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Clinical Update: Literature Abstracts

MEASURES

Developing a cancer-specific geriatric assessment: A feasibility study

Hurria, A., Gupta, S., Zauderer, M., Zuckerman, E.L., Cohen, H.J., Muss, H., Rodin, M., Panageas, K.S., Holland, J.C., Saltz, L., Kris, M.G., Noy, A., Gomez, J., Jakubowski, A., Hudis, C., and Kornblith, A.B.

Cancer, *9* (2005), 1998–2005

As the U.S. population ages, there is an emerging need to characterize the "functional age" of older patients with cancer to tailor treatment decisions and stratify outcomes based on factors other than chronologic age. The goals of the current study were to develop a brief, but comprehensive, primarily self-administered cancer-specific geriatric assessment measure and to determine its feasibility as measured by (1) the percentage of patients able to complete the measure on their own, (2) the length of time to complete, and (3) patient satisfaction with the measure. The geriatric and oncology literature was reviewed to choose validated measures of geriatric assessment across the following domains: functional status, comorbidity, cognition, psychological status, social functioning and support, and nutritional status. Criteria applied to geriatric assessment measurements included reliability, validity, brevity, and ability to self-administer. The measure was administered to patients with breast carcinoma, lung carcinoma, colorectal carcinoma, or lymphoma who were fluent in English and receiving chemotherapy at Memorial Sloan-Kettering Cancer Center (New York, NY) or the University of Chicago (Chicago, IL). The instrument was completed by 43 patients (mean age, 74 years; range, 65–87 years). The majority had AJCC Stage IV disease (68%). The mean time to completion of the assessment was 27 min (range, 8–45 min). Most patients were able to complete the self-administered portion of the assessment without assistance (78%) and were satisfied with the questionnaire length (90%). There was no association noted between age ($p = 0.56$) or educational level ($p = 0.99$) and the ability to complete the assessment without assistance. In this cohort, this brief but comprehensive geriatric assessment could be completed by the majority of patients without assistance. Prospective trials of its generalizability, reliability, and validity are justified. © 2005 American Cancer Society.

Validation of Toolkit After-Death Bereaved Family Member Interview

Teno, J.M., Clarridge, B., Casey, V., Edgman-Levitan, S., and Fowler, J.

Journal of Pain and Symptom Management, *22* (2001), 752–758

The purpose of this study was to examine the reliability and validity of the Toolkit After-Death Bereaved Family Member Interview to measure quality of care at the end of life from the unique perspective of family members. The survey included proposed problem scores (a count of the opportunity to improve the quality of care) and scales. Data were collected through a retrospective telephone survey with a family member who was interviewed between 3 and 6 months after the death of the patient. The setting was an outpatient hospice service, a consortium of nursing homes, and a hospital in New England. One hundred fifty-six family members from across these settings participated. The eight proposed domains of care, as represented by problem scores or scales, were based on a conceptual model of patient-focused, family-centered medical care. The survey design emphasized face validity in order to provide actionable information to health care providers. A correlational and factor analysis

was undertaken of the eight proposed problem scores or scales. Cronbach's alpha scores varied from 0.58 to 0.87, with two problem scores (each of which had only three survey items) having a low alpha of 0.58. The mean item-to-total correlations for the other problem scores varied from 0.36 to 0.69, and the mean item-to-item correlations were between 0.32 and 0.70. The proposed problem scores or scales, with the exception of closure and advance care planning, demonstrated a moderate correlation (i.e., from 0.44 to 0.52) with the overall rating of satisfaction (as measured by a five-point, *excellent* to *poor* scale). Family members of persons who died with hospice service reported fewer problems in each of the six domains of medical care, gave a higher rating of the quality of care, and reported higher self-efficacy in caring for their loved ones. These results indicate that seven of the eight proposed problem scores or scales demonstrated psychometric properties that warrant further testing. The domain of closure demonstrated a poor correlation with overall satisfaction and requires further work. This survey could provide information to help guide quality improvement efforts to enhance the care of the dying.

An Item Response Theory-Based Pain Item Bank Can Enhance Measurement Precision

Lai, J.S., Dineen, K., Reeve, B.B., Von Roenn, J., Shervin, D., McGuire, M., Bode, R.K., Paice, J., and Cella, D.

Journal of Pain and Symptom Management, *30* (2005), 278–288

Cancer-related pain is often underrecognized and undertreated. This is partly due to the lack of appropriate assessments, which need to be comprehensive and precise yet easily integrated into clinics. Computerized adaptive testing (CAT) can enable precise, yet brief, assessments by only selecting the most informative items from a calibrated item bank. The purpose of this study was to create such a bank. The sample included 400 cancer patients who were asked to complete 61 pain-related items. Data were analyzed using factor analysis and the Rasch model. The final bank consisted of 43 items that satisfied the measurement requirement of factor analysis and the Rasch model, demonstrated high internal consistency and reasonable item-total correlations, and discriminated patients with differing degrees of pain. We conclude that this bank demonstrates good psychometric properties, is sensitive to pain reported by patients, and can be used as the foundation for a CAT pain-testing platform for use in clinical practice.

