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Clinical Update: Literature Abstracts

MEASURES

Screening for Depression in the Medically Ill: A Comparison of Self-Report Measures, Clinician Judgment, and DSM-IV Diagnoses

Wilhelm, K., Kotze, B., Waterhouse, M., Hadzi-Pavlovic, D., and Parker, G.

Psychosomatics, *45* (2004), 461–469

The performance of the self-report 10-item Depression in the Medically Ill scale was observed in 210 patients as part of clinical assessment by consultation-liaison psychiatry clinicians. Both the Depression in the Medically Ill scale and the Beck Depression Inventory for Primary Care were completed by the patient, and the clinicians made their judgment of the presence and severity of "clinical depression" and DSM-IV affective disorder diagnoses. Both the Depression in the Medically Ill scale and the Beck Depression Inventory for Primary Care detected 85% of patients with DSM-IV major depressive episode. The Depression in the Medically Ill scale was slightly superior to the Beck Depression Inventory for Primary Care in its relationship to clinicians' judgments of clinical depression caseness.

Development of an Impact Thermometer for Use in Combination with the Distress Thermometer as a Brief Screening Tool for Adjustment Disorders and/or Major Depression in Cancer Patients

Akizuki, N., Yamawaki, S., Akechi, T., Nakano, T., and Uchitomi, Y.

Journal of Pain and Symptom Management, *29* (2005), 91–99

Screening cancer patients for adjustment disorders and major depression is important, because both are prevalent and often underrecognized. The purpose of this study was to validate the Distress and Impact Thermometer, a 2-item questionnaire, which was newly developed as a brief screening tool for detection of adjustment disorders and/or major depression. Two hundred ninety-five cancer patients completed the Distress and Impact Thermometer and the Hospital Anxiety and Depression Scale (HADS), and were examined by psychiatrists based on DSM-IV criteria. Using cutoff points for detection of adjustment disorders and major depression of "3/4" on the "distress" score and "2/3" on "impact," the sensitivity and specificity were 0.82 and 0.82, respectively. Screening performance of the Distress and Impact Thermometer was comparable to that of the Hospital Anxiety and Depression Scale. Its brevity and good performance suggest that the Distress and Impact Thermometer is an effective tool for routine screening in clinical oncology settings.

Quality-of-Life Assessment in the Symptom Management Trials of the National Cancer Institute-Supported Community Clinical Oncology Program

Buchanan, D.R., O'Mara, A.M., Kelaghan, J.W., and Minasian, L.M.

Journal of Clinical Oncology, *23* (2005), 591–598

This paper examines 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). 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. 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. 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.

Evaluation of the Missoula-VITAS Quality of Life Index—Revised: Research Tool or Clinical Tool?

Schwartz, C.E., Merriman, M.P., Reed, G., and Byock, I.

Journal of Palliative Medicine, *8* (2005), 121–135

Quality of life (QOL) is a central outcome measure in caring for seriously ill patients. The Missoula-VITAS Quality of Life Index (MVQOLI) is a 25-item patient-centered index that weights each of five QOL dimensions (symptoms, function, interpersonal, well-being, transcendence) by its importance to the respondent. The measure has been used to assess QOL for hospice patients, and has been found to be somewhat complex to use and analyze. This study aimed to simplify the measure, and evaluate the reliability and validity of a revised version as either a research or clinical tool (i.e., "psychometric" vs. "clinimetric"). Two data collection efforts are described. The psychometric study collected QOL data from 175 patients at baseline, 3–5 days, and 21 days later. The implementation study evaluated the feasibility and utility of the MVQOLI-R during over 6 weeks of use. Setting/subjects: End-stage renal patients on dialysis, hospice, or long-term care patients participated in the psychometric study. The implementation study was done in hospice, home health, and palliative care settings. The MVQOLI-R and the Memorial Symptom Assessment Scale: The psychometric and implementation studies suggest that the MVQOLI-R performs well as a clinical tool but is not powerful as an outcome research instrument. The MVQOLI-R has the heterogeneous structure of clinimetric tools, and demonstrated both relevance and responsiveness. Additionally, in a clinical setting the MVQOLI-R was useful therapeutically for stimulating communication about the psychosocial and spiritual issues important to the tasks of life completion and life closure. The MVQOLI-R has clinical utility as a patient QOL assessment tool and may have therapeutic utility as a tool for fostering discussion among patients and their clinicians, as well as for helping patients identify sources of suffering and opportunities during this time in their lives.

Assessment of Pain Quality in Chronic Neuropathic and Nociceptive Pain Clinical Trials with the Neuropathic Pain Scale

Jensen, M.P., Dworkin, R.H., Gammaitoni, A.R., Olaleye, D.O., Oleka, N., and Galer, B.S.

The Journal of Pain, *4* (2005), 98–106

Although a number of measures of pain qualities exist, little research has examined the potential for these measures to identify the unique effects of pain treatments on different pain qualities. We examined the utility of the Neuropathic Pain Scale (NPS) for assessing changes in pain qualities after open label lidocaine patch 5% in three samples of patients: patients with peripheral neuropathic pain, low back pain, and osteoarthritis. With one exception ("cold" pain in subjects with low back pain), each of the NPS items showed significant change after open label lidocaine patch. In addition, significantly larger changes were observed for the NPS items reflecting global pain intensity and pain unpleasantness and for items assessing sharp and deep pain than for items assessing cold, sensitive, and itchy pain. The pattern of changes in pain qualities did not differ across the three diagnostic groups, but it did differ from the patterns of changes in pain qualities associated with other analgesic treatments. The results support the potential utility of the NPS for assessing the patterns of changes in pain qualities that can be observed after pain treatment.

Item Analysis of Cancer Patient Responses to the Multidimensional Affect and Pain Survey Demonstrates High Inter-item Consistency and Discriminability and Determines the Content of a Short Form

Griswold, G.A. and Clark, W.C.

