Updated Oncology Nursing Society Putting Evidence Into Practice Resources

Oncology Nursing Society Putting Evidence Into Practice Project Teams

Ensuring that nursing practice is based on the most current evidence available is a priority for the Oncology Nursing Society (ONS). In 2005, ONS initiated a project to develop resources for nursing interventions designed to ensure high-quality, cost-effective patient care. Putting Evidence Into Practice (PEP) resources debuted in 2006 with the availability of evidence-based nursing interventions for four outcomes in patients with cancer: fatigue, chemotherapy-induced nausea and vomiting, prevention of infection, and sleep-wake disturbances. Since then, 12 more resources have been developed.

ONS advanced practice nurses, staff nurses, and nurse scientists developed the ONS PEP resources through the review, critique, and synthesis of the scientific literature on interventions for specific outcomes for patients with cancer. With each outcome, a card was developed for nurses to carry in addition to more detailed information offered at the ONS Outcomes Resource Area at www.ons.org/outcomes.

The *Clinical Journal of Oncology Nursing* also publishes a manuscript for each topic, describing scientific evidence for the evidence-based nursing interventions.

In 2008, the ONS PEP project teams began updating the content for their respective topics. Because of the sheer number of topics included, ONS decided to provide the updated resources in a book format, realizing that the handling and use of 16 pocket cards was getting unwieldy. The resources, including the background information on the synthesis of the evidence, will be available on the ONS Outcomes Resource Area (www.ons.org/outcomes).

Some of the project teams that reviewed the latest scientific literature for updates to the resources discovered that not very much had changed since the original work was done (anorexia, anxiety, and prevention of bleeding). However, changes were made for the other topics. To help nurses easily understand what the new scientific evidence revealed, a brief explanation of the updates is provided in this article.

Caregiver Strain and Burden (2007)

The ONS PEP project team for caregiver strain and burden updated the list of interventions nurses can use to assist family caregivers in reducing their strain and burden. To date, nine studies using outcome measures of caregiver burden or caregiver strain from 21 articles have been found.

Recommended for Practice

Cognitive behavioral interventions: Cognitive behavioral interventions now are recommended for practice. Cognitive behavioral interventions focus on changing caregivers' perceptions of their ability to control a situation, including challenging negative thoughts that encourage problematic behaviors, using strategies that facilitate development of problem-solving abilities, and focusing on managing time, work, and emotional reactions. The team found the interventions most effective in female caregivers or caregivers younger than the patient receiving care.

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Constipation (2007)

The primary changes in the original constipation resource include the addition of new medications: alvimopan; methylnaltrexone; colchicine; and lubiprostone, misoprostol, and polyethylene glycol. Tegaserod was taken off the market. Hydrolysed guar gum, a nonpharmacologic product, was added. The use of polyethylene glycol with or without electrolytes showed a higher level of evidence for use in patients without cancer and was moved to likely to be effective.

New information was added regarding clarification of the use of enemas in infants and children as well as the use of mineral oil, polyethylene glycol, and Milk of Magnesia® (Bayer AG) in children.

Also, new cautions were identified regarding the use of phosphate enemas in the very young and old with chronic renal failure, diseases altering gastrointestinal motility, tumor lysis syndrome, and bowel obstruction. In addition, cautions were added for use of mineral oil in patients with gastroesophageal reflux disease or cerebral palsy because of the potential for aspiration (Zanetti, Marchiori, Gasparetto, Escuissato, & Souza, 2007).

