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Clinical Update: Literature Abstracts

PSYCHIATRIC SYMPTOMS

Depression and Anxiety Disorders in Palliative Cancer Care

Wilson, K.G., Chochinov, H.M., Skirko, M.G., Allard, P., Chary, S., Gagnon, P.R., Macmillan, K., De Luca, M., O'Shea, F., Kuhl, D., Fainsinger, R.L., and Clinch, J.J.

Journal of Pain and Symptom Management, *33* (2007), 118–129.

Depression and anxiety disorders are thought to be common in palliative cancer care, but there is inconsistent evidence regarding their relevance for other aspects of quality of life. In the Canadian National Palliative Care Survey, semistructured interviews assessing depression and anxiety disorders were administered to 381 patients who were receiving palliative care for cancer. There were 212 women and 169 men, with a median survival of 63 days. We found that 93 participants (24.4%, 95% confidence interval = 20.2–29.0) fulfilled *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition, diagnostic criteria for at least one anxiety or depressive disorder (20.7% prevalence of depressive disorders, 13.9% prevalence of anxiety disorders). The most frequent individual diagnosis was major depression (13.1%, 95% confidence interval = 9.9–16.9). Comorbidity was common, with 10.2% of participants meeting criteria for more than one disorder. Those diagnosed with a disorder were significantly younger than other participants ($p = .002$). They also had lower performance status ($p = .017$), smaller social networks ($p = 0.008$), and less participation in organized religious services ($p = 0.007$). In addition, they reported more severe distress on 14 of 18 physical symptoms, social concerns, and existential issues. Of those with a disorder, 39.8% were being treated with antidepressant medication, and 66.7% had been prescribed a benzodiazepine. In conclusion, it appears that depression and anxiety disorders are indeed common among patients receiving palliative care. These disorders contribute to a greatly diminished quality of life among people who are dying of cancer.

The Association of Depression and Anxiety with Medical Symptom Burden in Patients with Chronic Medical Illness

Katon, W., Lin, E.H., and Kroenke, K.

General Hospital Psychiatry, *29* (2007), 147–155.

Primary care patients with anxiety and depression often describe multiple physical symptoms, but no systematic review has studied the effect of anxiety and depressive comorbidity in patients with chronic medical illnesses. MEDLINE databases were searched from 1966 through 2006, using the combined search terms "diabetes," "coronary artery disease (CAD)," "congestive heart failure (CHF)," "asthma," "COPD," "osteoarthritis (OA)," "rheumatoid arthritis (RA)," with "depression," "anxiety," and "symptoms." Cross-sectional and longitudinal studies with >100 patients were included as were all randomized controlled trials that measure the impact of improving anxiety and depressive symptoms on medical symptom outcomes. Thirty-one studies involving 16,922 patients met our inclusion criteria. Patients with chronic medical illness and comorbid depression or anxiety compared to those with chronic medical illness alone reported significantly higher numbers of medical symptoms when controlling for severity of medical disorder. Across the four categories of common medical disorders examined (diabetes, pulmonary disease, heart disease, arthritis), somatic symptoms were at least as strongly associated with depression and anxiety as were objective physiologic measures. Two treatment studies also showed that improvement in depression outcome was associated with decreased somatic symptoms without improvement in physiologic measures. Accurate diagnosis of comorbid depressive and anxiety disorders in patients with chronic medical illness is essential in understanding the cause and in optimizing the management of somatic symptom burden.

An Empirical Examination of the Stage Theory of Grief

Maciejewski, P.K., Zhang, B., Block, S.D., and Prigerson, H.G.

JAMA, *297* (2007), 716–723.

