

Nausea and Vomiting

Evidence Table

(Literature search completed through May 2008)

Author and Year	Characteristics of the Intervention	Sample Characteristics, Setting Characteristics, Study Design, and Conceptual Model	Measures	Results and Conclusions	Limitations, Major and Minor Flaws, Cautions and/or Contraindications, Special Training Needs, and Costs
Effectiveness of Ondansetron and Granisetron: PEP Weight-of-Evidence Category: Recommended for Practice					
Vrabel, 2007	A review of the literature was conducted to identify trials that compared antiemetic effectiveness of ondansetron and granisetron in reducing chemotherapy-induced nausea and vomiting (CINV) in adult patients with cancer, by searching PubMed®, Ovid, MEDLINE®, CINHAL®, and Evidence-Based Medicine Reviews databases. Six trials were identified.	<p>Del Giglio et al. (2000) provided a meta-analysis of 14 randomized controlled trials (RCT) with 6,467 patients that compared the antiemetic efficacy of ondansetron and granisetron for prophylaxis of CINV.</p> <p>Forni et al. (2000) compared the antiemetic efficacy of ondansetron, granisetron, and tropisetron in prevention of acute CINV through a double-blinded RCT with 90 patients.</p> <p>de Wit et al. (2001) conducted a double-blinded RCT to compare ondansetron plus dexamethasone to granisetron plus dexamethasone during the first 24 hours after highly emetogenic chemotherapy (HEC). Forty patients, predominately women, participated in this crossover study.</p> <p>Watters et al. (2001) evaluated the response success and side effects of ondansetron, granisetron, and tropisetron in the prevention of CINV in a quasi-experimental prospective</p>	The instruments to evaluate efficacy and adverse effects were not described in this review.	<p>According to Del Giglio et al. (2000), no statistically significant differences were identified in the eight types of CINV scenarios studied.</p> <p>According to Forni et al. (2000), no significant differences were found among the three agents for antiemetic control.</p> <p>de Wit et al. found that of the 19 patients on ondansetron who crossed over to granisetron, 9 obtained complete control of emesis. Only 1 of 21 patients continuing with ondansetron obtained complete control of emesis.</p> <p>Watters et al. (2001) reported no statistically significant differences among these three agents for efficacy or side effects.</p> <p>Dempsey et al. (2004): Overall, granisetron 1 mg IV and ondansetron 32 mg IV appeared to be more effective than ondansetron 8 mg IV in preventing acute CINV. In both logistical regression models (one model controlled for radiation therapy and dexamethasone use and one model that did not), Ondansetron 8 mg IV had a higher risk than granisetron for</p>	<p>Ondansetron and granisetron are equally effective in reducing or eliminating CINV in adult patients with cancer with no significant differences in adverse effects.</p> <p>Patients who experience side effects from one of these agents can be safely crossed over to the other. This review of the literature</p> <p>The impact of cost of the selection of antiemetic agents was not described.</p>

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		<p>cohort study of 274 patients undergoing chemotherapy with high risk for emesis in single-site hospital setting.</p> <p>Dempsey et al. (2004) evaluated antiemetic effectiveness of ondansetron 8 mg IV, ondansetron 32 mg IV, and granisetron 1 mg IV as prophylaxis in patients with breast cancer receiving cyclophosphamide-containing regimens (N=224). It was a descriptive, correlational, multi-center retrospective trial.</p> <p>Walsh et al. (2004) compared efficacy and adverse effects of ondansetron and granisetron, in combination with other antiemetics for the prevention of acute CINV through a double-blinded RCT with 96 patients undergoing hematopoietic stem cell transplantation for any malignancy in two hospital settings.</p>		<p>acute CINV. No significant differences were found between ondansetron 32 mg and granisetron 1 mg.</p> <p>Walsh et al. (2004) found no statistically significant differences between ondansetron and granisetron. None of the adverse effects occurred more frequently with ondansetron or granisetron.</p>	
Pharmacologic Interventions: PEP Weight-of-Evidence Category: Recommended for Practice					
Abali et al., 2007	A comparison of efficacy, side effects, and cost of tropisetron, ondansetron, and granisetron for control of chemotherapy-induced emesis.	Prospective, open-label, observational study of 158 patients receiving highly and moderately emetogenic chemotherapy (MEC) in a university outpatient setting in Turkey to evaluate efficacy, side effects, and cost. Participants	Five-day questionnaire to evaluate response using definitions for complete, moderate, minor responses and failure related to emesis and high, moderate, low, and absent for nausea.	No differences were apparent among these three serotonin antagonists in the efficacy or side effect profile for patients with CINV from HEC or MEC chemotherapy. Tropisetron is the least	No control for type of cancer or chemotherapy regimens was incorporated into the review. More women than men participated in the study with a median age of 48 years. The older adult population was