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Chemotherapy-Induced Nausea and Vomiting (2006)

The updated nausea and vomiting resource includes new pharmacologic agents to prevent and treat nausea and vomiting, specifically the addition of tropisetron as a 5-hydroxytryptamine 3 (5-HT_3) receptor antagonist choice. The neurokinin 1 (NK1) receptor antagonist aprepitant is now available in an IV formulation (fosaprepitant 115 mg IV) and may be considered if the oral route is contraindicated. For a highly emetogenic regimen, a three-drug antiemetic combination (NK1 receptor antagonist, 5-HT_3 receptor antagonist, and a corticosteroid) is recommended. With regimens containing doxorubicin and cyclophosphamide, the evidence supports use of the three-drug antiemetic combination (Kris et al., 2006; Multinational Association of Supportive Care in Cancer, 2008; National Comprehensive Cancer Center, 2008a). For breakthrough/refractory nausea and vomiting, a second cannabinoid option, nabilone, is now available. Reviews on Chinese herbal medicine and one study describing a yoga intervention were evaluated and added to the effectiveness not established category.

More studies evaluating the effectiveness of acupressure and acupuncture in relieving nausea and vomiting are available; however, the ONS PEP weight-of-evidence category remains at likely to be effective. Nonetheless, behavioral or nonpharmacologic interventions should be considered and used in combination with state-of-the-art pharmacologic interventions to prevent and manage nausea and vomiting. Additional general points to highlight include an awareness of prescribing appropriate pharmacologic agents for patients who receive multiday emetogenic therapy, in which delayed nausea can last as long as 10 days depending on the sequence of the regimen and the emetogenicity of the last chemotherapy agent administered. The recommended antiemetics must be administered for as long as the delayed nausea is expected to occur and not discontinued prematurely.

Lastly, antiemetic regimens have shown better efficacy in controlling acute and delayed vomiting than nausea. Trials show poorer control of nausea; indeed, the prevalence of anticipatory, acute, and delayed nausea is greater than the prevalence of vomiting.

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Depression (2007)

Additional study references in the depression PEP resource endorse the existing practice recommendations. Palliative care guidelines were included that support the benefit of using antidepressant medications for patients with cancer and depression. Specifically endorsed by palliative care guidelines are tricyclic antidepressants or selective serotonin receptor inhibitors.

The only intervention added was exercise. Exercise shows promise as an intervention to improve mood in patients with cancer, but current studies are small and their limitations prevent sufficient evidence for recommendation. Therefore, effectiveness is not established for exercise.

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Diarrhea (2008)

The diarrhea PEP resource underwent some revisions. Two key differences are the change in the definition for diarrhea as well as clarification of what cancer therapies were researched.

Diarrhea was harder to define than the group anticipated. No literature reviewed had a good definition and most referred to the National Cancer Institute Common Terminology Criteria for Adverse Events. The group believed that a more comprehensive definition was needed. Therefore, diarrhea is defined as an abnormal increase in stool liquidity and stool frequency greater than or equal to four to six stools per day over baseline with or without nocturnal bowel movements that may be accompanied by abdominal cramping.

The best available evidence for managing cancer treatment–related diarrhea involved standard chemotherapy and pelvic and abdominal radiation therapy. Biologic and targeted therapies did not have good evidence other than expert opinion. This information was added.

Likely to Be Effective

Octreotide: Octreotide 150 mcg subcutaneously three times daily results in near-complete resolution of diarrhea in patients with rectal carcinoma with grades 2 or 3 diarrhea receiving concomitant 5-fluorouracil (5-FU) and pelvic radiation therapy who are refractory to loperamide (Topkan & Karaoglu, 2006).

Benefits Balanced With Harms

Neomycin: Two studies addressed the use of neomycin for the prevention of irinotecan-induced diarrhea.

In one double-blind, randomized, placebo-controlled trial, the group receiving neomycin versus placebo had a 45% lower incidence of grade 3 diarrhea. Neomycin 660 mg was administered orally three times per day for three consecutive days starting two days before chemotherapy. The treatment with neomycin did not result in a significantly shorter duration of diarrhea in days and the patients receiving neomycin had a 4.5 higher risk for grade 2 nausea than those receiving placebo (de Jong et al., 2006).