Patient Autonomy Problems in Palliative Care: Systematic Development and Evaluation of a Questionnaire

Vernooij-Dassen, M.J., Osse, B.H., Schade, E., and Grol, R.P.

Journal of Pain and Symptom Management, *30* (2005), 264–270

No instrument to assess autonomy problems in palliative care is currently available. The purpose of this study was to develop a comprehensive and concise questionnaire to measure autonomy problems in palliative cancer patients and to study its validity and reliability. We systematically developed a questionnaire through (a) a literature review of the concepts and elements of autonomy, (b) qualitative analysis of interviews with patients and professional carers, (c) the construction of questionnaires, and (d) testing validity and reliability. The basic conceptual elements were dependency, losing control, and limitation of activities. Patients with disseminated cancer in the palliative stage of the disease ($n = 64$) participated in the study. A 9-item Patient Autonomy Questionnaire (PAQ) was developed (Cronbach's alpha 0.86), followed by a concise 4-item version (PAQs) (Cronbach's alpha 0.71). Autonomy problems were more prevalent than pain problems. The development of the PAQ may help draw attention to autonomy problems.

Assessment of Beliefs about Psychotropic Medication and Psychotherapy: Development of a Measure for Patients with Anxiety Disorders

Bystritsky, A., Wagner, A.W., Russo, J.E., Stein, M.B., Sherbourne, C.D., Craske, M.G., and Roy-Byrne, P.P.

General Hospital Psychiatry, *5* (2005), 313–318

This study presents the psychometric properties of a brief measure to assess beliefs about psychotropic medications and psychotherapy among patients with anxiety disorders. Data were collected on a large sample of primary care patients with a range of anxiety disorders, as part of the Collaborative Care for Anxiety and Panic study. Factor analyses using principal axis factoring with Varimax rotations were used to determine the factor structure of the beliefs scale. Internal consistency, concurrent validity, and predictive validity of the resulting subscales were examined. Two subscales emerged, one reflecting beliefs about psychotropic medications and the other assessing beliefs about psychotherapy. Both showed strong internal consistency and concurrent validity. The beliefs about psychotropic medication demon-

strated strong predictive validity. This measure may be a useful tool for assessing treatment beliefs among patients with anxiety disorders toward the provision of more quality treatment for this population. Its brevity may make it particularly useful in primary health care settings

SYMPTOM CONTROL

Topical Amitriptyline and Ketamine in Neuropathic Pain Syndromes: An Open-Label Study

Lynch, M.E., Clark, A.J., Sawynok, J., and Sullivan, M.J.

Journal of Pain, *10* (2005), 644–649

Twenty-eight subjects with refractory, moderate to severe peripheral neuropathic pain participated in an open label prospective trial examining perceived analgesic effect, patient satisfaction, and safety of topical amitriptyline 2%/ketamine 1% cream. Outcome measures included an 11-point numerical rating scale for pain intensity (NRS-PI), a 5-point satisfaction scale, blood chemistry screen, drug and metabolite levels, urinalyses, electrocardiogram (ECG), and physical examination. Adverse events were monitored. Twenty-one subjects completed the trial. At 6 months, subjects reported an average long-term reduction in pain of 34% (standard deviation [*SD*] = 37%); 5 subjects (25%) achieved 50% or greater reduction in pain and 1 subject (5%) achieved 100% reduction in pain. At 12 months, the average reduction in pain was 37% (*SD* = 40%); 7 subjects (40%) achieved 50% or greater pain reduction. At the end of the study, 89% of subjects rated their satisfaction as 3/5 or greater and 2 subjects (10%) were pain free. Minimal adverse events were reported and there were no serious medication-related adverse events. Blood levels revealed minimal systemic absorption. In conclusion, topical 2% amitriptyline/1% ketamine cream was associated with long-term reduction (6–12 months) in perceived pain, moderate to complete satisfaction, and was well tolerated in treatment of neuropathic pain. There was no significant systemic absorption of amitriptyline or ketamine. This study demonstrates that topical 2% amitriptyline/1% ketamine, given over 6–12 months, is associated with long-term perceived analgesic effectiveness in treatment of neuropathic pain. Antidepressants and ketamine both produce multiple pharmacologic effects that may contribute to peripheral analgesia; such actions include blockage of peripheral N-methyl-D-aspartate receptors, local anesthetic properties, and interactions with adenosine systems.

Rapid Switching between Transdermal Fentanyl and Methadone in Cancer Patients

Mercadante, S., Ferrera, P., Villari, P., and Casuccio, A.