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		<p>were required to have a single day protocol or HEC or MEC administered on the first day of the schedule with agents on subsequent days with low emetogenic potential. Patients with intracranial metastases, gastrointestinal complications, and vertigo; patients receiving other drugs that affect emesis; and patients receiving radiotherapy were excluded. Participants were given a five-day questionnaire developed for the study, following a brief instructions on how to fill it out, and a schedule of how to take their medications. They filled out the questionnaire at home and returned it later. Antiemetic doses were standardized pre- and post-chemotherapy treatment, and three arms were created.</p>	<p>Cost analysis prices were obtained for antiemetics from the Web site of Turkish Health Ministry of Health. Dexamethasone price was not obtained for analysis because it was the same dose for three arms of treatment.</p>	<p>expensive at current prices. Preferences among serotonin antagonists must be based on other factors.</p>	<p>limited. Cost analysis was based on one Turkish Health Ministry's database. The availability of these agents in other countries and cost analysis will vary by country.</p>
<p>Pharmacologic Intervention: Aprepitant and 5-HT₃ Antagonist Plus Corticosteroid Effect of Gender: PEP Weight-of-Evidence Category: Recommended for Practice</p>					
<p>Hesketh et al., 2006</p>	<p>The data from two phase III studies of aprepitant plus a 5-HT₃ antagonist and corticosteroid for the prevention of CINV were pooled to assess the effect of gender on treatment response.</p>	<p>Two identically designed, randomized, double-blind parallel group, placebo-controlled trials of 1,044 patients receiving more than 70 mg/m² Of cisplatin randomly assigned to control regimen or aprepitant regimen. The studies were conducted in the United States and the Netherlands, predominately in university cancer centers. Patients were</p>	<p>Visual Analogue Scales (VASs) and patient diaries</p>	<p>In the control group, women had an overall complete response (CR) of 41% compared with 53% of men. In the aprepitant group, 66% of women had an overall CR compared with 69% of men. The enhanced efficacy of aprepitant regimen in women occurred during acute and delayed phases and resulted in</p>	<p>Details of design, primary efficacy, and tolerability are not included, but the results of the studies are published elsewhere.</p>

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		<p>older than 18 years with a Karnofsky score greater than 60 and were scheduled for first their cycle of chemotherapy, including cisplatin. Patients were randomized to one of the treatment groups and stratified by gender. Patients used a diary to document emetic episodes, severity ratings of nausea (100 mm horizontal visual analogue scale), and any use of rescue medications.</p>		<p>similar rates of antiemetic control for men and women.</p> <p>The aprepitant regimen partly maintained improvement over multiple cycles for men and women.</p> <p>The addition of aprepitant may reverse the risk of gender for CINV in women receiving HEC.</p>	
<p>Aprepitant for Prevention of CINV With Highly-Emetogenic Chemotherapy: PEP Weight-of-Evidence Category: Recommended for Practice</p>					
<p>Schmoll et al., 2006</p>	<p>Comparison of aprepitant regimen (oral aprepitant on days 1-3, ondansetron on day 1 only, and oral placebo twice a day on days 2-4, dex on days 1-4) to ondansetron/dex regimen (ondansetron and dex on days 1-4 and aprepitant placebo on days 1-3)</p>	<p>489 patients with solid malignancies receiving chemotherapy (patients were cisplatin-naïve) were randomized to the treatment arm (aprepitant) or control group (ondansetron and dex). n = 231 in the treatment arm and n = 229 in the comparison group. Prospective, randomized, double-blind trial with sponsor blinding.</p>	<p>Diary to record number of episodes of vomiting and use of rescue medication, nausea VAS.</p> <p>Patients considered treatment failures if they needed to take rescue medication.</p>	<p>CR is defined as no vomiting and no rescue medication in the overall period (days 1-5 after cisplatin infusion).</p> <p>Aprepitant regimen is superior to the control arm in the overall treatment period (CR = 72% versus 61%, p = 0.003).</p> <p>No significant difference was observed among groups in control of nausea.</p> <p>Aprepitant group had higher rate of drug-related adverse events</p>	<p>The addition of aprepitant to prevention of CINV provides an objective improvement in control of vomiting as compared to ondansetron and dex alone; however, the triple drug combination is recommended for practice.</p> <p>Efficacy might be further improved if ondansetron is given on days 1-4 as well (as per guidelines), rather than only on day 1 as done in this study.</p>
<p>Palonosetron for Prevention of CINV With Highly Emetogenic Chemotherapy: PEP Weight-of-Evidence Category: Recommended for Practice</p>					
<p>Aapro et al., 2006</p>	<p>To evaluate the safety and efficacy of palonosetron at two different doses (0.25 mg versus 0.75 mg) compared with a single dose of ondansetron</p>	<p>Phase III, multinational, randomized, double-blind, double dummy, stratified, parallel-group, active-comparator trial with three</p>	<p>Patient diaries to record emetic episodes, nausea, and use of rescue medications</p> <p>Functional Living Index-Emesis</p>	<p>Equal results for palonosetron and ondansetron in the first 24 hours; however, palonosetron (no difference based on dose) with higher CR rates compared</p>	

