earlier (5 +/- 27 months after AC, $p < 0.0001$). At baseline, pain, sleep, dyspnea, well-being, and total symptom distress were significantly worse among CAGE+ patients. Both groups showed similar improvement in symptoms. CAGE+ patients were more frequently on opioids upon referral (47/100 versus 29/100, $p < 0.05$) and follow-up (27/65 versus 16/68, $p < 0.05$). At follow-up, opioid doses did not show significant changes. **CONCLUSION:** Seventeen percent of the patients

were CAGE+. These patients were referred earlier to palliative care, had more symptom expression, and were more frequently on opioids. The palliative care team successfully improved symptom control in both groups without opioid dose escalation.

Pat, K., C. Doms, et al. (2008). "Systematic review of symptom control and quality of life in studies on chemotherapy for advanced non-small cell lung cancer: how CONSORTed are the data?" *Lung Cancer* **62**(1): 126-38.

BACKGROUND: The effect of chemotherapy on survival of patients with advanced NSCLC is modest, therefore patient reported outcomes (PRO's) are of high interest in randomized controlled trials (RCTs). CONSORT (CONsolidated Standards On Reporting Trials) is a quality checklist of 22 items for the conduct and reporting of RCTs. The aim of this report was to analyse to what extent the different RCTs with information on PRO's adhere to the CONSORT statement. **METHODS:** Systematic review of RCTs using PRO's either as primary or secondary endpoint. Compliance with the (revised) CONSORT statement was checked by 2 independent reviewers by making for each study the simple sum of the 22 CONSORT items, or a weighted score with a maximum rating of 31 points. **RESULTS:** The median weighted CONSORT score of the different RCTs was 25, with a remarkable difference from 12 till 30. There was no significant change over time, nor difference between academic and commercial studies, but a significant correlation between CONSORT agreement and journal type ($P < 0.0001$). Adherence to CONSORT was similar for studies comparing chemotherapy with best supportive care alone, comparing different first-line chemotherapies with PRO either as primary or secondary endpoint, or studies looking at second-line chemotherapy. Benefit in PRO's was reported in all of these settings. **CONCLUSION:** The overall adherence of peer-reviewed RCTs to CONSORT is reasonable, with nonetheless major differences between journals, and with no clear sign of change over time. Apart from modest survival differences, benefits in PRO endpoints are present in all categories of studies we analysed.

Patrick, D. L., S. L. Ferketich, et al. (2004). "National Institutes of Health State-of-the-Science Conference Statement: Symptom management in cancer: pain, depression, and fatigue, July 15-17, 2002." *J Natl Cancer Inst Monogr*(32): 9-16.

BACKGROUND: Despite advances in early detection and effective treatment, cancer remains one of the most feared diseases. Among the most common side effects of cancer and treatments for cancer are

pain, depression, and fatigue. Although research is producing increasingly hopeful insights into the causes and cures for cancer, efforts to manage the side effects of the disease and its treatments have not kept pace. The challenge that faces us is how to increase awareness of the importance of recognizing and actively addressing cancer-related distress. The National Institutes of Health (NIH) convened a State-of-the-Science Conference on Symptom Management in Cancer: Pain, Depression, and Fatigue to examine the current state of knowledge regarding the management of pain, depression, and fatigue in individuals with cancer and to identify directions for future research. Specifically, the conference examined how to identify individuals who are at risk for cancer-related pain, depression, and/or fatigue; what treatments work best to address these symptoms when they occur; and what is the best way to deliver interventions across the continuum of care. STATE-OF-THE-SCIENCE PROCESS: A non-advocate, non-Federal, 14-member panel of experts representing the fields of oncology, radiology, psychology, nursing, public health, social work, and epidemiology prepared the statement. In addition, 24 experts in medical oncology, geriatrics, pharmacology, psychology, and neurology presented data to the panel and to the conference audience during the first 1.5 days of the conference. The panel then prepared its statement, addressing the five predetermined questions and drawing on submitted literature, the speakers' presentations, and discussions held at the conference. The statement was presented to the conference audience, followed by a press conference to allow the panel to respond to questions from the media. After its release at the conference, the draft statement was made available on the Internet. The panel's final statement is available at <http://consensus.nih.gov>. CONCLUSIONS: The panel concluded that the available evidence supports a variety of interventions for treating cancer patients' pain, depression, and fatigue. Clinicians should routinely use brief assessment tools to ask patients about pain, depression, and fatigue and to initiate evidence-based treatments. Assessment should include discussion about common symptoms experienced by cancer patients, and these discussions should continue over the duration of the illness. Impediments to effective symptom management in cancer patients can arise from different sources and interactions among providers, patients and their families, and the health care system. Numerous factors could interfere with adequate symptom management. Among these factors are incomplete effectiveness of some treatments, a lack of sufficient knowledge regarding effective treatment strategies, patient reluctance to report symptoms to caregivers, a belief that such symptoms

are simply a part of the cancer experience that must be tolerated, and inadequate coverage and reimbursement for some treatments. Additional research is needed on the definition, occurrence, the treatment of pain, depression, and fatigue, alone and in combination, in adequately funded prospective studies. The panel also concluded that the state of the science in cancer symptom management should be reassessed periodically.

Phianmongkhol, Y. and N. Suwan (2008). "Symptom management in patients with cancer of the female reproductive system receiving chemotherapy." *Asian Pac J Cancer Prev* 9(4): 741-5.

This study was conducted to examine the feelings, symptom management, and needs of patients with gynecological cancer receiving chemotherapy at Chiang Mai University Hospital, Chiang Mai, Thailand. During the period July 2006 and June 2007, 286 patients were recruited. The most common chemotherapeutic regimen was paclitaxel and carboplatin followed by single carboplatin and weekly cisplatin. Five severe and frequent complications were as follows: alopecia, anorexia, fatigue, nausea, and vomiting. Some 41.9% could well tolerate with such complications but 50.3% had various feelings including irritability, boredom, dejection, fear, stress, and anxiety. Anorexia was the symptom that the majority of them could best manage, 17.4% by eating as much as they can and 32.6% by selecting different foods from normal, such as fruit, sweetmeats, noodles, milk. For nausea and vomiting, 31.3% managed by eating fruit, drinking sour juice, and holding sour fruit in mouth, and 16.0% used the breathing method, eating something cold, such as ice-cream, or hot food like noodles. For health needs, 41.0% needed encouragement, care, health education, and information from doctors and nurses, and 5.0% needed care and encouragement from their family, and sympathy from neighbors and colleagues. In conclusion, gynecological cancer patients receiving chemotherapy experience a variety of feelings, symptom management, and health needs. Nurses need to explain the pathology of the occurring symptoms so that the patients can understand and accept the symptoms to lessen their negative impact.

Phipps, E., L. E. Braitman, et al. (2008). "Quality of life and symptom attribution in long-term colon cancer survivors." *J Eval Clin Pract* 14(2): 254-8.

AIMS AND OBJECTIVES: This study investigates how long-term colon cancer survivors evaluate their health, functional status and quality of life, and whether there are differences based on age, gender or ethnicity. METHODS: Thirty long-term survivors of at least stage I colon cancer were

interviewed in person between December 2004 and May 2005. The interview protocol included the Medical Outcomes Study 36-Item Short Form, Quality of Life--Cancer Survivor, and study-specific questions that asked about physical and non-physical problems they attributed to colon cancer. RESULTS: Substantial percentages of survivors attributed their problems with lack of energy (83%), sexual functioning (67%), bowel problems (63%), poor body image (47%) and emotional problems (40%) to having had colon cancer. Of those problems attributed to colon cancer, sexual functioning and pain were given the highest severity rankings by survivors. The majority of long-term colon cancer survivors reported distress regarding future diagnostic tests, a second cancer, and spread of cancer. Women reported greater problems completing daily activities as a result of physical problems ($P = 0.003$) and more pain ($P = 0.07$) than men. African Americans appear to report marginally better overall quality of life ($P = 0.07$) and psychological well-being than whites ($P = 0.07$). CONCLUSION: The majority of long-term colon cancer survivors with resected colon cancer and disease-free for 5 years reported problems with low energy, sexual functioning and bowel problems.

Podnos, Y. D., T. R. Borneman, et al. (2007). "Symptom concerns and resource utilization in patients with lung cancer." *J Palliat Med* 10(4): 899-903.

OBJECTIVE: Lung cancer remains a major source of death in the United States. With the aging of the population, health policy makers are challenged to develop systems of care for the complex needs of these patients. This study sought to determine quality of life and symptom concerns in lung cancer patients. The study also sought to determine how supportive care resources were being used to address these concerns. METHODS: One hundred consecutive patients with newly diagnosed lung cancer presenting over a 12-month period were selected from the tumor registry. Charts were reviewed for demographic data, treatment history, treatment received, number and type of practitioner encounters, readmissions, and complications for a 6-month period. RESULTS: Of the 100 charts retrospectively reviewed, 4 patients had small cell and 96 patients had non-small cell lung cancer. The median age was 67 years. Fifty-three patients were men. The most common symptoms were pain, cough, dyspnea, and fatigue. A total of 114 referrals in 57 patients were made. Nutrition consultation was the most common. CONCLUSIONS: This study serves to guide the institution in the development of more effective support services for patients with lung cancer to address quality of life

concerns through collaboration between clinicians and researchers.

Rao, A. and H. J. Cohen (2004). "Symptom management in the elderly cancer patient: fatigue, pain, and depression." *J Natl Cancer Inst Monogr*(32): 150-7.

Patients who are $>$ or $=65$ years of age are the fastest growing segment of the U.S. population. These patients with already existing physiologic decline and comorbidities, when diagnosed with cancer, provide considerable challenges in management issues. Along with therapy for the tumor the practicing oncologist must also keep in mind the various symptoms, like fatigue, pain, and depression, that may occur due to the tumor itself or due to therapy. The prevalence of fatigue is greater than 50-70% in advanced cancer. The tools to measure fatigue are all subjective in nature and no one tool has been tested in the elderly cancer patient. Treatment of fatigue in the elderly may involve education, antidepressants, treatment of anemia, exercise, and use of psychostimulants. Pain is present in 80% of elderly patients with advanced cancer. Pain should be assessed in a systematic way and it has been shown that the Visual Descriptor Scale is the tool most preferred by the elderly. Several guidelines for management of pain exist and options include acetaminophen, nonsteroidal anti-inflammatory drugs, opioids, adjuvant analgesics, and education of patients and caregivers. Depression is also a prevalent symptom arising from a variety of causes. There are many validated tools to measure depression in the elderly like the Geriatric Depression Scale. Treatment includes use of education, selective serotonin reuptake inhibitors, psychotherapy, and electroconvulsive therapy. There exists an interplay of many of these symptoms and quite often they can occur simultaneously in the elderly cancer patient. Future research is needed to expand our base of knowledge on the occurrence and management of each of these symptoms and to better understand how aging systems interact with these phenomena to produce unique situations in older adults.

Rao, D., Z. Butt, et al. (2009). "A Comparison of the Renal Cell Carcinoma-Symptom Index (RCC-SI) and the Functional Assessment of Cancer Therapy-Kidney Symptom Index (FKSI)." *J Pain Symptom Manage* 38(2): 291-8.

The development and validation of measures that provide disease-specific, patient-reported outcomes have become increasingly relevant in the care of cancer patients, especially for assessing symptoms from the patient's perspective. Recently, two patient symptom questionnaires were developed

for kidney cancer patients, the Renal Cell Carcinoma-Symptom Index (RCC-SI) and the Functional Assessment of Cancer Therapy-Kidney Symptom Index (FKSI). This article describes the development of the revised FKSI scale (FKSI-19) and reconciles its use with the RCC-SI. Fifty participants with advanced kidney cancer commented on their symptoms and concerns about kidney cancer and this input was used to revise FKSI items. These patients also completed the RCC-SI, the Functional Assessment of Cancer Therapy-General (FACT-G), and an older version of the FKSI scale. We qualitatively reviewed item wording and content coverage across the two instruments, examined correlations between the scales, and calculated basic psychometrics on each scale. We found that the FKSI-19 and the RCC-SI addressed similar symptoms. Qualitative and descriptive statistical analyses demonstrated considerable overlap between the two instruments ($\rho=0.88$, $P<0.001$). Cronbach's alpha for the FKSI-19 and RCC-SI were both good, at 0.86 and 0.92, respectively. The FKSI-19 has some advantages over the RCC-SI. The FKSI-19 has more clarity in item phrasing, is shorter in length, and covers a similar breadth of disease-based symptoms when compared to the RCC-SI.

Recklitis, C. J., S. K. Parsons, et al. (2006). "Factor structure of the brief symptom inventory--18 in adult survivors of childhood cancer: results from the childhood cancer survivor study." *Psychol Assess* **18**(1): 22-32.

The factor structure of the Brief Symptom Inventory--18 (BSI-18; L. R. Derogatis, 2000) was investigated in a sample of adult survivors of childhood cancer enrolled in the Childhood Cancer Survivor Study (CCSS; $N = 8,945$). An exploratory factor analysis with a randomly chosen subsample supported a 3-factor structure closely corresponding to the 3 BSI-18 subscales: Depression, Anxiety, and Somatization. Confirmatory factor analysis with structural equation modeling validated this 3-dimensional structure in a separate subsample, though an alternative 4-factor model also fit the data. Analysis of the 3-factor model showed consistent fit in male and female participants. Compared with available community-based norms, survivors reported fewer symptoms of psychological distress. Together, results support the hypothesized 3-dimensional structure of the BSI-18 and indicate the measure may be useful in assessing psychological distress in this growing population of cancer survivors.

Recklitis, C. J. and P. Rodriguez (2007). "Screening childhood cancer survivors with the brief symptom inventory-18: classification agreement with the

symptom checklist-90-revised." *Psychooncology* **16**(5): 429-36.

The Brief Symptom Inventory-18 (BSI-18) is an 18-item symptom checklist used as a brief distress screening in cancer and other medical patients. This study evaluated the validity of the BSI-18 in a sample of 221 adult survivors of childhood cancers ages 18-55 (median = 26). Validity of the BSI-18 was compared to the Symptom Checklist-90-Revised (SCL-90-R). Results indicated the BSI-18 scales had acceptable internal consistency ($\alpha >0.80$) and were highly correlated with the corresponding SCL-90-R subscales (correlations from 0.88 to 0.94). When subjects were classified as case positive (significantly distressed) using the BSI-18 manual case-rule, classification agreement with the SCL-90-R was poor as evidenced by low sensitivity (41.78%). An alternative BSI-18 case-rule previously developed for cancer patients using the General Severity Index (GSI; GSI t-score ≥ 57) demonstrated better sensitivity (83.54%). ROC analysis indicated the BSI-18 had strong diagnostic utility relative to the SCL-90-R (AUC = 0.98) and several possible GSI cut-off scores were evaluated. The optimal cut-off score was a t-score ≥ 50 which had a sensitivity of 97.47% and a specificity of 85.21%. Results support use of the BSI-18 with adult survivors of childhood cancer but indicate an alternative case-rule must be used.

Reid, C. M., R. Gooberman-Hill, et al. (2008). "Opioid analgesics for cancer pain: symptom control for the living or comfort for the dying? A qualitative study to investigate the factors influencing the decision to accept morphine for pain caused by cancer." *Ann Oncol* **19**(1): 44-8.

BACKGROUND: Morphine and other opioids are the mainstay of cancer pain management, yet considerable fears surrounding them present barriers to pain control. Research in groups already using opioids has examined their concerns, but there is little evidence about how patients react when first offered opioids. We explored the factors influencing the decision to accept or reject morphine when first offered to patients with cancer. **PATIENTS AND METHODS:** A qualitative in-depth interview study nested within a cancer pain management trial. Interviews were conducted with 18 patients (nine females), aged 42-88 years. **RESULTS:** The categories that surrounded decisions about commencement of opioids were: anticipation of death; morphine as a last resort; the role of the professional; and 'no choice' but to commence. Participants rejected morphine as a medical intervention to control pain and promote quality of life because they saw it only as a comfort measure for the dying. However, opioids were more acceptable if health care providers had

confidence in opioids and side-effects were well managed. **CONCLUSION:** Among cancer patients the idea that opioids represent a comfort measure for the dying and not legitimate analgesics may represent a greater barrier to their uptake than concerns about tolerance or addiction.

Reuter, K., S. Raugust, et al. (2004). "Depressive symptom patterns and their consequences for diagnosis of affective disorders in cancer patients." Support Care Cancer **12**(12): 864-70.

GOALS OF WORK: In order to obtain references for adequate diagnostic procedures of depressive syndromes in cancer patients, the present study analyzes first the prevalence of somatic, emotional, and cognitive symptoms of depression. In a second part, the ability of diagnostic procedures to discriminate between patients with and without comorbid affective disorder is investigated. **PATIENTS AND METHODS:** From a cross-sectional survey investigating comorbid mental disorders in cancer patients with standardized clinical assessment, a subsample of 71 patients with current affective disorders and depressive symptoms according to the Diagnostic and Statistic Manual of Mental Disorders, 4th edition (DSM-IV) were analyzed. In addition to patients' symptom patterns, a discriminant analysis including all depressive symptoms was conducted. **MAIN RESULTS:** Cognitive symptoms are less prevalent in cancer patients than somatic and emotional symptoms. Loss of interest discriminated best between patients with and without diagnosis of comorbid affective disorder. Additionally, decreased energy and fatigue proved to have discriminatory value. **CONCLUSIONS:** Cognitive symptoms should receive special attention in diagnostic procedures for affective disorders in cancer patients. In spite of possible symptom overlap with the cancer disease and its treatment, fatigue proves to be a useful criteria for diagnosis of depression.

Ribi, K., J. Bernhard, et al. (2007). "Endocrine symptom assessment in women with breast cancer: what a simple "yes" means." Support Care Cancer **15**(12): 1349-56.

GOALS OF WORK: To investigate the self-reported symptoms related to endocrine therapy in women with early or advanced breast cancer and the impact of these symptoms on quality of life (QL) indicators. **MATERIALS AND METHODS:** Symptom occurrence was assessed by the Checklist for Patients on Endocrine Therapy (C-PET) and symptom intensity was assessed by linear analogue self-assessment (LASA) indicators. Patients also responded to global LASA indicators for physical well-being, mood, coping effort and treatment burden.

Associations between symptoms and these indicators were analysed by linear regression models. **MAIN RESULTS:** Among 373 women, the distribution of symptom intensity showed considerable variation in patients reporting a symptom as present. Even though patients recorded a symptom as absent, some patients reported having experienced that symptom when responding to symptom intensity, as seen for decreased sex drive, tiredness and vaginal dryness. Six of 13 symptoms and lower age had a detrimental impact on the global indicators, particularly tiredness and irritability. **CONCLUSIONS:** Patients' experience of endocrine symptoms needs to be considered both in patient care and research, when interpreting the association between symptoms and QL.

Rich, T. A. (2006). "Cancer symptom complexes related to alterations in molecular circadian axis signaling." Conf Proc IEEE Eng Med Biol Soc **1**: 171-2.

One of the most common symptoms in cancer patients is fatigue that is often associated with appetite loss and sleep disruption. Quality of life indices and objective measures of these symptoms are now possible and continue to improve our understanding of how these symptoms are caused. Disruption of 24 hour rest/activity patterns measured by actigraphy is one example where there is overlap of the objective measurement of symptoms and the circadian axis. This paper reviews new data relevant to understanding mechanisms involving inhibition of the circadian system and the production of symptom complexes in cancer patients through hypothalamic signaling by tumor produced members of the epidermal growth factor receptor.

Rich, T. A. (2007). "Symptom clusters in cancer patients and their relation to EGFR ligand modulation of the circadian axis." J Support Oncol **5**(4): 167-74; discussion 176-7.

