Chemotherapy-induced nausea and vomiting (CINV) continues to have a considerable effect on the physical and psychological well-being of patients with cancer, despite significant advances in antiemetic drugs since the 1990s. This article reviews and summarizes past and current empirical evidence related to interventions for CINV. A resource that summarizes evidence-based interventions for CINV is critical for effective management of this distressing symptom. Pharmacologic and nonpharmacologic interventions are appraised. Finally, gaps in the literature and opportunities for research, education, and practice changes are discussed.

Nursing-sensitive patient outcomes are outcomes that are attained through or are significantly impacted by nursing interventions. The interventions must be within the scope of nursing practice and integral to the processes of nursing care.

Methods

The definitions of nausea and vomiting from the Oncology Nursing Sensitive Patient Outcomes Measurement Summaries (ONS, n.d.) were used to guide the review of strategies to manage CINV.

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The purpose of the measurement summaries is to provide a centralized resource regarding the measurement of specific oncology nursing-sensitive patient outcomes. In addition to definitions, the summaries provide references to integrative reviews and meta-analyses, guidelines and standards of practice, tables of tools, outcome measurement instrument references, summaries of key evidence and gaps, recommendations, and links to current research. Nausea is defined as “an unpleasant feeling in the back of the throat and stomach that may or may not result in vomiting” (Rhodes & McDaniel, 2004, p. 1). Vomiting is defined as “a forceful contraction of the abdominal (stomach) muscles to cause stomach contents to come up through the mouth” (Rhodes & McDaniel, 2004, p. 1). Specific types of nausea are defined because some interventions are more effective for certain types of nausea. Anticipatory nausea occurs before patients receive their chemotherapy treatments. It is a conditioned response and can occur after a prior negative experience with chemotherapy. Prevention is key, especially early in therapy (National Comprehensive Cancer Network [NCCN], 2007). Acute nausea usually occurs within a few minutes to several hours after chemotherapy administration and often resolves in the first 24 hours (NCCN). Delayed nausea occurs more than 24 hours after chemotherapy administration. It often peaks 48–72 hours after chemotherapy and can last six to seven days (NCCN).

A systematic database search was conducted to identify research on interventions for nausea and vomiting. Computerized searches of CINAHL®, MEDLINE®, HealthSTAR, Biological Abstracts®, Dissertation Abstracts, ProQuest® Digital Dissertations and Theses, the Cochrane Collection, Database of Abstracts of Reviews of Effects, EMBASE, PsycINFO, and Health Source: Nursing/Academic Edition (via EBSCO) databases were performed using the search terms listed in Figure 1. Database searches were performed by the project team leader, researcher, and the ONS information resources supervisor, who is a medical librarian. At first, citations from 2000–2005 were searched and retrieved. But because data were limited for nonpharmacologic interventions, the search was expanded to cover publications from 1988–2005. The abstract of each study was reviewed, and those meeting the inclusion criteria were identified for further critique. The articles’ reference lists also supplied additional studies.

Studies were selected based on the following inclusion criteria: findings were published in English, the sample consisted of adult patients with cancer who were receiving or had received chemotherapy, the publication was a complete report of a study, nausea and/or vomiting were the dependent variable(s), nausea and/or vomiting were measured using an instrument designed to measure the variables or were a subscale of an instrument that was reported separately, and the publication contained guidelines for prevention, management, or treatment for nausea and/or vomiting.

### Critical Review of the Evidence

Three subgroups of the project team, each which included an advanced practice nurse and a staff nurse, reviewed the articles using standardized worksheets to promote a systematic examination of each study. The subgroups had guidance from a nurse researcher experienced in CINV and an ONS Research Team member. The research nurse provided guidance and mentored the subgroups in review of the literature and in practical questions and applications. The subgroups prepared tables of evidence organized by intervention category or subcategory, including the following information: author and year, intervention characteristics (e.g., delivery method, dose), sample characteristics (e.g., size, age, gender, race, ethnicity, disease and treatment characteristics, treatment phase), setting (e.g., inpatient, outpatient, community; number of sites), study design, conceptual model, nausea and vomiting measures, results and conclusions, limitations, cautions or contraindications, special training to deliver the intervention and its cost, ONS levels of evidence rating, ONS PEP weight-of-evidence category rating (see Table 1), and comments or directions for future research.