The stage theory of grief remains a widely accepted model of bereavement adjustment still taught in medical schools, espoused by physicians, and applied in diverse contexts. Nevertheless, the stage theory of grief has previously not been tested empirically. The aim of our study was to examine the relative magnitudes and patterns of change over time postloss of five grief indicators for consistency with the stage theory of grief. We used a longitudinal cohort study (Yale Bereavement Study) of 233 bereaved individuals living in Connecticut, with data collected between January 2000 and January 2003. The main outcome measures were five rater-administered items assessing disbelief, yearning, anger, depression, and acceptance of the death from 1 to 24 months postloss. Counter to stage theory, disbelief was not the initial, dominant grief indicator. Acceptance was the most frequently endorsed item and yearning was the dominant negative grief indicator from 1 to 24 months postloss. In models that take into account the rise and fall of psychological responses, once rescaled, disbelief decreased from an initial high at 1 month postloss, yearning peaked at 4 months postloss, anger peaked at 5 months postloss, and depression peaked at 6 months postloss. Acceptance increased throughout the study observation period. The five grief indicators achieved their respective maximum values in the sequence (disbelief, yearning, anger, depression, and acceptance) predicted by the stage theory of grief. Identification of the normal stages of grief following a death from natural causes enhances understanding of how the average person cognitively and emotionally processes the loss of a family member. Given that the negative grief indicators all peak within approximately 6 months postloss, those who score high on these indicators beyond 6 months postloss might benefit from further evaluation.

Tamoxifen Treatment and New-Onset Depression in Breast Cancer Patients

Lee, K.C., Ray, G.T., Hunkeler, E.M., and Finley, P.R.

Psychosomatics, *48* (2007), 205–210.

The authors conducted a retrospective cohort study of female patients diagnosed with breast cancer (BRCA), evaluating the risk of new-onset depression associated with tamoxifen treatment among those with estrogen receptor-positive (ER+) tumors, versus estrogen receptor-negative (ER–) tumors, who were not receiving tamoxifen. A total cohort of 2943 patients was identified. The hazard ratio for new-onset depression in the tamoxifen group was nonsignificant. A *post hoc* analysis revealed that chemotherapy and ER+ status were significantly and independently associated with an increased risk for developing depression.

Do Anxiety, Body Image, Social Support and Coping Strategies Predict Survival in Breast Cancer? A Ten-Year Follow-Up Study

Cousson-Gélie, F., Bruchon-Schweitzer, M., Dilhuydy, J.M., and Jutand, M.A.

Psychosomatics, *48* (2007), 211–216.

A longitudinal study enrolled 75 women with primary breast cancer. Before the confirmation of diagnosis, authors measured trait-anxiety and body satisfaction. Three weeks after diagnosis, coping strategies and state-anxiety were evaluated. The number of days of survival was measured 10 years after diagnosis. In Cox proportional-hazards models adjusting for severity of disease and age, high social support and low state-anxiety predicted an increased risk of death from breast cancer. A significant increased risk of death in women with low scores on the Body Image Questionnaire appeared only in the univariate model.

Subtypes of Pediatric Delirium: A Treatment Algorithm

Karnik, N.S., Joshi, S.V., Paterno, C., and Shaw, R.

Psychosomatics, *48* (2007), 253–257.

Delirium in adult populations of hospitalized patients has been well characterized into hyperactive, hypoactive, and mixed subtypes. The degree to which these subtypes apply to pediatric populations has yet to be fully demonstrated. In this case report, the authors present two cases of delirium that serve as examples of the hyperactive and hypoactive/mixed types and then discuss treatment. They find marked differences in the response of different delirium subtypes to haloperidol and risperidone and theorize as to the neurochemical pathways by which these pharmacological agents might work. This framework provides an algorithm for the treatment of pediatric delirium.

SYMPTOM CONTROL

Asking the Right Question of Informal Caregivers about Patient Symptom Experiences: Multiple Proxy Perspectives and Reducing Interrater Gap

Lobchuk, M.M., McClement, S.E., Daeninck, P.J., Shay, C., and Elands, H.

Journal of Pain and Symptom Management, *33* (2007), 130–145.