Journal of Pain, *6* (2005), 67–74

To construct a short form (SMAPS-CP), item analysis was used to select 30 items, 1 from each of the 30 subclusters in the 101-item Multidimensional Affect and Pain Survey (101-MAPS). Representation of each of the subclusters ensured that the structure of the MAPS dendrogram obtained by cluster analysis was maintained in SMAPS-CP. Responses of outpatients with cancer to the 101-MAPS were treated by item analysis to obtain measures of inter-

item consistency (criterion between 0.40 and 0.80) and discriminability (criterion above 0.35) for each of the 101-MAPS questions. Both of these criteria for acceptance were met by 53 of the 57 questions in Supercluster I, Somatosensory Pain, by 25 of the 26 questions in Supercluster II, Emotional Pain, and by all 18 of the questions in Supercluster III, Well-being. The item within each cluster that best met the item analysis criteria was selected for the 30-item SMAPS-CP questionnaire.

SYMPTOM CONTROL

Efficacy, Safety, and Steady-State Pharmacokinetics of Once-a-Day Controlled-Release Morphine (MS Contin XL) in Cancer Pain

Hagen, N.A., Thirlwell, M., Eisenhoffer, J., Quigley, P., Harsanyi, Z., and Darke, A.

Journal of Pain and Symptom Management, *29* (2005), 80–90

The efficacy, safety, and pharmacokinetics of a novel once-daily morphine formulation (OAD morphine) and a 12-hourly formulation (twice-daily CR morphine) were compared in a double-blind, multicentered crossover study. Chronic cancer pain patients ($n = 25$) were randomized to OAD morphine (mean 238 ± 319 mg q24h) or twice-daily CR morphine (mean 119 ± 159 mg q12h) for 1 week. They then crossed over to the alternate drug, which also was taken for 1 week. There was no difference between treatments for evaluations of overall pain intensity, analgesic efficacy, or adverse events. However, whereas pain scores increased during the day on twice-daily CR morphine ($p = 0.0108$), they remained stable on OAD morphine. Most patients (68%) chose once-daily dosing for continuing pain management ($p = 0.015$). The AUC ratio was 100.3%, indicating equivalent absorption. Fluctuation indices were 93.5 ± 28.8% and 179.3 ± 41.3% ($p = 0.0001$) for OAD morphine and twice-daily CR morphine, respectively. OAD morphine provides analgesia similar to twice-daily CR morphine with reduced fluctuation in plasma morphine concentration and more stable pain control.

Barriers to Effective Symptom Management in Hospice

Johnson, D.C., Kassner, C.T., Houser, J., and Kutner, J.S.

Journal of Pain and Symptom Management, *29* (2005), 69–79

The barriers to effective symptom management in hospice are not well described. We surveyed nurses of hospices affiliated with the Population-based Palliative Care Research Network (PoPCRN) to identify barriers to the effective management of common symptoms in terminally ill patients. Some 867/1710 (51%) nurses from 67 hospices in 25 U.S. states returned surveys. Of 32 symptoms, nurses reported agitation (45%), pain (40%), and dyspnea (34%) as the "most difficult to manage." The most common perceived barriers to effective symptom management were inability of family care providers to implement or maintain recommended treatments (38%), patients or families not wanting recommended treatments (38%), and competing demands from other distressing symptoms (37%). Patterns of barriers varied by symptom. These nurses endorsed multiple barriers contributing to unrelieved symptom distress in patients receiving hospice care. Interventions to improve symptom management in hospice may need to account for these differing barrier patterns.

Perceived Adverse Effects of Antiretroviral Therapy

Johnson, M.O., Charlebois, E., Morin, S.F., Catz, S.L., Goldstein, R.B., Remien, R.H., Rotheram-Borus, M.J., Mickalian, J.D., Kittel, L., Samimy-Muzaffar, F., Lightfoot, M.A., Gore-Felton, C., Chesney, M.A., and the NIMH Healthy Living Project Team

Journal of Pain and Symptom Management, *29* (2005), 193–205

Adverse effects from antiretroviral therapy (ARV) for HIV are associated with medication nonadherence. The purposes of this study were to explore group differences in the reporting of adverse effects, identify individual adverse effects that are linked to nonadherence, and to explore the role of coping in the relationship between adverse effects and adherence. Cross-sectional interviews of 2,765 HIV-positive adults on ARV therapies in four U.S. cities were performed using a computerized assessment of self-reported adverse effects, coping self-efficacy, and adherence. There were no gender differences in the rate or severity of adverse effects reported. Latino respondents reported more adverse effects than either White or African Americans. Those taking a protease inhibitor (PI) reported a higher rate and greater severity of adverse effects. Older participants reported fewer adverse effects despite being more likely to be on a regimen containing a PI. Respondents with less than 90% adherence reported greater numbers and severity

of adverse effects overall. In multivariate analyses, nausea, skin problems, vomiting, and memory adverse effects were independently related to less than 90% adherence over the prior 3 days. Coping moderated the relationship between nausea and adherence such that individuals who reported lower coping self-efficacy and experienced nausea were at increased risk for nonadherence, regardless of the length of time on the current ARV regimen. Women and men are similar in their overall reports of adverse effects, and Latinos report more adverse effects to ARVs than White or African American patients. Specific adverse effects (skin problems, memory problems, vomiting, and nausea) are more likely than others to be associated with missing ARV medications. Increasing adaptive coping self-efficacy among patients experiencing nausea may be a particularly effective strategy in increasing medication adherence.

Predictors and Correlates of Fatigue in HIV/AIDS

Voss, J.G.

Journal of Pain and Symptom Management, *29* (2005), 73–184

Variation in the intensity of fatigue according to selected demographic, cultural, and health/illness variables was explored in 372 patients with HIV/AIDS, and the contribution of fatigue to physical and mental health in this population was investigated within the UCSF Symptom Management Model (UCSF-SMM). The sample included 73% African Americans and 63% males. Moderate to severe fatigue intensity was reported by 58% of the total sample. Women, Hispanics, the disabled, and those with inadequate income or insurance reported higher fatigue intensity scores. Two hierarchical regression models explored the contributions of fatigue to physical and mental health. Fatigue contributed 2% to the total variance (37.4%) in physical health, but did not contribute as an independent predictor of the total variance (23.2%) in mental health. The results of this study imply the need for further gender and ethnic-specific fatigue research, as well as symptom cluster research.