### Effective Interventions for Prevention and Treatment

Pharmacologic interventions to prevent, manage, and treat CINV were the only interventions that were supported by enough strong empirical evidence of effectiveness to allow them to be recommended for practice. The research on nonpharmacologic interventions lacked sufficient empirical evidence to be recommended for practice. However, several nonpharmacologic interventions were evaluated as likely to be effective for the prevention, management, and treatment of CINV when used in conjunction with pharmacologic interventions. Interventions that are likely to be effective are supported by evidence that is less well established than for those listed under recommended for practice. Examples include one well-conducted randomized, controlled trial with fewer than 100 patients or at one or more study sites and guidelines developed by consensus or expert opinion without synthesis or quality rating. Included in the likely to be effective interventions are acupuncture, acupressure, guided imagery, music therapy, progressive muscle relaxation, and psychoeducational support and information. Figures 2 and 3 summarize the interventions supported by empirical studies, or lack thereof, and by expert opinion.

Pharmacologic interventions for nausea and vomiting are recommended based on the type of nausea and/or vomiting and the emetogenicity of the chemotherapy. The NCCN (2007) Antiemesis Practice Guidelines and the results of the 2004 Perugia International Antiemesis Consensus Conference (Roila, Hesketh, & Herrstedt, 2006) support the use of benzodiazepines such as alprazolam and lorazepam for anticipatory nausea and vomiting. A 5-HT<sub>3</sub> receptor antagonist such as palonosetron, granisetron, ondansetron, or dolasetron; a corticosteroid such as dexamethasone; and aprepitant and a benzodiazepine are...
recommended for acute nausea and vomiting associated with moderately and highly emetogenic chemotherapy.

Acupuncture involves the insertion of wire-thin needles into acupoints along a specific meridian of the body. Acupuncture at the P6 point (see Figure 4) is used frequently to treat nausea and vomiting. The P6 acupoint is the most commonly investigated and accessible acupoint, located on the anterior surface of the forearm, approximately three finger widths from the wrist crease (Klein & Griffiths, 2004). A review of the literature that examined the effect of acupuncture on CINV found that P6 acupuncture plus antiemetics was more effective than antiemetics alone or antiemetics with placebo acupuncture (Mayer, 2000). Electroacupuncture with antiemetics was more effective in controlling emesis than placebo acupuncture with antiemetics or antiemetics alone in a randomized, controlled trial of 104 women receiving chemotherapy (Shen et al., 2000). A meta-analysis by Ezzo et al. (2005) found that acupuncture was effective in reducing the incidence of acute vomiting but not the severity of acute nausea. Three studies reviewed by Ezzo et al. evaluated delayed vomiting and did not support the intervention. The pooled results of 11 studies using acupuncture-point stimulation plus antiemetics for CINV showed significant reduction in acute vomiting and marginal statistical significance for reducing acute nausea.

Acupressure is the application of pressure to acupoints digitally and may be beneficial for patients who cannot tolerate needles. The P6 point is the most commonly used acupressure point because of ease of access. Two controlled trials with a total of 482 adult subjects found that acupressure may decrease nausea in patients receiving chemotherapy (Klein & Griffiths, 2004). Acupressure was effective in Korean patients with gastric cancer receiving chemotherapy (Shin, Kim, Shin, & Juon, 2004). Additional work is needed before conclusively advising patients on the efficacy of acupressure in preventing and treating CINV.

A systematic review, a meta-analysis, and five randomized, controlled trials (Arakawa, 1997; Ezzone, Baker, Rosselet, & Terepka, 1998; Luebbert, Dahme, & Hasenbring, 2001; Molassiotis, Yung, Yam, Chan, & Mok, 2002; Redd, Montgomery, & DuHamel, 2001; Sahler, Hunter, & Liesveld, 2003; Troesch, Rodehaver, Delaney, & Yanes, 1993) found that guided imagery, music therapy, and progressive muscle relaxation reduce nausea and/or vomiting. The nonpharmacologic interventions may be useful in combination with antiemetics. Many of the strategies may be helpful interventions for the prevention and treatment of anticipatory nausea and vomiting. In many studies, at least two interventions were used together (e.g., guided imagery with music therapy).