Recent conceptual work on multiple proxy perspectives indicates that clinicians should be more reflective in terms of how they question or prompt informal caregivers to report on patient illness experiences. There are different ways in which therapeutic questions might be posed that can influence perceptual agreement between patients and caregivers. The purpose of this randomized, between-subjects study was to test the hypothesis that "The interrater gap between patient self-assessment and caregiver assessment on patient multidimensional symptom experiences will be reduced when caregivers are prompted to imagine-patient perspective-take." We also tested the hypothesis that "Regardless of the perspective-taking prompt provided to the caregiver, gender will have no impact on patient and caregiver discrepancy scores on patient symptom experiences." This study comprised a convenience sample of 126 dyads consisting of breast and prostate cancer patients, and their informal caregivers. Patients provided self-reports on the abbreviated Memorial Symptom Assessment Scale (MSAS). Informal caregivers also completed the abbreviated MSAS under one of three randomly assigned instructional set conditions: neutral, imagine-patient perspective-taking, and imagine-self perspective-taking. The imagine-patient prompt was effective in reducing caregiver discrepancy across symptoms and underlying dimensions in comparison to the imagine-self prompt. However, the least discrepancy between patients and caregivers occurred in the neutral condition. The greatest discrepancy by caregivers occurred in the imagine-self condition. For the most part, there was no significant interaction effect between caregiver gender and induced perspective-taking across each of the symptoms and underlying frequency, severity, and distress. These results lend support for Pickard and Knight's multiple proxy perspectives model in that different perspective-taking prompts can result in varying levels of perceptual agreement, of which clinicians need to be aware to deliver sensitive patient and family centered care.

Factors Influencing Agreement in Symptom Ratings by Lung Cancer Patients and their Significant Others

Wennman-Larsen, A., Tishelman, C., Wengstrom, Y., and Gustavsson, P.

Journal of Pain and Symptom Management, *33* (2007), 146–155.

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

Symptom Profiles Differ in Patients with Neuropathic versus Non-neuropathic Pain

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

The Journal of Pain, *8* (2007), 118–126.

The distinction between neuropathic and non-neuropathic pain reflects partially distinct mechanisms and patterns of treatment response. It was therefore hypothesized that patients with neuropathic and non-neuropathic pain have different profiles of symptoms and signs. To test this hypothesis, pain intensity, unpleasantness, quality, and spatial characteristics were examined in 618 patients with one of three peripheral neuropathic pain conditions (painful diabetic peripheral neuropathy, painful idiopathic sensory polyneuropathy, or postherpetic neuralgia), osteoarthritis pain, or low back pain. These assessments were conducted before treatment had begun in clinical trials of lidocaine patch 5% administered alone or with stable dosages of other analgesics. Patients with osteoarthritis pain and low back pain did not differ in their profile of pain quality and spatial characteristics and were combined to form a group of patients with

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non-neuropathic pain. In univariate analyses, patients with peripheral neuropathic pain reported significantly more intense hot, cold, sensitive, itchy, and surface pain and significantly less intense dull and deep pain than patients with non-neuropathic pain. In a multivariate analysis, the overall pattern of pain quality and spatial characteristics differed significantly between patients with neuropathic and non-neuropathic pain. In addition, specific pain quality and spatial characteristics improved the discrimination of patients with neuropathic and non-neuropathic pain in a logistic regression model that adjusted for demographic covariates and overall pain intensity and unpleasantness. The results indicate that the distinction between neuropathic and non-neuropathic pain is reflected in different profiles of pain quality and spatial characteristics and suggest that the assessment of patterns of pain symptoms might contribute to the identification of distinct pathophysiologic mechanisms and the development of mechanism-based treatment approaches.

A Phase III Randomized, Double-Blind, Placebo-Controlled Study Evaluating Dextromethorphan plus Slow-Release Morphine for Chronic Cancer Pain Relief in Terminally Ill Patients

Dudgeon, D.J., Bruera, E., Gagnon, B., Watanabe, S.M., Allan, S.J., Warr, D.G., MacDonald, S.M., Savage, C., Tu, D., and Pater, J.L.

Journal of Pain and Symptom Management, *33* (2007), 365–371.