Journal of Clinical Oncology, *23* (2005), 5229–5234

The aim of this study was to examine the clinical effects of switching from transdermal (TTS) fentanyl to methadone, or vice versa, in patients with a poor response to the previous opioid. A prospective study was carried out on 31 patients who switched from TTS fentanyl to oral methadone, or vice versa, because of poor opioid response. A fixed conversion ratio of fentanyl to methadone of 1:20 was started and assisted by rescue doses of opioids, and then doses were changed according to clinical response. Pain and symptom intensity, expressed as distress score, were recorded before switching doses of the two opioids and after subsequent doses. The number of changes of the daily doses, time to achieve stabilization, and hospital stay were also recorded. Eighteen patients were switched from TTS fentanyl to methadone, and seven patients were switched from methadone to TTS fentanyl. A significant decrease in pain and symptom intensity, expressed as symptom distress score, was found within 24 h after switching took place in both directions. Unsuccessful switching occurred in six patients, who were subsequently treated with an alternative therapy. A rapid switching using an initial fixed ratio of fentanyl to methadone of 1:20 is an effective method to improve the balance between analgesia and adverse effects in cancer patients with poor response to the previous opioid. No relationship between the final opioid dose and the dose of the previous opioid has been found.

Trends in Abuse of Oxycontin and Other Opioid Analgesics in the United States: 2002%–2004

Cicero, T.J., Inciardi, J.A., and Munoz, A.

Journal of Pain, *6* (2005), 662–672

OxyContin (Purdue Pharma L.P., Stamford, Conn) was approved by the Food and Drug Administration (FDA) in 1995 as a sustained-release preparation of oxycodone hydrochloride and was thought to have much lower abuse potential than immediate-release oxycodone because of its slow-release properties. However, beginning in 2000, widespread reports of OxyContin abuse surfaced. In response, Purdue Pharma L.P. sponsored the development of a proactive abuse surveillance program, named the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS) system. In this paper,

we describe results obtained from one aspect of RADARS—the use of drug abuse experts (i.e., key informants)—as a source of data on the prevalence and magnitude of abuse of prescription drugs. The results indicate that prescription drug abuse has become prevalent, with cases reported in 60% of the zip codes surveyed. The prevalence of abuse was rank ordered as follows: OxyContin ≥ hydrocodone > other oxycodone > methadone > morphine > hydromorphone > fentanyl > buprenorphine. In terms of the magnitude of abuse (≥5 cases/100,000 persons in a 3-digit zip code), modest growth was seen with all analgesics over the 10 calendar quarters we monitored, but was most pronounced with OxyContin and hydrocodone. These results indicate that OxyContin abuse is a pervasive problem in this country, but that it needs to be considered in the context of a general pattern of increasing prescription drug abuse. Over the past 5 years, there have been reports, frequently anecdotal, that opioid analgesic abuse has evolved into a national epidemic. In this study, we report systematic data to indicate that opioid analgesic abuse has in fact increased among street and recreational drug users, with OxyContin and hydrocodone products the most frequently abused. Steps need to be taken to reduce prescription drug abuse, but very great care needs to be exercised in the nature of these actions so the legitimate and appropriate use of these drugs in the treatment of pain is not compromised as a result.

Frequency, Severity, Clinical Course, and Correlates of Fatigue in 372 Patients during 5 Weeks of Radiotherapy for Cancer

Hickok, J.T., Roscoe, J.A., Morrow, G.R., Mustian, K., Okunieff, P., and Bole, C.W.

Cancer, *15* (2005), 1772–1778

Patients often describe fatigue as the most distressing of the symptoms they experienced during their cancer treatment. Fatigue may increase from initial levels experienced during cancer treatment with the addition of radiotherapy (RT). Three hundred seventy-two patients completed a Symptom Inventory at the initiation of RT and weekly for 4 weeks thereafter. Descriptive statistics were used to evaluate differences in fatigue at baseline by demographics and diagnosis. Changes over the course of treatment were evaluated by repeated-measures analysis of variance and Student *t* tests for paired data. The effect of diagnosis, age, gender, and previous treatment on fatigue was investigated by linear and hierarchical regression. Fifty-seven percent of patients reported some degree of fatigue at the initiation of RT. The proportion increased to 76% by week 3 and then to 78% at week 5. Eighty-four percent of patients with initial fatigue remained fatigued throughout the 5-week course. Of the 160 patients without initial fatigue, 70% subsequently developed it. By week 5, only 13% of patients had never reported any fatigue. Severity was found to be related to diagnosis, with patients with prostate carcinoma reporting the least severe fatigue and patients with lung, alimentary, and head and neck carcinoma reporting the most severe fatigue. Neither gender, age, nor total dose of RT predicted significant variance in severity. Fatigue was a common adverse effect of RT for cancer, reported by more than three-fourths of patients by the third to fifth weeks of treatment. Cancer diagnosis was the only factor found to be significantly related to variation in fatigue severity. Additional studies should be devised to identify other underlying causes of RT-related fatigue.