Pharmacological Treatment of Neuropsychiatric Symptoms of Dementia; A Review of the Evidence

Sink, K.M., Holden, K.F., and Yaffe, K.

JAMA, *293* (2005), 596–608

Neuropsychiatric symptoms of dementia are common and associated with poor outcomes for patients and caregivers. Although nonpharmacological interventions should be the first line of treatment, a wide variety of pharmacological agents are used in the management of neuropsychiatric symptoms; therefore, concise, current, evidence-based recommendations are needed. The objective of this paper is to evaluate the efficacy of pharmacological agents used in the treatment of neuropsychiatric symptoms of dementia. A systematic review of English-language articles published from 1966 to July 2004 using MEDLINE, the Cochrane Database of Systematic Reviews, and a manual search of bibliographies was conducted. Inclusion criteria were double-blind, placebo-controlled, randomized controlled trials (RCTs) or meta-analyses of any drug therapy for patients with dementia that included neuropsychiatric outcomes. Trials reporting only depression outcomes were excluded. Data on the inclusion criteria, patients, methods, results, and quality of each study were independently abstracted. Twenty-nine articles met inclusion criteria. For typical antipsychotics, two meta-analyses and two RCTs were included. Generally, no difference among specific agents was found, efficacy was small at best, and adverse effects were common. Six RCTs with atypical antipsychotics were included; results showed modest, statistically significant efficacy of olanzapine and risperidone, with minimal adverse effects at lower doses. Atypical antipsychotics are associated with an increased risk of stroke. There have been no RCTs designed to directly compare the efficacy of typical and atypical antipsychotics. Five trials of antidepressants were included; results showed no efficacy for treating neuropsychiatric symptoms other than depression, with the exception of one study of citalopram. For mood stabilizers, three RCTs investigating valproate showed no efficacy. Two small RCTs of carbamazepine had conflicting results. Two meta-analyses and six RCTs of cholinesterase inhibitors generally showed small, although statistically significant, efficacy. Two RCTs of memantine also had conflicting results for treatment of neuropsychiatric symptoms. Pharmacological therapies are not particularly effective for management of neuropsychiatric symptoms of dementia. Of the agents reviewed, the atypical antipsychotics risperidone and olanzapine currently have the best evidence for efficacy. However, the effects are modest and further complicated by an increased risk of stroke. Additional trials of cholinesterase inhibitors enrolling patients with high levels of neuropsychiatric symptoms may be warranted.

Does a History of Childhood Sexual Abuse Affect Sexual Outcomes in Breast Cancer Survivors?

Wyatt, G.E., Loeb, T.B., Desmond, K.A., and Ganz, P.A.

Journal of Clinical Oncology, *23* (2005), 1261–1269

Little is known about a history of childhood sexual abuse (CSA) in breast cancer survivors and its relationship to sexual functioning after cancer. As part of a larger survey study examining sexuality and intimacy in breast cancer survivors, we conducted in-person interviews with a subsample of participants. A total of 147 women in Los Angeles, CA, and Washington, DC, completed a structured interview that addressed sexual socialization and a history of sexual abuse. Trained female interviewers conducted the interviews. Descriptive statistics and regression analyses were used to examine the prevalence of CSA, and its potential impact on sexual health and functioning. One in three women reported at least one CSA incident. Among women who had experienced CSA, 71% reported a single incident, and 22% reported a penetrative form of sexual contact. In multivariate regression analyses examining physical and psychological aspects of sexuality and body image, CSA was not a significant predictor of physical discomfort. However, a history of penetrative CSA was a significant predictor of psychological discomfort ($p = 0.02$). The prevalence of CSA in this sample was similar to the general population literature on this topic. In this small sample, a past history of CSA did not contribute significantly to the physical discomforts associated with sexual intimacy after breast cancer; however, our findings suggest that a past history of penetrative CSA is associated with increased psychological discomfort, and may warrant additional examination in future research.

Effects of Parenteral Hydration in Terminally Ill Cancer Patients: A Preliminary Study

Bruera, E., Sala, R., Rico, M.A., Moyano, J., Centeno, C., Willey, J., and Palmer, J.L.

Journal of Clinical Oncology, *23* (2005), 2366–2371

Most patients with cancer develop decreased oral intake and dehydration before death. This study aimed to determine the effect of parenteral hydration on overall symptom control in terminally ill cancer patients with dehydration. Patients with clinical evidence of mild to moderate dehydration and a liquid oral intake less than 1,000 ml/day were randomly assigned to receive either parenteral hydration with 1,000 ml (treatment group) or placebo with 100 ml normal saline administered over 4 hours for 2 days. Patients were evaluated for target symptoms (hallucinations, myoclonus, fatigue, and sedation), global well-being, and overall benefit. Twenty-seven patients randomly assigned to the treatment group had improvement in 53 (73%) of their 73 target symptoms versus 33 (49%) of 67 target symptoms in the placebo group ($n = 22$; $p = 0.005$). Fifteen (83%) of 18 and 15 (83%) of 18 patients had improved myoclonus and sedation after hydration versus 8 (47%) of 17 and 5 (33%) of 15 patients after placebo ($p = 0.035$ and $p = 0.005$, respectively). There were no significant differences of improvement in hallucinations or fatigue between groups. When blinded to treatment, patients (17 [63%] of 77) and investigators (20 [74%] of 27) perceived hydration as effective compared with placebo in 9 (41%) of 22 patients ($p = 0.78$) and 12 (54%) of 22 investigators ($p = 0.15$), respectively. The intensity of pain and swelling at the injection site were not significantly different between groups. Parenteral hydration decreased symptoms of dehydration in terminally ill cancer patients who had decreased fluid intake. Hydration was well tolerated, and a placebo effect was observed. Studies with larger samples and a longer follow-up period are justified.

Weight, Weight Gain, and Survival after Breast Cancer Diagnosis

Kroenke, C.H., Chen, W.Y., Rosner, B., and Holmes, M.D.