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	32 mg in preventing CINV after highly-emetogenic chemotherapy	treatment arms (palonosetron 0.25 mg, palonosetron 0.75 mg and ondansetron 32 mg); a total of N = 673 patients were randomized and final data reported on N = 667 patients	(FLIE)	with ondansetron during the delayed and overall phases.	
Palonosetron Plus Dexamethasone for Prevention of CINV With Moderately Emetogenic Chemotherapy: PEP Weight-of-Evidence Category: Recommended for Practice					
Hajdenberg et al., 2006	Palonosetron 0.25 mg admixed with dexamethasone 8 mg in 50 ml infusion solution prior to chemotherapy	Nonblinded (open-label) phase II study that enrolled 33 patients from three sites to evaluate the efficacy and safety of palonosetron and dexamethasone as an anti-emetic regimen. Eligible patients received palonosetron plus dexamethasone infusion as an anti-emetic treatment. Patients self-recorded efficacy data in diary and were contacted on day 3 at home to review diary completion and inquire about other possible anti-emetic treatments. Patients then returned to the clinic between days 6 and 8 after chemotherapy for final study procedures.	Four-point Likert scale to rate nausea intensity; number of emetic episodes and use of rescue medication also were documented in a patient diary	<p>Twenty-nine (91%) patients had no emetic episodes during the acute interval, 26 (81%) had no emesis during the delayed interval, and 23 (72%) had no emesis during the overall interval.</p> <p>Emesis-free rates for the acute, delayed, and overall intervals for the historic population were 79%, 72%, and 66%, respectively.</p> <p>There were no significant differences in any of the outcomes of interest between groups.</p> <p>The report states that the addition of dexamethasone increased in the benefit in the acute interval by 12%, but this is not significant.</p>	The study refers to a historic population as the control rather than having a control group. The historic control is not described other than that patients received palonosetron without concomitant dexamethasone.
Pharmacologic Intervention: Dronabinol for Delayed CINV: PEP Weight-of-Evidence Category: Likely to Be Effective					
Meiri et al., 2007	Efficacy of dronabinol alone or in combination with ondansetron versus ondansetron alone for delayed CINV	Randomized, double-blind, placebo-controlled, parallel-group five-day study to compare the effectiveness of dronabinol alone or in combination with	Visual Analog Scale (VAS), total response, intensity of nausea, Eastern Cooperative Oncology Group (ECOG) performance status, and McCorkle Symptom	The efficacy of dronabinol alone was comparable with ondansetron for the treatment of delayed CINV in patients with cancer receiving HEC or MEC.	Patients had difficulties with potential for randomization to placebo when receiving HEC or MEC.

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		<p>ondansetron versus ondansetron alone for delayed CINV among patients receiving HEC or MEC in multiple cancer centers; sixty-four participants were aged 18 years or older, had a malignancy that did not involve bone marrow, were undergoing a chemotherapy regimen, and had a performance status of 0–2 at screening. They were able to receive concurrent radiation except to the abdomen and changing regimens with last antiemetics seven days prior to study enrollment. For women, a negative pregnancy test at baseline was required. Patients had a primary malignancy of the brain, spinal cord, or nervous system; brain metastases; severe brain trauma or surgery; leukemias; or lymphomas. Marijuana use within 30 days or antiemetics within 7 days were excluded. Participants were randomized to four treatment groups: dronabinol alone, ondansetron alone, combination with both drugs, and placebo. Standard pretreatment medications, fixed doses on day 2, and flexible doses days 3-5 were administered. Participants were assessed from patient telephone diary entries each morning to report on the previous day through the Interactive Voice Response System.</p>	<p>Distress Scale</p>	<p>Combination therapy with dronabinol and ondansetron was not more effective than either agent alone.</p> <p>Difficulties in enrollment led to early termination of this study.</p>	<p>Early discontinuation of the study reduced the number of participants enrolled in each treatment group.</p> <p>Heterogeneous population</p> <p>No control chemotherapy treatment</p> <p>The majority of patients had a breast or lung cancer.</p>