The use of guided imagery was supported by a meta-analysis of 15 studies. Clinically significant reductions in nausea were found, but the effect on vomiting could not be analyzed because of the low incidence of vomiting in the studies that were reviewed (Lueebbert et al., 2001). Molassiotis et al. (2002), in an experimental study of 71 Chinese women with breast cancer, found that 25 minutes of progressive muscle relaxation with 5 minutes of guided imagery was superior to standard antiemetic treatment alone in managing acute and delayed nausea and vomiting. In many studies, at least two interventions were used together (e.g., guided imagery with music therapy).

Progressive muscle relaxation as a complementary therapy may be beneficial for preventing or managing nausea and vomiting in patients receiving chemotherapy. Several studies examined progressive muscle relaxation either alone or in combination with other interventions. An experimental study of 71 patients...
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and it engages the senses simultaneously (Schneider, Prince-Paul, 2004). A case-control study of bone marrow transplant recipients also demonstrated decreased nausea with music therapy (Ezzone et al., 1998). A randomized study with 33 patients undergoing bone marrow transplantation found less nausea and fewer instances of vomiting in the group that received music therapy (Ezzone et al., 1998). A case-control study of bone marrow transplant recipients also demonstrated decreased nausea with music therapy (Sahler et al., 2003).

The use of psychoeducational support and information as an intervention may be effective in managing CINV. Informational massage and aromatherapy as interventions for nausea. The massage groups experienced a complete remission of anticipatory nausea and vomiting. Fourteen of 16 patients experienced a significant decrease in nausea following the first massage and a significant reduction in nausea after massage overall. The effect of aromatherapy was more difficult to assess overall. The effect of aromatherapy was more difficult to assess overall. The effect of aromatherapy was more difficult to assess overall.

The following interventions may be effective in the prevention and management of chemotherapy-induced nausea and vomiting.

- Oral and IV antiemetics are equally effective.
- The period of expected nausea and vomiting should be covered with appropriate antiemetics (anticipatory, acute, and delayed period for at least four days).
- The lowest efficacious dose of the antiemetics should be used.
- Selection of antiemetics should be based on emetic potential of the chemotherapy agent(s), as well as patient factors.
- Consider the potential causes of nausea and emesis in patients with cancer that may be contributing factors.

Although evidence is limited, experts recommend the following dietary interventions in patients receiving chemotherapy to minimize nausea and vomiting.

- Eat smaller, more frequent meals.
- Reduce food aromas and other stimuli with strong odors.
- Avoid foods that are spicy, fatty, or highly salty.
- Take antiemetics prior to meals so that the effect is present during and after meals.
- Repeat previous measures and foods that minimize nausea (e.g., "comfort foods").

Figure 3. Chemotherapy-Induced Nausea and Vomiting Interventions and General Principles Supported by Expert Opinion

Note. Based on information from Polovich et al., 2005.
Anecdotal evidence supports the efficacy of lemon, peppermint, and chamomile, but no research has examined their use in CINV. With the increased attention on complementary and integrative therapies in cancer, additional studies are needed to validate the safety of herbal interventions as well as the combination with other traditional interventions to prevent, manage, and treat CINV.

Oncology nursing staff must be educated about evidence-based interventions and assessment of individual patient characteristics. For example, nurses should assess risk factors for nausea and vomiting, a patient’s physical and psychological capability of participating in or performing the interventions, and accessibility and cost of the interventions before developing plans of care. ONS PEP resources (pocket cards and the Outcomes Resource Area located at www.ons.org/outcomes), and discussion of the resources in a journal club format, are strategies that can be used in practice to educate nurses about evidence-based interventions for nausea and vomiting. Staff knowledge of an intervention, including the definition, and staff members’ ability to learn, perform, and teach the intervention should be assessed and developed when implementing evidence-based interventions.