Journal of Clinical Oncology, *23* (2005), 1370–1378

The purpose of this paper is to determine whether weight prior to diagnosis and weight gain after diagnosis are predictive of breast cancer survival. Patients included 5,204 Nurses' Health Study participants diagnosed with incident, invasive, nonmetastatic breast cancer between 1976 and 2000; 860 total deaths, 533 breast cancer deaths, and 681 recurrences (defined as secondary lung, brain, bone, or liver cancer, and death from breast cancer) accrued to 2002. We computed the change in body mass index (BMI) from before to the first BMI reported ≥12 months after the date of diagnosis. Cox proportional hazards models were used to evaluate associations of categories of BMI before diagnosis and of BMI change with time to event. We stratified by smoking, menopausal status, and breast cancer–related variables. In multivariate-adjusted analyses, weight before diagnosis was positively associated with breast cancer recurrence and death, but this was apparent only in never smokers. Sim-

ilarly, among never-smoking women, those who gained between 0.5 and 2.0 kg/m^2 (median gain, 6.0 lb; relative risk [RR], 1.35; 95% CI, 0.93 to 1.95) or more than 2.0 kg/m^2 (median gain, 17.0 lb; RR, 1.64; 95% CI, 1.07 to 2.51) after diagnosis had an elevated risk of breast cancer death during follow-up (median, 9 years), compared with women who maintained their weight (test for linear trend, $p = 0.03$). Associations with weight were stronger in premenopausal than in postmenopausal women. Similar findings were noted for breast cancer.

Sedation for Terminally Ill Patients with Cancer with Uncontrollable Physical Distress

Kohara, H., Ueoka, H., Takeyama, H., Murakami, T., and Morita, T.

Journal of Palliative Medicine, *8* (2005), 20–25

Relief of distressful symptoms in terminally ill patients with cancer is of prime importance. Use of sedation to accomplish this has been the focus of recent medical studies in countries other than Japan. We investigated the influence on consciousness of sedative drugs in a Japanese hospice. We defined sedation as medical procedure to decrease level of consciousness in order to relieve severe physical distress refractory to standard interventions. We excluded increases in doses of morphine or other analgesic drugs resulting in secondary somnolence from the present study. We reviewed medical records of patients receiving sedation among 124 consecutive patients admitted to our palliative care unit between January and December in 1999. The 63 patients who received sedation (50.3%) died an average of 3.4 days after its initiation. Major symptoms requiring sedation were dyspnea, general malaise/restlessness, pain, agitation, and nausea/vomiting. The Palliative Performance Status (PPS) just before sedation was 20 or less in 83% of patients. Drugs administered for sedation were midazolam, haloperidol, scopolamine hydrobromide, and chlorpromazine. During the few days before death, sedated patients were significantly more drowsy and less responsive than those receiving nonsedative treatment. Our data suggest the effectiveness of sedation in relieving severe, refractory physical symptoms in terminally ill Japanese patients with cancer. Further investigation to confirm safety and effectiveness of sedation in this context is warranted.

The Correlation between Fatigue, Physical Function, the Systemic Inflammatory Response, and Psychological Distress in Patients with Advanced Lung Cancer

Brown, D.J.F., McMillan, D.C., and Milroy, R.

Cancer, *103* (2005), 377–382

Functional disability is reported frequently in fatigued cancer patients, but little is known about the correlation between fatigue and objective physical function. In addition, from previous work, the systemic inflammatory response and psychological distress appear to be related to fatigue. Thirty-eight patients with metastatic or locally advanced lung carcinoma and 15 age-matched and gender-matched healthy controls completed the Functional Assessment of Chronic Illness Therapy–Fatigue scale, a visual analogue weakness score, and the Hospital Anxiety and Depression (HAD) scale. Hemoglobin concentrations, C-reactive protein (CRP) concentrations, creatine kinase concentrations, white blood cell count, body composition, Karnofsky performance status (KPS), grip strength, and chair-rise time also were measured in both groups. The cancer patients were then grouped into tertiles on the basis of fatigue scores. The cancer patients had greater fatigue compared with the control group ($p < 0.001$). They also weighed less, had lower hemoglobin and creatine kinase levels and higher CRP levels, and had lower KPS, poorer grip strength, longer chair-rise times, and increased HAD scale scores (all $p < 0.01$). KPS and chair-rise time were correlated strongly ($r^2 = 0.565$; $p < 0.001$). With increasing fatigue, KPS was lower, and chair-rise time and HAD scale scores were greater ($p < 0.01$). On multiple regression analysis, only KPS, weakness, and HAD scale scores were correlated independently with fatigue ($r^2 = 0.570$; $p < 0.001$). Objective physical function (as measured by chair-rise time) in patients with advanced lung cancer was poorer with increasing fatigue. Results of the current study suggest that fatigue is not a result primarily of weight loss or anemia but is related to KPS and psychological distress.

Forgiveness and Chronic Low Back Pain: A Preliminary Study Examining the Relationship of Forgiveness to Pain, Anger, and Psychological Distress

Carsona, J.W., Keefea, F.J., Golia, V., Frasa, A.M., Lyncha, T.R., Thorpa, S.R., and Buechle, J.L.

The Journal of Pain, *6* (2005), 84–91

Clinical observations suggest that many patients with chronic pain have difficulty forgiving persons they perceive as having unjustly offended them in some way. By using a sample of 61 patients with chronic low back pain, this study sought to determine the reliability and variability of forgiveness

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assessments in patients and to examine the relationship of forgiveness to pain, anger, and psychological distress. Standardized measures were used to assess patients' current levels of forgiveness, forgiveness self-efficacy, pain, anger, and psychological distress. Results showed that forgiveness-related constructs can be reliably assessed in patients with persistent pain, and that patients vary considerably along dimensions of forgiveness. Furthermore, correlational analyses showed that patients who had higher scores on forgiveness-related variables reported lower levels of pain, anger, and psychological distress. Additional analyses indicated that state anger largely mediated the association between forgiveness and psychological distress, as well as some of the associations between forgiveness and pain. These findings indicate that forgiveness can be reliably assessed in patients with persistent pain, and that a relationship appears to exist between forgiveness and important aspects of living with persistent pain.