Recent studies in chronobiology and the neurosciences have led to rapid growth in our understanding of the molecular biology of the human timekeeping apparatus and the neuroanatomic sites involved in signaling between the "master clock" in the hypothalamus and other parts of the brain. The circadian axis comprises a central clock mechanism and a downstream network of hypothalamic relay stations that modulate arousal, feeding, and sleeping behavior. Communication between the clock and these hypothalamic signaling centers is mediated, in part, by diffusible substances that include ligands of the epidermal growth factor receptor (EGFR). Preclinical studies reveal that EGFR ligands such as transforming growth factor-alpha (TGF-alpha) inhibit hypothalamic signaling of rhythmic behavior; clinical

observations show that elevated levels of TGF- α are associated with fatigue, flattened circadian rhythms, and loss of appetite in patients with metastatic colorectal cancer. These data support the hypothesis that a symptom cluster of fatigue, appetite loss, and sleep disruption commonly seen in cancer patients may be related to EGFR ligands, released either by the cancer itself or by the host in response to the stress of cancer, and suggest that further examination of their role in the production of symptom clustering is warranted.

Ridner, S. H. (2005). "Quality of life and a symptom cluster associated with breast cancer treatment-related lymphedema." *Support Care Cancer* **13**(11): 904-11.

OBJECTIVES: The aim of this study was to compare quality of life and symptoms between breast cancer survivors who have developed and undergone treatment for chronic lymphedema with those who have not developed lymphedema. **PATIENTS AND METHODS:** The cross-sectional, mixed-methods design included 64 breast cancer survivors with lymphedema and 64 breast cancer survivors without lymphedema. Variables assessed quantitatively included sociodemographic information, medical data, body mass index (BMI), arm extracellular fluid volume, quality of life (QOL), and physical and emotional symptoms. For the qualitative component, individuals with lymphedema responded in writing to the question: During the past week what other difficulties have you experienced because of your lymphedema? **RESULTS:** Compared with those without lymphedema, breast cancer survivors with lymphedema reported poorer QOL. A symptom cluster that included alteration in limb sensation, loss of confidence in body, decreased physical activity, fatigue, and psychological distress was identified. Perception of limb size influenced the cumulative symptom experience more than objective arm volume. Qualitative data revealed multiple QOL, physical health, and psychological concerns. BMI correlated with multiple outcomes. **CONCLUSIONS:** Findings suggest that current lymphedema treatments, although beneficial, may not provide complete relief of symptoms associated with lymphedema and complementary interventions are needed. The poorer QOL in breast cancer survivors with lymphedema may relate to the presence of an untreated symptom cluster.

Riechelmann, R. P., M. K. Krzyzanowska, et al. (2007). "Symptom and medication profiles among cancer patients attending a palliative care clinic." *Support Care Cancer* **15**(12): 1407-12.

BACKGROUND: Patients with advanced cancer frequently experience distressful symptoms

and receive numerous medications. We describe the symptomatology and medication profile of ambulatory cancer patients receiving exclusively supportive care at the Princess Margaret Hospital. **MATERIALS AND METHODS:** This was a retrospective, cross-sectional study. We reviewed the charts of consecutive adult cancer patients attending palliative care clinics and who were no longer receiving cancer-directed therapy. From the medical records, we collected information about self-reported symptoms [screened for with the numerical Edmonton symptom assessment system (ESAS) scale; range, 0-10, with 10=worst symptom] and medication profiles. Summary statistics were used to describe the results. **RESULTS:** Two hundred fifty five patients met the inclusion criteria. The most frequent self-reported symptoms of any severity were fatigue (77%), pain (75%), and lack of appetite (66%). These were also the most severe symptoms: fatigue (median ESAS score=7), pain (median ESAS=5), and lack of appetite (median ESAS=5). The median number of medications per patient after consultation in the palliative care service was 6, and the most common classes of drugs prescribed were opioids (67%), laxatives/stool softeners (54%), corticosteroids (41%), and acetaminophen (41%). Palliative care physicians made at least one medication change in 75% of the patients, with the most frequent change being the addition of new medication(s); dexamethasone was the most commonly added individual drug (18% of the patients). **CONCLUSION:** Among patients with advanced cancer not receiving antineoplastic therapy, the most frequent and severe symptoms were fatigue, pain, and lack of appetite. The medication profile represented drugs that could both alleviate and contribute to these symptoms. Audit of patient symptoms and medication prescription in palliative care may inform clinical practice and help the development of research specific to patient symptoms.

Rippy, L. and J. Marsden (2006). "Is HRT justified for symptom management in women at higher risk of developing breast cancer?" *Climacteric* **9**(6): 404-15.

Hormone replacement therapy (HRT) is the most efficacious intervention for the treatment of estrogen-deficiency symptoms. Prescriptions for HRT have fallen over the last 3 years due to anxiety provoked about breast cancer risk and recurrence that has been generated by recent clinical trials. In women at population risk of breast cancer, these trials have not shown risks greater than estimates from clinical trial evidence that predated them. For women at increased breast cancer risk due to a family history or high-risk benign breast conditions, clinical trial data are limited but suggest a lack of an additive effect of HRT on risk. In symptomatic breast cancer survivors,

observational data suggest no increase in recurrence but these data are open to bias. Interim analyses of large, randomized trials have shown contradictory outcomes and, as a result, three large HRT randomized trials have now been closed. The randomized LIBERATE trial evaluating tibolone in breast cancer survivors is fully recruited and continuing. The current clinical climate is 'HRT adverse' but, due to a lack of effective alternatives for symptom relief, women at higher breast cancer risk and breast cancer survivors are still requesting information about HRT. In this situation, discussion of the current clinical uncertainty surrounding the use of HRT must be undertaken to ensure that women are adequately informed.

Rogers, L. Q., J. Malone, et al. (2009). "Exercise preferences among patients with head and neck cancer: prevalence and associations with quality of life, symptom severity, depression, and rural residence." *Head Neck* 31(8): 994-1005.

BACKGROUND: Our aim was to determine exercise preferences among patients with head and neck cancer and their associations with quality of life, symptom severity, depression, and rural residence. **METHODS:** This study involved a cross-sectional chart review and self-administered survey, with 90 outpatients with head and neck cancer (response rate = 83%). **RESULTS:** The majority were <65 years old (65%), male (78%), and white (96%) with stage > or = III (81%). Lack of preference was the most frequent option for counseling source (66%), counseling delivery (47%), and exercise variability (52%). Popular specific preferences included outdoors (49%), morning (47%), and alone (50%). Significant adjusted associations occurred for patients' interest with lower functional well-being, alone with higher functional well-being, and morning with higher total quality of life and emotional, social, and functional well-being. No significant associations occurred with symptoms, depression, or rural residence. **CONCLUSION:** Patients with head and neck cancer may be open to a variety of exercise options. Quality of life may influence interest and preference for exercising alone or in the morning.

Rosenthal, D. I., T. R. Mendoza, et al. (2007). "Measuring head and neck cancer symptom burden: the development and validation of the M. D. Anderson symptom inventory, head and neck module." *Head Neck* 29(10): 923-31.

BACKGROUND: The aim of this study was to develop and validate a symptom inventory for patients with head and neck cancer and to assess the occurrence and severity of symptoms, the overall symptom burden, and the interference the symptoms

cause in daily life. **METHODS:** Items were generated from a comprehensive literature review, our prior work, and focus groups with head and neck cancer patients, symptom researchers, and a multidisciplinary group of head and neck cancer health care workers. We selected 11 provisional head and neck cancer-specific items for addition to the core M. D. Anderson Symptom Inventory (MDASI), and conducted a cross-sectional validation study among patients with head and neck cancer. **RESULTS:** Construct validity was established using principal axis factoring with direct oblimin rotation, and tests of concurrent and known-groups validity were conducted. Two items were dropped because of low severity scores and low frequency of complaint, leaving 9 final head and neck cancer-specific items. The coefficient alpha reliabilities were 0.88, 0.83, and 0.92 for the 13 core MDASI items, the 9 head and neck cancer-specific items, and the 6 interference items, respectively. The most prevalent severe symptoms were problems with mucus, mouth/throat sores, tasting food, difficulty with chewing or swallowing, dry mouth, pain, and fatigue. **CONCLUSIONS:** The M. D. Anderson Symptom Inventory-Head and Neck (MDASI-HN) is a reliable and valid instrument to measure head and neck cancer symptom burden, and the interference symptoms cause in the major aspects of a patient's daily life. A subset of specifically distressing symptoms was identified, many of which are not included in commonly used head and neck cancer quality of life instruments.

Royer, H. R., C. H. Phelan, et al. (2009). "Older breast cancer survivors' symptom beliefs." *Oncol Nurs Forum* 36(4): 463-70.

PURPOSE/OBJECTIVES: To use Leventhal's Common Sense Model (CSM) to describe older breast cancer survivors' symptom representations, symptom management strategies, and perceived barriers to symptom management. **DESIGN:** A secondary analysis was conducted using data from three pilot studies that tested a theory-based intervention to improve symptom management in older breast cancer survivors. **SETTING:** Advanced practice nurses conducted open-ended interviews with older breast cancer survivors either in their homes or via telephone. **SAMPLE:** Participants were recruited from the community, an oncology clinic, and a state tumor registry. The women (N = 61, X age = 69.5) were an average of 4.7 years after breast cancer diagnosis and reported an average of 17 symptoms. **METHODS:** Content analysis was conducted with field notes taken during baseline interviews. **MAIN RESEARCH VARIABLES:** Symptom representations, symptom management strategies, and perceived barriers to symptom management.

FINDINGS: Women described their symptoms as chronic, incurable, and uncontrollable, with multiple causes (usually not aging) and numerous negative consequences. Women described an average of six symptom management strategies, most typically self-care. The most frequent barrier to symptom management was communicating with healthcare providers. **CONCLUSIONS:** The CSM is a useful framework for understanding the symptom beliefs of older breast cancer survivors. **IMPLICATIONS FOR NURSING:** Addressing women's beliefs and barriers may result in better communication with healthcare providers and more effective interventions for symptom management.

Ruiter, R. A., J. de Nooijer, et al. (2008). "Intended coping responses to cancer symptoms in healthy adults: the roles of symptom knowledge, detection behavior, and perceived threat." *Cancer Epidemiol Biomarkers Prev* **17**(4): 818-26.

BACKGROUND: To date, the causal effects of the knowledge of cancer-related symptoms and detection behavior on coping with cancer-related symptoms have not been identified. Therefore, the current study explored the effects of active or passive detection of supposedly well-known or less-known cancer-related symptoms on intended coping responses. In addition, we were interested in the extent to which these effects are driven by heightened perceptions of threat. **METHODS:** In an experimental study using a 2 x 2 within-subject design, 221 Dutch adults from the general population responded to a survey study sent to their homes (18.4% response). They were asked to read scenario information about four cancer-related symptoms that were (a) well known or less known and (b) actively or passively detected (e.g., self-examination versus unusual blood loss). The authors measured intended coping responses to the detection of cancer-related symptoms as either adaptive (e.g., visiting a general practitioner) or maladaptive (e.g., denial of the symptom). **RESULTS:** As expected, the findings revealed that well-known symptoms resulted in more anticipated adaptive coping and less anticipated maladaptive coping than less-known symptoms. Unfortunately, the findings also suggest that the active as opposed to passive detection of cancer symptoms (e.g., self-examination versus unusual blood loss) is likely to result in more maladaptive coping. These effects were mediated by heightened perceptions of threat. **CONCLUSIONS:** Future health education programs that aim to motivate people to be more active in the early detection of cancer symptoms should first focus on increasing people's knowledge about the early warning signs of cancer.

Sagar, S. M. (2008). "Acupuncture as an evidence-based option for symptom control in cancer patients." *Curr Treat Options Oncol* **9**(2-3): 117-26.

OPINION STATEMENT: Current technology suggests that acupuncture modulates neurological processes within the central nervous system, especially the spinal cord gating mechanisms, cerebral subcortical nuclei, and the hypothalamic-endocrine axis. Many single arm clinical studies report the effectiveness of acupuncture for controlling symptoms in cancer patients. However, the challenge has been to separate the nonspecific effects of the practitioner, as well as regression to the mean, from the neurophysiological effects of needle penetration. Recently, randomized controlled trials have attempted to answer this question, with mixed results. For example, needle penetration (or equivalent stimulation) is effective for nausea and vomiting, whereas it does not appear to be a major factor in reducing hot flashes. Safety and quality are priorities, so regulation of the practice of acupuncture is important, as well as excellent communication between practitioners. In addition, continuing research is mandatory, using validated methodology and reporting principles as outlined in the CONSORT and STRICTA recommendations.

Sarna, L., M. E. Cooley, et al. (2008). "Symptom severity 1 to 4 months after thoracotomy for lung cancer." *Am J Crit Care* **17**(5): 455-67; quiz 468.

BACKGROUND: Information about the severity of symptoms during recovery from surgery for lung cancer can be useful in planning and anticipating needs for recovery. **OBJECTIVES:** To describe symptom severity during the first 4 months after thoracotomy for non-small cell lung cancer and factors associated with overall symptom severity at 1 and 4 months. **METHODS:** Ninety-four patients were assessed at 1, 2, and 4 months after thoracotomy by using the Lung Cancer Symptom Scale, Brief Pain Inventory, Schwartz Fatigue Scale, Dyspnea Index, and Center for Epidemiology Studies-Depression Scale (CES-D). Clinically meaningful changes, decrease in the proportion of patients with severe symptoms, and relationships among symptoms were determined. Mixed effects models for repeated measures were used to evaluate changes in severity. Multiple regression models were used to examine correlates of overall symptoms. **RESULTS:** Mean symptom severity significantly decreased over time for most symptoms. Only disrupted appetite, pain, and dyspnea had clinically meaningful improvement at 4 months. Severe symptoms included fatigue (57%), dyspnea (49%), cough (29%), and pain (20%). Prevalence of depressed mood decreased at 4 months. Most patients (77%) had comorbid conditions.

Number of comorbid conditions and CES-D explained 54% of the variance in symptom severity at 1 month; comorbid conditions, male sex, neoadjuvant treatment, and CES-D score explained 50% of the variance at 4 months. CONCLUSIONS: Severe symptoms continued 4 months after surgery for some patients, indicating the need for support during recovery, especially for patients with multiple comorbid conditions and depressed mood.

Sarna, L. and M. S. Riedinger (2004). "Assessment of quality of life and symptom improvement in lung cancer clinical trials." *Semin Oncol* 31(3 Suppl 9): 1-10.

The majority of lung cancers are diagnosed at advanced stages when treatment options are limited and mainly palliative. In advanced lung cancer, quality-of-life (QOL) issues have become an integral part of making decisions about various treatment options. Recent clinical trials in patients with lung cancer have assessed symptom improvement and QOL as important endpoints. There are several valid and reliable QOL assessment instruments that specifically evaluate symptoms of lung cancer. These questionnaires evaluate a variety of factors related to emotional, physical, and social well-being. Several key factors, including age, gender, comorbidities, and quality of supportive care may affect symptoms and QOL in patients with lung cancer. Overall, QOL is important for patients with advanced lung cancer; therefore, symptom and QOL assessments are becoming vital in evaluating the efficacy of emerging cancer treatments.

Schonwetter, R. S., L. A. Roscoe, et al. (2006). "Quality of life and symptom control in hospice patients with cancer receiving chemotherapy." *J Palliat Med* 9(3): 638-45.

The value of palliative chemotherapy for hospice patients is difficult to quantify and little is known about outcomes from these treatments. This study examined quality of life and symptom control in hospice patients with cancer receiving chemotherapy and in a control group of hospice patients with cancer who had not received chemotherapy for at least 3 months. Using a case-control study design matching patients by age, gender, race, and cancer diagnosis, patients receiving chemotherapy reported a similar number of symptoms as patients off chemotherapy. Global symptom distress was comparable in both groups as was quality of life. Patients in both groups were similar at the symptom-specific level, however, patients on chemotherapy had better symptom outcomes for urination problems ($p=0.03$), numbness/tingling ($p=0.03$), muscle weakness ($p=0.07$), and pain ($p=0.09$). Patients on

chemotherapy had poorer symptom control involving change in taste ($p=0.01$) and cough ($p=0.01$). Patients on chemotherapy were more likely than those off chemotherapy to report that chemotherapy "made them feel better" ($p=0.01$) and "allowed better symptom control" ($p=0.01$), indicating that patients taking chemotherapy had more subjective benefit from chemotherapy when compared to those off chemotherapy. The two groups showed no difference in the rate of survival.

Schwartzberg, L. S., B. V. Fortner, et al. (2005). "Sex differences in patients who have cancer with mild anemia: symptom burden and quality of life." *Support Cancer Ther* 2(4): 241-6.

The same criterion for mild anemia ($10 < \text{hemoglobin [Hgb]} < 12 \text{ g/dL}$) has been used for male and female patients. Mild anemia is associated with greater symptom burden and reduced quality of life (QOL). We compared male and female patients who have mild anemia with each other and with their respective normal groups. Patients ($N = 3553$) from a community oncology database were sorted by sex and Hgb level into 3 anemic and 2 normal groups: men with $10 \leq \text{Hgb} < 12 \text{ g/dL}$, men with $12 \leq \text{Hgb} < 14 \text{ g/dL}$, women with $10 \leq \text{Hgb} < 12 \text{ g/dL}$, men with $\text{Hgb} \geq 14 \text{ g/dL}$, and women with $\text{Hgb} \geq 12 \text{ g/dL}$. Patients receiving chemotherapy (< 30 days) and/or growth factor (< 60 days) were excluded. Each case provided same-day scores on the Cancer Care Monitor, a validated measure of symptom burden, functioning, and health-related QOL comprising 7 scales. Compared with respective normal groups, male and female patients with mild anemia showed greater symptom burden, lower functioning, and worse QOL ($P < 0.05$). Compared with normal men and women, patients with mild anemia showed clinically significant differences in terms of effect size (Cohen's d , 0.11- 0.91). Men with $10 \leq \text{Hgb} < 12 \text{ g/dL}$ were significantly more impaired and had worse QOL than men with $12 \leq \text{Hgb} < 14 \text{ g/dL}$ or women with $10 \leq \text{Hgb} < 12 \text{ g/dL}$. Impact of mild anemia on QOL is significant, and treating men and women by the same standards (Hgb level $< 12 \text{ g/dL}$) is likely incorrect. Mild anemia may be undertreated, especially for men with $12 \leq \text{Hgb} < 14 \text{ g/dL}$.

Sela, R. A. (2007). "Screening for depression in palliative cancer patients attending a pain and symptom control clinic." *Palliat Support Care* 5(3): 207-17.

OBJECTIVE: Depression in palliative care patients is often underrecognized. Screening can increase case recognition. The aims of this study were to assess the prevalence of depression in palliative cancer patients attending a pain and symptom control

clinic and to investigate the validity and utility of a depression visual analogue scale in detecting depression in the advanced cancer outpatient population. **METHOD:** One hundred and thirty-two oncology outpatients who came for consultation at a multidisciplinary pain and symptom control clinic were asked and agreed to complete the Brief Zung Self-Rating Depression Scale (BZSDS; Dugan et al., 1998) and depression visual analogue scale (DVAS). **RESULTS:** The majority of participants (72%) indicated clinically significant depressive symptoms according to the BZSDS (21% in the "mild" depressive symptoms range, 32% in the "moderate" range, and 19% in the "severe" range). Participants indicated low endorsement rates of items related to overt manifestation of depression (e.g., sadness, tearfulness, irritability, and suicide ideation). The DVAS showed high correlation with the BZSDS ($r = .82$) and is a potentially useful screening instrument for detecting depressive disorder in palliative care cancer patients. **SIGNIFICANCE OF RESULTS:** The results of the study underline the importance of routine screening to detect depressive disorder in palliative care patients to improve their quality of care. The depression visual analogue scale was found to be an effective simple screening tool, easy to administer and use.

Sela, R. A., S. Watanabe, et al. (2005). "Sleep disturbances in palliative cancer patients attending a pain and symptom control clinic." *Palliat Support Care* 3(1): 23-31.

