

## FEATURE ARTICLE

# Putting Evidence Into Practice: Evidence-Based Interventions to Prevent, Manage, and Treat Chemotherapy-Induced Nausea and Vomiting

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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.**

*Editor's note.* This article is the third in a series on Oncology Nursing Society's Putting Evidence Into Practice project, in which best practices for patient care are presented.

**N**ausea and vomiting continue to be among the most distressing side effects of chemotherapy, despite the development of more efficacious antiemetic agents (Rhodes & McDaniel, 2001). Research has documented that the incidence of acute and delayed postchemotherapy nausea and vomiting is greater than 50% (Liau et al., 2005; Neymark & Crott, 2005), even after antiemetic prophylaxis.

Successful interventions to prevent, manage, and treat nausea and vomiting decrease the distress associated with the symptoms and promote well-being and quality of life for patients and their families (Bender et al., 2002). This article describes the process and results of an Oncology Nursing Society (ONS) initiative to examine and evaluate current evidence-based interventions to prevent, man-

age, and treat chemotherapy-induced nausea and vomiting (CINV) in adults. The ONS Putting Evidence Into Practice (PEP) project is a collaborative effort that demonstrates commitment to quality care in the development of resources regarding nursing-sensitive patient outcomes. The nausea team united researchers, advanced practice nurses, and staff nurses to develop the ONS PEP resources that provide evidence-based guidelines for CINV interventions.

## 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

### Computerized searches were performed using the listed terms, with and without cancer, neoplasms, and oncology.

Nausea	Exercise
Anticipatory nausea	Ginger
Vomiting	Herbal treatments for nausea
Acupuncture	Massage
Acupressure	Music therapy
Acustimulation	Psychoeducation
Cannabis	Guided imagery
Chemotherapy	Relaxation
Complementary and alternative therapy/treatment	Progressive muscle relaxation
Education	Virtual reality

**Figure 1. Database Search Terms**

**Table 1. Putting Evidence Into Practice Weight-of-Evidence Classification Schema**

WEIGHT-OF-EVIDENCE CATEGORY	DESCRIPTION	EXAMPLES
Recommended for practice	Effectiveness is demonstrated by strong evidence from rigorously designed studies, meta-analyses, or systematic reviews. Expected benefit exceeds expected harms.	At least two multisite, well-conducted, randomized, controlled trials (RCTs) with at least 100 subjects Panel of expert recommendation derived from explicit literature search strategy; includes thorough analysis, quality rating, and synthesis of evidence
Likely to be effective	Evidence is less well established than for those listed under recommended for practice.	One well-conducted RCT with fewer than 100 patients or at one or more study sites Guidelines developed by consensus or expert opinion without synthesis or quality rating
Benefits balanced with harms	Clinicians and patients should weigh the beneficial and harmful effects according to individual circumstances and priorities.	RCTs, meta-analyses, or systematic reviews with documented adverse effects in certain populations
Effectiveness not established	Data currently are insufficient or are of inadequate quality.	Well-conducted case control study or poorly controlled RCT Conflicting evidence or statistically insignificant results
Effectiveness unlikely	Lack of effectiveness is less well established than those listed under not recommended for practice.	Single RCT with at least 100 subjects that showed no benefit No benefit and unacceptable toxicities found in observational or experimental studies
Not recommended for practice	Ineffectiveness or harm clearly is demonstrated, or cost or burden exceeds potential benefit.	No benefit or excess costs or burden from at least two multisite, well-conducted RCTs with at least 100 subjects Discouraged by expert recommendation derived from explicit literature search strategy; includes thorough analysis, quality rating, and synthesis of evidence

*Note.* Based on information from Mitchell & Friese, n.d.

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 for breast cancer (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 or with acustimulation bands; again, the P6 point is used most commonly 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 (Luebbert 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.

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

### Recommended for Practice

- Pharmacologic interventions, including benzodiazepines, 5-HT<sub>3</sub> receptor antagonists, corticosteroids, and NK1 receptor antagonists

### Likely to Be Effective

- Acupuncture
- Acupressure
- Guided imagery
- Music therapy
- Progressive muscle relaxation
- Psychoeducational support and information

### Benefits Balanced With Harms

- Virtual reality

### Effectiveness Not Yet Established

- Exercise
- Hypnosis
- Massage and aromatherapy
- Acustimulation with wristband device
- Ginger

## Figure 2. Interventions for Nausea and Vomiting Supported by Empirical Studies

with breast cancer in Hong Kong found that progressive muscle relaxation training decreased the duration of nausea and vomiting considerably (Molassiotis et al., 2002). A meta-analysis of 15 studies from the United States, Sweden, and the United Kingdom found the effects of relaxation to significantly decrease nausea (Luebbert et al., 2001). Because of limited data on vomiting, no conclusion could be drawn regarding the effectiveness (Luebbert et al.). Consistent positive results in meta-analyses showed clinically significant reductions in nausea and other symptoms. Progressive muscle relaxation reduced delayed nausea and vomiting in a group of 60 Japanese patients who were receiving chemotherapy (Ara-kawa, 1997). The study did confirm the usefulness of progressive muscle relaxation in decreasing the incidence of vomiting.