In a nonrandomized study, seven evaluable patients received irinotecan alone in cycle 1 with resultant grade 2 diarrhea. In cycle 2 they were treated with irinotecan plus oral neomycin 1,000 mg three times per day for seven consecutive days starting two days before chemotherapy. Six out of seven of these patients had a decrease in diarrhea. By reducing the level of bacterial B-glucorinidase, neomycin plays a crucial role in reducing irinotecan-induced diarrhea without altering the efficacy of irinotecan. However, this is an extremely small study (Kehrer et al., 2001).

Effectiveness Not Established

Cholestyramine/levofloxacin: In one small phase II trial, patients were treated with levofloxacin 500 mg once daily and cholestyramine 4 g three times a day for three consecutive days starting the day before each irinotecan administration. Treatment led to a decreased incidence of World Health Organization grades 3–4 diarrhea (Flieger et al., 2007).

Expert Opinion

See Figure 1 for general diet strategies to manage diarrhea.

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Dyspnea (2007)

Eight new studies were located in the dyspnea literature to update the evidence supporting what nurses can do to assist people with cancer-related dyspnea. It is encouraging that more evidence is being generated for this symptom, which is difficult to study.

Three new studies continue to support the use of oral and parenteral opioids for management of dyspnea. Research is still needed to specify the opioid, dose, and schedule that are most effective. Although new research has been reported about transmucosal fentanyl and nebulized furosemide as interventions to relieve dyspnea, data are insufficient to make a recommendation for practice regarding those medications at this time.

With respect to use of supplemental oxygen to relieve dyspnea, two additional, randomized, controlled trials did not demonstrate a significant difference between air and oxygen in the hypoxic subgroups. On average, patients improved subjectively with air and oxygen. The evidence, however, is not strong or sufficient enough to make a practice recommendation, and use of oxygen or air to palliate dyspnea remains in the effectiveness not established category.

Three new research studies are added to the nonpharmacologic evidence. Two continue to support the effectiveness of a comprehensive cognitive behavioral approach, and one fails to show the benefit of acupuncture to relieve dyspnea. Again, the data are not considered conclusive to move those interventions out of the effectiveness not established category. Future research findings are anticipated and needed to build the evidence base for this challenging and sometimes refractory symptom.

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- Consume at least 8–10 8 oz servings of liquid per day. Choose liquids such as Gatorade®, diluted fruit juice (50:50 juice and water), broth, or noncaffeinated soft drinks.
- Avoid substances that contain sorbitol, such as sugar-free candy and sugar-free chewing gum. (Foods, beverages, and medications can contain sorbitol.)
- Choose foods that bulk stools.
  - **High in soluble fiber (pectin-containing foods):** applesauce, oatmeal, bananas, cooked carrots, and rice
  - **Low in insoluble fiber:** rice, noodles, Cream of Wheat®, well-cooked eggs, bananas, white toast, canned or cooked fruit without skin, bananas, skinned turkey or chicken, fish, and mashed potatoes
- Choose foods high in sodium and potassium (e.g., bananas, peach nectar, apricot nectar, oranges, potatoes) because of the loss of those electrolytes.

Figure 1. General Diet Strategies to Manage Diarrhea

Fatigue (2006)

The systematic critical appraisal of the evidence supporting interventions to prevent and treat fatigue during and following cancer recently was updated through July 2008. Search strategies comparable to those used in the initial review were applied (Mitchell, Beck, Hood, Moore, & Tanner, 2007). More than 150 studies, systematic reviews, and meta-analyses were identified for critical appraisal, almost double the number analyzed in 2005. Exercise was still the only intervention supported by sufficient weight of evidence that it could be recommended for practice. Additional evidence was available in support of interventions that were likely to be effective, such as screening for potential etiologic factors, energy conservation and activity management, education, measures to optimize sleep quality, relaxation, massage, and healing touch. Adding to the empiric evidence that complementary, energy-based interventions may be valuable in fatigue management, a single-arm pilot trial provided preliminary support that polarity therapy, an intervention hypothesized to promote healing, relaxation, and well-being by balancing energy flow, may be effective in reducing fatigue. However, the additional empiric evidence in support of those interventions was predominantly from small randomized trials performed at single centers or from pilot studies. Moreover, in some cases those studies were underpowered or showed negative results for the outcome of fatigue.