QUALITY OF PALLIATIVE CARE

Psychosocial Function after Hematopoietic Stem Cell Transplantation

Chang, G., Orav, E.J., McNamara, T.K., Tong, M.-Y., and Antin, J.H.

Psychosomatics, *46* (2005), 34–40

The authors report on a prospective cohort study of patients with chronic myelogenous leukemia undergoing allogeneic hematopoietic stem cell transplantation. The purpose was to evaluate the progression of quality of life and mood, as well as patterns of alcohol consumption, a behavior with potential adverse health consequences. Of the 84 subjects who completed serial measures and other interviews at admission for hematopoietic stem cell transplantation and 6-month follow-up, 75 provided data 12 months later. The main findings of this study were that quality of life improves, measures of depressive symptoms decline, and patients drink less alcohol overall. Time was the most important variable accounting for these changes.

Understanding the Will to Live in Patients Nearing Death

Chochinov, H.M., Hack, T., Hassard, T., Kristjanson, L.J., McClement, S., and Harlos, M.

Psychosomatics, *46* (2005), 7–10

This study examined concurrent influences on the will to live in 189 patients with end-stage cancer. The authors found significant correlations between the will to live and existential, psychological, social, and, to a lesser degree, physical sources of distress. Existential variables proved to have the most influence, with hopelessness, burden to others, and dignity entering into the final model. Health care providers must learn to appreciate the importance of existential issues and their ability to influence the will to live among patients nearing death.

Levels of Depressive Symptoms in Spouses of People with Lung Cancer: Effects of Personality, Social Support, and Caregiving Burden

Kim, Y., Duberstein, P.R., and Sörensen, S.

Psychosomatics, *46* (2005), 123–130

The authors sought to identify the personality correlates of depressive symptoms in 120 spouses of people with lung cancer. Spouses completed questionnaires, including measures of personality (neuroticism, extraversion, and interpersonal self-efficacy), social support, and caregiving burden. Their level of depressive symptoms was measured with self-report (Center for Epidemiologic Studies Depression Scale) and interviewer (Hamilton Depression Rating Scale) ratings. Structural equation modeling showed that neuroticism was directly associated with greater depressive symptoms and indirectly associated with less social support and greater caregiving burden. Interpersonal self-efficacy was indirectly associated with the severity of depressive symptoms through both social support and caregiving burden. These findings have implications for identifying spouses of individuals with lung cancer who are vulnerable to depression and could inform the design of programs to reduce depressive symptoms in the context of cancer caregiving.

Contracts, Covenants and Advance Care Planning: An Empirical Study of the Moral Obligations of Patient and Proxy

Fins, J.J., Maltby, B.S., Friedmann, E., Greene, M.G., Norris, K., Adelman, R., and Byock, I.

Journal of Pain and Symptom Management, *29* (2005), 55–68

Previously we had speculated that the patient–proxy relationship existed on a contractual to covenantal continuum. In order to assess this hypothesis, and to better understand the moral obligations of the patient–proxy relationship, we surveyed 50 patient–proxy pairs as well as 52 individuals who had acted as proxies for someone who

had died. Using structured vignettes representative of three distinct disease trajectories (cancer, acute stroke, and congestive heart failure), we assessed whether respondents believed that proxies should follow explicit instructions regarding life-sustaining therapy and act contractually or whether more discretionary or covenantal judgments were ethically permissible. Additional variables included the valence of initial patient instructions—for example, "to do nothing" or "to do everything"—as well as the quality of information available to the proxy. Responses were graded on a contractual to covenantal continuum using a modified Likert scale employing a prospectively scored survey instrument. Our data indicate that the patient–proxy relationship exists on a contractual to covenantal continuum and that variables such as disease trajectory, the clarity of prognosis, instructional valence, and the quality of patient instructions result in statistically significant differences in response. The use of interpretative or covenantal judgment was desired by patients and proxies when the prognosis was grim, even if initial instructions were to pursue more aggressive care. Nonetheless, there was a valence effect: Patients and proxies intended that negative instructions to be left alone be heeded. These data suggest that the delegation of patient self-determination is morally complex. Advance care planning should take into account both the exercise of autonomy and the interpretative burdens assumed by the proxy. Patients and proxies think inductively and contextually. Neither group viewed deviation from patient instructions as a violation of the principal's autonomy. Instead of adhering to narrow notions of patient self-determination, respondents made nuanced and contextually informed moral judgments. These findings have implications for patient education as well as the legal norms that guide advance care planning.

Transformative Aspects of Caregiving at Life's End

Salmon, J.R., Kwak, J., Acquaviva, K.D., Brandt, K., and Egan, K.A.

Journal of Pain and Symptom Management, *29* (2005), 121–129

We do not know to what extent the needs of caregivers involved with patients at the end of life are being met by care providers and whether caregiving at life's end can be a positive experience. We used the Hospice Experience Model of Care as a framework for understanding the effect of transformative tasks on caregiving at life's end. We compared current and bereaved caregivers and then, holding background characteristics constant, tested the independent effects of three transformative mediators: self-acceptance, meaning, and closure, as well as comfort with caregiving on several stressors when explaining differences in caregiver burden and gain. Transformative aspects of caregiving do not mediate the stressors associated with burden but do mediate one stressor associated with caregiver gain. Two mediators reduce caregiver burden and all four of the mediators improve caregiver gain. Caregivers who are able to attend to these transformative aspects find more gain in the caregiving experience.

Dealing with Conflict in Caring for the Seriously Ill: "It Was Just Out of the Question"

Back, A.L. and Arnold, R.M.

JAMA, *293* (2005), 1374–1381

Physicians often assume that conflict is undesirable and destructive, yet conflict handled well can be productive, and the clarity that results can lead to clearer decision making and greater family, patient, and clinician satisfaction. We review the course of Mrs. B, an 84-year-old woman with advanced dementia and an advance directive stating no artificial hydration or nutrition. Over the course of her illness, her family and physicians had conflicting opinions about the use of short-term tube feeding and intravenous hydration in her care. We describe the conflicts that arose between her physicians and family and a typology of conflicts common in care of patients who are seriously ill (family vs. team, team member vs. team member). Drawing from the business, psychology, and mediation literature, we describe useful communication tools and common pitfalls. We outline a step-wise approach that physicians can use to deal with conflicts and the use of treatment trials as a strategy to address conflicts about the use of life-sustaining medical interventions.