OBJECTIVE: The nature of sleep disturbances in palliative cancer patients has not been delineated clearly or fully understood due to limited clinical information. The purpose of this study was to describe sleep disturbance patterns, treatments, and communication in an advanced cancer outpatient population attending a pain and symptom control clinic. **METHOD:** One hundred oncology outpatients who came for consultation at a multidisciplinary pain and symptom control clinic were asked and agreed to complete a self-report questionnaire that elicited information about their sleeping habits, sleep concerns, sleep enhancement strategies, and related communication with health care providers. **RESULTS:** The majority of participants (72%) reported a wide variety of sleep disturbances, after cancer diagnosis, with the three most frequent elevated symptoms ($> \text{ or } = 5$) being not feeling rested in the morning (72%), difficulty staying asleep (63%), and difficulty falling asleep (40%). Approximately one-fifth of participants (19%) reported having insomnia problems prior to their cancer diagnosis. In a correlational comparison with four other symptoms (i.e., fatigue, pain, anxiety, depression), the three

highest correlations were between difficulty falling asleep and fatigue ($r = 0.612$), early awakening and fatigue ($r = 0.596$), and difficulty falling asleep and anxiety ($r = 0.572$). Fifty-three percent of participants reported using a variety of interventions for their sleep problems, the most frequent being sleep medication (37%). Of the 52 participants who reported an elevated level of concern about their sleeping difficulties ($> \text{ or } = 5$), 48 (92%) discussed their concerns with a health care provider. However, of the 20 participants with elevated symptoms ($> \text{ or } = 5$) and low levels of concern (< 5), only 7 (35%) communicated their concerns to a health care provider. **SIGNIFICANCE OF RESULTS:** The results of this study underline the importance of routine clinical assessments to detect sleep problems and interventions designed specifically to improve the overall sleep quality of cancer patients.

Shelby, R. A., D. M. Golden-Kreutz, et al. (2005). "Mismatch of posttraumatic stress disorder (PTSD) symptoms and DSM-IV symptom clusters in a cancer sample: exploratory factor analysis of the PTSD Checklist-Civilian Version." *J Trauma Stress* 18(4): 347-57.

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV; American Psychiatric Association, 1994a) conceptualization of posttraumatic stress disorder (PTSD) includes three symptom clusters: reexperiencing, avoidance/numbing, and arousal. The PTSD Checklist-Civilian Version (PCL-C) corresponds to the DSM-IV PTSD symptoms. In the current study, we conducted exploratory factor analysis (EFA) of the PCL-C with two aims: (a) to examine whether the PCL-C evidenced the three-factor solution implied by the DSM-IV symptom clusters, and (b) to identify a factor solution for the PCL-C in a cancer sample. Women ($N = 148$) with Stage II or III breast cancer completed the PCL-C after completion of cancer treatment. We extracted two-, three-, four-, and five-factor solutions using EFA. Our data did not support the DSM-IV PTSD symptom clusters. Instead, EFA identified a four-factor solution including reexperiencing, avoidance, numbing, and arousal factors. Four symptom items, which may be confounded with illness and cancer treatment-related symptoms, exhibited poor factor loadings. Using these symptom items in cancer samples may lead to overdiagnosis of PTSD and inflated rates of PTSD symptoms.

Sherman, D. W., X. Y. Ye, et al. (2007). "Symptom assessment of patients with advanced cancer and AIDS and their family caregivers: the results of a

quality-of-life pilot study." Am J Hosp Palliat Care 24(5): 350-65.

This longitudinal pilot study examined differences in demographic characteristics of 101 patients with advanced illness (cancer, AIDS) and 81 Family caregivers, evaluated the reliability of the Memorial Symptom Assessment Scale for these patients and their family caregivers; obtained preliminary data regarding similarities or differences in the symptom experience of these patients and their family caregivers and changes in symptoms over time; and identified demographic variables that may be potential covariates related to the symptom experience. All demographic variables were significantly different for patients with advanced cancer and AIDS, and their symptom experience is similar only with regard to psychologic symptoms; however, based on the Memorial Symptom Assessment Scale, cancer and AIDS patients and their family caregivers have similar symptom experiences, indicating the need for palliative care for both patients and family. Further research is needed to establish the reliability of the Memorial Symptom Assessment Scale for use with family caregivers.

Sherwood, P., B. A. Given, et al. (2005). "A cognitive behavioral intervention for symptom management in patients with advanced cancer." Oncol Nurs Forum 32(6): 1190-8.

PURPOSE/OBJECTIVES: To evaluate the effectiveness of a cognitive behavioral intervention in decreasing symptom severity in patients with advanced cancer undergoing chemotherapy. **DESIGN:** Prospective, randomized clinical trial based on cognitive behavioral theory. **SETTING:** Six urban cancer centers in the midwestern United States. **SAMPLE:** 124 patients 21 years of age or older were recruited and randomized to receive conventional care or conventional care and an intervention. Participants were newly diagnosed with stage III, stage IV, or recurrent cancer (solid tumor or non-Hodgkin lymphoma), undergoing chemotherapy, cognitively intact, and able to read and speak English. **METHODS:** Data were gathered via telephone interviews at baseline and 10 and 20 weeks after randomization. Nurses with experience in oncology delivered a five-contact, eight-week intervention aimed at teaching patients problem-solving techniques to affect symptom severity. **MAIN RESEARCH VARIABLES:** Gender, site of cancer, age, symptom severity and depressive symptoms at baseline, group (i.e., experimental versus control), and total symptom severity. **FINDINGS:** Patients in the experimental group and those with lower symptom severity at baseline had significantly lower symptom severity at 10 and 20 weeks; the experimental difference at 20

weeks occurred primarily in those 60 years of age and younger. Depressive symptoms at baseline predicted symptom severity at 20 weeks; however, age, gender, and site of cancer did not affect symptom severity at either time point. **CONCLUSIONS:** A cognitive behavioral intervention to teach problem-solving skills can be effective for patient symptom self-management during and following an intervention. **IMPLICATIONS FOR NURSING:** Problem-solving strategies should be included in educational programs for patients with advanced cancer, particularly those 60 years of age and younger.

Shih, Y. C., X. S. Wang, et al. (2006). "The association between symptom burdens and utility in Chinese cancer patients." Qual Life Res 15(8): 1427-38.

OBJECTIVES: This study explored the relationship between the M. D. Anderson Symptom Inventory (MDASI), an instrument measuring the severity of symptoms common to patients with cancer, and utility derived from the SF-36. **METHODS:** Cancer patients from Tianjin Cancer Hospital in China (n = 249) completed a demographic questionnaire and Chinese versions of the MDASI and SF-36. Using a published algorithm converting SF-36 scores to standard gamble (SG) utilities, we examined the association between utility and individual symptoms using Spearman's rank correlation, and explored the association between utility and aggregate symptom scores through multivariate regression analyses. **RESULTS:** The mean SG utility was 0.81 (SD = 0.11); utilities were significantly but moderately correlated with the majority of symptoms, especially those of distress, sadness, fatigue, and pain. Regression models showed a significantly negative association between the total symptom score and the utility. After controlling for sociodemographics, cancer stage and performance status, a significantly negative association between the total symptom scores and utility was found in the multivariate analyses. We also found the total number of severe symptoms to be a stronger predictor of "disutility." **CONCLUSIONS:** Symptom measures were significantly albeit moderately associated with utility derived from the SF-36 scores, suggesting that a full study with rigorously collected utilities is worth exploring.

Sikorskii, A., C. W. Given, et al. (2007). "Symptom management for cancer patients: a trial comparing two multimodal interventions." J Pain Symptom Manage 34(3): 253-64.

The results of a randomized controlled trial that tested the effects of eight-week, six-contact multidimensional interactive interventions for symptom management are presented. Four hundred

and thirty-five cancer patients with solid tumors undergoing chemotherapy were randomized to receive either nurse-assisted symptom management (NASM) or automated telephone symptom management (ATSM). A prior trial established the effectiveness of NASM compared with conventional care. Seventeen symptoms commonly experienced by patients undergoing chemotherapy were rated on a scale from 0 to 10 and were evaluated at baseline, at each of the six intervention contacts, and postintervention observation at 10 weeks. Both groups achieved significant reduction in symptom severity over baseline, and there was no difference between groups on symptom severity at 10 weeks. Randomization accounted for possible reductions in severity due to response shifts. Severity of symptoms reported by patients at each of the six intervention contacts was measured using a Rasch model. Symptom pattern was different for lung and non-lung cancer patients, and they were analyzed separately. Longitudinal analyses revealed that lung cancer patients with greater symptom severity withdrew from later intervention contacts of the ATSM. The results suggest that both NASM and ATSM achieved a clinically significant reduction in symptom severity. The NASM may be more effective than ATSM in retaining lung cancer patients in the intervention. Further testing of ATSM supplemented by NASM for patients with severe symptoms is warranted.

Skerman, H. M., P. M. Yates, et al. (2009). "Multivariate methods to identify cancer-related symptom clusters." *Res Nurs Health* **32**(3): 345-60.

Multivariate methods are required to assess the interrelationships among multiple, concurrent symptoms. We examined the conceptual and contextual appropriateness of commonly used multivariate methods for cancer symptom cluster identification. From 178 publications identified in an online database search of Medline, CINAHL, and PsycINFO, limited to articles published in English, 10 years prior to March 2007, 13 cross-sectional studies met the inclusion criteria. Conceptually, common factor analysis (FA) and hierarchical cluster analysis (HCA) are appropriate for symptom cluster identification, not principal component analysis. As a basis for new directions in symptom management, FA methods are more appropriate than HCA. Principal axis factoring or maximum likelihood factoring, the scree plot, oblique rotation, and clinical interpretation are recommended approaches to symptom cluster identification.

Skrutkowski, M., A. Saucier, et al. (2008). "Impact of a pivot nurse in oncology on patients with lung or breast cancer: symptom distress, fatigue, quality of

life, and use of healthcare resources." *Oncol Nurs Forum* **35**(6): 948-54.

PURPOSE/OBJECTIVES: To examine the impact on continuity of nursing care delivered by a pivot nurse in oncology to improve symptom relief and outcomes for patients with lung or breast cancer. **DESIGN:** Randomized controlled trial in which participants were randomly assigned to an intervention group (n = 93) with care by a pivot nurse in oncology and usual care by clinic nurses or to a control group (n = 97) with usual care only. **SETTING:** Three outpatient ambulatory oncology clinics in a large university health center in Quebec, Canada. **Sample:** 113 patients with lung cancer and 77 patients with breast cancer. **METHODS:** Participants in both groups completed the Symptom Distress Scale, Brief Fatigue Inventory, and Functional Assessment of Cancer Therapy Scale-General version 4 at eight intervals over six months. Healthcare usage was evaluated through a review of hospital records. **MAIN RESEARCH VARIABLES:** Symptom distress, fatigue level, quality of life, and healthcare usage. **FINDINGS:** Researchers found no significant differences in symptom distress, fatigue, quality of life, and healthcare usage between groups. **CONCLUSIONS:** The new nursing role did not have an impact on the patient outcomes under study. **IMPLICATIONS FOR NURSING:** Experienced nurses with specialized knowledge of oncology symptom assessment and management may reduce the symptom burden experienced by ambulatory patients with breast or lung cancer during active treatment.

Slaughter, L. A., C. M. Ruland, et al. (2006). "Constructing an effective information architecture for a pediatric cancer symptom assessment tool." *AMIA Annu Symp Proc*: 1102.

We are in the process of creating a classification structure of health concepts (symptoms) that will be used within the user interface of a children's symptom management system called PedsCHOICE. Through studies conducted during the development process, we have learned that there are many factors that influence the structure of the symptom categorization that go beyond the user's cognition and ways of thinking. Restraints such as emotional reactions/acknowledging illness, children's development of motor skills, in addition to children's conceptualizations of categories all affect how a health application should present content.

Slim, I., K. Ach, et al. (2009). "Diabetes mellitus as an early symptom of pancreatic cancer diagnosed three years later." *Ann Endocrinol (Paris)* **70**(1): 76-9.

We present a case of a 40-year-old man with strong family history of diabetes. His pancreatic

ultrasonography was normal at the discovery of his diabetes. Anti-pancreatic antibodies were negative. The patient was treated by insulin and continued to lose weight. His diabetes remained unstable during the follow-up. Three years later, a pancreatic adenocarcinoma was diagnosed which was locally advanced and could not be removed surgically. This observation argues among several mechanisms explaining diabetes in subjects with pancreatic cancer, in favor of tumor-derived diabetogenic substance and suggests that diabetes mellitus could reveal pancreatic cancer even in the presence of conventional risk factors of type 2 diabetes.

Sloan, J. A., L. Berk, et al. (2007). "Integrating patient-reported outcomes into cancer symptom management clinical trials supported by the National Cancer Institute-sponsored clinical trials networks." *J Clin Oncol* **25**(32): 5070-7.

Patient-reported outcomes (PROs) are often the primary end point in symptom management trials. The scientific field of PROs is evolving, as evidenced by the US Food and Drug Administration's February 2007 release of a draft guidance for using PROs in effectiveness claims for drug labeling. This article presents issues encountered during use of PROs in National Cancer Institute-sponsored symptom management trials. Selected trials are presented that exemplify the challenges often seen in symptom management trials, and solutions are described. The examples presented include defining the appropriate end point, selecting and validating assessments, and answering the research questions through statistical analysis and interpretation. Progress has been made in addressing some of the unique challenges of PRO-based symptom management research. Many challenges still remain, but a foundational body of work now exists for more consistent and rigorous application of PROs into symptom management trials. There remains a need for more research in several methodologic aspects of design, analysis, and interpretation of symptom management trials.

So, W. K., G. Marsh, et al. (2009). "The symptom cluster of fatigue, pain, anxiety, and depression and the effect on the quality of life of women receiving treatment for breast cancer: a multicenter study." *Oncol Nurs Forum* **36**(4): E205-14.

PURPOSE/OBJECTIVES: To examine the symptom cluster of fatigue, pain, anxiety, and depression and its effect on the quality of life (QOL) of women receiving chemotherapy or radiotherapy for breast cancer. **DESIGN:** Descriptive. **SETTING:** Oncology outpatient sections of four public hospitals in Hong Kong. **SAMPLE:** 215 ethnic Chinese women who were midway through treatment for breast

cancer. **METHODS:** Chinese versions of the Brief Fatigue Inventory, Hospital Anxiety and Depression Scale, Brief Pain Inventory, Functional Assessment of Chronic Illness Therapy for Breast Cancer, and Medical Outcomes Study Social Support Survey were used. Spearman rho correlation and structural equation modeling were used to examine the relationships among the study variables. **MAIN RESEARCH VARIABLES:** Breast cancer, fatigue, pain, anxiety, depression, and QOL. **FINDINGS:** Most participants reported mild-to-moderate levels of fatigue and pain. Twenty-one percent and 36% of patients might have had an anxiety or depression disorder, respectively. Significant correlations among the four symptoms supported the existence of the symptom cluster. The participants receiving chemotherapy had inadequate social support, experienced higher levels of symptoms, and were more likely to have a poorer QOL. **CONCLUSIONS:** The findings supported the existence of the symptom cluster that had detrimental effects on QOL. **IMPLICATIONS FOR NURSING:** This study shed light on a contemporary approach of grouping several related symptoms together. The findings enhance nurses' clinical sensitivity when identifying patients in high-risk groups and provide useful information for designing and prioritizing symptom-management strategies to meet patients' needs.

Solano, J. P., B. Gomes, et al. (2006). "A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease." *J Pain Symptom Manage* **31**(1): 58-69.

Little attention has been paid to the symptom management needs of patients with life-threatening diseases other than cancer. In this study, we aimed to determine to what extent patients with progressive chronic diseases have similar symptom profiles. A systematic search of medical databases (MEDLINE, EMBASE, and PsycINFO) and textbooks identified 64 original studies reporting the prevalence of 11 common symptoms among end-stage patients with cancer, acquired immunodeficiency syndrome (AIDS), heart disease, chronic obstructive pulmonary disease, or renal disease. Analyzing the data in a comparative table (a grid), we found that the prevalence of the 11 symptoms was often widely but homogeneously spread across the five diseases. Three symptoms-pain, breathlessness, and fatigue-were found among more than 50% of patients, for all five diseases. There appears to be a common pathway toward death for malignant and nonmalignant diseases. The designs of symptom prevalence studies need to be improved because of methodological disparities in symptom assessment and designs.

Stanton, A. L., C. A. Bernaards, et al. (2005). "The BCPT symptom scales: a measure of physical symptoms for women diagnosed with or at risk for breast cancer." *J Natl Cancer Inst* 97(6): 448-56.

BACKGROUND: Documentation of concurrent and late side effects of medical interventions to prevent and treat breast cancer is important in research and clinical practice. We used the Breast Cancer Prevention Trial (BCPT) Symptom Checklist to develop an instrument (BCPT Symptom Scales) that could be used to assess side effects and to examine correlates of the derived symptom dimensions among patient populations. **METHODS:** Exploratory and confirmatory factor analyses were conducted using data from the 42-item BCPT Symptom Checklist completed by four distinct patient populations (N = 2208) who had previously been diagnosed with breast cancer or were at risk for the disease. We examined associations among the resulting BCPT Symptom Scales and demographic and cancer-related variables and a widely used measure of health-related quality of life. **RESULTS:** Exploratory and confirmatory factor analyses revealed eight factors corresponding to physical symptoms associated with cancer treatment, chemoprevention, menopause, and normal aging: hot flashes, nausea, bladder control, vaginal problems, musculoskeletal pain, cognitive problems, weight problems, and arm problems. On the derived BCPT Symptom Scales, women reported somewhat higher mean scores on scales for hot flashes, pain, and weight problems than on scales for the other symptoms. Demographic and cancer-related variables accounted for up to 15% of the interindividual variance in how women responded to the symptom scales. The most consistent predictors of reporting greater symptoms included lower education level and previous receipt of chemotherapy. **CONCLUSIONS:** Meaningful symptom dimensions, identified across four samples of women, were associated with demographic and breast cancer-related variables. The BCPT Symptom Scales offer a valuable refinement of the original BCPT Symptom Checklist to assess side effects associated with the treatment and prevention of breast cancer.

Stapley, S., T. J. Peters, et al. (2006). "The mortality of colorectal cancer in relation to the initial symptom at presentation to primary care and to the duration of symptoms: a cohort study using medical records." *Br J Cancer* 95(10): 1321-5.

The association between the staging of colorectal cancer and mortality is well known. Much less researched is the relationship between the duration of symptoms and outcome, and whether particular initial symptoms carry a different prognosis.

We performed a cohort study of 349 patients with primary colorectal cancer in whom all their prediagnostic symptoms and investigation results were known. Survival data for 3-8 years after diagnosis were taken from the cancer registry. Six features were studied: rectal bleeding, abdominal pain, diarrhoea, constipation, weight loss, and anaemia. Two of these were significantly associated with different staging and mortality. Rectal bleeding as an initial symptom was associated with less advanced staging (odds ratio from one Duke's stage to the next 0.50, 95% confidence interval 0.31, 0.79; P=0.003) and with reduced mortality (Cox's proportional hazard ratio (HR) 0.56 (0.41, 0.79); P=0.001. Mild anaemia, with a haemoglobin of 10.0-12.9 g dl(-1), was associated with more advanced staging (odds ratio 2.2 (1.2, 4.3); P=0.021) and worse mortality (HR 1.5 (0.98, 2.3); P=0.064). When corrected for emergency admission, sex, and the site of the tumour, the HR for mild anaemia was 1.7 (1.1, 2.6); P=0.015. No relationship was found between the duration of symptoms and staging or mortality.

Stepanski, E. J., A. C. Houts, et al. (2009). "Second- and third-line treatment of patients with non-small-cell lung cancer with erlotinib in the community setting: retrospective study of patient healthcare utilization and symptom burden." *Clin Lung Cancer* 10(6): 426-32.