Evidence continues to support the correction of anemia less than 10 g/dl with erythropoiesis stimulating agents (ESAs) as effective in the treatment of fatigue. However, the use of these agents specifically for the management of fatigue must be considered in light of mounting evidence that ESAs can have serious adverse events, including an increased risk of thrombotic events. Another concern is that ESAs may support or extend tumor growth in patients with certain types of cancer. The potential benefits of ESAs therefore must be balanced with their potential to create harm. The authors of the PEP resources concluded that, although ESAs may improve fatigue in severely anemic patients with cancer, national clinical practice guidelines and the guidance of the U.S. Food and Drug Administration should be used to direct the management of individual patients receiving ESAs, including decisions about treatment initiation and discontinuation, monitoring, and the use of supplemental iron.

Interventions that continue to have some support for their effectiveness in managing fatigue included individual and group psychotherapy and the pharmacologic agents paroxetine, methylphenidate, donepezil, bupropion, and modafinil. Interventions added to the effectiveness not established category and for which preliminary evidence showed they may be effective for cancer-related fatigue included cognitive behavioral therapy for fatigue or concurrent symptoms, structured rehabilitation, Reiki, hypnosis, mindfulness-based stress reduction, and art or music therapy. However, for all of those interventions, the data supporting their efficacy were still of insufficient quality because of nonrandomized study designs or flaws in the conduct of the study, data analysis, or reporting.

Although more research is needed, new evidence also has emerged in support of several additional pharmacologic agents that offer the potential to improve fatigue. Pharmacologic treatments for which preliminary evidence exists of potential benefit include venlafaxine, sertraline,

infliximab, etancercept, the nutraceuticals, lectin standardized mistletoe extract, essiac, and a combination of dietary supplements, lipid replacement, and antioxidant supplementation. The evidence in support of these interventions is underdeveloped. The studies were limited by small sample sizes; nonrandomized, uncontrolled study designs; and failure to control for baseline differences in fatigue between the study and comparison groups.

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Prevention of Infection (2006)

Cancer and cancer treatment-related immune dysfunction predispose patients with cancer to infection. Infection is a major cause of morbidity and mortality, and nurses play an integral role in infection prevention. The PEP resource establishes recommendations for interventions to prevent infection based on current research and the strength of the evidence. The summary will highlight the updates to the PEP resource based on the literature through May 2008.

The most important intervention to prevent infection is hand hygiene. When hands are not visibly soiled or contaminated, hands may be cleansed with soap and water or alcohol-based hand rubs. If hands are visibly soiled or contaminated with proteinaceous material, then soap and water should be used.

This recommendation was amended to specify that if patients have suspected or known infection with *C. difficile* or *bacillus*, mechanical removal with soap and water is required for hand hygiene because spore-forming bacteria are not killed by alcohol (Boyce, Pittet, Healthcare Infection Control Practices Advisory Committee, Society for Healthcare Epidemiology of America, Association for Professionals in Infection Control, & Infectious Diseases Society of America, Hand Hygiene Task Force, 2002; Siegel, Rhinehart, Jackson, & Chiarello, 2007a).

Updated guidelines for isolation precautions to prevent the transmission of infection in healthcare settings were published by the Centers for Disease Control and Prevention (Siegel et al., 2007a). Private rooms are recommended to decrease the transmission of infection for all patients. Routine donning of gowns when entering high-risk units now is deemed unnecessary. However, contact precautions, including gowns and gloves, are indicated if patients have a multidrug-resistant infection (Siegel et al., 2007a, 2007b).

