Putting Evidence Into Practice: Evidence-Based Interventions for Depression

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Depression is a distressing emotion that occurs during various times of the cancer trajectory. Depression often goes unrecognized and untreated, which can significantly affect cost, quality of life, and treatment adherence. The Oncology Nursing Society’s Putting Evidence Into Practice depression project team reviewed current literature to identify evidence-based interventions to reduce depression in people with cancer. Pharmacologic and nonpharmacologic interventions were evaluated, and opportunities for nurses to integrate recommendations into practice are offered in this article.

Depression often accompanies a cancer diagnosis and its treatment, occurring in as many as 52% of patients (Massie, Lloyd-Williams, Irving, & Miller, 2011). Differing definitions of depression, time of assessment, and measurement tools exist. Depressive disorders may be preexisting and chronic (dysthymia), episodic, or related to medical or even medication-induced conditions; however, the common feature is the presence of sad, empty, or irritable mood accompanied by somatic and cognitive changes that significantly affect functioning (American Psychiatric Association, 2013). Depressive symptoms are sometimes difficult to distinguish in patients with cancer because treatment side effects, such as fatigue and sleep and appetite disturbances, may mimic depression. More telling are the psychological symptoms of hopelessness, worthlessness, guilt, loss of confidence, anxiety, irritability, and the inability to experience pleasure (Kleiboer et al., 2011; Miller & Massie, 2006), which are not effects of typical cancer treatment.

In addition, not participating in medical care and withdrawing socially are markers of moderately severe depression; the inability to be cheered up or respond to good news or humor may mark more severe depression (Akechi, Ietsugu, et al., 2009). Different cancers also carry a higher prevalence of comorbid depression, with lung, breast, pancreatic, and oropharyngeal cancers rating highest (Massie, 2004; National Cancer Institute, 2013). Cancer-related risk factors include advanced disease, poorly managed pain, increased physical disability, and perceived lack of support (Miller & Massie, 2010; National Cancer Institute, 2013).

Depression affects quality of life and treatment adherence in significant ways. Patients who are depressed have difficulty making decisions and plans, avoid health-promoting activities, use community resources less, socially withdraw, and have difficulty tolerating treatment side effects (DiMatteo & Haskard-Zolnierek, 2011). Some studies attribute increased mortality to patients with coexisting depression (Satin, Linden, & Phillips, 2009). As a result, identification and management of depression is critical to compassionate and quality care.

Methods

This article reviews evidence retrieved from May 1, 2008, through December 31, 2013, and updates two previous publications (Fulcher & Badger, 2009; Fulcher, Badger, Gunter, Marrs, & Reese, 2008). English-language articles were searched for depression and therapy or systematic or neoplasms or oncology. A PubMed search provided 1,557 citations, and a CINAHL® search
identified 461 citations. In addition, the National Comprehensive Cancer Network’s (2013) clinical guidelines for distress management were reviewed. Studies were included if they were full research reports, systematic reviews, guidelines, or meta-analysis; reported the measurement of depression and depressive symptoms; examined a depression intervention; and included patients with cancer. Based on the Oncology’s Nursing Society’s (Mitchell & Friese, n.d.) evidence evaluation criteria, each intervention is categorized (see Figure 1).

Levels of Evidence
Recommended for Practice

Antidepressant medications generally are effective in reducing depression in patients with physical illnesses (odds ratio [OR] = 2.33, p < 0.00001 for short-term response; OR = 2.13, p = 0.002 for long-term response) (Rayner et al., 2010). Two reviews also showed antidepressant benefit (Laoutidis & Mathiak, 2013; Walker et al., 2013). In other trials among patients with cancer, the effects of newer drugs were examined. A large-sample (N = 180) randomized, controlled trial showed a reduction in depression after patients used fluoxetine (Navari, Brenner, & Wilson, 2008). Small-sample, open-label, single-group trials reported positive effects of mirtazapine (Cankurtaran et al., 2008; Ersoy, Noyan, & Elbi, 2008), fluvoxamine (Suzuki et al., 2011), escitalopram (Park, Lee, Kim, Bae, & Hahn, 2012), paroxetine (Amodeo et al., 2011), duloxetine (Torta, Leombruni, Borio, & Castelli, 2011), and sertraline (Torta, Siri, & Caldera, 2008). Risk of developing depression was reduced in studies that examined the prophylactic use of citalopram (Lydiatt, Denman, McNelley, Puumula, & Burke, 2008) or escitalopram (Lydiatt, Bessette, Schmid, Sayles, & Burke, 2013) in 23 and 148 patients with head and neck cancer, respectively. It is unknown if a specific antidepressant would be more appropriate for a cancer population or if antidepressants would be effective in patients in specific stages or cancer type.