INTRODUCTION: The purpose of this study was to describe treatment use patterns and outcomes with single-agent erlotinib among patients with advanced non-small-cell lung cancer (NSCLC) in the community oncology setting. **PATIENTS AND METHODS:** Retrospective chart review identified patients treated with single-agent erlotinib as either second- or third-line therapy from 4 community oncology clinics. Medical records were extracted for medical outcomes and resource utilization. Patients reported outcome measures of symptom burden and functioning. **RESULTS:** A total of 45 patients with stage IIIB/IV disease in second- (n = 27) or third-line (n = 18) therapy were 44% female and 84% white (16% black), with mean age of 66.7 years (SD, 9.2). Over 93% of the patients had previous platinum-based chemotherapy. Patients were treated with erlotinib for an average of 24 weeks. Dose reductions (24%) and treatment delays (29%) were due to skin reactions, diarrhea, and fatigue. The most common reasons for stopping erlotinib therapy were disease progression (53%), death (22%), and toxicities (11%). Patients' physical functioning improved during the first 3 months of erlotinib therapy. Hospitalizations (22%) were not due to erlotinib complications, and unplanned medical visits to the clinics were rare. **CONCLUSION:** Data from this community sample

were generally in agreement with the major clinical trial of erlotinib. Erlotinib is well tolerated by second- and third-line patients with advanced NSCLC in the community setting.

Storey, D. J., R. A. Waters, et al. (2007). "Clinically relevant fatigue in cancer outpatients: the Edinburgh Cancer Centre symptom study." *Ann Oncol* **18**(11): 1861-9.

BACKGROUND: Fatigue is associated with cancer and its treatment but we know little about how many and which patients suffer fatigue of clinical severity. We aimed to determine the prevalence of clinically relevant fatigue (CRF) and its associations in outpatients with various cancer diagnoses. **PATIENTS AND METHODS:** A survey of outpatients with colorectal, breast, gynaecological, genitourinary, sarcoma, melanoma and miscellaneous tumours at a regional cancer centre. Patients completed the European Organisation for Research and Treatment of Cancer (EORTC) fatigue subscale and the Hospital Anxiety and Depression Scale (HADS). These self-report data were linked to demographic and clinical variables. Data were available on 2867 outpatients. **RESULTS:** The prevalence of CRF (EORTC fatigue subscale $>$ or $=40$) was 32% (95% confidence interval 31-34%). The variables independently associated with CRF were primary cancer site, having disease present, type of cancer treatment and emotional distress (total HADS score $>$ or $=15$). Emotional distress had the strongest association with fatigue but half the cases of CRF were not distressed. **CONCLUSION:** CRF is common in cancer outpatients and is associated with type of disease and treatment, as well as with emotional distress. The association between CRF and emotional distress is strong but they are not equivalent conditions.

Strasser, F., C. Sweeney, et al. (2004). "Impact of a half-day multidisciplinary symptom control and palliative care outpatient clinic in a comprehensive cancer center on recommendations, symptom intensity, and patient satisfaction: a retrospective descriptive study." *J Pain Symptom Manage* **27**(6): 481-91.

To characterize a new, one-stop multidisciplinary palliative care (MD) clinic which offers standardized multidisciplinary assessment, specific care recommendations, patient and family education, and on-site counseling, we retrospectively compared the assessments of 138 consecutive patients with advanced cancer referred to the MD clinic and 77 patients referred to a traditional pain and symptom management (PSM) clinic. The two groups were similar in tumor type, demographics, and symptom

distress. The MD clinic team (physicians; nurses; pharmacists; physical, speech, and occupational therapists; social workers; chaplains; nutritionists; psychiatric nurse practitioner) delivered 1,066 non-physician recommendations (median 4 per patient, range 0-37). The PSM clinic team made no non-physician recommendations, but referred 14 patients to other medical specialists. In 80 (58%) MD-clinic patients with follow-up 9 days (median) after assessment, significant improvement was observed in pain, nausea, depression, anxiety, sleep, dyspnea, and well-being, but not in fatigue, anorexia, or drowsiness. In 83 patients interviewed after the MD clinic, satisfaction was rated as excellent (5 out of 5) in 86-97% of seven areas. Assessment at an MD clinic results in a high number of patient care recommendations, improved symptoms, and high levels of patient satisfaction.

Strong, V., R. Waters, et al. (2007). "Emotional distress in cancer patients: the Edinburgh Cancer Centre symptom study." *Br J Cancer* **96**(6): 868-74.

To: (1) estimate the prevalence of clinically significant emotional distress in patients attending a cancer outpatient department and (2) determine the associations between distress and demographic and clinical variables, we conducted a survey of outpatients attending selected clinics of a regional cancer centre in Edinburgh, UK. Patients completed the Hospital Anxiety and Depression Scale (HADS) on touch-screen computers and the scores were linked to clinical variables on the hospital database. Nearly one quarter of the cancer outpatients 674 out of 3071 (22%; 95% confidence interval (CI) 20-23%) met our criterion for clinically significant emotional distress (total HADS score 15 or more). Univariate analysis identified the following statistically significant associations: age $<$ 65, female gender, cancer type and extent of disease. Multivariate analysis indicated that age $<$ 65 (odds ratio 1.41; 95% CI 1.18-1.69), female gender (odds ratio 1.58; 95% CI 1.31-1.92) and active disease (odds ratio 1.72; 95% CI 1.43-2.05) but not cancer diagnosis, were the independent predictors of clinically significant emotional distress. Services to treat distress in cancer patients should be organised to target patients by characteristics other than their cancer diagnosis.

Sun, C. C., D. C. Bodurka, et al. (2005). "Rankings and symptom assessments of side effects from chemotherapy: insights from experienced patients with ovarian cancer." *Support Care Cancer* **13**(4): 219-27.

GOALS OF WORK: Although many patients with ovarian cancer achieve favorable responses to primary chemotherapy, the majority of

women will experience recurrence of their cancer. Selection of second- or third-line chemotherapy ultimately depends on patient preferences for different side effects. To better understand this process, we evaluated preferences and symptom distress in patients with ovarian cancer. **PATIENTS AND METHODS:** A total of 70 women with ovarian cancer who had previously received at least three cycles of platinum-based chemotherapy and currently undergoing chemotherapy for newly diagnosed or recurrent disease were interviewed in an outpatient chemotherapy clinic. The patients were asked to rank order 27 health states using a modified visual analog scale and to complete the Memorial Symptom Assessment Scale (MSAS). **MAIN RESULTS:** Most favorable health states included perfect health, clinical remission and complete control of chemotherapy-induced nausea and vomiting (CINV). Least favorable health states included more severe CINV health states and death. Patients on first-line chemotherapy had less symptom distress, and rated sexual dysfunction, fatigue and memory loss more favorably than patients on second- or third-line chemotherapy ($P < 0.05$). Married patients generally had less symptom distress compared to patients who were not married, but married patients indicated more distress with sexual dysfunction ($P = 0.04$). Married patients rated alopecia less favorably than unmarried patients ($P = 0.03$), but married patients viewed certain CINV health states more favorably ($P = 0.02-0.04$). **CONCLUSIONS:** CINV remains one of the most dreaded side effects of chemotherapy. Separate preference profiles exist for patients with newly diagnosed and recurrent disease, as well as for married versus unmarried patients. While MSAS scores and VAS rankings showed consistency across some health states, this was not true for CINV, suggesting that current symptom status may only influence patient preferences for selected side effects.

Sun, Y. and M. T. Knobf (2008). "Concept analysis of symptom disclosure in the context of cancer." *ANS Adv Nurs Sci* **31**(4): 332-41.

Although symptoms suggestive of cancer are the most common reason that people seek healthcare, the process undertaken to disclose the symptoms is unclear. The purpose of this article is to critically analyze the concept of symptom disclosure in the context of cancer. Rodgers' evolutionary approach was applied to analyze the concept of symptom disclosure. Concept analysis indicates that symptom disclosure is a decision-making process in which a person chooses to tell significant others and a healthcare provider about self-identified symptoms. Characteristics of the concept include symptom interpretation, weighing the risks and benefits of

disclosure, and taking action. Influencing factors are knowledge, cancer risk perception, personal or family history of cancer, socioeconomic and cultural factors, and access to care. The concept analysis of symptom disclosure provides guidance for developing strategies to promote healthcare-seeking behavior in practice and suggest areas for future research.

Swore Fletcher, B. A., M. J. Dodd, et al. (2008). "Symptom experience of family caregivers of patients with cancer." *Oncol Nurs Forum* **35**(2): E23-44.

OBJECTIVES: To review the literature on depression, anxiety, sleep disturbance, fatigue, and pain in family caregivers of patients with cancer in the context of the Symptom Management Model (SMM) developed at the University of California, San Francisco (UCSF). **DATA SOURCES:** Published research studies and systematic reviews from 1990-2007. **DATA SYNTHESIS:** Studies of depressive symptoms in caregivers of patients with cancer were the most numerous. A limited number of studies examined anxiety, fatigue, sleep disturbance, and pain. Most studies focused on the symptom experience dimension of the UCSF SMM. **CONCLUSIONS:** Based on the small sample sizes, cross-sectional nature of the studies, and lack of comparison groups, little is known about the prevalence and effects of symptoms in caregivers of patients with cancer. **IMPLICATIONS FOR NURSING:** Additional research is needed to determine the prevalence, severity, and effects of symptoms on caregivers. Better descriptive, correlational studies will lead to the development of interventions to improve symptom management for this group of caregivers.

Tanaka, N., K. Fujimoto, et al. (2009). "Variations in international prostate symptom scores, uroflowmetric parameters, and prostate volume after (125)I permanent brachytherapy for localized prostate cancer." *Urology* **74**(2): 407-11.

OBJECTIVES: To evaluate the chronologic changes in the International Prostate Symptom Score (IPSS), uroflowmetric parameters, and prostate volume (PV) in patients who received low-dose-rate brachytherapy. **METHODS:** Between July 2004 and December 2006, 110 patients received low-dose-rate brachytherapy. Of the 110 patients, 82 were treated with seed implantation alone and 28 with combined external beam radiotherapy. The IPSS, uroflowmetric parameters, and PV were evaluated before seed implantation and at 1, 3, 6, and 12 months after seed implantation. **RESULTS:** The mean IPSS showed a significant increase at 1 and 6 months after seed implantation and had returned to baseline 12 months later. The maximal flow rate, voided volume, and

postvoid residual urine volume showed transient deterioration at 1 and 6 months after seed implantation and had returned to the baseline 12 months later. The mean PV compared with the baseline PV showed a significant 3.8-cm(3) decrease (11.2%) at 12 months after implantation. The patients who did not receive neoadjuvant hormonal therapy had a 5.9-cm(3) decrease in PV (20.2%) 12 months later. In contrast, those who received neoadjuvant hormonal therapy had no change in PV after seed implantation. CONCLUSIONS: This is the first report to evaluate the chronologic changes in subjective parameters (IPSS) and objective parameters (uroflowmetry) and PV, concurrently. The changes in subjective parameters correlated with the changes in objective parameters during the first 12 months after seed implantation. The change in the PV was different after seed implantation in patients with or without neoadjuvant hormonal therapy.

Tassinari, D., B. Poggi, et al. (2005). "Treating sialorrhea with transdermal scopolamine. Exploiting a side effect to treat an uncommon symptom in cancer patients." *Support Care Cancer* **13**(7): 559-61.

INTRODUCTION: Sialorrhea is a distressing symptom accompanying oral cancer and many heterogeneous cancer-related conditions (chemotherapy-induced nausea, bowel subocclusion, pharmacologic side effects), but its incidence is low in cancer patients. Conversely, it is frequent in patients with neurological damage, and some therapeutic options have been attempted such as botulinum toxins, anticholinergic agents, and surgical procedures. CASE REPORT: We report the case of an 80-year-old woman with peritoneal carcinomatosis and bowel subocclusion, suffering from distressing nausea and sialorrhea that rapidly improved using transdermal scopolamine. No relevant side effects occurred during the treatment, and the reduction of the abnormal salivation allowed the recovery of oral feeding. CONCLUSIONS: Anticholinergic drugs are classified as secondary options in the treatment of sialorrhea of patients with Parkinson's disease or cerebral palsy, owing to the relevant side effects occurring during prolonged treatments. However, they could be useful in cancer patients with bowel subocclusion, as the reduction of gastrointestinal secretions and intestinal motility (frequent side effects of anticholinergic drugs) could be effective in controlling nausea, vomiting, and abdominal pain. Moreover, the transdermal or sublingual route of administration can be of some interest, avoiding other more invasive parenteral approaches.

Temel, J. S., W. F. Pirl, et al. (2006). "Comprehensive symptom management in patients with advanced-

stage non-small-cell lung cancer." *Clin Lung Cancer* **7**(4): 241-9.

Although we have made steady improvements in the survival rates of patients with advanced-stage lung cancer, the majority of patients still experience distress and suffering. Although the symptom burden is greatest in patients in the end stages of life, many patients living with lung cancer suffer from troubling symptoms and side effects of therapy. Even long-term survivors with early-stage non-small-cell lung cancer (NSCLC) often experience respiratory symptoms, such as dyspnea and cough. Because of the high prevalence of NSCLC and the frequency with which it presents in an incurable stage, symptom management is a large component of the care of these patients. Dyspnea, cough, fatigue, anorexia/cachexia, and pain are the most common symptoms in patients with advanced-stage NSCLC. Cancer-directed therapy can improve some of these symptoms but often incompletely and temporarily. Therefore, comprehensive care of patients with advanced-stage NSCLC must include therapies targeted at these difficult and distressing symptoms.

Teunissen, S. C., A. de Graeff, et al. (2007). "Are anxiety and depressed mood related to physical symptom burden? A study in hospitalized advanced cancer patients." *Palliat Med* **21**(4): 341-6.

BACKGROUND: Anxiety and depressed mood are common symptoms in hospitalized advanced cancer patients. It is often presumed that anxiety and depression affect the occurrence and experience of physical symptoms. PURPOSE: To analyse the relation between anxiety, depressed mood and the presence and intensity of physical symptoms. PATIENTS AND METHODS: Anxiety and depressed mood were assessed in a hospitalized advanced cancer population (n = 79) primarily by the Hospital Anxiety and Depression Scale (HADS), and also by a single-item question ;Are you anxious and/or depressed?' and by the Edmonton Symptom Assessment System (ESAS). Physical symptoms were assessed by a semi-structured interview and by the ESAS. RESULTS: Thirty-four percent of the patients reported anxiety, 56% depressed mood and 29% both, as assessed by the HADS. The correlations between HADS, the single-item question and the ESAS were low. No association was found between anxiety or depressed mood and the presence of physical symptoms. Patients who were anxious or depressed had higher ESAS scores for insomnia and drowsiness; scores for pain, anorexia, asthenia, nausea and dyspnea were independent of anxiety and/or depressed mood. CONCLUSION: The relationship between anxiety, depressed mood and the presence and intensity of

physical symptoms in hospitalized advanced cancer patients is very limited.

Teunissen, S. C., W. Wesker, et al. (2007). "Symptom prevalence in patients with incurable cancer: a systematic review." *J Pain Symptom Manage* **34**(1): 94-104.

The suffering of patients with incurable cancer is determined to a large degree by the presence and intensity of the symptoms of their disease. Knowledge of symptom prevalence is important for clinical practice. The main aim of this study was to obtain a reliable estimation of symptom prevalence in patients with incurable cancer by performing a systematic review of studies assessing this topic. We included 44 studies (including 25,074 patients) on overall symptom prevalence (Group 1) and six studies (including 2,219 patients) on symptom prevalence during the last one to two weeks of life (Group 2). In these studies, symptom prevalence was assessed by a questionnaire, a standardized interview, or the medical record. We identified 37 symptoms assessed in at least five studies. Almost all symptoms occurred in more than 10% of the patients. Five symptoms (fatigue, pain, lack of energy, weakness, and appetite loss) occurred in more than 50% of the patients of Group 1. Weight loss occurred significantly more often in Group 2 compared to Group 1, and pain, nausea, and urinary symptoms occurred significantly less often. Generally, symptom prevalence was highest if assessed by a questionnaire. The results of this study should be used to guide doctors and nurses in symptom management. Proper attention to symptom burden and suffering should be the basis for individually tailored treatment aimed at improving or maintaining quality of life of patients in their last period of life.

Thompson, M. R., R. Perera, et al. (2007). "Predictive value of common symptom combinations in diagnosing colorectal cancer." *Br J Surg* **94**(10): 1260-5.

BACKGROUND: This study compared the diagnostic values of age and single symptoms of colorectal cancer with those of age and symptom combinations. **METHODS:** Consecutive patients with lower gastrointestinal symptoms referred to a surgical clinic over a 12-year period were studied prospectively. The diagnostic value of age and common symptoms of bowel cancer, individually and in combination, was determined by measuring positive predictive value, sensitivity and specificity. **RESULTS:** In total, 467 (5.5 per cent) of 8529 patients had colorectal cancer. Symptom combination analyses showed that patients presenting with rectal bleeding and change in bowel habit without anal

symptoms had the highest risk of cancer. Those with rectal bleeding and perianal symptoms without change in bowel habit were at the lowest risk of having cancer. Symptom subgroups defined by age had positive predictive values for cancer that varied from less than 1 to 35 per cent. **CONCLUSION:** Symptom combinations defined by age have greater diagnostic value than single symptoms alone.

Tishelman, C., L. M. Petersson, et al. (2007). "Symptom prevalence, intensity, and distress in patients with inoperable lung cancer in relation to time of death." *J Clin Oncol* **25**(34): 5381-9.

PURPOSE: To examine symptom prevalence, intensity, and association with distress in patients with inoperable lung cancer (LC), using time to death as point of reference. **PATIENTS AND METHODS:** A consecutive sample of 400 patients completed the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 plus a 13-item LC-specific scale and the Thurstone Scale of Symptom Distress-Lung Cancer at six time points during the first year after diagnosis. Patients were divided into subgroups, using data from the time point closest to death (< 1; 1 to 2; > 2 to 3; > 3 to 6; > 6 to 12; and > 12 months before death) for analysis. **RESULTS:** More than 50% of patients in all subgroups reported problems related to physical, role, and emotional functioning; fatigue; dyspnea; and cough. In general, functional levels were lower and symptoms higher in subgroups closer to death. Notably, clinically relevant differences were also found in role and social functioning and appetite loss between the two groups furthest from death. A consistent pattern was found among the six subgroups, with breathing, pain, and fatigue rated as the symptoms most associated with distress. **CONCLUSION:** High prevalence of symptoms was found in all subgroups, with higher intensity in subgroups closer to death, indicating a need for prophylactic and proactive symptom management. Less concordance was found among symptom prevalence, intensity, and association with distress in subgroups further from death. Future studies should investigate longitudinal associations between symptoms with low intensity and high distress, and examine their clinical implications.

Tokuda, Y., K. Chinen, et al. (2009). "Intervals between symptom onset and clinical presentation in cancer patients." *Intern Med* **48**(11): 899-905.

OBJECTIVE: We aimed to investigate relative values of the intervals between symptom onset and clinical presentation in cancer patients and to correlate them with diagnosis of distant metastasis. **METHODS:** Cancer registry and medical records of

all cancer patients for over a 10-year period in a medical center of Japan were reviewed. We examined the intervals of symptom onset to clinical presentation and the presence of metastasis at diagnosis. RESULTS: In 3,893 cancer patients, the mean interval of symptom onset to clinical presentation was 89 days (median, 30 days). The cancer group with a short interval of only days to weeks included hepatobiliary, ovary, brain, and acute leukemia. The group with a long interval of months to years included head and neck, thyroid, and skin cancers. Other types of cancer were included in the middle group with an interval of weeks to months. Among patients with head & neck, skin, and ovarian cancers, the longer interval was significantly associated with a lower likelihood of distant metastasis. A longer interval with an increment of each month was associated with a lower likelihood for distant metastasis with an odds ratio of 0.97 (95% CI, 0.96-0.99). CONCLUSION: Hepatobiliary, ovary, brain, and acute leukemia are among the cancer types with an interval of days to weeks, while head and neck, thyroid, and skin cancers are among the types with an interval of months to years. Among patients with solid tumors, those with metastasis are likely to present to a physician more promptly.