**Conclusion**

Clinicians should continually work to improve the symptom experience for patients receiving chemotherapy. Nausea and vomiting, despite many improvements in treatment, still are feared by patients and still are a challenge for clinicians to overcome. Prevention of CINV is key, and evidence-based interventions can help to better control the problem. The current review shows the critical need for improvements in the gaps of knowledge and research. Oncology nurses are in an ideal situation to be leaders or “symptom experts” by asking critical questions in practice, identifying evidence-based interventions, applying the interventions in the clinical setting, and assessing the impact of the interventions. These steps would enable oncology nurses to demonstrate the impact of nursing interventions on patient outcomes.

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Appendix. Putting Evidence Into Practice Card on Preventing and Treating Fatigue

What Interventions Are Effective in Preventing and Treating Chemotherapy-Induced Nausea and Vomiting?

**RECOMMENDED FOR PRACTICE**

Interventions for which effectiveness has been demonstrated by strong evidence from rigorously designed studies, meta-analyses, or systematic reviews and for which the expectation of harms is small compared to the benefits.

**Anticipatory nausea and/or vomiting**

Nausea and/or vomiting that occurs before patients receive their next chemotherapy treatment. It is a conditioned response and can occur after a negative past experience with chemotherapy. Prevention is key, especially early in therapy.

- **Benzodiazepines**
  - Alprazolam 0.5–2 mg po tid, beginning the night before treatment, or
  - Lorazepam 0.5–2 mg po on the night before and the morning of treatment

- Utilization of treatments for acute and delayed nausea and vomiting

**Acute and delayed nausea and/or vomiting: Moderately emetogenic chemotherapy**

Acute nausea and/or vomiting usually occurs within a few minutes to several hours after chemotherapy administration and often resolves within the first 24 hours. Delayed nausea and/or vomiting occurs more than 24 hours after chemotherapy administration. It often peaks 48–72 hours after chemotherapy and can last 6–7 days.

- **5-HT₁ receptor antagonists**
  - Palonosetron 0.25 mg IV on day 1, or
  - Granisetron 2 mg po, 1 mg po bid, or 1 mg IV on day 1, or
  - Ondansetron 16–24 mg po or 8–32 mg IV on day 1, or
  - Dolasetron 100 mg po or IV on day 1, and

- **Corticosteroids**
  - Dexamethasone 12 mg po or IV on day of treatment, or
  - Metoclopramide 20–40 mg po every 4–6 hours or 1–2 mg/kg every 3–4 hours ± diphenhydramine 25–50 mg po or IV every 4–6 hours, or
  - Benzodiazepine (may or may not be given with other antiemetics because of sedating effects)
    - Lorazepam 0.5–2 mg po or IV every 4–6 hours

**Acute and delayed nausea and/or vomiting: Low emetogenic chemotherapy**

Acute nausea and/or vomiting usually occurs within a few minutes to several hours after chemotherapy administration and often resolves within the first 24 hours. Delayed nausea and/or vomiting occurs more than 24 hours after chemotherapy administration. It often peaks 48–72 hours after chemotherapy and can last 6–7 days.

- **5-HT₁ receptor antagonists**
  - Ondansetron 8 mg po or IV daily, or
  - Granisetron 1–2 mg po daily, 1 mg po bid, or 1 mg IV, or
  - Dolasetron 100 mg po or IV

- **Corticosteroids**
  - Dexamethasone 8 mg po or IV daily, or

- **5-HT₁ receptor antagonists**
  - Ondansetron 8 mg po or IV daily, or
  - Granisetron 1–2 mg po daily, 1 mg po bid, or 1 mg IV, or
  - Dolasetron 100 mg po or IV

- **Substituted benzamides**
  - Metoclopramide 0.5 mg/kg po or IV every 6 hours or 20 mg po qid ± diphenhydramine 25–50 mg po or IV every 4–6 hours pm