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Acupressure: PEP Weight-of-Evidence Category: Likely to Be Effective					
Dibble et al., 2007	Acupressure for CINV	<p>A multicenter, longitudinal, randomized controlled trial throughout one cycle of chemotherapy to compare the differences in CINV among three groups: acupressure, acupressure placebo, and usual care of women undergoing chemotherapy for breast cancer. One-hundred and sixty women beginning their second or third cycle of chemotherapy for breast cancer with moderate nausea intensity scores with previous cycles, based on at least a score of 3 on the Morrow Assessment of Nausea and Emesis, and receiving treatment in community oncology programs associated with M.D. Anderson Cancer Center and nine independent sites; participants were able to read and write in English. Subjects were randomized to one of three groups: acupressure to P6 point (active), acupressure to S13 point (placebo), or usual care. Participants were taught to apply acupressure wrist device by research assistants unaware of the active pressure point. The participants completed a daily log for 21 days containing measures of nausea and vomiting and recorded methods for controlling the symptoms,</p>	<p>Rhodes Index of Nausea and Vomiting (three-item nausea; single-item vomiting subscales); nausea intensity also was rated with a descriptive, numeric rating scale, ranging 0–10, as well as the State-Trait Anxiety Index.</p>	<p>No significant differences in demographic data, disease, or treatment variables among groups.</p> <p>No significant differences were identified in acute nausea and vomiting among the treatment groups.</p> <p>With delayed nausea and vomiting, the acupressure group had statistically significant reduction in the amount of vomiting and intensity of nausea over time when compared with the placebo or usual care groups.</p> <p>No significant differences were found between placebo and usual care groups.</p> <p>In addition to pharmaceutical management of women undergoing treatment for breast cancer, acupressure at P6 reduces the amount and intensity of delayed CINV.</p> <p>Acupressure is a safe and effective tool to be offered to women undergoing breast cancer chemotherapy treatment.</p>	<p>Same research assistants and nurses taught both pressure points.</p> <p>Although most did not know which pressure point was active, a few referenced the Internet for the information.</p> <p>Patients with uncontrolled nausea broke the blind.</p> <p>Some challenges for participants in finding the location consistently; some needed markings on their wrist.</p> <p>Longer fingernails made the application of pressure difficult for two of the participants.</p> <p>Staff training on the technique and return demonstration</p> <p>No men or children in the study population</p>

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		<p>including antiemetics and acupressure. Research assistants, who received two hours of training on the study protocol, instructed participants. In an examination or private room, the participants were taught to find a quiet place each morning to perform the acupressure treatment to both P6 points sequentially either as treatment or practice. During the day, participants in the acupressure groups were encouraged to apply digital pressure to one of the points whenever nausea occurred regardless of where they were. Each session was six minutes in the morning and three minutes each during the rest of the day. Self-ratings were completed on a daily basis prior to bedtime. All participants were called or seen on day 8 for review of the log and coaching, if needed.</p>			
<p>Molassiotis et al., 2006</p>	<p>Effects of P6 acupressure in prophylaxis of CINV in breast patients with cancer</p>	<p>Randomized controlled trial to evaluate the effectiveness of using acupressure in P6 in managing CINV in patients with breast cancer; 36 participants were recruited from two centers in the United Kingdom: a general hospital and a cancer hospital. They were newly diagnosed and chemotherapy naïve, starting first cycle of chemotherapy for breast cancer, stages I-III, receiving doxorubicin or epirubicin and</p>	<p>Rhodes Index of Nausea and Vomiting</p>	<p>Nausea and retching experience and nausea, vomiting, and retching occurrence and distress were significantly lower in the acupressure group than the control group.</p> <p>High level of nausea, vomiting, and retching at day 3 in the acupressure group, equal to the control group.</p> <p>Acupressure at P6 is an effective intervention for managing CINV</p>	<p>Small sample size</p> <p>No control of antiemetics for delayed nausea and vomiting</p> <p>Completing daily questionnaires and returning them</p> <p>Easy to teach; minimal cost (bands)</p>

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		<p>cyclophosphamide. Patients were excluded if they received palliative chemotherapy, had a life expectancy was less than three months, had bowel obstruction, were receiving radiation therapy, or had lymphedema. Participants were randomized to the control or experimental arm and received standard antiemetics before chemotherapy with prescriptions for antiemetics for delayed CINV that were variable. For the experimental group, acupressure was applied using a Sea-Band® (Sea-Band Ltd.) for five days after chemotherapy administration. They were taught to wear them bilaterally with the stud pressing the P6 acupoint by researchers in a brief education session. They were given a daily log with the hours of the day and asked to put a mark at the hour each time that they pressed the wristband's stud. They were instructed to press the stud for two to three minutes every two hours throughout the day, marking it in their log. The control group was given antiemetics and told that they would receive acupressure instructions and wristbands with their next cycle. All participants completed questionnaires every evening after chemotherapy for five evenings. Completed questionnaires were returned</p>		<p>in patients with breast cancer.</p>	