This multicenter trial examined the efficacy and safety of dextromethorphan (DM) as an enhancer of analgesia and modulator of opioid tolerance in cancer patients with pain. Eligible patients were randomized to slow-release morphine plus DM or slow-release morphine plus placebo. The initial DM dose was 60 mg four times daily for 7 days, with an increase to 120 mg four times daily, if tolerated, for another 7 days. During the study, patients recorded medications and scores for pain, nausea, drowsiness, and insomnia. Sixty-five patients were randomized. Although average pain scores (12.6 vs. 15.8), number of breakthrough doses (9 vs. 11.3), and change in total morphine consumption (550.9 mg vs. 597.1 mg) were less in the DM group than placebo group, the differences were not statistically significant ($p = .31–.33$). Side-effect scores were not statistically significantly different. Dizziness was greater in the DM (58%) than placebo (36%) group. This study showed a statistically nonsignificant enhancement of analgesia or modulation of opioid tolerance in cancer patients with pain when DM was added to morphine. Participants receiving the DM also had more toxicity, particularly dizziness. This toxicity and the limited evidence of effect do not support the use of DM to enhance opioid analgesia or to modulate opioid tolerance in cancer patients.

Women Experience Higher Levels of Fatigue Than Men at the End of Life: A Longitudinal Home Palliative Care Study

Husain, A.F., Stewart, K., Arseneault, R., Moineddin, R., Cellarius, V., Librach, S.L., and Dudgeon, D.

Journal of Pain and Symptom Management, *33* (2007), 389–397.

Few studies have evaluated sex differences in the prevalence, severity, and correlates of fatigue at the end of life. The Brief Fatigue Inventory, McGill Quality of Life (MQOL) Questionnaire, and Karnofsky Performance Scale were administered at 2-week intervals to 102 patients in a home palliative program. Outcomes in the sample and a regional palliative database ($n = 3096$) were analyzed. Cancer was the diagnosis in 96% of patients enrolled. Prevalence ($p = .0091$) and severity of fatigue ($p < .001$) were higher in women at entry and in a repeated measures analysis over time (severity, $p = .0048$). Performance status did not explain this difference. MQOL scores were inversely correlated to fatigue (Spearman coefficient $= -.48$, $p < .0001$), but did not differ by sex. There was no difference in fatigue interference with MQOL in women and men. Although depression was higher in women ($p = .042$) and related to fatigue at entry, it did not explain the sex difference in fatigue scores. Of the sociodemographic variables examined, neither education nor living situation contributed to the fatigue difference. This study shows a sex effect in the fatigue experienced by patients with advanced illnesses, which is not explained by baseline differences in performance, depression, MQOL, education, or living situation. That fatigue interference with MQOL is the same for men and women suggests that higher fatigue scores in women reflect not only a difference in the dimension of fatigue severity, but are also relevant in relation to impact on QOL. Assessment of fatigue should include the dimension of QOL important for both women and men.

Clinical Trial Results with OROS((R)) Hydromorphone

Wallace, M.S., and Thipphawong, J.

Journal of Pain and Symptom Management, *33* (2007), S25–32.

OROS((R)) hydromorphone is a unique drug delivery system being evaluated for the once-daily oral treatment of moderate to severe chronic pain. Results of dose conversion studies indicate that most patients can be successfully titrated from prior opioid therapy to OROS((R)) hydromorphone using a 5:1 ratio to convert oral morphine equivalents to OROS((R)) hydromorphone in up to two dose titration steps. OROS((R)) hydromorphone is effective in both chronic cancer pain and chronic noncancer pain of moderate to severe intensity. It is at least as effective at controlling chronic pain, reducing the impact of pain on functionality, and improving quality of life as controlled-release morphine (cancer pain) and extended-release oxycodone (osteoarthritis pain). In all studies, OROS((R)) hydromorphone was generally well tolerated, with an adverse event profile similar to that of other long-acting opioid analgesics.

Taking Fatigue Seriously, II: Variability in Fatigue Levels in Cancer Patients

Dimsdale, J.E., Ancoli-Israel, S., Ayalon, L., Elsmore, T.F., and Gruen, W.

Psychosomatics, *48* (2007), 247–252.