Tsai, J. S., C. H. Wu, et al. (2006). "Symptom patterns of advanced cancer patients in a palliative care unit." *Palliat Med* 20(6): 617-22.

This study involved longitudinal evaluations of symptom severity and describes the symptom patterns of 77 terminal cancer patients (median age: 62 years; 61% female), selected from 537 consecutive patients admitted to the Palliative Care Unit of the National Taiwan University Hospital. The most common primary cancer sites in these patients were lung (23.4%), liver (15.6%), and stomach (13%). Nineteen physical and psychological symptoms were assessed using different scales. The median number of symptoms was 11 (range: 1-18) on admission, among which weakness, fatigue, anorexia, pain, and depression were the most common. A comparison of the initial symptom severity scores with those at one week after admission and two days before death suggested six symptom change patterns: A: continuous static (restless/heat, abdominal fullness, constipation, dizziness, and insomnia); B: static-increase (fatigue, weakness, nausea/vomiting, taste alteration, dysphagia, diarrhea, dry mouth, and night sweats); C: decrease-static (pain and depression); D: decrease-increase (anorexia and dyspnea); E: static-decrease (aggression); and F: gradually decrease (anxiety). These six symptom patterns can be divided into two categories on the basis of the relative severity of symptoms between one week after admission and two days before death. The first category included

patterns A, C, E and F, and the symptoms improved with palliative care. However, the symptoms in the second category (patterns B and D), which were associated with the anorexia-cachexia syndrome and dyspnea, did not show improvement. As symptom management is an essential component of palliative care, holistic care, which encompasses physical, psychosocial and spiritual aspects, represents a rational approach for the relief of these incurable symptoms at the end stage of life for these patients.

Tseng, T. H., C. S. Cleeland, et al. (2008). "Assessing cancer symptoms in adolescents with cancer using the Taiwanese version of the M. D. Anderson Symptom Inventory." *Cancer Nurs* 31(3): E9-16.

The purpose of this study was to evaluate the validity and reliability of the Taiwanese version of the M. D. Anderson Symptom Inventory (MDASI-T) in Taiwanese adolescent cancer patients. One hundred eight adolescent cancer patients were interviewed using the MDASI-T, and the results were then used to establish the psychometric properties of this instrument. Data were analyzed by factor analysis, cluster analysis, Pearson correlation, Mann-Whitney U test, and descriptive statistics. The construct validity was determined using a confirmatory factor analysis with oblimin rotation. The concurrent validity demonstrated moderate correlations between the MDASI-T subscale scores and the Medical Outcome Study 36-Item Short-Form Health Survey. Known-group validity was established by comparing MDASI-T scores between adolescent cancer patients with a low functional status and those with a high functional status (Karnofsky Performance Status scores ≤ 80 and >80 , respectively). The alpha coefficient of the symptoms severity and interference subscales demonstrated good internal consistency. There was acceptable test-retest stability of the MDASI-T in 35 adolescents during a 3-day interval. This study provides evidence that the MDASI-T is a reliable and valid instrument for measuring cancer-related symptoms in Taiwanese adolescents with cancer.

Vadiraja, S. H., M. R. Rao, et al. (2009). "Effects of yoga on symptom management in breast cancer patients: A randomized controlled trial." *Int J Yoga* 2(2): 73-9.

OBJECTIVES: This study compares the effects of an integrated yoga program with brief supportive therapy on distressful symptoms in breast cancer outpatients undergoing adjuvant radiotherapy. MATERIALS AND METHODS: Eighty-eight stage II and III breast cancer outpatients were randomly assigned to receive yoga (n = 44) or brief supportive therapy (n = 44) prior to their radiotherapy treatment. Intervention consisted of yoga sessions lasting 60 min

daily while the control group was imparted supportive therapy once in 10 days during the course of their adjuvant radiotherapy. Assessments included Rotterdam Symptom Check List and European Organization for Research in the Treatment of Cancer-Quality of Life (EORTC QoL C30) symptom scale. Assessments were done at baseline and after 6 weeks of radiotherapy treatment. RESULTS: A GLM repeated-measures ANOVA showed a significant decrease in psychological distress ($P = 0.01$), fatigue ($P = 0.007$), insomnia ($P = 0.001$), and appetite loss ($P = 0.002$) over time in the yoga group as compared to controls. There was significant improvement in the activity level ($P = 0.02$) in the yoga group as compared to controls. There was a significant positive correlation between physical and psychological distress and fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, and constipation. There was a significant negative correlation between the activity level and fatigue, nausea and vomiting, pain, dyspnea, insomnia, and appetite loss. CONCLUSION: The results suggest beneficial effects with yoga intervention in managing cancer-and treatment-related symptoms in breast cancer patients.

Visovsky, C. G., A. M. Berger, et al. (2008). "Methodological challenges of symptom management research in recurrent cancer." *Cancer Nurs* **31**(3): 175-81.

Completion of first-line treatment is an important milestone for adults newly diagnosed with cancer. However, for many adults, the cancer experience of the 21st century does not end with the completion of initial treatment. Decreased functional status, distressing symptoms, and residual effects of treatment impact the daily lives of cancer survivors. Cancer has evolved into a chronic illness, in which a disease-free period may be followed by recurrent cancer. Researchers face challenges in the design and analysis of symptom management studies in recurrent disease. Residual effects can preclude a true "baseline" measurement of the symptom(s) of interest to the researcher. In addition, as cancer survivors age, they are more likely to have comorbid conditions that increase the likelihood of developing toxicities and residual symptoms that are specific to cancer treatments. Research studies of cancer-related symptoms in adults with recurrent disease pose many methodological challenges. Selection of appropriate study design, sample inclusion and exclusion criteria, measures of comorbidity and symptoms, and advanced analysis techniques are among the strategies proposed to address these methodological challenges.

Wada, Y., R. Takahashi, et al. (2007). "Paradoxical cerebral embolism as the initial symptom in a patient

with ovarian cancer." *J Stroke Cerebrovasc Dis* **16**(2): 88-90.

This report concerns a 37-year-old patient with ovarian cancer and a paradoxical cerebral embolism as the initial symptom. She developed acute onset of left quadrantic hemianopia during coughing. Brain magnetic resonance imaging showed an acute multiple infarction, and a simultaneous acute pulmonary embolism was observed. Transesophageal echocardiography showed a patent foramen ovale, multidetector row computed tomography an ovarian tumor and infarction of the spleen, whereas multidetector row computed tomography venography showed right iliac vein compression by the ovarian tumor. The diagnosis was stage Ic ovarian cancer. Because blood stasis of the pelvic vein is a major risk factor for venous thrombosis, the presence of a patent foramen ovale should alert physicians to examine not only veins in the lower extremities but also the pelvic and intra-abdominal veins as a source paradoxical embolism.

Walsh, D. and L. Rybicki (2006). "Symptom clustering in advanced cancer." *Support Care Cancer* **14**(8): 831-6.

A major goal of palliative medicine is to control symptoms that interfere with quality of life. Identification of symptoms that occur together (cluster) may aid in symptom management, resulting in greater therapeutic benefit to the patient. An analysis of 25 symptoms from 922 patients with advanced cancer was undertaken to determine if symptom clusters could be identified. Cluster analysis was done using an agglomerative hierarchical method with average linkage; the absolute value of the correlation between pairs of symptoms was used as the measure of similarity. A correlation of ≥ 0.68 was used to define the final clusters. Seven clusters were identified: (1) fatigue; anorexia-cachexia; (2) neuropsychological; (3) upper gastrointestinal; (4) nausea and vomiting; (5) aerodigestive; (6) debility; (7) pain. Recognition of symptom clusters should help understand symptom pathophysiology and target therapies that perhaps can be used to relieve multiple symptoms in that cluster. This could result in improved quality of life for patients with advanced cancer and perhaps reduce polypharmacy, lessen drug side effects, and have pharmacoeconomic benefits.

Wang, J., F. Liu, et al. (2008). "The symptom-to-treatment delay and stage at the time of treatment in cancer of esophagus." *Jpn J Clin Oncol* **38**(2): 87-91.

OBJECTIVE: The main purpose of this investigation was to measure the delay from the first symptom to treatment in esophageal cancer and to analyse the relation between the delay and stage at the

time of treatment. **METHODS:** A total of 80 patients who were consecutively found to have esophageal cancer between 1 January 2007 and 30 July 2007 at Qilu Hospital of Shandong University in Jinan (China) were included in the retrospective study. Two groups of patients were compared, one group with good prognosis (patients in Stages I and II) and the other group with poor prognosis (patients in Stages III and IV). The symptom-to-treatment delay between the two patient groups was compared using the Mann-Whitney U-test. **RESULTS:** The median symptom-to-treatment delay was 2.1 months (range from 0.5 to 24). The total symptom-to-treatment delay was made up with the following components: (i) delay from the first symptoms to first contacting the health-care system (69%); (ii) delay from first contacting the health-care system to histological diagnosis of esophageal cancer (20%); and (iii) delay from histological diagnosis to end point (11%). A significantly shorter median symptom-to-treatment delay was found for patients with Stages I and II compared with III and IV ($P = 0.0177$). **CONCLUSIONS:** Long delays still occur in patients with esophageal cancer. A few months delay before final treatment of esophageal cancer may have an impact on the stage of the cancer, and thereby on the patients' prognosis. Shorting the delay may result in early detection of esophageal cancer.

Wang, S. Y., C. W. Lee, et al. (2005). "Symptom distress changes during first postoperative month in newly diagnosed Taiwanese breast cancer patients: a longitudinal study." *Cancer Nurs* **28**(4): 263-9.

The purpose of this longitudinal study was to explore changes in symptom distress in newly diagnosed Taiwanese breast cancer patients during the initial 4-week postoperative period. The research instruments, including a demographic questionnaire and the Symptom Distress Scale, were used to obtain data on postoperative day 2 and at weeks 2, 3, and 4. In total, 39 patients with a mean age of 48 years participated in this study. Data were analyzed using descriptive statistics, t tests, one-way ANOVA, and repeated-measures ANOVA. Results revealed that the level of symptom distress significantly decreased from postoperative day 2 to week 4. Loss of appetite and a poor outlook increased; nausea frequency, fatigue, and insomnia decreased then increased; and frequency and the level of pain, coughing, tightness/tenderness in the chest wall, weakness, and numbness in the arm of the operative side all decreased over the 4-week study period. Age, stage of disease, and type of surgery were all related to symptom distress. Results of this study may provide reassurances about what can be expected after breast cancer surgery.

Wang, S. Y., C. M. Tsai, et al. (2008). "Symptom clusters and relationships to symptom interference with daily life in Taiwanese lung cancer patients." *J Pain Symptom Manage* **35**(3): 258-66.

The number one cause of cancer death in Taiwan is lung cancer. Of the few studies describing the experience of patients living with lung cancer, most use bivariate analyses to test associations between individual symptoms. Few have systematically investigated multiple symptoms. This prospective study was undertaken to explore the phenomenon of symptom distress, to investigate the presence of symptom clusters, and to examine the relationship of symptom clusters to symptom interference with daily life in Taiwanese lung cancer patients. A sample of 108 lung cancer patients was recruited using the Taiwanese version of the M. D. Anderson Symptom Inventory. Data were analyzed by hierarchical cluster analysis, factor analysis, Pearson correlation, t-test, and regression analysis. The top five most-severe symptoms were fatigue, sleep disturbance, lack of appetite, shortness of breath, and general distress. Factor analysis generated a two-factor solution (general and gastrointestinal symptoms) for symptom severity items. Consistent with the result from factor analysis, cluster analysis also indicated the same two cluster groups (general and gastrointestinal symptoms). Both clusters were significantly correlated with symptom interference items; however, the general symptom cluster presented higher correlation coefficients than did the gastrointestinal symptom cluster. These results provide an important basis for developing novel strategies to manage multiple symptoms in lung cancer patients and thereby improve their well-being.

Wang, X. S., A. V. Laudico, et al. (2006). "Filipino version of the M. D. Anderson Symptom Inventory: validation and multisymptom measurement in cancer patients." *J Pain Symptom Manage* **31**(6): 542-52.

Assessing cancer-related symptoms requires a brief, reliable, valid, and culturally adapted symptom screening tool. In the Philippines, cancer patients ($n=206$) and community-dwelling adults ($n=170$) participated in a cross-sectional validation study of the Filipino version of the M. D. Anderson Symptom Inventory (MDASI-F). Both exploratory factor analysis and hierarchical cluster analysis revealed two underlying symptom severity constructs--general and gastrointestinal symptoms--consistent with the English, Japanese, and Chinese versions of the MDASI. Cronbach alpha coefficients of 0.79 and 0.77, respectively, demonstrated acceptable internal consistency for the two factors. Known-group validity was confirmed by significant differences on MDASI-F items by performance status ($P<0.01$ or $P<0.001$).

Fatigue, sadness, distress, and pain were significant predictors of symptom interference. Cancer patients reported significantly greater symptom severity on multiple items than did the community sample. The MDASI-F is reliable and valid for evaluating cancer-related symptoms and their impact on Filipino cancer patients.

Wang, X. S., Y. Wang, et al. (2004). "Chinese version of the M. D. Anderson Symptom Inventory: validation and application of symptom measurement in cancer patients." *Cancer* **101**(8): 1890-901.

BACKGROUND: Symptom management is an essential component of cancer treatment for patients of every culture and nationality. Symptom assessment depends on subjective reporting, mandating linguistically equivalent versions of symptom assessment scales. Because disease-related and treatment-related symptoms most often occur in clusters, there is a global need for a standardized multiple-symptom assessment tool. **METHODS:** The authors sought to validate the Chinese version of the M. D. Anderson Symptom Inventory (MDASI-C) by enrolling patients who had received various diagnoses of and different types of treatment for cancer ($n = 249$) in a cross-sectional symptom study conducted at an urban cancer center in China. **RESULTS:** Factor analysis identified 2 underlying constructs, general symptoms and gastrointestinal symptoms, which had Cronbach alpha coefficients of 0.86 and 0.84, respectively. These results were consistent with English- and Japanese-language MDASI validation studies. Known-group validity was supported by the MDASI-C's ability to detect significant differences in symptom and interference levels according to Eastern Cooperative Oncology Group performance status (ECOG PS; $P < 0.001$) and chemotherapy status ($P < 0.05$). Fifty-five percent of the study cohort had ≥ 1 symptom that was considered severe (score ≥ 7 on a 0-10 scale). ECOG PS was strongly associated with symptom burden (total interference score: $R(2) = 0.26$; $P < 0.001$). Fatigue, sadness, drowsiness, and lack of appetite accounted for most of the variability in the total interference score ($R(2) = 0.49$; $P < 0.05$). **CONCLUSIONS:** The authors demonstrated that the MDASI-C is a valid, reliable, and concise tool for measuring symptom severity and interference with functioning in Chinese cancer patients.

Wennman-Larsen, A., C. Tishelman, et al. (2007). "Factors influencing agreement in symptom ratings by lung cancer patients and their significant others." *J Pain Symptom Manage* **33**(2): 146-55.

Comparisons of symptom ratings and health-related quality of life between significant others and patients have been the focus of numerous studies

during the past decades. Additional studies are needed to assess the discrepancies identified in this work. In the present cross-sectional exploratory study, focus has been on evaluating the accuracy of significant other proxy ratings and on investigating factors that influence agreement between lung cancer patients and significant others based on dyadic assessments from 52 patients and 54 significant others. Results indicate that the levels of agreement are fair to good, but that significant others consistently rate the patients' symptoms higher and functioning lower than the patients do themselves. Factors found to influence agreement in various dimensions of symptoms and functioning were gender, patient age, and significant others' self-reported lack of family support, health problems, and caregiver esteem.

Wilkinson, S., K. Barnes, et al. (2008). "Massage for symptom relief in patients with cancer: systematic review." *J Adv Nurs* **63**(5): 430-9.

AIM: This paper is a report of a review to assess evidence of the effectiveness of massage for patients with cancer, in terms of reducing physical or psychological symptoms, improving quality of life, or producing unwanted side effects. **BACKGROUND:** Patients with cancer may use complementary therapies, including massage and aromatherapy massage. However, their use and provision by state-financed healthcare services is controversial. **DATA SOURCES:** A systematic review was carried out, using the Cochrane principles. No meta-analysis was appropriate. An initial comprehensive search of electronic databases search was carried out in 2003 and updated in 2006. Eligible trials were randomized controlled trials, controlled before-and-after (pre-post) studies and interrupted time-series studies. Participants were adults with a diagnosis of cancer and receiving care in any healthcare setting. Interventions were limited to massage and/or aromatherapy massage carried out by a qualified therapist. Outcome measures to be included were patient-reported levels of physical and psychological indices of symptom distress and quality of life (measured using validated assessment tools). **FINDINGS:** In the review, 1325 papers were considered. Ten trials met the inclusion criteria and their results suggest that massage might reduce anxiety in patients with cancer in the short term and may have a beneficial effect on physical symptoms of cancer, such as pain and nausea. However, the lack of rigorous research evidence precludes drawing definitive conclusions. **CONCLUSION:** Further well-designed large trials with longer follow-up periods are needed to be able to draw firm conclusions about the efficacy and effectiveness of massage for cancer patients.

Wilkinson, S., K. Lockhart, et al. (2008). "Reflexology for symptom relief in patients with cancer." *Cancer Nurs* **31**(5): 354-60; quiz 361-2.

Complementary therapies are increasingly being used in hospices and hospitals alongside orthodox treatments in an attempt to improve patients' emotional, spiritual, psychological, and physical well-being. An average of 31% of UK patients with cancer use some form of complementary therapy. Many UK cancer centers, out-patient units, and hospices are providing complementary services. There is strong anecdotal evidence that complementary therapies assist in the palliation of physical and psychological symptoms. This systematic review examines the research evidence base for the effectiveness of reflexology in cancer care. The study reports the results of a systematic review following the Cochrane principles of systematic reviewing. No meta-analysis was possible. Studies were retrieved from a comprehensive search of electronic databases from their start dates. An initial search was carried out in 2003 and updated in 2005 to 2006. Eligible studies were randomized controlled trials, controlled before and after studies, and interrupted time-series studies. Participants were adults with a diagnosis of cancer, receiving care in any healthcare setting. Interventions were limited to reflexology carried out by a qualified therapist as distinguished from another healthcare professional carrying out a reflexology intervention. Outcome measures were patient-reported levels of physical and psychological indices of symptom distress and quality of life (measured using validated assessment tools).

Williams, P. D., U. Piamjariyakul, et al. (2006). "Cancer treatment, symptom monitoring, and self-care in adults: pilot study." *Cancer Nurs* **29**(5): 347-55.

A descriptive study was conducted on self-reported symptoms and self-care by 37 adults receiving chemotherapy primarily for leukemia, lymphomas, or breast cancer or radiation therapy for head and neck or lung cancers. The Therapy-Related Symptom Checklist and demographic and interview forms on self-care for identified symptoms were used. Severe symptoms on the Therapy-Related Symptom Checklist subscales fatigue, eating, nausea, pain, numbness in fingers/toes, hair loss, and constipation were reported by patients on chemotherapy. Those on radiation therapy reported severe symptoms on the eating, fatigue, skin changes, oropharynx, and constipation subscales. Self-care strategies were in the following categories, using complementary medicine as framework: diet/nutrition/lifestyle change (eg, use of nutritional supplements; modifications of food and of eating habits; naps, sleep, and rest); mind/body

control (eg, relaxation methods, prayer, music, attending granddaughter's sports events); biologic treatments (vitamins); herbal treatments (green mint tea); and ethnomedicine (lime juice and garlic). The first category was predominantly used by patients in both treatment types. Medications were prescribed also to help control symptoms (eg, pain and nausea). Symptom monitoring and self-care for symptoms identified may be facilitated by the Therapy-Related Symptom Checklist; based on reported symptom severity, care providers may prioritize interventions. A larger study needs to be done on (a) the use of the Therapy-Related Symptom Checklist as a clinical tool to assess symptoms that oncology patients experience during therapy; (b) whether care providers, based on patient-reported symptom severity, can prioritize interventions--and how this influences the efficiency of care; (c) the self-care strategies used by patients on chemotherapy or radiation therapy or both; and (d) how useful these strategies are in alleviating symptoms.