Music therapy may be effective as an intervention for nausea and vomiting. 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 audiotapes on self-care behaviors and the occurrence and intensity of common side effects were useful in managing side effects of chemotherapy in a study of 70 women with breast cancer (Williams & Schreier, 2004); however, the study did not use controls to obtain any additional information outside of the intervention. A meta-analysis of 116 intervention studies indicated that psychoeducational and psychosocial care have beneficial effects for nausea and vomiting in cancer (Devine & Westlake, 1995).

Virtual reality is an intervention for nausea and vomiting that may have benefit balanced with harms. It is 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 (Schneider, Prince-Paul,

Allen, Silverman, & Talaba, 2004). Schneider et al. used a crossover design with 20 subjects who were randomly assigned to receive a virtual reality distraction intervention during one chemotherapy treatment and received no distraction intervention (control condition) during an alternate chemotherapy treatment. A significant decrease in symptom distress was noted immediately following chemotherapy treatments when women used the virtual reality intervention. Oyama, Kaneda, Katsumata, Akechi, and Ohsuga (2000) found a decrease in emesis three to five days after chemotherapy when patients received a virtual reality intervention. Although the intervention may be effective, it can cause motion sickness, which may increase nausea and vomiting. Also, use of the intervention may be limited because of the cost of the virtual reality system.

Exercise, hypnosis, massage and aromatherapy, acustimulation with wristband device, and consumption of ginger have been examined for use in nausea and vomiting but do not have established effectiveness. A randomized, controlled study of aerobic exercise in women with breast cancer showed marked improvement in nausea in the treatment group (Winningham & MacVicar, 1988). The study results suggest that moderate aerobic activity may be beneficial as an adjunct to antiemetic therapy in controlling CINV and in promoting physical well-being. To date, no other studies examining the effect of exercise on nausea and vomiting have been published.

Hypnosis was examined as an intervention for patients who experienced anticipatory nausea and vomiting. Fourteen of 16 patients experienced a complete remission of anticipatory nausea and vomiting following hypnotherapy (Marchioro et al., 2000).

Two randomized, controlled studies examined massage and aromatherapy as interventions for nausea. The massage groups 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

### 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.





**Figure 4. Acupuncture at the P6 Point**

because different essential oils were used (Fellowes, Barnes, & Wilkinson, 2004).

The use of acustimulation with wristbands for prevention and management of nausea and vomiting has been examined in several studies with conflicting findings. Two studies had positive but inconclusive results with the use of the bands, and two other studies found no significant differences (Roscoe et al., 2003, 2005; Roscoe, Morrow, Matteson, Bushunow, & Tian, 2002; Treish et al., 2003). In a systematic review, Collins and Thomas (2004) found no benefit with the use of acustimulation bands.

Although anecdotal evidence supports the consumption of ginger to manage and treat CINV, the treatment is not supported by research. A systematic review on the effectiveness of ginger on various types of nausea and vomiting did not support the effectiveness of ginger in treating CINV in 40 patients with leukemia (Ernst & Pittler, 2000). In a randomized, crossover study with 40 patients being treated for gynecologic cancer, ginger was not found to be effective in treating acute nausea, nor was it significantly different from metoclopramide in delayed nausea (Manusirivithaya et al., 2004).

## Implications

Only pharmacologic interventions are supported by sufficient strong empirical evidence of effectiveness to allow them to be recommended for practice. Evidence for nonpharmacologic interventions is limited. However, evidence does support several interventions as likely to be effective to prevent, manage, and treat CINV when used in conjunction with pharmacologic interventions.

Additional research on nonpharmacologic interventions for CINV needs to be conducted. Many nonpharmacologic interventions are inexpensive and require minimal patient teaching, such as exercise. Randomized clinical trials with large samples are needed for interventions that have the potential to prevent and manage nausea and vomiting. Studies are needed to include patients with different types of cancers, ethnic and cultural groups, and genders. Caucasian women with breast cancer were the subjects of many of the reviewed articles.

Herbal interventions such as ginger lack dose regulation. Treatments must be consistent across studies to allow for comparison.

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](http://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<sup>1-5</sup>

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: Highly emetogenic chemotherapy<sup>1-5</sup>

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-HT<sub>3</sub> 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
- Corticosteroid
  - Dexamethasone 12 mg po or IV on day 1, 8 mg po or IV daily on days 2–4, and
- NK1 receptor antagonist
  - Aprepitant 125 mg po on day 1, 80 mg po daily on days 2 and 3, and
- Benzodiazepine (may or may not be given with other antiemetics because of sedating effects)
  - Lorazepam 0.5–2 mg po, IV, or SL every 4–6 hours on days 1–4

##### Acute and delayed nausea and/or vomiting: Moderately emetogenic chemotherapy<sup>1-5</sup>

- 5-HT<sub>3</sub> receptor antagonists
  - Palonosetron 0.25 mg IV on day 1, or
  - Granisetron 1–2 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
- Corticosteroid
  - Dexamethasone 12 mg po or IV on day 1, and
- Benzodiazepine (may or may not be given with other antiemetics because of sedating effects)
  - Lorazepam 0.5–2 mg po, IV, or SL every 4–6 hours, and
- Aprepitant 125 mg po on day 1, 80 mg po on days 2 and 3