Fatigue is a common and distressing complaint of cancer patients. It is typically measured with symptom inventories that reflect the patient's experience over the previous days or weeks. This study examined short-term variation in fatigue levels in a heterogeneous group of cancer patients over a 3-day period to examine the feasibility of such repeated assessments and to characterize the extent and pattern of fatigue symptoms in cancer patients. Thirty-four cancer outpatients with diverse malignancies wore a prototype fatigue watch monitor for three consecutive 24-h periods and provided fatigue ratings every hour while awake for the 3 days. Patients completed an average of 40 self-reports over 72 h. These reports revealed a diurnal variation in fatigue, with increasing levels in the evening. The reports also revealed considerable differences across individuals and within individuals in terms of fatigue ratings. Multiple ratings of fatigue within short periods of time can be obtained and reveal that fatigue levels are quite variable, even within an individual. Cancer patients experience their fatigue as "moderate to extreme" 33% of the time.

MEASURES

Taiwanese Version of the M. D. Anderson Symptom Inventory: Symptom Assessment in Cancer Patients

Lin, C.C., Chang, A.P., Cleeland, C.S., Mendoza, T.R., and Wang, X.S.

Journal of Pain and Symptom Management, *33* (2007), 180–188.

The purpose of this study was to validate the Taiwanese version of the M. D. Anderson Symptom Inventory (MDASI-T) in a sample of 556 Taiwanese patients with multiple diagnoses of cancer. The internal consistency Cronbach alpha was .89 for symptom severity items and .94 for interference items. The test–retest reliability was .97 for the severity composite score and .96 for the interference composite score over a 3-day interval in a sample of 12 patients. Construct validity was established by factor analysis, which revealed a two-factor structure. Concurrent validity was examined by correlating the MADSI-T scores and scores of the Medical Outcome Study 36-Item Short-Form Health Survey. Known-group validity was established by comparing MDASI-T scores between patients having low functional status and those having high functional status (Karnofsky Performance Status scores $\leq$50 or $>$50, respectively) and between inpatients and outpatients. The MDASI-T's sensitivity (its ability to detect small differences in reporting variations) was examined by comparing the MDASI-T composite symptom scores and composite interference scores before, during, and 1 week after treatment in a sample of 20 breast cancer patients receiving chemotherapy. The MDASI-T is a reliable, valid, and sensitive instrument for measuring the severity and interference with daily life of cancer-related symptoms among Taiwanese cancer patients.

Validation of the Missoula-Vitas Quality-of-Life Index among Patients with Advanced AIDS in Urban Kampala, Uganda

Namisango, E., Katabira, E., Karamagi, C., and Baguma, P.

Journal of Pain and Symptom Management, *33* (2007), 189–202.

The Missoula-Vitas Quality-of-Life Index (MVQOLI) is a unique tool specifically designed to measure quality of life (QOL) in advanced illness in a palliative care setting. The aim of this study was to explore its cross-cultural validity. We used a culturally adapted version in a local language, Luganda, and

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tested the MVQOLI-M in 200 patients with advanced AIDS in urban Kampala, Uganda. Content validity was assessed using the content validity ratio approach. Reliability was assessed using Cronbach's alpha, and test–retest reliability was evaluated using the intraclass correlation coefficient. All items and domains were rated content valid and there was good construct validity. The instrument demonstrated good internal consistency (alpha = .83). The transcendence domain was the best predictor of overall QOL. The MVQOLI-M is an acceptable, valid, and reliable measure of QOL for people with advanced AIDS and findings demonstrate the importance of measuring the transcendence domain in QOL in advanced illness.

EXISTENTIAL ISSUES

Healing Connections: On Moving from Suffering to a Sense of Well-being

Mount, B.M., Boston, P.H., and Cohen, S.R.

Journal of Pain and Symptom Management, *33* (2007), 372–388.

Life-threatening illness is an assault on the whole person—physical, psychological, social, and spiritual. It frequently presents caregiver and sufferer with a paradox—suffering does not correlate with physical well-being alone. Drawing on a purposive sample of 21 participants, a phenomenological study was carried out to explore the relevance of the existential and spiritual domains to suffering, healing, and quality of life (QOL). The phenomenological method was used to achieve an in-depth description of both existential suffering and, conversely, the experience of integrity and wholeness in persons with life-threatening illness, to identify "inner life" and existential contributors to suffering and subjective well-being in advanced illness, and to develop a narrative account of these QOL extremes. The importance of meaning-based adaptation to advanced illness was supported, as were Frankl's sources of meaning and Yalom's sources of existential anguish. Divergent themes characteristic of the two QOL extremes were identified. Four types of "healing connections" involving a sense of bonding to self, others, the phenomenal world, and ultimate meaning, respectively, were identified. They situated the participant in a context that was greater and more enduring than the self, thus leading to enhanced meaning and QOL. The assumptions underlying the construct "health-related QOL" are questioned.