Epidemiology of Cancer-Related Fatigue in the Swedish Twin Registry

Forlenza, M.J., Hall, P., Lichtenstein, P., Evengard, B., and Sullivan, P.F.

Cancer, *104* (2005), 2022–2031

Estimates of the prevalence of cancer-related fatigue (CRF) are wide, and data suggest that fatigue is more prevalent among cancer patients than among the general population. However, most studies examining the prevalence of CRF have been hospital-based or clinic-based studies, which often are subject to bias. Point prevalence and prevalence odds ratios of fatigue were estimated using data from a large, population-based cohort that was screened for fatigue and linked with national registry-based data about cancer. Prevalence odds ratios and 95% confidence intervals were calculated using logistic regression with general estimating equations. Approximately 23% of cancer registrants reported abnormal fatigue in the previous 6 months, 19% reported abnormal fatigue that lasted for at least 1 month, 14% reported abnormal fatigue that lasted at least 6 months, and 11% reported abnormal fatigue that lasted at least 6 months and caused significant functional impairment. Individuals who were listed in the cancer registry within the last 5 years were more likely to report experiencing fatigue than individuals who were not listed. There was an elevated prevalence of fatigue among those who were registered with carcinomas of the lung,

uterine cervix, colon-rectum, ovaries, and prostate. Both women and men who were listed recently in the cancer registry were more likely to experience any level of fatigue than the comparison group. However, a greater proportion of women experienced fatigue relative to men. A greater proportion of individuals who were listed in a national cancer registry reported experiencing fatigue compared with individuals in the general population.

Symptoms in Patients with Lung Carcinoma: Distinguishing Distress from Intensity

Tishelman, C., Degner, L.F., Rudman, A., Bertilsson, K., Bond, R., Broberger, E., Doukkali, E., and Levealahti, H.

Cancer, *104* (2005), 2013–2021

The patient perspective on distress associated with lung carcinoma is important, yet understudied. Previous research on symptom experience generally had not differentiated the dimension symptom intensity/frequency from which symptoms are associated with most distress. The objective of the current study was to determine whether patterns of symptom intensity were similar to patterns of symptom distress, whether patterns were consistent at different time points, whether patterns varied by subgroups, and whether high symptom intensity was equivalent to distress. Four hundred adults who were newly diagnosed with inoperable lung carcinoma completed a measure of symptom intensity/frequency and a new measure of distress associated with symptoms at six time points during the first year after diagnosis. These data were supplemented by field notes by research nurses and by less structured, qualitative interviews. The mean ranking of distress in the total group and in all subgroups remained constant at all time points, with breathing, pain, and fatigue associated with the most distress. In contrast, the pattern of mean rank order of symptom intensity showed little consistency; however, fatigue had the highest intensity scores at all time points. The current data challenged the uncritical use of summated scores of different symptom items in the context of lung carcinoma. Breathing and pain appeared to function as icons representing threats associated with lung carcinoma, with distress described as related to the past and the present and to expectations for the future. One of the most promising implications of these data was in fostering a preventive paradigm for symptom palliation.

Assessment of Quality of Life in the Supportive Care Setting of the Big Lung Trial in Non-Small-Cell Lung Cancer

Brown, J., Thorpe, H., Napp, V., Fairlamb, D.J., Gower, N.H., Milroy, R., Parmar, M.K., Rudd, R.M., Spiro, S.G., Stephens, R.J., Waller, D., West, P., and Peake, M.D.

Journal of Clinical Oncology, *23* (2005), 7417–7427

The Big Lung Trial (BLT) was a large, pragmatic trial to evaluate the addition of chemotherapy to primary treatment (i.e., surgery, radical radiotherapy, or supportive care) in non-small-cell lung cancer (NSCLC). In the supportive care group, there was a small but significant survival benefit in patients treated with chemotherapy compared with supportive care alone (no chemotherapy). A substudy was undertaken to evaluate the quality of life (QoL) implications of the treatment options. QoL was assessed using European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaires C30 (QLQ-C30) and LC17 and daily diary cards. EORTC QLQ-C30 and LC17 were collected at 0, 6–8, 12, 18, and 24 weeks. Diary cards were completed during the first 12 weeks of the study. The primary end point was global QoL at 12 weeks. A total of 273 patients were randomly assigned, 138 to no chemotherapy and 135 to chemotherapy. There was no evidence of a large detrimental effect on QoL of chemotherapy. No statistically significant differences in global QoL or physical/emotional functioning, fatigue and dyspnea, and pain were detected at 12 weeks. Higher rates of palliative radiotherapy in the no chemotherapy arm may have lessened differences in QoL. Global QoL, role functioning, fatigue, appetite loss, and constipation were prognostic indicators of survival at 12 weeks. There were no important adverse effects of chemotherapy on QoL.