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		directly to researchers or pre-paid envelopes.			
Acupuncture and Acupressure: PEP Weight-of-Evidence Category: Likely to Be Effective					
Choo et al., 2006	Patients identified as having refractory emesis received electroacupuncture in addition to standard antiemetic prophylaxis. Acupuncture was started 10 minutes prior to start of chemotherapy infusion and then continued for an additional 20 minutes. The P6 acupuncture point was used and a second needle was inserted at a different point and electrical stimulation was delivered.	Prospective trial with only an intervention group of patients receiving second cycle of doxorubicin and cyclophosphamide; cyclophosphamide, doxorubicin, and prednisone; or doxorubicin only. Patients were defined as having refractory emesis (defined as vomiting three or more times 24-48 hours after cycle 1). Twenty-seven female patients with breast cancer were enrolled. Patients received standard antiemetic prophylaxis.	Attitudes toward acupuncture questionnaire Vomit diary Telephone interview by trained doctor 24-48 hours after chemotherapy to assess National Cancer Institute Common Toxicity Criteria (NCI-CTC) grade of nausea and vomiting	Thirty-seven percent of the sample (n = 10 patients) had no vomiting after the second cycle of chemotherapy with the addition of electroacupuncture Ninety-six percent of the sample (n = 26) had significantly less nausea and vomiting, and one patient had increased vomiting after electroacupuncture. Overall, mean emetic episodes decreased from seven to three after the intervention (p < 0.0001). NCI grade of vomiting decreased significantly (p = 0.0120) less patients with grade 3-4 vomiting after the electroacupuncture (14 subjects pre at this level and 5 subjects post at this level. NCI grade of nausea improved as well after the intervention (p < 0.0001). Most patients (25/27) thought that electroacupuncture was an acceptable procedure and helpful in reducing emesis.	No control group Two subjects complained of severe headache after the electroacupuncture, lasting for several days; otherwise it was well-tolerated. Intervention was delivered by trained acupuncturists.
Dibble et al., 2000	To compare differences in nausea and intensity with usual care (regular antiemetics) versus usual care with	N = 17 adult women undergoing chemotherapy for breast cancer (cyclophosphamide, methotrexate and fluorouracil) or	Baseline and post-study questionnaires and a daily log Nausea was measured with the	Significant differences existed between the two groups in regard to nausea experience (p < 0.01) and nausea intensity (p <	Single cycle of treatment, small sample size, and women limited to those with breast cancer were limitations.

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	<p>acupressure training or treatment in women undergoing chemotherapy for breast cancer</p> <p>The intervention included finger acupressure bilaterally at the P6 and ST36 acupressure points located on the forearm and knee for a maximum of three minutes for each point every morning or as needed for nausea. Baseline and post-study questionnaires and a daily log were used to collect data.</p>	<p>doxorubicin-containing regimens) 9 in control group, 8 in experimental group with acupressure</p> <p>The mean age of both groups was 49 years. 59% were Caucasian.</p> <p>Outpatient oncology clinic in a major teaching medical center and a private outpatient oncology practice (two sites) located in urban areas in the western United States</p>	<p>Rhodes Inventory of Nausea, Vomiting and Retching, and nausea intensity.</p>	<p>0.04) during the first 10 days of the chemotherapy cycle, with the acupressure group reporting less intensity and experience of nausea.</p>	<p>The ST36 acupressure point was difficult to reach.</p>
<p>Gardani et al., 2007</p>	<p>To confirm the potential therapeutic efficacy of PC6 stimulation by acupressure in patients with cancer with CINV after failure with pharmacologic approach.</p>	<p>100 consecutive patients with metastatic solid tumors were admitted to receive chemotherapy for advanced disease in Italy. Inclusion criteria were histologically proven metastatic solid tumor, measurable lesions, no double tumor, no brain metastasis, no previous chemotherapy for metastatic disease, no concomitant illnesses other than cancer, vomiting grade 3 or 4, and no response to conventional antiemetic therapies. The intervention was stimulation of PC6 acupoint by acupressure with a button (P6 nausea control Sea-Band) for eight hours per day at home, starting before the onset of chemotherapy, and for at least three days after chemotherapy.</p>	<p>World Health Organization criteria</p>	<p>A control of emesis was achieved for 68% of patients.</p> <p>No significant differences in efficacy were observed in relation to tumor histotype.</p> <p>The percentage of efficacy varied in relation to type of chemotherapy.</p> <p>The lowest results were observed in patients treated with anthracyclines, whereas more benefit was seen in patients with other chemotherapy agents. However, the efficacy achieved was greater than 50% in the treatment of vomiting because of anthracyclines.</p> <p>The study confirms the efficacy of acupressure in the treatment of CINV with a larger number of</p>	<p>Only vomiting was measured; nausea was not measured.</p> <p>Heterogeneous population with different tumor types and chemotherapy agents</p> <p>Antiemetics before and after chemotherapy were not described.</p> <p>No specific exclusion criteria were listed.</p> <p>Several questions related to the intervention: who taught the patient how to use the Sea-Bands; what training did that person have; and how, when, and who evaluated the effectiveness of the intervention</p>