Communicating with Realism and Hope: Incurable Cancer Patients' Views on the Disclosure of Prognosis

Hagerty, R.G., Butow, P.N., Ellis, P.M., Lobb, E.A., Pendlebury, S.C., Leighl, N., Leod, C.M., and Tattersall, M.H.N.

Journal of Clinical Oncology, *23* (2005), 1278–1288

The purpose of this study was to identify preferences for the process of prognostic discussion among patients with incurable metastatic cancer and variables associated with those preferences. One hun-

dred twenty-six (58%) of 218 patients invited into the study participated. Eligible patients were the consecutive metastatic cancer patients of 30 oncologists, who were diagnosed within 6 weeks to 6 months before recruitment, over 18 years of age, and without known mental illness. Patients completed a postal survey measuring patient preferences for the manner of delivery of prognostic information, including how doctors might instill hope. Ninety-eight percent of patients wanted their doctor to be realistic, provide an opportunity to ask questions, and acknowledge them as an individual when discussing prognosis. Doctor behaviors rated the most hope giving included offering the most up-to-date treatment (90%), appearing to know all there is to know about the patient's cancer (87%), and saying that pain will be controlled (87%). The majority of patients indicated that the doctor appearing to be nervous or uncomfortable (91%), giving the prognosis to the family first (87%), or using euphemisms (82%) would not facilitate hope. Factor analysis revealed six general styles and three hope factors; the most strongly endorsed styles were realism and individualized care and the expert/positive/collaborative approach. A range of demographic, psychological, and disease factors were associated with preferred general and hope-giving styles, including anxiety, information-seeking behavior, expected survival, and age. The majority of patients preferred a realistic and individualized approach from the cancer specialist and detailed information when discussing prognosis.

Attitudes of Patients with Incurable Cancer toward Medical Treatment in the Last Phase of Life

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Journal of Clinical Oncology, *23* (2005), 2012–2019

When cancer has advanced to a stage in which cure becomes unlikely, patients may have to consider the aim of further treatment. We studied the relationship of patients' attitudes toward treatment with advance care planning and the development of these attitudes after diagnosis of incurable cancer. Patients with incurable cancer were interviewed and asked to fill out a written questionnaire about their attitudes concerning life-prolonging treatment and end-of-life decision making. These questions were repeated after 6 and 12 months. One hundred twenty-two patients (mean age, 64 years; standard deviation, 10.5 years; 53% women) participated in the study. Patients' attitudes toward treatment could be categorized into the following three different profiles: striving for quality of life, striving for length of life, and no clear preference. Patients who were older, more tired, or had less positive feelings and patients who had more often taken initiatives to engage in advance care planning were more inclined to strive for quality of life than others. Patients with a history of cancer of less than 6 months were more inclined to prefer life prolongation than patients with a longer history of cancer. During follow-up, no changes in attitudes toward treatment were found, except for patients with a short history of cancer in whom the inclination to strive for length decreased. Patients who appreciate advance care planning were more inclined to strive for quality of life than other patients. Shortly after the diagnosis of cancer, patients typically seem to prefer life-prolonging treatment, whereas quality of life becomes more important when death is nearing.

Long-Term Health-Related Quality of Life, Growth, and Spiritual Well-Being after Hematopoietic Stem-Cell Transplantation

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Our aim was to examine health-related quality of life (HRQOL) and growth, and spiritual well-being in adult survivors of hematopoietic stem-cell transplantation (HSCT) for a malignant disease. HSCT survivors (n = 662) were recruited through the International Bone Marrow Transplant Registry/Autologous Blood and Marrow Transplant Registry and were drawn from 40 transplantation centers. HSCT survivors completed a telephone interview and a set of questionnaires a mean of 7.0 years post-HSCT (range: 1.8–22.6 years). Study measures included a variety of standardized measures of HRQOL and growth and spiritual well-being. An age- and sex-matched healthy comparison (HC) group (n = 158) was recruited using a peer nomination method. The HC group completed a parallel telephone interview and set of questionnaires. Multivariate analyses of variance found the HSCT survivor group reported poorer status relative to the HC group for all HRQOL outcome clusters including physical health, physical functioning, social functioning, psychological adjustment, and dyadic adjustment. In contrast, the HSCT survivor group reported more psychological and interpersonal growth. Mean effect size for the 24 outcome indices examined was 0.36 standard deviations, an effect size often considered clinically meaningful or im-

portant. The largest group differences were found for measures of general health, physical function and well-being, depression, cognitive function, and fatigue. The experience of HSCT for a malignant disease has a wide-ranging, longstanding, and profound impact on adult recipients. Relative to healthy controls, HSCT survivors reported poorer physical, psychological, and social functioning but, conversely, more psychological and interpersonal growth, differences that appeared to persist many years after HSCT.

Service Preferences among Family Caregivers of the Terminally Ill

Brazil, K., Bedard, M., Krueger, P., Abernathy, T., Lohfeld, L., and Willison, K.