Quality of Life and Sexual Functioning in Cervical Cancer Survivors

Frumovitz, M., Sun, C.C., Schover, L.R., Munsell, M.F., Jhingran, A., Wharton, J.T., Eifel, P., Bevers, T.B., Levenback, C.F., Gershenson, D.M., and Bodurka, D.C.

Journal of Clinical Oncology, *23* (2005), 7428–7436

The objective was to compare quality of life and sexual functioning in cervical cancer survivors treated with either radical hysterectomy and lymph node dissection or radiotherapy. Women were in-

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terviewed at least 5 years after initial treatment for cervical cancer. Eligible women had squamous cell tumors smaller than 6 cm at diagnosis, were currently disease free, and had either undergone surgery or radiotherapy, but not both. The two treatment groups were then compared using univariate analysis and multivariate linear regression with a control group of age- and race-matched women with no history of cancer. One hundred fourteen patients (37 surgery, 37 radiotherapy, 40 controls) were included for analysis. When compared with surgery patients and controls using univariate analysis, radiation patients had significantly poorer scores on standardized questionnaires measuring health-related quality of life (physical and mental health), psychosocial distress, and sexual functioning. The disparity in sexual function remained significant in a multivariate analysis. Univariate and multivariate analyses did not show significant differences between radical hysterectomy patients and controls on any of the outcome measures. Cervical cancer survivors treated with radiotherapy had worse sexual functioning than did those treated with radical hysterectomy and lymph node dissection. In contrast, these data suggest that cervical cancer survivors treated with surgery alone can expect overall quality of life and sexual function not unlike that of peers without a history of cancer.

Paroxetine is an Effective Treatment for Hot Flashes: Results from a Prospective Randomized Clinical Trial

Stearns, V., Slack, R., Greep, N., Henry-Tilman, R., Osborne, M., Bunnell, C., Ullmer, L., Gallagher, A., Cullen, J., Gehan, E., Hayes, D.F., and Isaacs, C.

Journal of Clinical Oncology, *23* (2005), 6919–6930

In an open-label trial we have previously demonstrated that paroxetine reduces hot flashes. We initiated a stratified, randomized, double-blind, cross-over, placebo-controlled trial to investigate the efficacy of paroxetine 10 mg and 20 mg compared to placebo in reducing hot flash frequency and composite score. A secondary objective was to evaluate quality of life (QOL) parameters. Women who suffered at least two hot flashes a day for 1 month or longer were eligible. Women were randomly assigned to 4 weeks of paroxetine 10 mg or 20 mg followed by placebo for 4 weeks, or placebo for 4 weeks followed by paroxetine 10 mg or 20 mg for 4 weeks. Participants completed baseline daily hot flash diaries for 1 week prior to the start of the study and throughout the study, and QOL questionnaires at baseline, week 5 and week 9. Two hundred seventy-nine women were screened, and 151 were randomly assigned. Paroxetine 10 mg reduced hot flash frequency and composite score by 40.6% and 45.6%, respectively, compared to 13.7% and 13.7% for placebo ($p = 0.0006$ and $p = 0.0008$, respectively). Paroxetine 20 mg reduced hot flash frequency and composite score by 51.7% and 56.1%, respectively, compared with 26.6% and 28.8% for placebo ($p = 0.002$ and $p = 0.004$, respectively). Efficacy was similar between the two doses, but women were less likely to discontinue low-dose paroxetine. Paroxetine 10 mg was associated with a significant improvement in sleep compared with placebo ($p = 0.01$). Paroxetine is an effective treatment for hot flashes in women with or without a prior breast cancer.

Pilot Evaluation of Citalopram for the Treatment of Hot Flashes in Women with Inadequate Benefit from Venlafaxine

Loprinzi, C.L., Flynn, P.J., Carpenter, L.A., Atherton, P., Barton, D.L., Shanafelt, T.D., Rummans, T.A., Sloan, J.A., Adjei, A.A., Mincey, B.A., Fitch, T.R., and Collins, M.

Journal of Palliative Medicine, *8* (2005), 924–930

Although newer antidepressants, such as venlafaxine and paroxetine, substantially decrease hot flashes, there is no published information with regards to whether a different antidepressant will be effective when one antidepressant does not adequately relieve hot flashes. The objective of this trial was to provide pilot information with regards to whether citalopram would effectively reduce hot flashes in patients who did not receive adequate enough hot flash reduction with venlafaxine. This was a prospective pilot trial. Validated patient-completed hot flash diary questionnaires were utilized for measuring hot flashes. Thirty patients were recruited to this trial, 22 of whom were fully evaluable. Compared to a baseline week, hot flash scores were reduced by 53% 4 weeks later. The citalopram appeared to be well tolerated with many quality-of-life and potential toxicity symptoms much improved compared to the baseline week. At the end of the 4-week treatment, 19 patients (63% of patients entering the study and 86% of the patient completing the study treatment) chose to continue to use citalopram. This pilot information supports the hypothesis that citalopram will reduce hot flashes in patients with inadequate hot flash relief while taking venlafaxine.