Suffering with Advanced Cancer

Wilson, K.G., Chochinov, H.M., McPherson, C.J., LeMay, K., Allard, P., Chary, S., Gagnon, P.R., Macmillan, K., De Luca, M., O'Shea, F., Kuhl, D., and Fainsinger, R.L.

Journal of Clinical Oncology, *25* (2007), 1691–1697.

The alleviation of suffering is a central goal of palliative care, but little research has addressed the construct of suffering as a global experience of the whole person. We inquired into the sense of suffering among patients with advanced cancer to investigate its causes and correlates. Semistructured interviews were administered to 381 patients. The interviews inquired about physical symptoms, social concerns, psychological problems, and existential issues. We also asked, "In an overall, general sense, do you feel that you are suffering?" Almost half (49.3%) of respondents did not consider themselves to be suffering, and 24.9% felt that they suffered only mildly. However, 98 participants (25.7%) were suffering at a moderate to extreme level. The latter participants were more likely to experience significant distress on 20 of the 21 items addressing symptoms and concerns; the highest correlations were with general malaise (rho = .56), weakness (rho = .42), pain (rho = .40), and depression (rho = .39). In regression analyses, physical symptoms, psychological distress, and existential concerns, but not social issues, contributed to the prediction of suffering. In qualitative narratives, physical problems accounted for approximately half (49.5%) of patient reports of suffering, with psychological, existential, and social concerns accounting for 14.0%, 17.7%, and 18.8%, respectively. Many patients with advanced cancer do not consider themselves to be suffering. For those who do, suffering is a multidimensional experience related most strongly to physical symptoms, but with contributions from psychological distress, existential concerns, and social-relational worries.

CAREGIVERS

Caregiver Thoughts and Feelings in Response to Different Perspective-Taking Prompts

Lobchuk, M.M., McClement, S.E., Daeninck, P.J., and Elands, H.

Journal of Pain and Symptom Management, *33* (2007), 420–433.

Both conceptual and empirical evidence in the caregiving literature suggest that "how" informal caregivers are prompted to think about patient

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experiences can impact their ability to achieve perceptual agreement with patients on symptom events. Researchers have begun to test the effects of different clinical questions with caregivers or a proxy on their perceptual agreement with patient self-reports. However, there are gaps in understanding caregivers' underlying thoughts and feelings when they are prompted to take different vantage points on the patient's symptom experiences. To assess these thoughts and feelings, content analysis was performed on verbal responses to an open-ended interview schedule in which caregivers were questioned about their thoughts and feelings in one of three randomly assigned instructional conditions—neutral, imagine-patient, and imagine-self perspective taking. Responses were classified into one of five cue categories: patient-oriented, caregiver-oriented, generalized other, feeling distanced, and other. Caregivers tended to respond to patient symptom experiences in ways that suggest it is innate for caregivers in intimate relationships to make an effort to imagine the patient's viewpoint on symptom events. When caregivers were prompted to imagine the patient's perspective, "labeling" processes were also triggered that denote a categorization process in which caregivers interpreted the meaning of simple patient information arising in the care situation. A large portion of caregivers in the neutral and imagine-patient conditions reported feeling distanced from patients in light of perceived communication difficulties.

Benefits of Training Family Caregivers on Experiences of Closure during End-of-Life Care

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

Journal of Pain and Symptom Management, *33* (2007), 434–445.