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				<p>patients than previously studied.</p> <p>Acupressure appears to be effective in reducing vomiting due to most commonly used chemotherapy agents.</p>	
<p>Melchart et al., 2006</p>	<p>The effectiveness of acupuncture and acupressure in reducing chemotherapy-induced nausea</p>	<p>Randomized crossover pilot study of 28 patients receiving MEC or HEC in hematology and gastroenterology departments of a large university hospital in Germany were treated for one cycle of chemotherapy with acupuncture and acupressure at point P6 and for one cycle at a close sham point. Patients were eligible if they were aged 18-75 years, scheduled to receive MEC or HEC and standard antiemesis additional medication for rescue predefined for two cycles of chemotherapy, and had Karnofsky index of 50%. Patients were excluded if they had received chemotherapy within the last three months; had anticipatory nausea and vomiting, cerebral metastasis, chronic ileus or subileus, or lymphedema in arms; or had knowledge of acupressure points. Participants were randomized to acupuncture at P6 or at a close nonacupuncture point, and it was delivered by one of two physicians with training and experience in acupuncture. Participants wore acupressure bands for 72 hours</p>	<p>Morrow Assessment of Nausea and Vomiting (MANE); shortened version Intensity, frequency, and duration of nausea through patient diaries</p>	<p>There was no difference between combined acupuncture and acupressure at P6 point and at the sham point. The study was stopped early due to recruitment problems and low incidence of nausea and vomiting was low in the sham group. Half of the participants reported an irradiating feeling which is a sign of effective acupuncture.</p>	<p>It was a small sample and low incidence of nausea in the sham group. There was a no acupuncture control group. There was no control for type of cancer or chemotherapy regimen. The sham point may have been too close to P6 or the needle was too deep.</p>

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		<p>at the same points on both arms and could wear them for an additional four days if needed. It was covered with a mull bandage to blind the staff. Participants completed diaries for seven days, documenting intensity (rating 0-6), frequency, and duration of nausea and vomiting; additional antiemetics taken; and, on day 7, rate the effectiveness of side effects or impairment by acupuncture or acupressure. They completed the MANE. Oncology staff checked that the diary was completed accurately, standard antiemetics regimen were followed, and for any adverse reactions related to acupuncture.</p>			
Shen et al., 2000	<p>Participants were randomly assigned to one of three groups.</p> <ol style="list-style-type: none"> 1) Low-frequency electroacupuncture at classic antiemetic acupuncture points once daily for five days 2) Minimal needling at control points with mock electrostimulation once daily for five days <p>No adjunct needling</p>	<p>N = 104 women with high-risk breast cancer undergoing myeloablative (high-dose) chemotherapy; the mean age was 46 years (range = 18–62 years). Women had histologically proven resected breast cancer; Karnofsky score were more than 80 (0–100 scale). Life expectancy was at least six months, and patients were appropriate for a bone marrow transplantation program.</p> <p>Patients with brain metastases, cardiac pacemakers, life-threatening concurrent nonmalignant conditions, or active skin infections over proposed treatment area were</p>	<p>The total number of emetic episodes that occurred during the five-day study period and the proportion of emesis-free days across the treatment groups</p>	<p>The electroacupuncture group had significantly fewer emesis episodes than the minimal needling group or the pharmacotherapy group alone ($p < 0.001$). The minimal needling group had significantly fewer episodes of emesis than the pharmacotherapy group alone ($p = 0.01$).</p> <p>The electroacupuncture group had a greater proportion of emesis-free days than the other groups ($p < 0.001$).</p> <p>No significant difference existed between the groups from days 6–14.</p>	<p>Homogeneity of sample (standard chemotherapy and supportive care) helped to increase the precision in measurement; however, generalizability is limited.</p> <p>The study did not include 5-HT₃ antagonists or corticosteroids.</p> <p>The beneficial effect may be related to attention and clinician-patient interaction. Minimal needling led to a reduction in emesis, which could have been a placebo effect.</p> <p>Electroacupuncture has been thought to modulate serotonin, substance P, and endogenous opioids (similar to drugs that are</p>