Cognitive-behavioral interventions (CBIs) are designed to help patients identify negative or unhelpful thoughts, beliefs, and behaviors, establish goals to change them, and develop skills to implement helpful behaviors. CBIs can be provided in individual or group settings, in person, or via telephone. In two meta-analyses, CBIs showed moderate-to-strong statistical effects on depression (Hart et al., 2012; Naaman, Radwan, Fergusson, & Johnson, 2009). In a systematic review of seven CBI studies, short-term improvement was found in depressive symptoms in patients with prostate cancer (Chien, Liu, Chien, & Liu, 2014). However, findings from individual studies are mixed: Some reported positive effects (Brothers, Yang, Strunk, & Andersen, 2011; Given et al., 2004; Guo et al., 2013; Osborn, Demoncada, & Feuerstein, 2006; Qiu et al., 2013), whereas others reported no effect (Boesen et al., 2011; Fleming, Randell, Harvey, & Espie, 2014; Greer et al., 2012; Groarke, Curtis, & Kerin, 2013; Kangas, Milross, Taylor, & Bryant, 2012; Korstjens et al., 2011; Pitceathly et al., 2009; Serfaty, Wilkinson, Freeman, Mannix, & King, 2012). The format, frequency, and timing of the intervention program varied across studies. Content can also be diverse and often includes education or relaxation-training activities. That diversity may have contributed to inconsistent results across studies. Whether individual or group therapy is more beneficial for specific patient groups or whether the intervention has long-term effects is unclear (Naaman et al., 2009; Osborn et al., 2006).

Mindfulness-based stress reduction (MBSR) aims to teach people to more positively address experiences through present awareness of feelings, thoughts, and bodily sensations. MBSR techniques include body scans, simple yoga exercises, and meditation. Six to eight weeks of MBSR interventions are recommended to reduce depression, with sessions typically lasting two hours (Ando et al., 2009; Garland, Tamagawa, Todd, Speca, & Carlson, 2013; Hofmann, Sawyer, Witt, & Oh, 2012; Lengacher et al., 2012; Sharplin et al., 2010; Würtzen et al., 2013). A randomized, controlled trial of 336 patients with breast cancer showed positive effects in eight weekly group sessions at 6 and 12 months (Würtzen et al., 2013). A meta-analysis estimated a...
Psychoeducation or psychoeducational interventions cover a broad range of educational activities in combination with counseling and support. Education often includes information on treatments, symptoms, resources and services, training to provide care and respond to disease-related problems, and problem-solving strategies to cope with cancer. Interventions may be delivered individually or in groups, may be tailored or standardized, and may be provided online or via telephone.

Psychoeducational interventions consistently reduce depression, but effect size is small (Aashing & Rosales, 2013; Chien et al., 2014; Ell et al., 2011; Galway et al., 2012; Hopko et al., 2011; Ram, Narayanasamy, & Barua, 2013; Rottman et al., 2012; van der Meulen et al., 2013). Bruera et al. (2013) found psychoeducation plus placebo improved depression, as opposed to psychoeducation plus methylphenidate. Meta-analyses indicated psychoeducation may be more effective in early-stage disease and early phases of care (Galway et al., 2012; Zimmerman, Heinrichs, & Baum, 2007). Badger et al. (2011) reported effects from telephone psychoeducation counseling and a support intervention of health education, but Komatsu et al. (2012) reported no differences among education, counseling, and support groups in a small sample with many limitations.

Studies using psychoeducational interventions tend to vary substantially in content, format, frequency, and intervention timing. An interpersonal relationship with the provider appears to be an important component in the intervention format, given that self-directed interventions of CD use were not effective (Ramachandra, Booth, Pieters, Vrotsou, & Huppert, 2009). Whether one type or length of an intervention is superior to others is unclear. Further study is indicated to determine standardized formats of intervention and delivery methods that are most effective and efficient.