The National Comprehensive Cancer Network 2008b guidelines changed their focus from febrile neutropenia to a more inclusive document on cancer-related infections, reflecting the heterogeneity of immune compromise in patients with cancer. Recommendations that were added to the PEP resource based on the guidelines include: penicillin prophylaxis to prevent pneumococcal infection in patients who have undergone splenectomy or who are functionally asplenic, cytomegalovirus prophylaxis for high-risk patients, and hepatitis B prophylaxis for at-risk patients.

The most noteworthy update to the PEP resource is a change in the recommendation for neutropenic (low-microbial) diets from effectiveness not established to effectiveness unlikely. In the 1970s, research established that foods, particularly fresh fruits and vegetables, contain *Escherichia coli*, *Pseudomonas aeruginosa*, and other Gram-negative bacilli that can cause life-threatening sepsis and pneumonia (Gardner et al., 2008). Those observations led to the use of a neutropenic diet that restricts fresh fruits and vegetables. Although dietary restrictions for neutropenic patients with cancer have been common practice for more than three decades, a surprising paucity of research links pathogens from fresh fruits and vegetables with infection in neutropenic patients. Almost all institutions recommend dietary restrictions for neutropenic patients with cancer and the most common recommendation is to avoid unwashed fruits and vegetables (Larson & Nirenberg, 2004; Moody, Charlson, & Finlay, 2002; Smith & Besser, 2000; Somerville, 1986; Wilson, 2002). Most studies evaluating the effect of a neutropenic diet on the risk of infection are confounded by insufficient sample size and institutional manipulations such as protected environments and variation in dietary restrictions. However, research is accumulating that demonstrates that neutropenic diets are unlikely to decrease the risk of infection. Thirty percent of 23 outpatients participating in a study of the effect of this diet on infection rate were not compliant with the neutropenic diet and infection rates were similar in compliant and noncompliant patients (DeMille, Deming, Lupinacci, & Jacobs, 2006). A small trial in 19 children found no difference in rates of febrile neutropenia according to whether patients were randomly assigned to a U.S. Food and Drug Administration–approved food safety diet or a diet that included restriction of fresh fruits and vegetables. Similarly, a randomized trial of 20 patients with hematologic malignancies found no differences in gut colonization or infection according to whether a normal hospital diet or a low-bacterial diet was used (van Tiel et al., 2007). The largest trial to date is a well-designed study including 153 patients who were receiving induction chemotherapy for acute myelogenous leukemia (AML) or myelodysplastic syndrome (MDS) in a protective environment (HEPA-filtered private room) who were randomized to a diet with fresh fruits and vegetables or a diet that restricted raw fruits and vegetables (Gardner et al.). Patients received routine antimicrobial prophylaxis with levofloxacin, valacyclovir and an antifungal agent (itraconazole, voriconazole, or lipid amphotericin B) per protocol; growth colonizing stimulating factor was not used routinely. No significant difference in the rate of infection, bacteremia, fungemia, fever of unknown origin, rate of enteric organisms cultured from the blood, pneumonia, or survival was observed. The authors concluded that a diet including raw fruits and vegetables did not increase the risk of infection or death in patients with MDS or AML treated with remission induction chemotherapy in a protective environment when compared to a diet that restricts raw fruits and vegetables. Additional research is warranted to replicate the findings and confirm the results in other populations of patients with cancer, particularly patients with solid tumors undergoing chemotherapy and patients not treated with routine antibiotic prophylaxis. Nonetheless, the existing data suggest that low microbial diets are unlikely to be effective to prevent infection in neutropenic patients with cancer.

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Lymphedema (2008)

Although the lymphedema PEP resource was released in May 2008, at that time the review of the literature was about eight months old. By May 2008, significant contributions to the research warranted adding new categories and further supported the evidence in other categories. In addition, one category was moved based on additional review and discussion.