PSYCHOSOCIAL ISSUES IN PALLIATIVE CARE

How Well Are We Caring for Caregivers? Prevalence of Grief-Related Symptoms and Need for Bereavement Support among Long-Term Care Staff

Rickerson, E.M., Somers, C., Allen, C.M., Lewis, B., Strumpf, N., and Casarett, D.J.

Journal of Pain and Symptom Management, *30* (2005), 227–233

To define the prevalence and correlates of grief-related symptoms among long-term care staff who care for patients near the end of life, a cross-sectional survey was conducted at six Program of All-inclusive Care for the Elderly (PACE) organizations that provide long-term care in the home and in institutions. All clinical and nonclinical program staff were surveyed to examine the prevalence of 20 grief-related symptoms and assess current sources of bereavement support, as well as willingness to use additional sources of support. Surveys were completed by 203/236 staff (86%), who described a wide variety of symptoms they attributed to the death of one of their patients in the past month. Most staff (147/203; 72%) reported at least one symptom. Staff with more symptoms had experienced more patient deaths in the past month (Spearman rho = 0.20, $p = 0.007$), had worked for a longer time at a PACE organization (Spearman rho = 0.16, $p = 0.031$), and reported a closer and longer relationship with the last patient who died (Spearman rho = 0.32, $p < 0.001$; rho = 0.24, $p = 0.001$). Although staff identified several informal sources of bereavement support (mean 2.3 sources, range 0–6), almost all ($n = 194$; 96%) said they would use additional support services if they were offered. These community-based long-term care staff experience a variety of symptoms attributable to the deaths of their patients, and would welcome additional sources of bereavement support.

Care-Related Distress: A Nationwide Study of Parents Who Lost Their Child to Cancer

Kreicbergs, U., Valdimarsdottir, U., Onelov, E., Bjork, O., Steineck, G., and Henter, J.I.

Journal of Clinical Oncology, *23* (2005), 9162–9171

Palliative care is an important part of cancer treatment. However, little is known about how care-related factors affect bereaved intimates in a long-term perspective. We conducted a population-based, nationwide study addressing this issue, focusing on potential care-related stressors in parents losing a child to cancer. In 2001, we attempted to contact all parents in Sweden who had lost a child to cancer in 1992 to 1997. The parents were asked, through an anonymous postal questionnaire, about their experience of the care given and to what extent these experiences still affect them today. Information was supplied by 449 (80%) of 561 eligible parents. Among 196 parents of children whose pain could not be relieved, 111 (57%) were still affected by it 4 to 9 years after bereavement. Among 138 parents reporting that the child had a difficult moment of death, 78 (57%) were still affected by it at follow-up. The probability of parents reporting that their child had a difficult moment of death was increased (relative risk = 1.4; 95% CI, 1.0–1.8) if staff were not present at the moment of death. Ten percent of the parents (25 of 251 parents) were not satisfied with the care given during the last month at a pediatric hematology/oncology center; the corresponding figure for care at other hospitals was 20% (33 of 168 parents; $p = 0.0163$). Physical pain and the moment of death are two important issues to address in end-of-life care of children with cancer in trying to reduce long-term distress in bereaved parents.

Posttraumatic Stress Symptoms during Treatment in Parents of Children with Cancer

Kazak, A.E., Boeving, C.A., Alderfer, M.A., Hwang, W.T., and Reilly, A.

Journal of Clinical Oncology, *23* (2005), 7405–7410

The conceptualization of childhood cancer and its treatment as traumatic has gained increasing support in the growing literature on medically related posttraumatic stress. Posttraumatic stress symptoms (PTSS) such as intrusive thoughts, physiologic arousal, and avoidance have been documented in mothers and fathers of childhood cancer survivors. In this study we investigated the presence of PTSS in parents of children currently in treatment and their association with treatment intensity and length of time since diagnosis. Mothers ($N = 119$) and fathers ($N = 52$) of children currently in treatment for a childhood malignancy completed questionnaire measures of PTSS. Outcomes on these measures were compared with a sample of parents of childhood cancer survivors from our hospital. Oncologist ratings of treatment intensity were obtained based on diagnosis, treatment modalities, and protocol number. All but 1 parent reported PTSS. Mean scores indicated moderate PTSS for both mothers and fathers. In families with two participating parents, nearly 80% had at least 1 parent with moderate to severe PTSS. There were minimal associations between PTSS and length of

time since diagnosis. PTSS are common among parents of children currently undergoing cancer treatment. Trauma-informed psychosocial interventions can be used to help patients and families, including normalizing the experience as potentially traumatic and using evidence-based interventions that are emerging to facilitate long-term well-being.