Caregiving at Life's End (CGLE) is a program for family caregivers caring for someone during the last years of life that focuses on the emotional, spiritual, and practical aspects of life and relationship completion and closure. This study evaluated the effectiveness of CGLE in improving three major outcomes: comfort with caregiving, closure, and caregiver gain. Family caregivers ($n = 2025$) participated in programs facilitated by health and human service professionals ($n = 142$) who completed a CGLE train-the-trainer workshop conducted by The Hospice Institute of the Florida Suncoast. The caregivers completed training rosters and pre- and/or postsurveys. Group differences are reported in baseline characteristics and change in three outcomes for caregivers who completed (1) both pre- and postsurvey, (2) presurvey only, and (3) postsurvey only. For those who completed both surveys ($n = 926$), paired t tests and multiple linear regression tested the impact of program length on caregiver outcomes. Caregivers participated in, on average, four sessions and 7.7 h of training. The majority of caregivers were Caucasian (88%), female (81%), and, on average, 60 years old. Significant improvement was found in all three outcomes ($p < .001$). The program length made a difference for improvement in comfort with caregiving and closure but not in caregiver gain. Caregivers who are caring for someone during the last years of life benefit from a program that focuses on the life-changing or transformative aspects of caregiving in the last years of life, as well as practical aspects of caregiving. The ability to support caregivers in this relatively low impact intervention can be used in hospice and nonhospice settings.

PSYCHOSOCIAL INTERVENTIONS

Clinical Response and Risk for Reported Suicidal Ideation and Suicide Attempts in Pediatric Antidepressant Treatment: A Meta-analysis of Randomized Controlled Trials

Bridge, J.A., Iyengar, S., Salary, C.B., Barbe, R.P., Birmaher, B., Pincus, H.A., Ren, L., and Brent, D.A.

JAMA, *297* (2007), 1568–1576.

The U.S. Food and Drug Administration (FDA) has issued warnings that use of antidepressant medications poses a small but significantly increased risk of suicidal ideation/suicide attempt for children and adolescents. This objective of this paper is to assess the efficacy and risk of reported suicidal ideation/suicide attempt of antidepressants for treatment of pediatric major depressive disorder (MDD), obsessive-compulsive disorder (OCD), and non-OCD anxiety disorders. Data were obtained from PubMed (1988 to July 2006), relevant U.S. and British regulatory agency reports, published abstracts of important scientific meetings (1998–2006), clinical trial registries, and information from authors. Studies were published and unpublished randomized, placebo-controlled, parallel-group trials of second-generation antidepressants (selective serotonin reuptake inhibitors, nefazodone, venlafaxine, and mirtazapine) in participants younger than 19 years with MDD, OCD, or non-OCD anxiety disorders. Information was extracted on study characteristics, efficacy outcomes, and spontaneously reported suicidal ideation/suicide attempt. Twenty-seven trials of pediatric MDD

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($n = 15$), OCD ($n = 6$), and non-OCD anxiety disorders ($n = 6$) were selected, and risk differences for response and for suicidal ideation/suicide attempt estimated by random-effects methods. Pooled risk differences in rates of primary study-defined measures of responder status significantly favored antidepressants for MDD (11.0%; 95% confidence interval [CI], 7.1%–14.9%), OCD (19.8%; 95% CI, 13.0%–26.6%), and non-OCD anxiety disorders (37.1%; 95% CI, 22.5%–51.7%]), corresponding to a number needed to treat (NNT) of 10 (95% CI, 7–15), 6 (4–8), and 3 (2–5), respectively. Although there was increased risk difference of suicidal ideation/suicide attempt across all trials and indications for drug versus placebo (0.7%; 95% CI, 0.1%–1.3%) (number needed to harm, 143; 95% CI, 77–1000), the pooled risk differences within each indication were not statistically significant: 0.9% (95% CI, −0.1%–1.9%) for MDD, 0.5% (−1.2%–2.2%) for OCD, and 0.7% (−0.4%–1.8%) for non-OCD anxiety disorders. There were no completed suicides. Age-stratified analyses showed that for children younger than 12 years with MDD, only fluoxetine showed benefit over placebo. In MDD trials, efficacy was moderated by age, duration of depression, and number of sites in the treatment trial. Relative to placebo, antidepressants are efficacious for pediatric MDD, OCD, and non-OCD anxiety disorders, although the effects are strongest in non-OCD anxiety disorders, intermediate in OCD, and more modest in MDD. Benefits of antidepressants appear to be much greater than risks from suicidal ideation/suicide attempt across indications, although comparison of benefit to risk varies as a function of indication, age, chronicity, and study conditions.

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