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		<p>excluded.</p> <p>Participants were from an inpatient unit at a tertiary hospital with a comprehensive cancer center. Patients were recruited from oncology clinics.</p> <p>The study design was random, without stratification.</p>			<p>available now).</p> <p>Training is required for electroacupuncture and minimal needling. This was a grant-funded project. The two investigators administered the procedure (training completed with 3–20 years of experience). Time commitment was 30 minutes a day for five days.</p>
Shin et al., 2004	<p>Control and intervention groups received regular antiemetics, and the intervention group received acupressure training and was instructed to perform the finger acupressure maneuver for five minutes on the P6 point at least three times per day before chemotherapy and mealtimes or as needed.</p> <p>Both groups received frequent nursing visits and consultations.</p>	<p>N = 40 (20 in control group, 20 in intervention group); age range= 47–52 years. All were postoperative gastric patients with cancer.</p> <p>Intervention was given with first cycle of 5-fluorouracil and cisplatin chemotherapy</p> <p>Setting was a university medical center in metropolitan South Korea. Participants were on inpatient oncology wards.</p> <p>Study design was a nonequivalent control group design for a single cycle of chemotherapy.</p>	<p>Demographic data: family background, diagnosis and treatment, assessment of nausea and vomiting</p> <p>Rhode's Index of Nausea, Vomiting and Retching translated into Korean and back-translated to English to ensure equivalency</p> <p>Daily log rating of nausea experience using a four-point scale and intensity of nausea experience measured during the past 24 hours rated by patient</p>	<p>Significant differences existed between control and intervention groups in the severity of nausea and vomiting, duration of nausea, and frequency of vomiting.</p>	<p>Self-report has some degree of measurement error.</p> <p>Generalizability is limited because of regional study and small sample size.</p>
Assessment of Risk Factors: PEP Weight-of-Evidence Category: Likely to Be Effective					
Booth et al., 2007	CINV in patients with breast cancer	Prospective, multicenter, observational study evaluated emetic control in patients with breast cancer over multiple cycles of chemotherapy and compared prevalence and severity of CINV in randomized clinical trials. Patients received	<p>Potential Predictive Factors for CINV (e.g. motion sickness, morning sickness, and amount of alcohol consumed daily)</p> <p>Prior to each cycle, data was collected on scheduled antiemetics, anticancer agent</p>	The prevalence of nausea and vomiting were low when compared RCTs. Several risk factors were associated with severe emesis during the first 24 hours: age younger than 40, recent surgery, use of anthracycline-based	<p>Most patients were women with early-stage breast cancer</p> <p>Chemotherapy agents were limited with anthracycline-based therapies.</p> <p>General adherence to evidence-</p>

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		<p>treatment in three comprehensive cancer centers in Canada. Breast cancer patients (N = 143), receiving new chemotherapy treatment in outpatient setting for a total of 766 cycles were evaluated. Most patients had early-stage breast cancer with a mean age of 51.4, receiving anthracycline-based therapy. Patients were included with previous chemotherapy regimens if three weeks had elapsed since last treatment. Patients had a good command of English language. Patients were excluded if they currently were receiving chemotherapy, had an estimated survival of less than three months, or had preexisting medical or psychiatric conditions that might make completion of the study difficult. Patients were given daily diaries to record the number of vomiting episodes; the occurrence, intensity, and duration of nausea during first 24 hours and during days 2-5 following chemotherapy; and use of nonprescribed medications at home for emesis control. Patients were contacted via telephone or in person on day 2, day 6, and prior to the next cycle to ensure accurate completion of the diary. Patients were followed and data collected until either cessation of chemotherapy or completion of 6 cycles. Severe nausea and vomiting</p>	<p>administered, patient's expectation of nausea, food intake, anxiety level, and number of hours slept the preceding night.</p> <p>NCI-CTC version 2.0 grading nausea and vomiting 0-4 and four-point Likert Scale for nausea and vomiting (i.e., none, mild, moderate, or severe)</p>	<p>chemotherapy, nausea expectation, and not eating before treatment.</p> <p>The presence of a comorbid disease and the daily use of alcohol were associated with lower rates of acute emesis.</p> <p>The incidence of severe delayed emesis was higher in patients who expected nausea and vomiting, those with a history of morning sickness during pregnancy, and those who reported at least one episode of vomiting during the last 24 hours.</p> <p>Daily alcohol use was associated with lower incidence of severe symptoms during the delayed phase; however, the most common symptom was delayed nausea (70%).</p> <p>More than 60% of patients reported pretreatment anxiety and expectation of nausea and vomiting.</p> <p>These factors have been strongly associated with the development of severe symptoms.</p> <p>Receiving chemotherapy on an empty stomach has been linked to development of severe emesis.</p>	<p>based anti-emetic regimens</p> <p>No control group; patients were not blinded</p> <p>Study design and symptom scales used limit cross-study comparisons.</p>