Journal of Palliative Medicine, 8 (2005), 69–78

The ability of families to assume caregiving responsibilities is contingent on material, social, and professional support. Inadequate or inappropriate support to the terminally ill and their family caregivers can result in the misuse of resources and add burden to the family. In this report, we describe service preferences among informal caregivers of the terminally ill. Three hundred seventy-three caregivers participated in telephone interviews at two points in time: when the terminally ill person was designated as palliative and 5 months subsequent to the first interview. In the case that the care recipient died during the study period, the caregiver participated in the interview 3 months after the death. After reviewing possible services received by the care recipients and caregivers, caregivers were asked to identify the five services they found most valuable and which services they would have liked to have had or received more of when caregiving. The five services caregivers reported as most valuable included in-home nursing care (90.7%), family physicians (45.6%), medical specialists (46.4%), housekeeping (23.6%), and religious support (11.3%). The five most frequently reported services that family caregivers would have liked to have received or had more available included housekeeping (13.1%), caregiver respite (10.2%), in-home nursing care (8.0%), personal support workers (4.6%), and self-help/support groups (3.8%). Analyses revealed that most (64.8%) perceived service needs were of a supportive nature for caregivers. Caregiver perceptions of the value and perceived need of services were consistent over time and into bereavement. Logistic regression analyses suggested that younger caregivers who were not employed, reported higher levels of burden, and cared for someone with a diagnosis of cancer had greater perceived service needs. The findings reported in this paper provide important insights into caregiver perceptions of valued services when caring for a terminally ill family member. These finding also highlight the stability of caregiver service perceptions over time and into bereavement.

The Long-Term Impact of Dialysis Discontinuation on Families

McCole Phillips, J., Brennan, M., Schwartz, C.E., and Cohen, L.M.

Journal of Palliative Medicine, *8* (2005), 79–85

Little is known about the long-term psychological impact of stopping life support treatments on surviving loved ones. The authors sought to determine if there was an increase in pathologic grief in family members left behind after deaths that followed dialysis discontinuation. Phone interviews were used to collect data on demographics, attitudes, and families' comfort levels with the decision to withdraw dialysis. The Impact of Event Scale was administered to assess adaptation and stress levels. Avoidance and Intrusiveness subscales were calculated and associations with other survey data were examined using χ^2 tests and analysis of variance (ANOVA). The authors contacted families in New England who had previously participated in the Baystate Dialysis Discontinuation Study. Twenty-six family members (66% of the original study sample) were interviewed approximately 55 months after patient deaths. There was a low overall level of distress and the Avoidance subscale had insufficient variability for analysis. Intrusiveness was highest for spouses and primary caregivers. Only one respondent remembered the death as having been "bad," although 62% of patients were recalled as having suffered distressing symptoms in their last days. In ascending order of importance, respondents characterized good deaths as involving mental alertness, occurring at home, taking place while asleep, being peaceful, happening in the company of loved ones, and being painless or largely pain free. Almost all of the families reported becoming more comfortable with the decision to hasten death than originally. After nearly 5 years after dialysis discontinuation, families report low levels of distress. A higher frequency of intrusive thoughts was more likely if respondents were spouses or primary caregivers as compared to adult children, siblings, or other relatives. The findings suggest that families successfully adapt to the impact of dialysis withdrawal deaths.

PSYCHOSOCIAL INTERVENTIONS

Brief Psychotherapy at the Bedside: Countering Demoralization from Medical Illness

Griffith, J.L. and Gaby, L.

Psychosomatics, *46* (2005), 109–116

Bedside psychotherapy with medically ill patients can help counter their demoralization, which is the despair, helplessness, and sense of isolation that many patients experience when affected by illness and its treatments. Demoralization can be usefully regarded as the compilation of different existential postures that position a patient to withdraw from the challenges of illness. A fruitful interviewing strategy is to discern which existential themes are of most concern, then to tailor questions and interventions to address those specific themes. Illustrative cases show how such focused interviewing can help patients cope assertively by mobilizing existential postures of resilience, such as hope, agency, and communion with others.

Psychoeducational Intervention for Patients with Cutaneous Malignant Melanoma: A Replication Study

Boesen, E.H., Ross, L., Frederiksen, K., Thomsen, B.L., Dahlstrøm, K., Schmidt, G., Næsted, J., Krag, C., and Johansen, C.

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In 1993, a randomized intervention study among patients with malignant melanoma showed a significant decrease in psychological distress and increased coping capacity 6 months after the intervention and enhanced survival 6 years later. We applied a similar intervention with a few modifications in a randomized controlled trial among Danish patients with malignant melanoma and evaluated results on immediate and long-term effects on psychological distress and coping capacity. A total of 262 patients with primary cutaneous malignant melanoma were randomly assigned to the control or intervention group. Patients in the intervention group were offered six weekly sessions of 2 hours of psychoeducation, consisting of health education, enhancement of problem-solving skills, stress management, and psychological support. The participants were assessed at baseline before random assignment and 6 and 12 months after surgery. The analyses of the main effects of the intervention were based on analyses of covariance. The patients in the intervention group showed significantly less fatigue, greater vigor, and lower total mood disturbance compared with the controls, and they used significantly more active-behavioral and active-cognitive coping than the patients in the control group. The improvements were only significant at first follow-up. The findings of this study support the results of an earlier intervention study among patients with malignant melanoma and indicate that a psychoeducational group intervention for such patients can decrease psychological distress and enhance effective coping. However, this effect is short term and the clinical relevance is not obvious.

Psychological Impact of Genetic Testing for Hereditary Nonpolyposis Colorectal Cancer

Gritz, E.R., Peterson, S.K., Vernon, S.W., Marani, S.K., and Baile, W.F., B.G. Watts, C.I. Amos, M.L. Frazier, and P.M. Lynch

Journal of Clinical Oncology, *23* (2005), 1902–1910

This study examines the impact of hereditary nonpolyposis colorectal cancer (HNPCC) genetic test results on psychological outcomes among cancer-affected and -unaffected participants up to 1 year after results disclosure. A total of 155 persons completed study measures before HNPCC genetic testing and at 2 weeks and 6 and 12 months after disclosure of test results. Mean scores on all outcome measures remained stable and within normal limits for cancer-affected participants, regardless of mutation status. Among unaffected carriers of HNPCC-predisposing mutations, mean depression, state anxiety, and cancer worries scores increased from baseline to 2 weeks postdisclosure and decreased from 2 weeks to 6 months postdisclosure. Among unaffected noncarriers, mean depression and anxiety scores did not differ, but cancer worries scores decreased during the same time period. Affected and unaffected carriers had higher mean test-specific distress scores at 2 weeks postdisclosure compared with noncarriers in their respective groups; scores decreased for affected carriers and all unaffected participants from 2 weeks to 12 months postdisclosure. Classification of participants into high- versus low-distress clusters using mean scores on baseline psychological measures predicted significantly higher or lower follow-up scores, respectively, on depression, state anxiety, quality of life, and test-specific distress measures, regardless of mutation status. Although HNPCC genetic testing does not result in long-term adverse psychological outcomes, unaffected mutation carriers may experience increased distress during the immediate postdisclosure time period. Furthermore, those with higher levels of baseline mood disturbance, lower quality of life, and lower social support may be at risk for both.