On days 2–4, consider:

- Corticosteroid
  - Dexamethasone 8 mg po or IV daily, or

- 5-HT<sub>3</sub> receptor antagonists
  - Ondansetron 8 mg po bid, 16 mg po daily, or 8 mg IV, or
  - Granisetron 1–2 mg po daily, 1 mg po bid, or 1 mg IV, or
  - Dolasetron 100 mg po or IV
- Substituted benzamide
  - 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 prn

##### Acute and delayed nausea and/or vomiting: Low emetogenic chemotherapy<sup>1-5</sup>

- 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
- Substituted benzamide
  - 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<sup>1-5</sup>

Nausea and/or vomiting that occurs despite prophylactic antiemetics and requires “rescue” antiemetic therapy.<sup>1</sup>

Consider using a drug from a class not previously used.

- Corticosteroid
  - Dexamethasone 12 mg po or IV daily, if not previously given, or
- 5-HT<sub>3</sub> receptor antagonists
  - Granisetron 1–2 mg po daily, 1 mg po bid, or 1 mg IV, or
  - Ondansetron 8 mg po or IV daily, or
  - Dolasetron 100 mg po or IV daily, or
- Phenothiazine
  - Prochlorperazine 25 mg suppository every 12 hours, or 10 mg po or IV every 4–6 hours, or
- Substituted benzamide
  - Metoclopramide 20–40 mg po every 4–6 hours or 1–2 mg/kg IV every 3–4 hours ± diphenhydramine 25–50 mg po or IV every 4–6 hours, or
- Butyrophenones
  - Haloperidol 1–2 mg po every 4–6 hours or 1–3 mg IV every 4–6 hours, or
- Benzodiazepine
  - Lorazepam 0.5–2 mg po every 4–6 hours, or
- Cannabinoid
  - Dronabinol 5–10 mg po every 3–6 hours, or
- Olanzapine 2.5–5 mg po bid prn

#### 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.**



### 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.<sup>6</sup>

- Study populations: People with various carcinomas; women with high-risk breast cancer receiving myeloablative chemotherapy; and patients with mixed cancer types<sup>6-10</sup>

### 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.<sup>11</sup>

- 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 types<sup>11-13</sup>

### Guided imagery

Forming a relaxing, pleasing mental image, often preceded by relaxation techniques and/or music<sup>14</sup>

### 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.<sup>15</sup>

### 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.<sup>15</sup>

- 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 chemotherapy<sup>14-20</sup>

### 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 CINV<sup>21</sup>

- Study populations: Women receiving cisplatin-based chemotherapy for ovarian cancer; and women receiving chemotherapy for breast cancer<sup>21,22</sup>

## BENEFITS BALANCED WITH HARMS

Interventions for which clinicians and patients should weigh the beneficial and harmful effects according to individual circumstances and priorities

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

**Provide referral to appropriate practitioners as needed.**

### 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.<sup>23</sup>

- Study populations: Patients with mixed cancers, primarily women with breast and ovarian cancers<sup>24</sup>

## EFFECTIVENESS NOT ESTABLISHED

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.<sup>25,26</sup>

- Study population: Women with breast cancer receiving chemotherapy (not doxorubicin) who had received at least three treatments prior to study<sup>27</sup>

### 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.<sup>28</sup>

- Study population: Patients who had received at least four cycles of chemotherapy combined with a 5-HT<sub>3</sub> 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)<sup>28</sup>

### 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.<sup>29</sup>

- Study populations: Autologous bone marrow transplant recipients; hospital inpatients<sup>29-32</sup>

### 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 mAmps/pulse.<sup>33</sup>

- Study populations: Women with breast cancer receiving their second course of chemotherapy (doxorubicin-based); chemotherapy-naïve patients with mixed cancers receiving cisplatin or doxorubicin; and those with mixed cancers receiving moderately high to highly emetogenic chemotherapy<sup>33-36</sup>

### Ginger

A plant herb used in traditional Chinese and Indian medicine for the treatment of nausea and vomiting. Ginger has aromatic, spasmolytic,



carminative, and absorbent properties that suggest direct effects on the gastrointestinal tract.<sup>37</sup>

- Study populations: Patients with leukemia; patients with gynecologic cancers receiving cisplatin<sup>37,38</sup>

## EXPERT OPINION

Consensus<sup>1-5</sup> 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.<sup>5</sup>

- 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](http://www.ons.org/outcomes)  
Literature search completed through December 2005.

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**Note.** From *Putting Evidence Into Practice: Interventions for Chemotherapy-Induced Nausea and Vomiting* [PEP card], by J. Tipton, R. McDaniel, L. Barbour, M.P. Johnston, P. LeRoy, M. Kayne, et al., 2006, Pittsburgh, PA: Oncology Nursing Society. Copyright 2006 by the Oncology Nursing Society. Reprinted with permission.