Likely to Be Effective

Individual psychotherapy involves structured therapeutic interaction between a trained professional and a single client that addresses psychological challenges. A large randomized, controlled trial of patients with various cancers examined the effect of three-month individual psychotherapy sessions and reported that its effect was sustained at 12 months (Strong et al., 2008). In another randomized, controlled trial, individual psychotherapy significantly reduced anxiety and depression at the end of inpatient care and 12 months after discharge in a group of high-risk patients (Goering, Foerg, Sander, Schramm, & Schlag, 2011). Of note, the intervention was not effective in a low-risk group (Goering et al., 2011). Beutel et al. (2014) randomized women with breast cancer to usual care or short-term psychodynamic psychotherapy and found reduced depression in the intervention group. A meta-analysis suggested that depression in patients with advanced cancer can be effectively reduced with psychotherapy (Akechi, Okuyama, Onishi, Morita, & Furukawa, 2008). In their review, Naaman et al. (2009) noted effectiveness with psychotherapy treatment, but the overall effect size for individual intervention was \( -0.32 \) (95% confidence interval \([-0.8, 0.15]\)) and was not significant. The reviews included several types of psychotherapy, various durations and timing of intervention, and significant heterogeneity in results. In addition, clinically diagnosed depression was not documented and study quality was not high.

Peer counseling is the support and guidance provided by a trained nonprofessional with a similar symptom or health problem experience. A randomized, controlled trial with a small sample of patients with prostate cancer examined the effect of individual weekly peer support and reported that patients in the treatment group had significantly higher self-efficacy (\( p = 0.005 \)) and lower depression (\( p = 0.032 \)) at eight weeks (Weber et al., 2007). The study chose one-to-one peer counseling, believing men were unlikely to participate in support groups (Stegina, Pinnock, Gardiner, Gardiner, & Dunn, 2005). Whether the outcomes of one-to-one peer support are the same as support groups is unclear.

Relaxation therapies usually incorporate breathing exercises and ways to relax the body that often involve diversion or visualization. A meta-analysis of 15 randomized, controlled trials reported that relaxation has small significant positive effects on emotional-adjustment variables such as depression, anxiety, and hostility (Luebbert, Dahme, & Hasenbring, 2001). However, most studies in the review were older (from years 1981-1995) and had low study quality. Nunes et al. (2007) found a decline in depression in a small randomized, controlled trial combining relaxation and visualization. In a randomized, controlled trial with a small sample, no effect of relaxation on depression was reported (Lutgendorf et al., 2010).

Exercise effectiveness on depression was reviewed in eight randomized, controlled trials and three meta-analyses. The studies were conducted over varying periods, involving supervised group exercise programs, home- or hospital-based exercise or walking programs, information sessions, and spa and aquatic programs. Most took place during curative treatment. No significant effects on depression were reported (Kwiatkowski et al., 2013; Saarto et al., 2012), and differences were not found between groups (Berglund et al., 2007; Cantarero-Villanueva et al., 2013; Payne, Held, Thorpe, & Shaw, 2008). A number of studies reported reduced depression with results ranging from small to significant (Brown et al., 2012; Carayol et al., 2013; Craft, Vaniterson, Helenowski, Rademaker, & Courney, 2012; Ergun, Eyigor, Karaca, Kisim, & Uslu, 2013; Hanna, Avila, Meetre, Nicholas, & Kaminsky, 2008; Mehnert et al., 2011; Midtgaard et al., 2005; Yang, Tsai, Huang, & Lin, 2010). Jacobsen et al. (2013) found exercise combined with stress management training yielded significant reduction in depression (\( p = 0.048 \)) compared to usual care; supervised exercise and exercise offered in places conducive to interactions showed greater impact on depression (Craft et al., 2012). One review examined exercise in men on androgen-deprivation therapy and did not find sufficient evidence to determine its effect on depression (Chipperfield, Brooker, Fletcher, & Burney, 2013).

Effectiveness Not Established

Pharmacologic interventions include infliximab, a monoclonal antibody directed at inflammatory cytokines, and stimulants methylphenidate and modafinil. Gehring et al. (2012) reported...
that both stimulants showed improvement in depression, but findings are compounded by a small sample, different stimulants, dosing schedules, and the lack of a control group. Gong et al. (2014) found methylphenidate did not improve depression in two reviewed studies. In addition, infliximab did not improve depression (Raison et al., 2013).

Group psychotherapy was compared with a support group in patients with breast cancer (Bjorneklett et al., 2013; Vos, Visser, Garssen, Duivenvoorden, & de Haes, 2007), but no effect was found on depression. Herschbach et al. (2010) compared a cognitive-behavioral therapy group with a supportive experiential group in patients with cancer; neither intervention reduced depression. A systemic review suggested that group therapy appears to be superior to individual therapy in treating anxiety and depression; in addition, the study reported that patients with advanced breast cancer benefit more from long-term interventions that emphasize support (Naaman et al., 2009).