Williams, P. D., J. Schmideskamp, et al. (2006). "Symptom monitoring and dependent care during cancer treatment in children: pilot study." *Cancer Nurs* **29**(3): 188-97.

Symptom monitoring by parents/caregivers of children with cancer and what the caregiver and child did to help alleviate symptoms during chemotherapy were studied. The Therapy-Related Symptom Checklist (TRSC) child version was administered to parents/caregivers of 11 children and adolescents (mean age, 10.4 years; SD, 6.1 years; range, 2-18 years; 45% were boys). The Karnofsky scale was completed by clinicians to rate the child's functional status. The TRSC child version and functional status scores were inversely related. All children experienced nausea; the most frequent symptoms reported were in TRSC subscales: fatigue, nausea, eating, fever, oropharynx, pain, and hair loss. Care strategies that helped were distraction, massage, mouth rinses, and vitamins; some reported that their child received medications for pain, nausea, and vomiting. Using complementary medicine categories, the care strategies were diet/nutrition/lifestyle change (eg, more high-fat, high-calorie foods; new foods; any food the child likes; and much sleep and rest); mind/body control (eg, play, video games, television, reading, activity puzzle, breathing exercises, relaxation methods, and prayer); manual healing method (massage and skin-to-skin contact); and biologic treatments (vitamins). The first 2 categories were the most used. Systematic assessment with a self-report checklist enables the provider to identify and prioritize (according to reported severity) those symptoms needing intervention.

Woodgate, R. L. and L. F. Degner (2004). "Cancer symptom transition periods of children and families." *J Adv Nurs* **46**(4): 358-68.

BACKGROUND: Children with cancer are reported to experience many symptoms during the cancer trajectory. However, minimal qualitative research has been conducted that explores children's and families' experiences of symptoms. An understanding of the symptom trajectory, grounded in children's and families' experiences, is essential to providing comprehensive and sensitive care to children with cancer and their families. **AIM:** This paper reports a study designed to explore and describe the symptom course in childhood cancer as experienced by children and their families. **DESIGN:** Guided by the philosophy of interpretive interactionism, a longitudinal qualitative study was undertaken. A purposive sample of 39 families of children with cancer who resided in Western Canada participated. The children ranged in age from 4.5 to 18 years and varied in their cancer diagnoses. **METHODS:** Multiple data collection methods included formal and informal interviewing and participant observation. Data were analysed by the constant comparative method. Development of illness narratives added to an understanding of children's and families' experiences. **FINDINGS:** A substantive theory entitled 'Children's and Families' Lived Experience of Childhood Cancer Symptoms' emerged from the findings. This depicts the experience of cancer in relation to children's changing symptom trajectory. A core category of the theory, 'passage through the transition periods', shows how changing symptom experiences affected children's and families' ways of being in the world. These were reflected in six transition periods: (1) it is just the flu; (2) it is more than the flu; (3) it hits home; (4) it is nasty; (5) it is not so bad, it is pretty good; and (6) it is 'dragsville'. The changing roles and responsibilities of family members, and how the family existed in the cancer world, varied depending on the transition period through which they were passing. **CONCLUSIONS:** Transition periods not only reinforce the dynamic nature of the experience of childhood cancer but, more importantly, show how symptoms can greatly affect the quality of children's and families' day-to-day living. Interpreting cancer in the context of the symptom trajectory provides nurses with a new perspective for understanding childhood cancer, and will assist in the development of symptom relief strategies that will help to contain symptoms and improve overall quality of life for children and families.

Yamada, T., K. Furukawa, et al. (2008). "Case of meningeal carcinomatosis with gastric cancer which manifested meningeal signs as the initial symptom; the palliative benefit of radiotherapy." *J Nippon Med Sch* **75**(4): 216-20.

A 53-year-old male presenting with anorexia, intermittent diplopia, general fatigue, headache and vertigo was admitted to our hospital. He was diagnosed as having gastric cancer by endoscopy of his upper gastrointestinal tract. Brain computed tomography (CT) showed no abnormalities, but magnetic resonance imaging (MRI) showed slight enhancement in the cerebellar sulcus. Cytological examination of cerebrospinal fluid revealed malignant cells. He became blind one week after hospitalization. We diagnosed his condition as meningeal carcinomatosis (MC) and started radiotherapy. His vision improved after four weeks of treatment, and then he became totally blind again. Since his general condition remained poor, we did not perform chemotherapy. He died on the 127th day of hospitalization. MC is a rare pathosis of gastric cancer in comparison with leukemia and malignant lymphoma. This disease does not often show characteristic pictorial images, and early diagnosis is difficult. Moreover, it usually manifests itself in its late stages after several months or more of treatment, and it is rare for MC to be present at the time of initial diagnosis. We present a case of gastric cancer with meningeal signs present when the primary tumors were diagnosed. Radiotherapy alleviated some of the symptoms, and the patient survived for as long as patients undergoing enforced chemotherapy.

Yeh, C. H., Y. C. Chiang, et al. (2008). "Symptom clustering in older Taiwanese children with cancer." *Oncol Nurs Forum* **35**(2): 273-81.

PURPOSE/OBJECTIVES: To derive symptom clusters occurring in a large group of older pediatric patients with cancer in Taiwan and to examine whether each cluster differed based on gender, type of cancer and disease, pain, and functional status. **DESIGN:** Descriptive, correlational study. **SETTING:** Pediatric oncology inpatient unit and outpatient clinics in Taiwan. **SAMPLE:** 144 pediatric patients with cancer, aged 10-18 years. **METHODS:** Subjects completed the Memorial Symptom Assessment Scale 10-18, the Play Performance Scale for Children, and a demographic questionnaire. Medical records provided disease and treatment data. Cluster analysis techniques were used to identify the symptoms that clustered together by demographic characteristics, as well as disease, pain, and functional status. **MAIN RESEARCH VARIABLES:** Symptom cluster, pain status, and functional status. **FINDINGS:** Five clusters were

identified from the statistical analysis. The symptoms that clustered together were somewhat surprising, and some can be explained by cultural differences. Patients with pain reported statistically significant higher distress in all five clusters. **CONCLUSIONS:** Five symptom clusters are identified in older Taiwanese children with cancer. The way and possible rationale of how these symptoms clustered together is discussed. **IMPLICATIONS FOR NURSING:** This is the first study that used a statistical procedure to derive symptom clusters experienced by pediatric oncology patients. Knowledge from this study can provide a starting point to investigate the stability of symptom clusters with different states of disease, different populations, and over various periods of time.

Yennurajalingam, S., T. Zhang, et al. (2007). "The impact of the palliative care mobile team on symptom assessment and medication profiles in patients admitted to a comprehensive cancer center." Support Care Cancer **15**(5): 471-5.

GOALS OF WORK: In recent years, tertiary care hospitals and cancer centers have shown great interest in forming palliative care consultation teams. Thus, these centers may be interested in the types of care that such teams give, which could help the other centers put together their own teams. However, the availability of such information is limited. The purpose of our study was therefore to describe the experience of a palliative care team at our comprehensive cancer center. **MATERIALS AND METHODS:** We reviewed the medical records of 100 consecutive patients who were referred to our palliative care mobile team between November 2004 and January 2005; we then analyzed the primary interventions of this team. **RESULTS:** The median patient age was 61 years; 57 patients were female. The most frequent symptoms were fatigue in 78% and pain in 62% of patients. The main interventions by the palliative team were changes in medication types (opioids, antiemetics, neuroleptics, and laxatives) and in medication doses. **CONCLUSIONS:** Palliative care mobile teams make multiple changes in previous medications and provide almost universal counseling services to patients and families. The length of involvement with the patient and family is short; therefore, rapid stabilization and counseling are required. Our findings regarding medication changes could be helpful to tertiary care hospitals and cancer centers considering palliative care consultation teams.

Yoon, J., J. L. Malin, et al. (2008). "Symptom management after breast cancer treatment: is it influenced by patient characteristics?" Breast Cancer Res Treat **108**(1): 69-77.

PURPOSE: With improved patient survival from breast cancer, more interest has evolved regarding the symptoms women experience in association with breast cancer treatments. We studied the extent to which symptoms for women with incident breast cancer are addressed by their physicians and how symptom management varies with patient characteristics. **METHODS:** As part of the Los Angeles Women's (LAW) Study, we categorized women from a population-based study of incident breast cancer (n = 1,219) as having an unmet need if she had at least one severe symptom (any of the following: nausea/vomiting, arm problems, hot flashes, vaginal dryness, difficulty sleeping) for which she did not receive the help she wanted. Multivariable analyses predicted having any unmet need as a function of patient demographic and health characteristics. **RESULTS:** The prevalence of unmet need varied by the type of symptom with the highest proportion of women receiving help for nausea and vomiting (0.91) and the lowest for vaginal dryness (0.48). Black women (OR = 3.61, 95% CI: [1.57, 8.31]), and Spanish-speaking Hispanic women (OR = 2.69, 95% CI: [1.22, 5.94]) were significantly more likely than white women to report an unmet need. More black and Hispanic women compared to white women cited the doctor not thinking treatment would benefit her (P = 0.02), not appreciating how much the problem bothered her (P = 0.03), not knowing about treatments (P < 0.0001), or insurance/cost barriers (P = 0.009) as reasons for her unmet need. **CONCLUSION:** These results show the persistence of racial disparities in the receipt of appropriate care within the health care system.

Zaric, B., V. Canak, et al. (2007). "The effect of Nd:YAG laser resection on symptom control, time to progression and survival in lung cancer patients." J Buon **12**(3): 361-8.

PURPOSE: The aim of this study was to determine the effect of Nd:YAG laser resection of centrally located tumors on the control of various symptoms and signs, time to progression and survival in lung cancer patients. **PATIENTS AND METHODS:** We evaluated the effects of Nd: YAG laser resection in combination with high-dose rate (HDR) brachytherapy and external beam radiotherapy (EBRT) vs. combination of HDR brachytherapy and EBRT alone on lung cancer symptoms and signs, ECOG performance status, time to progression and overall survival in lung cancer patients. Patients in group I (n=81) were treated with combination of HDR brachytherapy and EBRT, while patients in group II (n=97) were treated with Nd:YAG laser in combination with HDR brachytherapy and EBRT. Patients were evaluated before and after treatment,

and were followed-up regularly every 3 months until the end of life. After RT +/- laser treatment all patients received standard chemotherapy (cisplatin plus etoposide) during the course of disease. RESULTS: After treatment in both groups significant improvement in all investigated parameters was seen. Improvement in dyspnoea, thoracic pain, body weight loss and ECOG performance status was significantly better in group II ($p < 0.05$), as were time to progression and overall survival ($p < 0.05$). CONCLUSION: Laser resection improves symptom control in lung cancer patients with central airway obstruction (CAO). Longer time to progression and survival of lung cancer patients could be the result of imminent airway desobstruction accomplished with Nd:YAG laser.

References

- Akechi, T., T. Ietsugu, et al. (2009). "Symptom indicator of severity of depression in cancer patients: a comparison of the DSM-IV criteria with alternative diagnostic criteria." *Gen Hosp Psychiatry* **31**(3): 225-32.
- Andrew, I. M., K. Waterfield, et al. (2009). "Quantifying the impact of standardized assessment and symptom management tools on symptoms associated with cancer-induced anorexia cachexia syndrome." *Palliat Med* **23**(8): 680-8.
- Annakkaya, A. N., P. Arbak, et al. (2007). "Effect of symptom-to-treatment interval on prognosis in lung cancer." *Tumori* **93**(1): 61-7.
- Armer, J. M., M. H. Henggeler, et al. (2008). "The Health Deviation of Post-Breast Cancer Lymphedema: Symptom Assessment and Impact on Self-Care Agency." *Self Care Depend Care Nurs* **16**(1): 14-21.
- Badger, T., C. Segrin, et al. (2005). "Telephone interpersonal counseling with women with breast cancer: symptom management and quality of life." *Oncol Nurs Forum* **32**(2): 273-9.
- Basch, E., A. Iasonos, et al. (2006). "Patient versus clinician symptom reporting using the National Cancer Institute Common Terminology Criteria for Adverse Events: results of a questionnaire-based study." *Lancet Oncol* **7**(11): 903-9.
- Beck, S. L., G. L. Towsley, et al. (2009). "Symptom experiences and quality of life of rural and urban older adult cancer survivors." *Cancer Nurs* **32**(5): 359-69.
- Beck, S. L., W. N. Dudley, et al. (2005). "Pain, sleep disturbance, and fatigue in patients with cancer: using a mediation model to test a symptom cluster." *Oncol Nurs Forum* **32**(3): 542.
- Bekelman, D. B., J. S. Rumsfeld, et al. (2009). "Symptom burden, depression, and spiritual well-being: a comparison of heart failure and advanced cancer patients." *J Gen Intern Med* **24**(5): 592-8.
- Bellizzi, K. M., D. M. Latini, et al. (2008). "Fear of recurrence, symptom burden, and health-related quality of life in men with prostate cancer." *Urology* **72**(6): 1269-73.
- Bender, C. M., S. J. Engberg, et al. (2008). "Symptom clusters in adults with chronic health problems and cancer as a comorbidity." *Oncol Nurs Forum* **35**(1): E1-E11.
- Berger, A. M., D. E. Neumark, et al. (2007). "Enhancing recruitment and retention in randomized clinical trials of cancer symptom management." *Oncol Nurs Forum* **34**(2): E17-22.
- Bezjak, A., D. Tu, et al. (2006). "Symptom improvement in lung cancer patients treated with erlotinib: quality of life analysis of the National Cancer Institute of Canada Clinical Trials Group Study BR.21." *J Clin Oncol* **24**(24): 3831-7.
- Bharucha, S., S. Hughes, et al. (2005). "Targets and elective colorectal cancer: outcome and symptom delay at surgical resection." *Colorectal Dis* **7**(2): 169-71.
- Boehmke, M. M. and S. S. Dickerson (2005). "Symptom, symptom experiences, and symptom distress encountered by women with breast cancer undergoing current treatment modalities." *Cancer Nurs* **28**(5): 382-9.
- Bornhak, S., E. Heidemann, et al. (2007). "Symptom-oriented follow-up of early breast cancer is not inferior to conventional control. Results of a prospective multicentre study." *Onkologie* **30**(8-9): 443-9.
- Bottomley, A., C. Debruyne, et al. (2008). "Symptom and quality of life results of an international randomised phase III study of adjuvant vaccination with Bec2/BCG in responding patients with limited disease small-cell lung cancer." *Eur J Cancer* **44**(15): 2178-84.
- Breen, S. J., C. M. Baravelli, et al. (2009). "Is symptom burden a predictor of anxiety and depression in patients with cancer about to commence chemotherapy?" *Med J Aust* **190**(7 Suppl): S99-104.
- Bruner, D. W. (2007). "Outcomes research in cancer symptom management trials: the Radiation Therapy Oncology Group (RTOG) conceptual model." *J Natl Cancer Inst Monogr* **37**: 12-5.
- Buchanan, D. R., A. M. O'Mara, et al. (2005). "Quality-of-life assessment in the symptom management trials of the National Cancer Institute-supported Community Clinical Oncology Program." *J Clin Oncol* **23**(3): 591-8.
- Buchanan, D. R., J. D. White, et al. (2005). "Research-design issues in cancer-symptom-management trials using complementary and alternative medicine: lessons from the National Cancer Institute Community Clinical Oncology Program experience." *J Clin Oncol* **23**(27): 6682-9.
- Burkett, V. S. and C. S. Cleeland (2007). "Symptom burden in cancer survivorship." *J Cancer Surviv* **1**(2): 167-75.
- Cella, D., D. Eton, et al. (2008). "Relationship between symptom change, objective tumor measurements, and performance status during chemotherapy for advanced lung cancer." *Clin Lung Cancer* **9**(1): 51-8.
- Cella, D., L. Wagner, et al. (2007). "Should health-related quality of life be measured in cancer symptom management clinical trials? Lessons learned using the functional assessment of cancer therapy." *J Natl Cancer Inst Monogr* **37**: 53-60.
- Cella, D., S. R. Land, et al. (2008). "Symptom measurement in the Breast Cancer Prevention Trial (BCPT) (P-1): psychometric properties of a new measure of symptoms for midlife women." *Breast Cancer Res Treat* **109**(3): 515-26.
- Cella, D., S. Yount, et al. (2006). "Development and validation of the Functional Assessment of Cancer Therapy-Kidney Symptom Index (FKSI)." *J Support Oncol* **4**(4): 191-9.
- Chan, C. W., A. Richardson, et al. (2005). "A study to assess the existence of the symptom cluster of breathlessness, fatigue and anxiety in patients with advanced lung cancer." *Eur J Oncol Nurs* **9**(4): 325-33.
- Chen, L., L. Antras, et al. (2007). "Psychometric validation of the Patient Symptom Assessment in Lung Cancer instrument for small cell lung cancer." *Curr Med Res Opin* **23**(11): 2741-52.
- Chen, L., L. Antras, et al. (2008). "Symptom assessment in relapsed small cell lung cancer: cross-validation of the patient symptom assessment in lung cancer instrument." *J Thorac Oncol* **3**(10): 1137-45.
- Chen, M. L. and C. C. Lin (2007). "Cancer symptom clusters: a validation study." *J Pain Symptom Manage* **34**(6): 590-9.