The first new category added was "maintaining optimal body weight: BMI (body mass index) less than 30 and weight loss as interventions for post-breast cancer lymphedema." Increasing evidence supports that being overweight is a risk factor for developing lymphedema; in one study, weight loss by whatever means appeared to benefit arm volume.

Another new category added was "compression garments." This category was added as effectiveness not established because studies are under way examining garments as a risk-reduction intervention. In addition, limited evidence supports garments as a stand-alone intervention for early lymphedema.

The other change to the resource was to move one intervention to a different level of evidence category. Low-level laser therapy was moved to effectiveness not established. Additional randomized clinical trials with larger samples, true control group, and longer follow-up are needed.

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Mucositis (2007)

Studies published through May 2008, were reviewed for the update to the original PEP resource for managing oral mucositis. The cryotherapy intervention was modified to indicate it is effective for mucotoxic chemotherapy (bolus 5-FU and melphalan) and that recent studies suggest a decrease in oral mucositis with longer durations of cryotherapy. The palifermin intervention was modified to indicate that it is now acceptable for use in allogeneic as well as autologous transplantation settings. Although one study (Rosen et al., 2008) did demonstrate a statistically significant reduction in grade 2 or higher mucositis for patients with colon cancer, the results have been questioned because cryotherapy was not used despite its known benefits with 5-FU–induced mucositis. Additional study of palifermin is needed to determine its use beyond the transplant setting.

The review also resulted in the inclusion of several new agents to the PEP resource. The following agents were added to the effectiveness not established category: caphosol, fluoride chewing gum, gelclair, honey, and L-alanyl-L-glutamine. Chlorhexidine, which previously was included only in the not recommended for practice section, also was added to this section because of a recent study that demonstrated a benefit of chlorhexidine rinse over normal saline and cryotherapy for severity and duration of mucositis. The study clearly stated that the chlorhexidine was alcohol-free (Sorensen, Skovsgaard, Bork, Damstrup, & Ingeberg, 2008). Chlorhexidine with alcohol has not been found to be effective in reducing mucositis and remains not recommended for practice. The evidence for povidone-iodine also has been updated because of two small trials that demonstrated a decreased incidence of severe mucositis.

New agents added to the effectiveness unlikely category include misoprostol, topical vitamin E, and proteolytic enzymes trialed under the name Wobe-Mugos E.

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Pain (2007)

The pain PEP resource recently was updated with several notable changes. Under recommended for practice, the opioids section includes the following changes and additions. Greater emphasis is placed on managing breakthrough pain with immediate-release opioids. Oral transmucosal formulations are effective immediate-release opioids that should be considered for breakthrough pain (Freye, Levy, & Braun, 2007; Mercadante et al., 2007; Slatkin, Xie, Messina, & Segal, 2007). Of note, buccal (transmucosal) fentanyl absorption does not appear to differ in patients with mucositis (Darwish, Kirby, Robertson, Tracewell, & Jiang, 2007). Regarding opioid side effects, evidence suggests that adverse effects differ among opioids, so providers should consider switching if adverse effects are significant (Rodriguez et al., 2007; Swarm et al., 2007). For dosing of opioids, recent research on fentanyl identified two factors that can affect dosing (Hagen, Fisher, Victorino, & Farrar, 2007). One is age; older individuals may require lower doses. Another factor is type of pain; individuals with neuropathic pain may require higher doses. Lastly, in the opioid section is an important note on tramadol. The concurrent use of tramadol and transdermal fentanyl has not been investigated thoroughly and should be administered with caution because some studies suggest a synergistic effect (Marinangeli et al., 2007).

Tetrodotoxin was added to effectiveness not established. Textrodotoxin is a neurotoxin used for nociceptive and neuropathic pain; however, the few studies with patients with cancer demonstrated mixed findings (Hagen, Fisher, Lapointe, et al., 2007; Hagen, Fisher, Victorino, et al., 2007; Hagen et al., 2008). In addition, a minimal efficacious dose has not been established.