**Acute and delayed nausea and/or vomiting: Low emetogenic chemotherapy**

- **No antiemetic agent**, or
- **Corticosteroid**
  - Dexamethasone 12 mg po or IV on day of treatment, or
- **Phenothiazine**
  - Prochlorperazine 10 mg po or IV every 4–6 hours, or
  - Metoclopramide 20–40 mg po every 4–6 hours or 1–2 mg/kg every 3–4 hours ± diphenhydramine 25–50 mg po or IV every 4–6 hours, or
  - Benzodiazepine (may or may not be given with other antiemetics because of sedating effects)
    - Lorazepam 0.5–2 mg po or IV every 4–6 hours

**Breakthrough nausea and/or vomiting**

Nausea and/or vomiting that occurs despite prophylactic antiemetics and requires “rescue” antiemetic therapy.

Consider using a drug from a class not previously used.

- **Corticosteroids**
  - Dexamethasone 12 mg po or IV daily, if not previously given, or
  - Metoclopramide 20–40 mg po every 4–6 hours or 1–2 mg/kg every 3–4 hours ± diphenhydramine 25–50 mg po or IV every 4–6 hours, or
  - Benzodiazepine (may or may not be given with other antiemetics because of sedating effects)
    - Lorazepam 0.5–2 mg po or IV every 4–6 hours

**Likely to be effective**

Interventions for which the evidence is less well established than for those listed under “Recommended for Practice”.

Nonpharmacologic interventions are to be used in conjunction with pharmacologic interventions.

Provide referral to appropriate practitioners as needed.

On days 2–4, consider:

- **Corticosteroids**
  - Dexamethasone 8 mg po or IV daily, or

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Acupuncture
A method of producing analgesia or altering the function of a body system by inserting fine, wire-thin needles (about the diameter of a strand of hair) into acupoints along a specific meridian on the body. The insertion of the needles may cause momentary discomfort. The needles are twirled or energized electronically or are warmed and left in place for approximately 20–30 minutes. The acupuncture point P6 is most commonly used for treatment of nausea and vomiting.6
• Study populations: People with various carcinomas; women with high-risk breast cancer receiving myeloablative chemotherapy; and patients with mixed cancer types6–10

Acupressure
A therapeutic technique of applying digital pressure or acustimulation bands in a specified way on designated points on the body. By applying pressure to one or more acupoints, practitioners can correct imbalances by stimulating or easing energy flow. The acupoint most commonly investigated and accessible is P6, which is located on the anterior surface of the forearm, approximately three finger-widths from the wrist crease.11
• Study populations: Women undergoing adjuvant chemotherapy for breast cancer, receiving CMF (cyclophosphamide, methotrexate, 5-fluorouracil) or a doxorubicin-containing regimen; postoperative patients with gastric cancer receiving their first cycle of chemotherapy with cisplatin and fluorouracil; and patients with other mixed cancer types11–13

Guided imagery
Forming a relaxing, pleasing mental image, often preceded by relaxation techniques and/or music14

Music therapy
The application of music to influence physiologic, psychological, and emotional functioning during chemotherapy. It often is used with other behavioral techniques, such as relaxation.15

Progressive muscle relaxation
Focusing on and isolating various muscle groups while moving progressively up or down the body to establish a state of deep relaxation. Focused breathing, with all attention centered on the sensations of breathing, including the rhythm and rise and fall of the chest, often is used along with progressive muscle relaxation.15
• Study populations: Patients with mixed cancer types; women with breast cancer receiving doxorubicin and cyclophosphamide; bone marrow transplant recipients with leukemia, lymphoma, and other solid tumors; and patients receiving cisplatin-based chemotherapy, some of whom were chemotherapy naive, whereas others had previously received chemotherapy14–20

Psychoeducational support and information
The use of counseling, support, and structured educational interventions, through the use of interactive media (audiotapes, computer-assisted, telephone, video) to provide specific information on self-care measures for patients with CINV21
• Study populations: Women receiving cisplatin-based chemotherapy for ovarian cancer; and women receiving chemotherapy for breast cancer21,22

Virtual reality
A computer-simulated technique that allows individuals to hear and feel stimuli that correspond with a visual image. Individuals wear a headset that projects an image with an accompanying sound. Virtual reality is interactive, and it engages the senses simultaneously.23
• Study populations: Patients with mixed cancers, primarily women with breast and ovarian cancers24

Interventions for which insufficient data or data of inadequate quality currently exist

Nonpharmacologic interventions are to be used in conjunction with pharmacologic interventions.
Provide referral to appropriate practitioners as needed.