Cancer Caregiving and Subjective Stress: A Multi-Site, Multi-Dimensional Analysis

Gaugler, J.E., Hanna, N., Linder, J, Given, C.W., Tolbert, V., Kataria, R., and Regine, W.F.

Psychooncology, *14* (2005), 771–785

Although research has emerged documenting the psychosocial impact of family care for cancer patients, few efforts capture the multi-dimensional nature of cancer caregiving stress, particularly among socioeconomically diverse samples. Utilizing data collected from cancer caregivers at a nonurban, Southern U.S. site and an inner-city, Northeastern U.S. site (N = 233), the present study identified predictors of multiple dimensions of caregivers' subjective stress (i.e., emotional appraisals of care demands). Various indicators representing the sociodemographic context of care, cancer care demands, and psychosocial resources were found to exacerbate or buffer caregivers from feelings of exhaustion, role entrapment, and loss of intimacy with the cancer patient. The multivariate regression model also emphasized the diffuse yet potent role care recipient mood problems and caregiver mastery/optimism have on multiple dimensions of subjective stress. The findings offer a number of recommendations for future research and practice focused on informal cancer care.

Psychiatric Disorders and Mental Health Service Use among Caregivers of Advanced Cancer Patients

Vanderwerker, L.C., Laff, R.E., Kadan-Lottick, N.S., McColl, S., and Prigerson, H.G.

Journal of Clinical Oncology, *23* (2005), 6899–6907

Despite research demonstrating the psychological burden of caregiving for advanced cancer patients, limited information exists on the prevalence of psychiatric disorders and mental health service use among these informal caregivers. Two hundred informal caregivers of advanced cancer patients were interviewed and administered the Structured Clinical Interview of the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition, and an assessment of mental health service use. Thirteen percent of caregivers met criteria for a psychiatric disorder; 25% accessed treatment for mental health concerns since the patient's cancer diagnosis. The frequencies of current psychiatric disorders were as follows: panic disorder, 8.0% (95% CI, 4.6%–12.7%), major depressive disorder, 4.5% (95% CI, 2.1%–8.4%), posttraumatic stress disorder, 4.0% (95% CI, 1.7%–7.7%), and generalized anxiety disorder, 3.5% (95% CI, 1.4%–7.1%). Among caregivers with a current psychiatric disorder, 81% discussed mental health concerns with a health professional before the patient's cancer diagnosis compared with 46% after the diagnosis (McNemar test = 5.40; p = 0.02). Only 46% of caregivers with a current psychiatric disorder accessed mental health services. Caregivers who discussed mental health concerns with a clinician before the patient's cancer diagnosis (odds ratio [OR] = 3.51; 95% CI, 1.42–8.71) and after the diagnosis (OR = 21.23; 95% CI, 9.02–49.94) were more likely than caregivers not having these discussions to receive mental health services. Many caregivers of advanced cancer patients either meet criteria or are being treated for psychiatric problems. Discussing mental health issues positively influences the receipt of mental health services and should be actively pursued in this vulnerable population.

Euthanasia and Depression: A Prospective Cohort Study among Terminally Ill Cancer Patients

van der Lee, M.L., van der Bom, J.G., Swarte, N.B., Heintz, A.P., de Graeff, A., and van den Bout, J.

Journal of Clinical Oncology, *20* (2005), 6607–6612

The objective was to study the association between depression and the incidence of explicit requests for euthanasia in terminally ill cancer patients. A prospective cohort study was conducted on 138 consecutive cancer patients with an estimated life expectancy of 3 months or less, in the period between September 1999 and August 2003. At inclusion, participants completed the Hospital Anxiety and Depression Scale. To identify "depressed mood" we used a cutoff score of 20. Kaplan–Meier curves and Cox regression analyses were used to assess the association between depressed mood and the risk of a request for euthanasia. Of 138 patients, 32 patients had depressed mood at inclusion. Thirty patients (22%) made an explicit request for euthanasia. The risk to request euthanasia for patients with depressed mood was 4.1 times higher than that of patients without depressed mood at inclusion (95% CI, 2.0–8.5). Depression in cancer pa-

tients with an estimated life expectancy of less than 3 months is associated with a higher likelihood of a request for euthanasia. The question of whether depressed mood can adequately be treated in this terminally ill population, and if so, whether it would lower the incidence of requests for euthanasia needs further investigation.