31. Chen, M. L. and H. C. Tseng (2006). "Symptom clusters in cancer patients." *Support Care Cancer* **14**(8): 825-30.
32. Cheng, K. K., E. M. Wong, et al. (2009). "Measuring the symptom experience of Chinese cancer patients: a validation of the Chinese version of the memorial symptom assessment scale." *J Pain Symptom Manage* **37**(1): 44-57.
33. Cheung, W. Y., N. Barmala, et al. (2009). "The association of physical and psychological symptom burden with time to death among palliative cancer outpatients." *J Pain Symptom Manage* **37**(3): 297-304.
34. Chow, E., G. Fan, et al. (2007). "Symptom clusters in cancer patients with bone metastases." *Support Care Cancer* **15**(9): 1035-43.
35. Chow, E., G. Fan, et al. (2008). "Symptom clusters in cancer patients with brain metastases." *Clin Oncol (R Coll Radiol)* **20**(1): 76-82.
36. Cirillo, M., M. Venturini, et al. (2009). "Clinician versus nurse symptom reporting using the National Cancer Institute-Common Terminology Criteria for Adverse Events during chemotherapy: results of a comparison based on patient's self-reported questionnaire." *Ann Oncol* **20**(12): 1929-35.
37. Cohen, M. Z., C. F. Musgrave, et al. (2005). "The cancer pain experience of Israeli adults 65 years and older: the influence of pain interference, symptom severity, and knowledge and attitudes on pain and pain control." *Support Care Cancer* **13**(9): 708-14.
38. Cruciani, R. A., E. Dvorkin, et al. (2006). "Safety, tolerability and symptom outcomes associated with L-carnitine supplementation in patients with cancer, fatigue, and carnitine deficiency: a phase I/II study." *J Pain Symptom Manage* **32**(6): 551-9.
39. Daly, B. J., S. L. Douglas, et al. (2007). "Psychosocial registry for persons with cancer: a method of facilitating quality of life and symptom research." *Psychooncology* **16**(4): 358-64.
40. Davis, K., S. Yount, et al. (2007). "An innovative symptom monitoring tool for people with advanced lung cancer: a pilot demonstration." *J Support Oncol* **5**(8): 381-7.
41. Davis, M. P., D. Walsh, et al. (2006). "Early satiety in cancer patients: a common and important but underrecognized symptom." *Support Care Cancer* **14**(7): 693-8.
42. de Marinis, F., J. R. Pereira, et al. (2008). "Lung Cancer Symptom Scale outcomes in relation to standard efficacy measures: an analysis of the phase III study of pemetrexed versus docetaxel in advanced non-small cell lung cancer." *J Thorac Oncol* **3**(1): 30-6.
43. Delgado-Guay, M. O., H. A. Parsons, et al. (2009). "Symptom distress, interventions, and outcomes of intensive care unit cancer patients referred to a palliative care consult team." *Cancer* **115**(2): 437-45.
44. Delgado-Guay, M., H. A. Parsons, et al. (2009). "Symptom distress in advanced cancer patients with anxiety and depression in the palliative care setting." *Support Care Cancer* **17**(5): 573-9.
45. Donovan, H. S., S. Ward, et al. (2008). "Evaluation of the Symptom Representation Questionnaire (SRQ) for assessing cancer-related symptoms." *J Pain Symptom Manage* **35**(3): 242-57.
46. Donovan, K. A. and P. B. Jacobsen (2007). "Fatigue, depression, and insomnia: evidence for a symptom cluster in cancer." *Semin Oncol Nurs* **23**(2): 127-35.
47. Dooms, C. A., K. E. Pat, et al. (2006). "The effect of chemotherapy on symptom control and quality of life in patients with advanced non-small cell lung cancer." *Expert Rev Anticancer Ther* **6**(4): 531-44.
48. Doorenbos, A. Z., C. W. Given, et al. (2006). "Symptom experience in the last year of life among individuals with cancer." *J Pain Symptom Manage* **32**(5): 403-12.
49. Doorenbos, A. Z., N. Verbitsky, et al. (2005). "An analytic strategy for modeling multiple-item responses: a breast cancer symptom example." *Nurs Res* **54**(4): 229-34.
50. Duncan, J. G., M. J. Bott, et al. (2009). "Symptom occurrence and associated clinical factors in nursing home residents with cancer." *Res Nurs Health* **32**(4): 453-64.
51. Duncan, J. G., S. Forbes-Thompson, et al. (2008). "Unmet symptom management needs of nursing home residents with cancer." *Cancer Nurs* **31**(4): 265-73.
52. Erridge, S. C., M. N. Gaze, et al. (2005). "Symptom control and quality of life in people with lung cancer: a randomised trial of two palliative radiotherapy fractionation schedules." *Clin Oncol (R Coll Radiol)* **17**(1): 61-7.
53. Eton, D. T., D. Cella, et al. (2007). "Validation of the functional assessment of cancer therapy--lung symptom index-12 (FLSI-12)." *Lung Cancer* **57**(3): 339-47.
54. Fadol, A., T. Mendoza, et al. (2008). "Psychometric testing of the MDASI-HF: a symptom assessment instrument for patients with cancer and concurrent heart failure." *J Card Fail* **14**(6): 497-507.
55. Fan, G., L. Filipczak, et al. (2007). "Symptom clusters in cancer patients: a review of the literature." *Curr Oncol* **14**(5): 173-9.
56. Fan, G., S. Hadi, et al. (2007). "Symptom clusters in patients with advanced-stage cancer referred for palliative radiation therapy in an outpatient setting." *Support Cancer Ther* **4**(3): 157-62.
57. Farah, R. and N. Makhoul (2009). "Pneumomediastinum as a presenting symptom of perforated sigmoid cancer: a case report." *Cases J* **2**: 7356.
58. Fellowes, D., K. Barnes, et al. (2008). "WITHDRAWN: Aromatherapy and massage for symptom relief in patients with cancer." *Cochrane Database Syst Rev*(4): CD002287.
59. Ferreira, K. A., M. Kimura, et al. (2008). "Impact of cancer-related symptom synergisms on health-related quality of life and performance status." *J Pain Symptom Manage* **35**(6): 604-16.
60. Fortner, B. V., L. S. Schwartzberg, et al. (2007). "Symptom Burden for Patients with Metastatic Colorectal Cancer Treated with First-Line FOLFOX or FOLFIRI with and Without Bevacizumab in the Community Setting." *Support Cancer Ther* **4**(4): 233-40.
61. Fox, S. W. and D. E. Lyon (2006). "Symptom clusters and quality of life in survivors of lung cancer." *Oncol Nurs Forum* **33**(5): 931-6.
62. Fox, S. W. and D. Lyon (2007). "Symptom clusters and quality of life in survivors of ovarian cancer." *Cancer Nurs* **30**(5): 354-61.
63. Francoeur, R. B. (2005). "The relationship of cancer symptom clusters to depressive affect in the initial phase of palliative radiation." *J Pain Symptom Manage* **29**(2): 130-55.
64. Friedlander, M., P. Butow, et al. (2009). "Symptom control in patients with recurrent ovarian cancer: measuring the benefit of palliative chemotherapy in women with platinum refractory/resistant ovarian cancer." *Int J Gynecol Cancer* **19** Suppl 2: S44-8.
65. Frostad, A. (2008). "Association between respiratory symptom score and 30-year cause-specific mortality and lung cancer incidence." *Clin Respir J* **2** Suppl 1: 53-8.
66. Fu, O. S., K. D. Crew, et al. (2009). "Ethnicity and persistent symptom burden in breast cancer survivors." *J Cancer Surviv* **3**(4): 241-50.
67. Gning, I., P. C. Trask, et al. (2009). "Development and initial validation of the thyroid cancer module of the M. D. Anderson Symptom Inventory." *Oncology* **76**(1): 59-68.
68. Goff, B. A., L. S. Mandel, et al. (2007). "Development of an ovarian cancer symptom index: possibilities for earlier detection." *Cancer* **109**(2): 221-7.

69. Goodell, T. T. and L. M. Nail (2005). "Operationalizing symptom distress in adults with cancer: a literature synthesis." *Oncol Nurs Forum* **32**(2): E42-7.
70. Goyal, S., J. Roscoe, et al. (2004). "Symptom interval in young people with bone cancer." *Eur J Cancer* **40**(15): 2280-6.
71. Gralla, R. J. (2004). "Quality-of-life considerations in patients with advanced lung cancer: effect of topotecan on symptom palliation and quality of life." *Oncologist* **9** Suppl **6**: 14-24.
72. Gralla, R. J., M. J. Edelman, et al. (2009). "Assessing quality of life following neoadjuvant therapy for early stage non-small cell lung cancer (NSCLC): results from a prospective analysis using the Lung Cancer Symptom Scale (LCSS)." *Support Care Cancer* **17**(3): 307-13.
73. Hadi, S., G. Fan, et al. (2008). "Symptom clusters in patients with cancer with metastatic bone pain." *J Palliat Med* **11**(4): 591-600.
74. Hedgepeth, R. C., J. Labo, et al. (2009). "Expanded Prostate Cancer Index Composite versus Incontinence Symptom Index and Sexual Health Inventory for Men to measure functional outcomes after prostatectomy." *J Urol* **182**(1): 221-7; discussion 227-8.
75. Heidrich, S. M., J. J. Egan, et al. (2006). "Symptoms, symptom beliefs, and quality of life of older breast cancer survivors: a comparative study." *Oncol Nurs Forum* **33**(2): 315-22.
76. Heidrich, S. M., R. L. Brown, et al. (2009). "An individualized representational intervention to improve symptom management (IRIS) in older breast cancer survivors: three pilot studies." *Oncol Nurs Forum* **36**(3): E133-43.
77. Hendrix, C. and C. Ray (2006). "Informal caregiver training on home care and cancer symptom management prior to hospital discharge: a feasibility study." *Oncol Nurs Forum* **33**(4): 793-8.
78. Hendrix, C. C., A. Abernethy, et al. (2009). "A pilot study on the influence of an individualized and experiential training on cancer caregiver's self-efficacy in home care and symptom management." *Home Healthc Nurse* **27**(5): 271-8.
79. Henoch, I., A. Ploner, et al. (2009). "Increasing stringency in symptom cluster research: a methodological exploration of symptom clusters in patients with inoperable lung cancer." *Oncol Nurs Forum* **36**(6): E282-92.
80. Hermansen-Kobulnicky, C. J. (2009). "Symptom-monitoring behaviors of rural cancer patients and survivors." *Support Care Cancer* **17**(6): 617-26.
81. Hockenberry, M. and M. C. Hooke (2007). "Symptom clusters in children with cancer." *Semin Oncol Nurs* **23**(2): 152-7.
82. Hoekstra, J., M. J. Vernooij-Dassen, et al. (2007). "The added value of assessing the 'most troublesome' symptom among patients with cancer in the palliative phase." *Patient Educ Couns* **65**(2): 223-9.
83. Hoekstra, J., P. J. Bindels, et al. (2004). "The symptom monitor. A diary for monitoring physical symptoms for cancer patients in palliative care: feasibility, reliability and compliance." *J Pain Symptom Manage* **27**(1): 24-35.
84. Hollen, P. J., R. J. Gralla, et al. (2004). "Adapting the Lung Cancer Symptom Scale (LCSS) to mesothelioma: using the LCSS-Meso conceptual model for validation." *Cancer* **101**(3): 587-95.
85. Hollen, P. J., R. J. Gralla, et al. (2005). "A comparison of visual analogue and numerical rating scale formats for the Lung Cancer Symptom Scale (LCSS): does format affect patient ratings of symptoms and quality of life?" *Qual Life Res* **14**(3): 837-47.
86. Hollen, P. J., R. J. Gralla, et al. (2006). "Measuring quality of life in patients with pleural mesothelioma using a modified version of the Lung Cancer Symptom Scale (LCSS): psychometric properties of the LCSS-Meso." *Support Care Cancer* **14**(1): 11-21.
87. Hopfgarten, T., J. Adolfsson, et al. (2006). "The choice between a therapy-induced long-term symptom and shortened survival due to prostate cancer." *Eur Urol* **50**(2): 280-9.
88. Hsiao, C. P., L. J. Loeschner, et al. (2007). "Symptoms and symptom distress in localized prostate cancer." *Cancer Nurs* **30**(6): E19-32.
89. Hwang, S. S., C. B. Scott, et al. (2004). "Prediction of survival for advanced cancer patients by recursive partitioning analysis: role of Karnofsky performance status, quality of life, and symptom distress." *Cancer Invest* **22**(5): 678-87.
90. Ivanova, M. O., T. I. Ionova, et al. (2005). "Cancer-related symptom assessment in Russia: validation and utility of the Russian M. D. Anderson Symptom Inventory." *J Pain Symptom Manage* **30**(5): 443-53.
91. Janz, N. K., M. Mujahid, et al. (2007). "Symptom experience and quality of life of women following breast cancer treatment." *J Womens Health (Larchmt)* **16**(9): 1348-61.
92. Jena, A., S. Taneja, et al. (2008). "Magnetic resonance (MR) patterns of brain metastasis in lung cancer patients: correlation of imaging findings with symptom." *J Thorac Oncol* **3**(2): 140-4.
93. Jensen, K., A. Bonde Jensen, et al. (2006). "The relationship between observer-based toxicity scoring and patient assessed symptom severity after treatment for head and neck cancer. A correlative cross sectional study of the DAHANCA toxicity scoring system and the EORTC quality of life questionnaires." *Radiother Oncol* **78**(3): 298-305.
94. Jeon, S., C. W. Given, et al. (2009). "The utility of screening in the design of trials for symptom management in cancer." *J Pain Symptom Manage* **38**(4): 606-14.
95. Johansson, E., A. Bill-Axelsson, et al. (2009). "Time, symptom burden, androgen deprivation, and self-assessed quality of life after radical prostatectomy or watchful waiting: the Randomized Scandinavian Prostate Cancer Group Study Number 4 (SPCG-4) clinical trial." *Eur Urol* **55**(2): 422-30.
96. Joly, F., J. Vardy, et al. (2007). "Quality of life and/or symptom control in randomized clinical trials for patients with advanced cancer." *Ann Oncol* **18**(12): 1935-42.
97. Kenefick, A. L. (2006). "Patterns of symptom distress in older women after surgical treatment for breast cancer." *Oncol Nurs Forum* **33**(2): 327-35.
98. Khattak, I., N. J. Eardley, et al. (2006). "Colorectal cancer--a prospective evaluation of symptom duration and GP referral patterns in an inner city teaching hospital." *Colorectal Dis* **8**(6): 518-21.
99. Kim, H. J. and I. L. Abraham (2008). "Statistical approaches to modeling symptom clusters in cancer patients." *Cancer Nurs* **31**(5): E1-10.
100. Kim, H. J., A. M. Barsevick, et al. (2008). "Treatment-related symptom clusters in breast cancer: a secondary analysis." *J Pain Symptom Manage* **36**(5): 468-79.
101. Kim, H. J., D. B. McGuire, et al. (2005). "Symptom clusters: concept analysis and clinical implications for cancer nursing." *Cancer Nurs* **28**(4): 270-82; quiz 283-4.
102. Kim, M. K., K. Kim, et al. (2009). "A hospital-based case-control study of identifying ovarian cancer using symptom index." *J Gynecol Oncol* **20**(4): 238-42.
103. Kirkova, J., M. P. Davis, et al. (2006). "Cancer symptom assessment instruments: a systematic review." *J Clin Oncol* **24**(9): 1459-73.
104. Kurtz, M. E., J. C. Kurtz, et al. (2006). "Effects of a symptom control intervention on utilization of health care services among cancer patients." *Med Sci Monit* **12**(7): CR319-24.

105. Labori, K. J., M. J. Hjermstad, et al. (2006). "Symptom profiles and palliative care in advanced pancreatic cancer: a prospective study." *Support Care Cancer* **14**(11): 1126-33.
106. Ladas, E. J., J. Post-White, et al. (2006). "Evidence for symptom management in the child with cancer." *J Pediatr Hematol Oncol* **28**(9): 601-15.
107. Lasheen, W., D. Walsh, et al. (2009). "Symptom variability during repeated measurement among hospice patients with advanced cancer." *Am J Hosp Palliat Care* **26**(5): 368-75.
108. Leak, A., J. Hu, et al. (2008). "Symptom distress, spirituality, and quality of life in African American breast cancer survivors." *Cancer Nurs* **31**(1): E15-21.
109. Lee, E. H. (2005). "Relationships of mood disturbance, symptom experience, and attentional function in women with breast cancer based upon the theory of unpleasant symptoms." *Taehan Kanho Hakhoe Chi* **35**(4): 728-36.
110. Lee, E. H., B. Yae Chung, et al. (2004). "Relationships of mood disturbance and social support to symptom experience in Korean women with breast cancer." *J Pain Symptom Manage* **27**(5): 425-33.
111. Lehrer, S., J. Cesaretti, et al. (2006). "Urinary symptom flare after brachytherapy for prostate cancer is associated with erectile dysfunction and more urinary symptoms before implantation." *BJU Int* **98**(5): 979-81.
112. Lin, C. C., A. P. Chang, et al. (2007). "Taiwanese version of the M. D. Anderson symptom inventory: symptom assessment in cancer patients." *J Pain Symptom Manage* **33**(2): 180-8.
113. Liu, L., L. Fiorentino, et al. (2009). "Pre-treatment symptom cluster in breast cancer patients is associated with worse sleep, fatigue and depression during chemotherapy." *Psychooncology* **18**(2): 187-94.
114. Lobchuk, M. M., L. F. Degner, et al. (2006). "Promoting enhanced patient and family caregiver congruence on lung cancer symptom experiences." *Oncol Nurs Forum* **33**(2): 273-82.
115. Loprinzi, C. L., S. L. Wolf, et al. (2008). "Symptom management in premenopausal patients with breast cancer." *Lancet Oncol* **9**(10): 993-1001.
116. Lovgren, M., H. Levealahti, et al. (2008). "Time spans from first symptom to treatment in patients with lung cancer--the influence of symptoms and demographic characteristics." *Acta Oncol* **47**(3): 397-405.
117. Lowe, K. A., M. R. Andersen, et al. (2009). "The temporal stability of the Symptom Index among women at high-risk for ovarian cancer." *Gynecol Oncol* **114**(2): 225-30.
118. Luo, X., J. C. Cappelleri, et al. (2009). "Using the Rasch model to validate and enhance the interpretation of the Functional Assessment of Cancer Therapy-Kidney Symptom Index--Disease-Related Symptoms scale." *Value Health* **12**(4): 580-6.
119. Maliski, S. L., L. Kwan, et al. (2008). "Symptom clusters related to treatment for prostate cancer." *Oncol Nurs Forum* **35**(5): 786-93.
120. Mallick, I., S. C. Sharma, et al. (2007). "Endobronchial brachytherapy for symptom palliation in non-small cell lung cancer--analysis of symptom response, endoscopic improvement and quality of life." *Lung Cancer* **55**(3): 313-8.
121. Manning-Walsh, J. (2005). "Social support as a mediator between symptom distress and quality of life in women with breast cancer." *J Obstet Gynecol Neonatal Nurs* **34**(4): 482-93.
122. Manning-Walsh, J. K. (2005). "Psychospiritual well-being and symptom distress in women with breast cancer." *Oncol Nurs Forum* **32**(3): 543.
123. Mansky, P. J. and D. B. Wallerstedt (2006). "Complementary medicine in palliative care and cancer symptom management." *Cancer J* **12**(5): 425-31.
124. Mao, J. J., K. Armstrong, et al. (2007). "Symptom burden among cancer survivors: impact of age and comorbidity." *J Am Board Fam Med* **20**(5): 434-43.
125. Mehling, W. E., B. Jacobs, et al. (2007). "Symptom management with massage and acupuncture in postoperative cancer patients: a randomized controlled trial." *J Pain Symptom Manage* **33**(3): 258-66.
126. Mehnert, A., C. Lehmann, et al. (2007). "Presence of symptom distress and prostate cancer-related anxiety in patients at the beginning of cancer rehabilitation." *Onkologie* **30**(11): 551-6.
127. Menczer, J., A. Chetrit, et al. (2009). "The effect of symptom duration in epithelial ovarian cancer on prognostic factors." *Arch Gynecol Obstet* **279**(6): 797-801.
128. Miaskowski, C., B. A. Cooper, et al. (2006). "Subgroups of patients with cancer with different symptom experiences and quality-of-life outcomes: a cluster analysis." *Oncol Nurs Forum* **33**(5): E79-89.
129. Miaskowski, C., B. E. Aouizerat, et al. (2007). "Conceptual issues in symptom clusters research and their implications for quality-of-life assessment in patients with cancer." *J Natl Cancer Inst Monogr* **37**: 39-46.
130. Miner, T. J., M. F. Brennan, et al. (2004). "A prospective, symptom related, outcomes analysis of 1022 palliative procedures for advanced cancer." *Ann Surg* **240**(4): 719-26; discussion 726-7.
131. Molassiotis, A., S. Brearley, et al. (2009). "Effectiveness of a home care nursing program in the symptom management of patients with colorectal and breast cancer receiving oral chemotherapy: a randomized, controlled trial." *J Clin Oncol* **27**(36): 6191-8.
132. Murakami, N., J. Itami, et al. (2008). "Urethral dose and increment of international prostate symptom score (IPSS) in transperineal permanent interstitial implant (TPI) of prostate cancer." *Strahlenther Onkol* **184**(10): 515-9.
133. Murphy, B. A. (2009). "Advances in quality of life and symptom management for head and neck cancer patients." *Curr Opin Oncol* **21**(3): 242-7.
134. Mystakidou, K., C. Cleeland, et al. (2004). "Greek M.D. Anderson Symptom Inventory: validation and utility in cancer patients." *Oncology* **67**(3-4): 203-10.
135. Mystakidou, K., E. Parpa, et al. (2009). "How is sleep quality affected by the psychological and symptom distress of advanced cancer patients?" *Palliat Med* **23**(1): 46-53.
136. Natale, R. B. (2004). "Epidermal growth factor receptor-targeted therapy with ZD1839: symptom improvement in non-small-cell lung cancer." *Int J Radiat Oncol Biol Phys* **59**(2 Suppl): 39-43.
137. Natale, R. B. (2004). "Inhibition of epidermal growth factor receptor and symptom improvement in advanced non-small cell lung cancer." *Semin Respir Crit Care Med* **25** Suppl 1: 29-32.
138. Nedstrand, E., Y. Wyon, et al. (2006). "Psychological well-being improves in women with breast cancer after treatment with applied relaxation or electro-acupuncture for vasomotor symptom." *J Psychosom Obstet Gynaecol* **27**(4): 193-9.
139. Nunobe, S., M. Sasako, et al. (2007). "Symptom evaluation of long-term postoperative outcomes after pylorus-preserving gastrectomy for early gastric cancer." *Gastric Cancer* **10**(3): 167-72.
140. Oh, E. G. (2004). "Symptom experience in Korean adults with lung cancer." *J Pain Symptom Manage* **28**(2): 133-9.
141. Oi-Ling, K., D. T. Man-Wah, et al. (2005). "Symptom distress as rated by advanced cancer patients, caregivers and physicians in the last week of life." *Palliat Med* **19**(3): 228-33.
142. Olson, K., L. Hayduk, et al. (2008). "The changing causal foundations of cancer-related symptom clustering during the final month of palliative care: a longitudinal study." *BMC Med Res Methodol* **8**: 36.