Effectiveness of Physical Activity on Cardiorespiratory Fitness and Health-Related Quality of Life in Young and Middle-Aged Cancer Patients Shortly after Chemotherapy

Thorsen, L., Skovlund, E., Strømme, S.B., Hornslien, K., Dahl, A.A., and Fosså, S.D.

Journal of Clinical Oncology, *23* (2005), 2378–2388

Our aim was to evaluate the effectiveness of a supervised home-based flexible training program on cardiorespiratory fitness (CRF), mental distress, and health-related quality of life (HRQOL) parameters in young and middle-aged cancer patients shortly after curative chemotherapy. One hundred eleven patients age 18 to 50 years who had received chemotherapy for lymphomas or breast, gynecologic, or testicular cancer completed the trial. These patients were randomly allocated to either an intervention group ($n = 59$), which underwent a 14-week training program, or a control group ($n = 52$) that received standard care. Primary outcome was change in CRF, as determined by Åstrand-Rhyming indirect bicycle ergometer test (maximum oxygen uptake [VO_{2max}]), between baseline (T0) and follow-up (T1). Secondary outcomes were mental distress, as assessed by the Hospital Anxiety and Depression Scale, and HRQOL, as assessed by the European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire. Two-way analysis of covariance was used to analyze changes from T0 to T1. VO_{2max} increased by 6.4 $ml/kg^{-1}/min^{-1}$ in patients in the intervention group and by 3.1 $ml/kg^{-1}/min^{-1}$ in patients in the control group ($p < 0.01$). The fatigue score decreased by 17.0 points in the control group compared with only 5.8 points in the intervention group ($p < 0.01$). There were no intergroup differences in mental distress or HRQOL. A supervised, home-based, flexible training program has significant effect on CRF in young and middle-aged cancer patients shortly after curative chemotherapy, but it has no favorable effect on patients' experience of fatigue, mental distress, or HRQOL.

Review of Exercise Intervention Studies in Cancer Patients

Galvão, D.A. and Newton, R.U.

Journal of Clinical Oncology, *23* (2005), 899–909

The purpose is to present an overview of exercise interventions in cancer patients during and after treatment and evaluate dose-training response considering type, frequency, volume, and intensity of training along with expected physiological outcomes. The review is divided into studies that incorporated cardiovascular training, combination of cardiovascular, resistance, and flexibility training, and resistance training alone during and after cancer management. Criteria for inclusion were based on studies sourced from electronic and nonelectronic databases and that incorporated preintervention and postintervention assessment with statistical analysis of data. Twenty-six published studies were summarized. The majority of the studies demonstrate physiological and psychological benefits. However, most of these studies suffer limitations because they are not randomized controlled trials and/or use small sample sizes. Predominantly, studies have been conducted with breast cancer patients using cardiovascular training rather than resistance exercise as the exercise modality. Recent evidence supports use of resistance exercise or "anabolic exercise" during cancer management as an exercise mode to counteract side effects of the disease and treatment. Evidence underlines the preliminary positive physiological and psychological benefits from exercise when undertaken during or after traditional cancer treatment. As such, other cancer groups, in addition to those with breast cancer, should also be included in clinical trials to address more specifically dose-response training for this population. Contemporary resistance training designs that provide strong anabolic effects for muscle and bone may have an impact on counteracting some of the side effects of cancer management, assisting patients to improve physical function and quality of life.

Dietary Counseling Improves Patient Outcomes: A Prospective, Randomized, Controlled Trial in Colorectal Cancer Patients Undergoing Radiotherapy

Ravasco, P., Monteiro-Grillo, I., Vidal, P.M., and Camilo, M.E.

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Our purpose was to investigate the impact of dietary counseling or nutritional supplements on outcomes in cancer patients: nutritional, morbidity, and quality of life (QoL) during and 3 months after radiotherapy. A total of 111 colorectal cancer outpatients referred for radiotherapy, stratified by staging, were randomly assigned: group 1 (G1; $n = 37$), dietary counseling (regular foods), group 2 (G2; $n = 37$), protein supplements; and group 3 (G3; $n = 37$), ad libitum intake. Nutritional intake (diet history), status (Ottery's Subjective Global Assessment), and QoL (European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire ver-

sion 3.0) were evaluated at baseline, at the end, and 3 months after radiotherapy. At radiotherapy completion, energy intake increased in G1/G2 ($p \leq 0.04$), G1 more than G2 ($p = 0.001$), and decreased in G3 ($p < 0.01$). Protein intake increased in G1/G2 ($p \leq 0.007$), G1 less than G2 (not significant), and decreased in G3 ($p < 0.01$). At 3 months, G1 maintained nutritional intake and G2/G3 returned to baseline. After radiotherapy and at 3 months, rates of anorexia, nausea, vomiting, and diarrhea were higher in G3 ($p < 0.05$). At radiotherapy completion, in G1 all QoL function scores improved proportionally to adequate intake or nutritional status ($p < 0.05$), whereas in G2 only three of six function scores improved proportionally to protein intake ($p = 0.04$), and in G3 all scores worsened ($p < 0.05$). At 3 months, G1 patients maintained/improved function, symptoms, and single-item scores ($p < 0.02$); in G2, only a few function and symptom scales improved ($p < 0.05$); in G3, QoL remained as poor as after radiotherapy. In G1/G2, respectively, improvement/deterioration of QoL correlated with better or poorer intake or nutritional status ($p < 0.003$). During radiotherapy, both interventions positively influenced outcomes; dietary counseling was of similar or higher benefit, whereas even 3 months after RT, it was the only method to sustain a significant impact on patient outcomes.

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