Risk of Death with Atypical Antipsychotic Drug Treatment for Dementia: Meta-Analysis of Randomized Placebo-Controlled Trials

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Atypical antipsychotic medications are widely used to treat delusions, aggression, and agitation in people with Alzheimer disease and other dementia; however, concerns have arisen about the increased risk for cerebrovascular adverse events, rapid cognitive decline, and mortality with their use. The objective was to assess the evidence for increased mortality from atypical antipsychotic drug treatment for people with dementia. Data sources were MEDLINE (1966 to April 2005), the Cochrane Controlled Trials Register (2005, Issue 1), meetings presentations (1997–2004), and information from the sponsors were searched using the terms for atypical antipsychotic drugs (aripiprazole, clozapine, olanzapine, quetiapine, risperidone, and ziprasidone), dementia, Alzheimer disease, and clinical trial. Study selection was published and unpublished randomized placebo-controlled, parallel-group clinical trials of atypical antipsychotic drugs marketed in the United States to treat patients with Alzheimer disease or dementia were selected by consensus of the authors. Trials, baseline characteristics, outcomes, all-cause dropouts, and deaths were extracted by one reviewer; treatment exposure was obtained or estimated. Data were checked by a second reviewer. Fifteen trials (9 unpublished), generally 10 to 12 weeks in duration, including 16 contrasts of atypical antipsychotic drugs with placebo met criteria (aripiprazole [$n = 3$], olanzapine [$n = 5$], quetiapine [$n = 3$], risperidone [$n = 5$]). A total of 3353 patients were randomized to study drug and 1757 were randomized to placebo. Outcomes were assessed using standard (with random- or fixed-effects models) to calculate odds ratios (ORs) and risk differences based on patients randomized and relative risks based on total exposure to treatment. There were no differences in dropouts. Death occurred more often among patients randomized to drugs (118 [3.5%] vs. 40 [2.3%]. The OR by meta-analysis was 1.54; 95% confidence interval [CI], 1.06–2.23; $p = 0.02$; and risk difference was 0.01; 95% CI, 0.004–0.02; $p = 0.01$). Sensitivity analyses did not show evidence for differential risks for individual drugs, severity, sample selection, or diagnosis. Atypical antipsychotic drugs may be associated with a small increased risk for death compared with placebo. This risk should be considered within the context of medical need for the drugs, efficacy evidence, medical comorbidity, and the efficacy and safety of alternatives. Individual patient analyses modeling survival and causes of death are needed.

Suicide Prevention Strategies: A Systematic Review

Mann, J.J., Apter, A., Bertolote, J., Beautrais, A., Currier, D., Haas, A., Hegerl, U., Lonnqvist, J., Malone, K., Marusic, A., Mehlum, L., Patton, G., Phillips, M., Rutz, W., Rihmer, Z., Schmidtke, A., Shaffer, D., Silverman, M., Takahashi, Y., Varnik, A., Wasserman, D., Yip, P., and Hendin, H.

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In 2002, an estimated 877,000 lives were lost worldwide through suicide. Some developed nations have implemented national suicide prevention plans. Although these plans generally propose multiple interventions, their effectiveness is rarely evaluated. Our goal was to examine evidence for the effectiveness of specific suicide-preventive interventions and to make recommendations for future prevention programs and research. Relevant publications were identified via electronic searches of MEDLINE, the Cochrane Library, and PsychINFO databases using multiple search terms related to suicide prevention. Studies, published between 1966 and June 2005, included those that evaluated preventative interventions in major domains, education and awareness for the general public and for professionals, screening tools for at-risk individuals, treatment of psychiatric disorders, restricting access to lethal means, and responsible media reporting of suicide. Data were extracted on primary outcomes of interest: suicidal behavior (completion, attempt, ideation), intermediary or secondary outcomes (treatment seeking, identification of at-risk individuals, antidepressant prescription/use rates, referrals), or both. Experts from 15 countries reviewed all studies. Included articles were those that reported on completed and attempted suicide and suicidal ideation or, where applicable, intermediate outcomes, including help-seeking behavior, identification of at-risk individuals, entry into treatment, and antidepressant prescription rates. We included three major types of studies for which the research ques-

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tion was clearly defined: systematic reviews and meta-analyses ($n = 10$); quantitative studies, either randomized controlled trials ($n = 18$) or cohort studies ($n = 24$); and ecological or population-based studies ($n = 41$). Heterogeneity of study populations and methodology did not permit formal meta-analysis; thus, a narrative synthesis is presented. Education of physicians and restricting access to lethal means were found to prevent suicide. Others, including public education, screening programs, and media education, need more testing. Physician education in depression recognition and treatment and restricting access to lethal means reduce suicide rates. Other interventions need more evidence of efficacy. Ascertaining which components of suicide prevention programs are effective in reducing rates of suicide and suicide attempt is essential in order to optimize use of limited resources.

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