143. Olsson, L., L. Bergkvist, et al. (2004). "Symptom duration versus survival in non-emergency colorectal cancer." *Scand J Gastroenterol* **39**(3): 252-8.
144. Ostlund, U., A. Wennman-Larsen, et al. (2007). "What symptom and functional dimensions can be predictors for global ratings of overall quality of life in lung cancer patients?" *Support Care Cancer* **15**(10): 1199-205.
145. Ott, J. J., A. Ullrich, et al. (2009). "The importance of early symptom recognition in the context of early detection and cancer survival." *Eur J Cancer* **45**(16): 2743-8.
146. Ozlu, T., Y. Bulbul, et al. (2004). "Time course from first symptom to the treatment of lung cancer in the Eastern Black Sea Region of Turkey." *Med Princ Pract* **13**(4): 211-4.
147. Paice, J. A. (2004). "Assessment of symptom clusters in people with cancer." *J Natl Cancer Inst Monogr*(32): 98-102.
148. Palmer, J. L. and M. J. Fisch (2005). "Association between symptom distress and survival in outpatients seen in a palliative care cancer center." *J Pain Symptom Manage* **29**(6): 565-71.
149. Papagoras, C., J. Kountouras, et al. (2007). "Rheumatic-like syndrome as a symptom of underlying gastric cancer." *Clin Rheumatol* **26**(6): 1029-31.
150. Parsons, H. A., M. O. Delgado-Guay, et al. (2008). "Alcoholism screening in patients with advanced cancer: impact on symptom burden and opioid use." *J Palliat Med* **11**(7): 964-8.
151. Pat, K., C. Dooms, et al. (2008). "Systematic review of symptom control and quality of life in studies on chemotherapy for advanced non-small cell lung cancer: how CONSORTed are the data?" *Lung Cancer* **62**(1): 126-38.
152. Patrick, D. L., S. L. Ferketich, et al. (2004). "National Institutes of Health State-of-the-Science Conference Statement: Symptom management in cancer: pain, depression, and fatigue, July 15-17, 2002." *J Natl Cancer Inst Monogr*(32): 9-16.
153. Phianmongkhol, Y. and N. Suwan (2008). "Symptom management in patients with cancer of the female reproductive system receiving chemotherapy." *Asian Pac J Cancer Prev* **9**(4): 741-5.
154. Phipps, E., L. E. Braitman, et al. (2008). "Quality of life and symptom attribution in long-term colon cancer survivors." *J Eval Clin Pract* **14**(2): 254-8.
155. Podnos, Y. D., T. R. Borneman, et al. (2007). "Symptom concerns and resource utilization in patients with lung cancer." *J Palliat Med* **10**(4): 899-903.
156. Rao, A. and H. J. Cohen (2004). "Symptom management in the elderly cancer patient: fatigue, pain, and depression." *J Natl Cancer Inst Monogr*(32): 150-7.
157. Rao, D., Z. Butt, et al. (2009). "A Comparison of the Renal Cell Carcinoma-Symptom Index (RCC-SI) and the Functional Assessment of Cancer Therapy-Kidney Symptom Index (FKSI)." *J Pain Symptom Manage* **38**(2): 291-8.
158. Recklitis, C. J. and P. Rodriguez (2007). "Screening childhood cancer survivors with the brief symptom inventory-18: classification agreement with the symptom checklist-90-revised." *Psychooncology* **16**(5): 429-36.
159. Recklitis, C. J., S. K. Parsons, et al. (2006). "Factor structure of the brief symptom inventory--18 in adult survivors of childhood cancer: results from the childhood cancer survivor study." *Psychol Assess* **18**(1): 22-32.
160. Reid, C. M., R. Gooberman-Hill, et al. (2008). "Opioid analgesics for cancer pain: symptom control for the living or comfort for the dying? A qualitative study to investigate the factors influencing the decision to accept morphine for pain caused by cancer." *Ann Oncol* **19**(1): 44-8.
161. Reuter, K., S. Raugust, et al. (2004). "Depressive symptom patterns and their consequences for diagnosis of affective disorders in cancer patients." *Support Care Cancer* **12**(12): 864-70.
162. Ribi, K., J. Bernhard, et al. (2007). "Endocrine symptom assessment in women with breast cancer: what a simple "yes" means." *Support Care Cancer* **15**(12): 1349-56.
163. Rich, T. A. (2006). "Cancer symptom complexes related to alterations in molecular circadian axis signaling." *Conf Proc IEEE Eng Med Biol Soc* **1**: 171-2.
164. Rich, T. A. (2007). "Symptom clusters in cancer patients and their relation to EGFR ligand modulation of the circadian axis." *J Support Oncol* **5**(4): 167-74; discussion 176-7.
165. Ridner, S. H. (2005). "Quality of life and a symptom cluster associated with breast cancer treatment-related lymphedema." *Support Care Cancer* **13**(11): 904-11.
166. Riechelmann, R. P., M. K. Krzyzanowska, et al. (2007). "Symptom and medication profiles among cancer patients attending a palliative care clinic." *Support Care Cancer* **15**(12): 1407-12.
167. Rippy, L. and J. Marsden (2006). "Is HRT justified for symptom management in women at higher risk of developing breast cancer?" *Climacteric* **9**(6): 404-15.
168. Rogers, L. Q., J. Malone, et al. (2009). "Exercise preferences among patients with head and neck cancer: prevalence and associations with quality of life, symptom severity, depression, and rural residence." *Head Neck* **31**(8): 994-1005.
169. Rosenthal, D. I., T. R. Mendoza, et al. (2007). "Measuring head and neck cancer symptom burden: the development and validation of the M. D. Anderson symptom inventory, head and neck module." *Head Neck* **29**(10): 923-31.
170. Royer, H. R., C. H. Phelan, et al. (2009). "Older breast cancer survivors' symptom beliefs." *Oncol Nurs Forum* **36**(4): 463-70.
171. Ruiter, R. A., J. de Nooijer, et al. (2008). "Intended coping responses to cancer symptoms in healthy adults: the roles of symptom knowledge, detection behavior, and perceived threat." *Cancer Epidemiol Biomarkers Prev* **17**(4): 818-26.
172. Sagar, S. M. (2008). "Acupuncture as an evidence-based option for symptom control in cancer patients." *Curr Treat Options Oncol* **9**(2-3): 117-26.
173. Sarna, L. and M. S. Riedinger (2004). "Assessment of quality of life and symptom improvement in lung cancer clinical trials." *Semin Oncol* **31**(3 Suppl 9): 1-10.
174. Sarna, L., M. E. Cooley, et al. (2008). "Symptom severity 1 to 4 months after thoracotomy for lung cancer." *Am J Crit Care* **17**(5): 455-67; quiz 468.
175. Schonwetter, R. S., L. A. Roscoe, et al. (2006). "Quality of life and symptom control in hospice patients with cancer receiving chemotherapy." *J Palliat Med* **9**(3): 638-45.
176. Schwartzberg, L. S., B. V. Fortner, et al. (2005). "Sex differences in patients who have cancer with mild anemia: symptom burden and quality of life." *Support Cancer Ther* **2**(4): 241-6.
177. Sela, R. A. (2007). "Screening for depression in palliative cancer patients attending a pain and symptom control clinic." *Palliat Support Care* **5**(3): 207-17.
178. Sela, R. A., S. Watanabe, et al. (2005). "Sleep disturbances in palliative cancer patients attending a pain and symptom control clinic." *Palliat Support Care* **3**(1): 23-31.
179. Shelby, R. A., D. M. Golden-Kreutz, et al. (2005). "Mismatch of posttraumatic stress disorder (PTSD) symptoms and DSM-IV symptom clusters in a cancer sample: exploratory factor analysis of the PTSD Checklist-Civilian Version." *J Trauma Stress* **18**(4): 347-57.
180. Sherman, D. W., X. Y. Ye, et al. (2007). "Symptom assessment of patients with advanced cancer and AIDS and their family caregivers: the results of a quality-of-life pilot study." *Am J Hosp Palliat Care* **24**(5): 350-65.
181. Sherwood, P., B. A. Given, et al. (2005). "A cognitive behavioral intervention for symptom management in patients with advanced cancer." *Oncol Nurs Forum* **32**(6): 1190-8.

182. Shih, Y. C., X. S. Wang, et al. (2006). "The association between symptom burdens and utility in Chinese cancer patients." *Qual Life Res* **15**(8): 1427-38.
183. Sikorskii, A., C. W. Given, et al. (2007). "Symptom management for cancer patients: a trial comparing two multimodal interventions." *J Pain Symptom Manage* **34**(3): 253-64.
184. Skerman, H. M., P. M. Yates, et al. (2009). "Multivariate methods to identify cancer-related symptom clusters." *Res Nurs Health* **32**(3): 345-60.
185. Skrutkowski, M., A. Saucier, et al. (2008). "Impact of a pivot nurse in oncology on patients with lung or breast cancer: symptom distress, fatigue, quality of life, and use of healthcare resources." *Oncol Nurs Forum* **35**(6): 948-54.
186. Slaughter, L. A., C. M. Ruland, et al. (2006). "Constructing an effective information architecture for a pediatric cancer symptom assessment tool." *AMIA Annu Symp Proc*: 1102.
187. Slim, I., K. Ach, et al. (2009). "Diabetes mellitus as an early symptom of pancreatic cancer diagnosed three years later." *Ann Endocrinol (Paris)* **70**(1): 76-9.
188. Sloan, J. A., L. Berk, et al. (2007). "Integrating patient-reported outcomes into cancer symptom management clinical trials supported by the National Cancer Institute-sponsored clinical trials networks." *J Clin Oncol* **25**(32): 5070-7.
189. So, W. K., G. Marsh, et al. (2009). "The symptom cluster of fatigue, pain, anxiety, and depression and the effect on the quality of life of women receiving treatment for breast cancer: a multicenter study." *Oncol Nurs Forum* **36**(4): E205-14.
190. Solano, J. P., B. Gomes, et al. (2006). "A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease." *J Pain Symptom Manage* **31**(1): 58-69.
191. Stanton, A. L., C. A. Bernards, et al. (2005). "The BCPT symptom scales: a measure of physical symptoms for women diagnosed with or at risk for breast cancer." *J Natl Cancer Inst* **97**(6): 448-56.
192. Stapley, S., T. J. Peters, et al. (2006). "The mortality of colorectal cancer in relation to the initial symptom at presentation to primary care and to the duration of symptoms: a cohort study using medical records." *Br J Cancer* **95**(10): 1321-5.
193. Stepanski, E. J., A. C. Houts, et al. (2009). "Second- and third-line treatment of patients with non-small-cell lung cancer with erlotinib in the community setting: retrospective study of patient healthcare utilization and symptom burden." *Clin Lung Cancer* **10**(6): 426-32.
194. Storey, D. J., R. A. Waters, et al. (2007). "Clinically relevant fatigue in cancer outpatients: the Edinburgh Cancer Centre symptom study." *Ann Oncol* **18**(11): 1861-9.
195. Strasser, F., C. Sweeney, et al. (2004). "Impact of a half-day multidisciplinary symptom control and palliative care outpatient clinic in a comprehensive cancer center on recommendations, symptom intensity, and patient satisfaction: a retrospective descriptive study." *J Pain Symptom Manage* **27**(6): 481-91.
196. Strong, V., R. Waters, et al. (2007). "Emotional distress in cancer patients: the Edinburgh Cancer Centre symptom study." *Br J Cancer* **96**(6): 868-74.
197. Sun, C. C., D. C. Bodurka, et al. (2005). "Rankings and symptom assessments of side effects from chemotherapy: insights from experienced patients with ovarian cancer." *Support Care Cancer* **13**(4): 219-27.
198. Sun, Y. and M. T. Knobf (2008). "Concept analysis of symptom disclosure in the context of cancer." *ANS Adv Nurs Sci* **31**(4): 332-41.
199. Swore Fletcher, B. A., M. J. Dodd, et al. (2008). "Symptom experience of family caregivers of patients with cancer." *Oncol Nurs Forum* **35**(2): E23-44.
200. Tanaka, N., K. Fujimoto, et al. (2009). "Variations in international prostate symptom scores, uroflowmetric parameters, and prostate volume after (125I) permanent brachytherapy for localized prostate cancer." *Urology* **74**(2): 407-11.
201. Tassinari, D., B. Poggi, et al. (2005). "Treating sialorrhea with transdermal scopolamine. Exploiting a side effect to treat an uncommon symptom in cancer patients." *Support Care Cancer* **13**(7): 559-61.
202. Temel, J. S., W. F. Pirl, et al. (2006). "Comprehensive symptom management in patients with advanced-stage non-small-cell lung cancer." *Clin Lung Cancer* **7**(4): 241-9.
203. Teunissen, S. C., A. de Graeff, et al. (2007). "Are anxiety and depressed mood related to physical symptom burden? A study in hospitalized advanced cancer patients." *Palliat Med* **21**(4): 341-6.
204. Teunissen, S. C., W. Wesker, et al. (2007). "Symptom prevalence in patients with incurable cancer: a systematic review." *J Pain Symptom Manage* **34**(1): 94-104.
205. Thompson, M. R., R. Perera, et al. (2007). "Predictive value of common symptom combinations in diagnosing colorectal cancer." *Br J Surg* **94**(10): 1260-5.
206. Tishelman, C., L. M. Petersson, et al. (2007). "Symptom prevalence, intensity, and distress in patients with inoperable lung cancer in relation to time of death." *J Clin Oncol* **25**(34): 5381-9.
207. Tokuda, Y., K. Chinen, et al. (2009). "Intervals between symptom onset and clinical presentation in cancer patients." *Intern Med* **48**(11): 899-905.
208. Tsai, J. S., C. H. Wu, et al. (2006). "Symptom patterns of advanced cancer patients in a palliative care unit." *Palliat Med* **20**(6): 617-22.
209. Tseng, T. H., C. S. Cleeland, et al. (2008). "Assessing cancer symptoms in adolescents with cancer using the Taiwanese version of the M. D. Anderson Symptom Inventory." *Cancer Nurs* **31**(3): E9-16.
210. Vadiraja, S. H., M. R. Rao, et al. (2009). "Effects of yoga on symptom management in breast cancer patients: A randomized controlled trial." *Int J Yoga* **2**(2): 73-9.
211. Visovsky, C. G., A. M. Berger, et al. (2008). "Methodological challenges of symptom management research in recurrent cancer." *Cancer Nurs* **31**(3): 175-81.
212. Wada, Y., R. Takahashi, et al. (2007). "Paradoxical cerebral embolism as the initial symptom in a patient with ovarian cancer." *J Stroke Cerebrovasc Dis* **16**(2): 88-90.
213. Walsh, D. and L. Rybicki (2006). "Symptom clustering in advanced cancer." *Support Care Cancer* **14**(8): 831-6.
214. Wang, J., F. Liu, et al. (2008). "The symptom-to-treatment delay and stage at the time of treatment in cancer of esophagus." *Jpn J Clin Oncol* **38**(2): 87-91.
215. Wang, S. Y., C. M. Tsai, et al. (2008). "Symptom clusters and relationships to symptom interference with daily life in Taiwanese lung cancer patients." *J Pain Symptom Manage* **35**(3): 258-66.
216. Wang, S. Y., C. W. Lee, et al. (2005). "Symptom distress changes during first postoperative month in newly diagnosed Taiwanese breast cancer patients: a longitudinal study." *Cancer Nurs* **28**(4): 263-9.
217. Wang, X. S., A. V. Laudico, et al. (2006). "Filipino version of the M. D. Anderson Symptom Inventory: validation and multisymptom measurement in cancer patients." *J Pain Symptom Manage* **31**(6): 542-52.
218. Wang, X. S., Y. Wang, et al. (2004). "Chinese version of the M. D. Anderson Symptom Inventory: validation and application of symptom measurement in cancer patients." *Cancer* **101**(8): 1890-901.
219. Wennman-Larsen, A., C. Tishelman, et al. (2007). "Factors influencing agreement in symptom ratings by lung cancer patients and their significant others." *J Pain Symptom Manage* **33**(2): 146-55.

220. Wilkinson, S., K. Barnes, et al. (2008). "Massage for symptom relief in patients with cancer: systematic review." *J Adv Nurs* **63**(5): 430-9.
221. Wilkinson, S., K. Lockhart, et al. (2008). "Reflexology for symptom relief in patients with cancer." *Cancer Nurs* **31**(5): 354-60; quiz 361-2.
222. Williams, P. D., J. Schmideskamp, et al. (2006). "Symptom monitoring and dependent care during cancer treatment in children: pilot study." *Cancer Nurs* **29**(3): 188-97.
223. Williams, P. D., U. Piamjariyakul, et al. (2006). "Cancer treatment, symptom monitoring, and self-care in adults: pilot study." *Cancer Nurs* **29**(5): 347-55.
224. Woodgate, R. L. and L. F. Degner (2004). "Cancer symptom transition periods of children and families." *J Adv Nurs* **46**(4): 358-68.
225. Yamada, T., K. Furukawa, et al. (2008). "Case of meningeal carcinomatosis with gastric cancer which manifested meningeal signs as the initial symptom; the palliative benefit of radiotherapy." *J Nippon Med Sch* **75**(4): 216-20.
226. Yeh, C. H., Y. C. Chiang, et al. (2008). "Symptom clustering in older Taiwanese children with cancer." *Oncol Nurs Forum* **35**(2): 273-81.
227. Yennurajalingam, S., T. Zhang, et al. (2007). "The impact of the palliative care mobile team on symptom assessment and medication profiles in patients admitted to a comprehensive cancer center." *Support Care Cancer* **15**(5): 471-5.
228. Yoon, J., J. L. Malin, et al. (2008). "Symptom management after breast cancer treatment: is it influenced by patient characteristics?" *Breast Cancer Res Treat* **108**(1): 69-77.
229. Zaric, B., V. Canak, et al. (2007). "The effect of Nd:YAG laser resection on symptom control, time to progression and survival in lung cancer patients." *J Buon* **12**(3): 361-8.
230. PubMed (2013). <http://www.ncbi.nlm.nih.gov/pubmed>.
231. Cancer. Wikipedia. (2013) <http://en.wikipedia.org/wiki/Cancer>.

2/3/2013