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Peripheral Neuropathy (2007)

Three new studies were added to the peripheral neuropathy PEP resource. Lamotrigine, an anti-epileptic and mood stabilizer, has been studied as a potential treatment for chemotherapy-induced peripheral neuropathy. Lamotrigine's mechanism of action is not fully known, but it is thought to act through an effect on sodium channels to stabilize neuronal membranes and modulate presynaptic transmitter release of excitatory amino acids. In a phase III, randomized, double-blind, placebo-controlled trial, 125 patients with chemotherapy-induced peripheral neuropathy were randomized to either lamotrigine or placebo. No significant differences were noted between the two groups on either pain or efficacy. The study concluded that lamotrigine was ineffective in treating chemotherapy-induced peripheral neuropathy (Rao et al., 2008).

Gabapentin, an anti-epileptic agent, was tested in a phase III, randomized, double-blind, controlled trial of 115 patients

with symptomatic chemotherapy-induced peripheral neuropathy. No significant differences were reported between the groups on scores of pain, symptom distress, or mood state, with the exception of the McGill Pain Rating Index, which showed lower pain in the gabapentin group at the end of the first six-week treatment period. The study failed to demonstrate the benefit of gabapentin to treat chemotherapy-induced peripheral neuropathy symptoms (Rao et al., 2008).

Glutamine, a naturally occurring nonessential amino acid, was tested in a nonrandomized pilot study to evaluate whether oral glutamine was effective in reducing the incidence and severity of peripheral neuropathy in patients receiving oxaliplatin. Eighty-six patients with colorectal cancer received glutamine 15 g twice daily for seven days every two weeks, starting on the day of treatment. Glutamine supplementation significantly reduced the incidence and severity of oxaliplatin-induced peripheral neuropathy. The percentage of grade 3–4 sensory neuropathy was lower in the glutamine group after six cycles of treatment. Results suggest glutamine has a potential neuroprotective effect in patients treated with oxaliplatin, but larger placebo-controlled, randomized trials are needed to confirm additional recommendations (Wang et al., 2007).

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Sleep-Wake Disturbances (2006)

The updated sleep-wake disturbances PEP resources include 13 new published studies. The intervention studies were categorized according to type of intervention determined during the development of original PEP resources and the strength of the evidence (Page, Berger, & Johnson, 2006).

The major revision to the 2008 PEP resource was that cognitive behavioral therapy (CBT) moved to the likely to be effective category. The recommendation is based on four large, well-conducted, randomized studies (Arving et al., 2007; Epstein & Dirksen, 2007; Espie et al., 2008; Vilela et al., 2006). All of the intervention studies reported positive benefits of the intervention on patients' self-reported sleep. Two studies were conducted during active treatment and two were tested among cancer survivors. Additional evidence from several smaller studies supported these findings. Key components of the CBT interventions include stimulus control, sleep restriction, and relaxation therapy. However, the studies in this intervention category have limitations. They occur at various times in the treatment trajectory, in various cancer populations, and involve various delivery formats. Evidence is mounting that CBT interventions improve sleep in patients with cancer.

Several recent studies reported positive benefits of complementary therapies to improve sleep-wake disturbances, but only one (Cohen & Fried, 2007) was a large randomized, controlled trial. Complementary therapies that have been tested to improve sleep include mindfulness-based stress reduction, autogenic training, healing touch, yoga, massage, muscle relaxation training, and expressive writing. Although evidence for this category has not been established, the interventions offer promise. No recent study tested a psycho-education/information intervention. One small study reported positive benefits on sleep from an intervention that tested the effects of relaxation and exercise. Large randomized clinical trials are needed to demonstrate the effectiveness of complementary therapies, education or information, and exercise interventions on sleep-wake disturbances.

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