Online support groups were explored in two articles. Samples were small and neither had a control group. Griffiths, Callear, and Banfield (2009) attempted to determine effectiveness of Internet support groups on depression in a systematic review. Little data on depression could be found. Klemm (2012) compared moderated with peer-led, online support groups for women with breast cancer and found no significant difference in depressive symptoms between the two groups.

Supportive care or telephone support was studied in a randomized, controlled trial by White et al. (2012) and in weekly counseling providing information by Gotay et al. (2007); no benefits were found. Telephone support by case workers was compared to oncologists (Girgis, Breen, Stacey, & Lecathelinais, 2009); no significant intervention effect was found on anxiety or depression. Kroenke et al. (2010) reported improvement in depression severity using calls by nurse-physician teams; however, varying intervention times and disease stages limits the ability to generalize to other populations. Aromatherapy was studied by Yim, Ng, Tsang, and Leung (2009). They reviewed three studies involving depression among patients with cancer and found many inconsistencies

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**Patient Education: Depression or Sadness**

Depression is a kind of sadness and is felt by many people being treated for cancer. It is often not noticed, and this leads to more doctor visits, more cost, and makes it harder to follow what the doctor says. Depression also makes it harder for people to enjoy their lives. It is important to tell your doctor or nurse about how you are feeling.

Studies show there are things you can do to help depression get better. They include the following.

- **Learn about the signs of depression.**
  - Too little sleep or sleeping all the time
  - Not caring about eating and losing weight
  - Not wanting to do the things you usually like to do
  - Feeling tired all the time
  - Having trouble remembering things
  - Feeling life is not worth living

- **Take medicine particularly to help with sadness or depression.**
- **Seek help from a specialist such as a counselor or therapist.**
- **Seek help from others who have the same kind of cancer.**
- **Learn ways to relax.**
- **Exercise regularly.**

There are many other ways people try to treat depression, but there is not enough research to recommend their use.

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*[Note. Full Oncology Nursing Society Putting Evidence Into Practice information for this topic and description of the categories of evidence are located at www.ons.org/practice-resources/dep/ped/depression. Users should refer to this resource for full dosages, references, and other essential information about the evidence.]*
in the aromatherapy interventions. Because aromatherapy is rarely used without massage, intervention effects are unclear. Massage effect was studied on perceived stress, mood, depression, and cytokine concentrations in patients with breast cancer (Krohn et al., 2011). Reduced depression scores were significant (p < 0.005) in the treatment group; however, the sample size was small and other confounding factors limited the findings.

Healing touch, an energy therapy, was compared to massage and relaxation in two randomized, controlled trials. One incorporated three groups to evaluate the effect of healing touch, relaxation, and usual care on quality of life, fatigue, depressed mood, and immune measures (Lutgendorf et al., 2010). The group receiving healing touch showed improved depression scores, but the sample size was small despite a lengthy recruitment period. The second trial, a crossover study, was conducted using massage, healing touch, and caring presence to examine effect on mood and anxiety (Post White et al., 2003). No clear evidence reported that one treatment was more effective than another; but mood disturbance decreased in all study participants over time.

Meditation was studied in patients with breast cancer in two randomized, controlled trials (Kim, Kim, Ahn, Seo, & Kim, 2013; Milbury et al., 2013). No effect was found on depression one month postintervention.

Yoga was reviewed in two randomized, controlled trials with small samples and showed mixed changes in depressive symptoms (Bower et al., 2012; Dhruva et al., 2012). A pre- and poststudy of an urban Zen initiative, an optimal healing environment created with color, lighting, and holistic techniques, included 163 inpatients with cancer and reported no change in the intervention group (Kligler et al., 2011). A systematic review of 90 mind-body therapies, six involving yoga, resulted in a mix of positive, negative, and unequivocal changes (D’Silva, Possablos, Habousha, Kogan, & Kligler, 2012). Mixed results were found in a systematic review of 18 randomized, controlled trials of patients with breast cancer (Harder, Parlour, & Jenkins, 2012). Three meta-analyses representing 32 studies found no effect of yoga on depression (Buffart et al., 2012; Sharma, Haider, & Knowlden, 2013; Zhang, Yang, Tian, & Wang, 2012). In addition, in their meta-analysis, Cramer, Lange, Klose, Paul, and Dobos (2012) found a short-term effect on depression that was not maintained at follow-up.