Exercise
Any planned, structured, and repetitive bodily movement performed that incorporates cardiovascular, strength, and/or flexibility conditioning of any intensity with the intent of improving or maintaining one or more components of physical fitness, performance, or health.25,26
• Study population: Women with breast cancer receiving chemotherapy (not doxorubicin) who had received at least three treatments prior to study27

Hypnosis
A behavioral intervention process whereby patients learn to focus attention on thoughts or images unrelated to a source of distress (i.e., nausea or vomiting). The patient is relaxed through a meditation-like excursion to pleasant locations and/or activities while a clinician introduces suggestions of calmness and well-being.28
• Study population: Patients who had received at least four cycles of chemotherapy combined with a 5-HT3 receptor antagonist who developed nausea and vomiting within the first six hours prior to receiving chemotherapy (drugs included cisplatin, carboplatin, cyclophosphamide, dacarbazine, doxorubicin, and epirubicin)28

Massage/aromatherapy
An ancient form of healing that involves the therapeutic manipulation of soft tissues of the body by various hand movements (e.g., rubbing, kneading, pressing, rolling, slapping, tapping). Massage therapy can elicit the relaxation response as measured by decreases in heart rate, blood pressure, and respiratory rate. Often, massage is complemented by the use of aromatherapy, which is the use of essential oils that are combined with a carrier cream or oil to manipulate the soft tissues.29
• Study populations: Autologous bone marrow transplant recipients; hospital inpatients29–32

Acustimulation with wristband device
Stimulation of the P6 point by transcutaneous electrical stimulation through a wristband device. A wristband device currently available is the ReliefBand®, a class-2 device approved by the U.S. Food and Drug Administration for the treatment of CINV. The device delivers slow, weak, electrical pulses to the P6 point via two metallic electrodes. Patients can adjust the electrical output to deliver 10–35 mAmmps/pulse.33
• Study populations: Women with breast cancer receiving their second course of chemotherapy (doxorubicin-based); chemotherapy-naive patients with mixed cancers receiving cisplatin or doxorubicin; and those with mixed cancers receiving moderately high to highly emetogenic chemotherapy33–36

Ginger
A plant herb used in traditional Chinese and Indian medicine for the treatment of nausea and vomiting. Ginger has aromatic, spasmyloytic,
carminative, and absorbent properties that suggest direct effects on the gastrointestinal tract.\textsuperscript{37}  
• Study populations: Patients with leukemia; patients with gynecologic cancers receiving cisplatin\textsuperscript{37,38}

**EXPERT OPINION**

Consensus\textsuperscript{1–5} exists recognizing the growing evidence that the following interventions may be effective in the prevention and management of CINV.

• Prevention of nausea and vomiting is the goal.
• Oral and IV antiemetics have equivalent effectiveness.
• The period of expected nausea and vomiting should be covered with appropriate antiemetics (anticipatory, acute, and delayed period for at least four days).
• The lowest efficacious dose of antiemetics should be used.
• Clinicians should base selection of antiemetics on the emetic potential of the chemotherapy agent(s), as well as on patient factors.
• Healthcare providers need to consider the many potential causes of nausea and emesis in patients with cancer that may be contributing factors.

Limited evidence exists, but experts recommend the following dietary interventions in patients receiving chemotherapy to minimize nausea and vomiting.\textsuperscript{5}

• Eat smaller, more frequent meals.
• Reduce food aromas and other stimuli with strong odors.
• Avoid foods that are spicy, fatty, and highly salty.
• Take antiemetics prior to meals so that the effect is present during and after meals.
• Repeat previous measures, and consume foods that minimize nausea and that are "comfort foods."

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Definitions of the interventions and full citations: www.ons.org/outcomes

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