Music and art therapies may be helpful interventions for patients with cancer (Australian Government National Health and Medical Research Council, 2003). Music therapy (Bradt, Dileo, Groteck, & Magill, 2011; Zhou, Li, Yan, Dang, & Wang, 2011) and art therapies (Bar-Sela, Atid, Danos, Gabay, & Epelbaum, 2007; Thyme et al., 2009) produced mixed results. Results showed positive effects of reduced anxiety (Bradt et al., 2011) and reduced depression (Zhou et al., 2011); however, limitations, such as the variety of music interventions (Bradt et al., 2011) and unclear use of music (Zhou et al., 2011), restricted the establishment of effectiveness. Art therapies produced positive results for anxiety and depression after more than four to five therapy sessions (Bar-Sela et al., 2007; Thyme et al., 2009), but limitations included sample size, self-referral, lack of randomization, and no attentional control.

Qigong is an ancient Chinese practice that integrates physical posture, breathing techniques, and focused intention. Chen et al. (2012) reported that women with breast cancer receiving radiotherapy plus qigong demonstrated less depression over time than usual care (p = 0.05). Liu et al. (2008) found that intervention and control groups improved similarly on Beck depression inventories; however, both studies were small and lacked attentional control.

Hypnosis was reviewed by Rajasekaran, Edmonds, and Higginson (2005). The poor quality of the studies (only one randomized, controlled trial) and heterogeneity of the study population limited evaluation.

Structured rehabilitation sessions were compared with usual care in an eight-week randomized, controlled trial of patients with breast cancer (Khan, Amatya, Pallant, Rajapaksa, & Brand, 2012) and in two 12-week multicomponent programs (Gagnon et al., 2013; Hanssens et al., 2011); improvement occurred in depression scores, but small samples and lack of a control group limited the establishment of effectiveness.

Structured assessment in the form of a 20-study systematic review found no data to support that screening for depression improves depression outcomes (Meijer et al., 2011). A large randomized, controlled trial reported improved depression scores with depression screening versus routine care (McMullan, Small, & Haley, 2011).

Early palliative care showed mixed results. Pirl et al. (2012) found patients with depression at baseline showed reduced scores with proactive palliative care team involvement; however, Kao, Hu, Chiu, and Chen (2014) found no effect on depression in a small study.

Tai chi in twice-weekly sessions showed depression declined in a small sample (Galantino, Callens, Cardena, Piela, & Mao, 2013).

Tailored information in packages of pamphlets, computer information, and DVDs showed depression decline in a single, nonrandomized study (D’Souza, Blouin, Zeitouni, Muller, & Allison, 2012).

Other interventions were represented by only one study with a small sample and showed no significant impact. They included narrative interviewing, an intervention in which patients were encouraged to discuss meaning, suffering, and well-being (Lloyd-Williams, Cobb, O’Connor, Dunn, & Shiels, 2012); the medical herb guarana (da Costa Miranda et al., 2009); and Reiki, a spiritual practice of hands-on healing (Potter, 2007). One study of computer games using virtual reality in pediatric patients showed improvement in depression scores, but sample bias and generalizability are limiting factors (Li, Chung, & Ho, 2011).

Effectiveness Unlikely

Quintard and Lakdja (2008) examined the effect of various beauty treatments (e.g., manicures, pedicures, makeup sessions, depilation, hairdressing, massages) provided by professionals in a randomized, controlled trial with 100 female patients with cancer. They found no differences in depression and anxiety between the intervention and control groups.

Expressive writing or emotional disclosure found a beneficial effect on psychological well-being in a meta-analysis in primarily healthy participants (Frattaroli, 2006). However, no study supports its benefit on depression in patients with health problems. A large randomized, controlled trial (Jensen-Johansen et al.,...
Implications for Practice

- Help patients identify unhelpful thoughts and behaviors, and plan approaches for effective coping and problem solving.
- Promote peer support through group-, disease-, or age-based organizations.
- Identify symptom clusters in which depression is common and seek evidence-based interventions through Putting Evidence Into Practice resources.

Many new studies, particularly nonpharmacologic interventions for depression, are appearing in the literature. With further study, more of those approaches may reach recommended effectiveness; evidence about timing of interventions on types and stages of cancers then may emerge. Nurses will ideally be among the researchers in those studies.

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