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		was defined as grade 3/4.		Several factors were identified in this study to help clinicians identify patients at higher risk for developing severe CINV; these patients may benefit from pre-treatment educational sessions and additional antiemetics.	
Chinese Herbal Medicine: PEP Weight-of-Evidence Category: Likely to Be Effective					
Mok et al., 2007	Chinese herbal medicine as complimentary therapy for the reduction of chemotherapy-induced toxicity	Double-blind, placebo-controlled, randomized study of Chinese herbal medicine (CHM) to reduce chemotherapy-induced toxicity was conducted on 120 patients with early-stage breast and colon cancer receiving adjuvant treatment in a university-based cancer center in Hong Kong. Patients were aged 18 years or older; had a ECOG performance status of less than 2; had no prior chemotherapy; and had normal hematologic, liver, and renal function. Patients who required concurrent radiotherapy, were unable to take or follow directions for daily oral medications, had evidence of distant metastasis, had concurrent medical illness, prior chemotherapy, or were females who were pregnant or breast feeding were excluded from the study. Patients were randomly assigned to one of three Chinese herbalists who evaluated and prescribed a combination, single-item, packaged herbal extract granules. Herbalists completed	NCI-CTC (version 2.0) Case report form Daily patient logs European Organization for Research and Treatment of Cancer Quality of Life Questionnaire 30	A formal interim analysis was conducted with half of the target accrual Slower rate of accrual because of patient's lack of interest in a placebo-controlled study and their preference for receiving true CHM The review committee terminated. CHM was not found efficacious for reducing hematologic toxicity associated with adjuvant chemotherapy for breast and colon cancer. CHM did reduce nausea grade 2 in the CHM group compared to the placebo group.	Patient accrual is difficult when the population believes CHM to be effective. Cost and storage is a barrier with the herbal or natural product granules. There are over 225 different types of preparations Trained and certified herbalists for CHM

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		<p>university training and licensed to practice CHM in Hong Kong and China. Patients were randomly assigned to each group and received either CHM or placebo packages with corresponding serial number in a 14-day supply at each clinic visit. The placebo package contained nontherapeutic herbs with an artificial smell and taste similar to typical herb tea. Each patient completed the log for each day's consumption. On days 1 and 14, the participant met with the herbalist in the clinic setting for evaluation and the herbalist documented in case report form. A quality of life questionnaire was completed at baseline, day 1 of each cycle, and at month 4 follow-up.</p>			
<p>Exercise: PEP Weight-of-Evidence Category: Likely to Be Effective</p>					
<p>Andersen et al., 2006</p>	<p>Effect of multidimensional exercise program on symptoms in patients with cancer undergoing chemotherapy as measured by semistructured diaries.</p>	<p>This prospective, exploratory study to evaluate the effectiveness of a six-week structured physical activity, relaxation, and body awareness training techniques as well as massage on self-reported symptoms of patients concurrently undergoing chemotherapy in university outpatient and inpatient settings in Denmark. Participants (N = 54) were aged 18-65 years with a diagnosis of cancer given at least one month prior receiving chemotherapy for adjuvant or</p>	<p>Semi-Structured Diary with 12 symptoms, including lack of appetite, nausea and vomiting, diarrhea, paraesthesia, constipation, physical fatigue, treatment-related fatigue, muscle pain, arthralgia, and other pain, defined by CTC (Cancer Therapy Evaluation Program, 1999).</p> <p>Participants completed daily logs, scoring (0-4) each symptom.</p>	<p>During the intervention, there was a decrease in 10 of 12 symptoms.</p> <p>Patients with evidence of disease scored higher in symptoms than those without evidence of disease.</p> <p>Both groups responded positively to the intervention based on sum of symptom scores.</p> <p>A six-week, multidimensional exercise intervention while</p>	<p>The use of daily diaries is time consuming for patients.</p> <p>There was missing data.</p> <p>Because this continued over time, participants may have recorded the previous score just to fill it in.</p> <p>The exercise program does take commitment-length of time for classes varied from high- and low-intensity groups.</p> <p>Space for workout room in</p>

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		<p>advanced disease with a performance status of 0-1 (WHO). Patients with documented brain metastases; who received anticoagulation treatment or treatment for arrhythmia or myocardial infarction within the past three months; who had dementia and psychotic conditions; or who were unable to read and write in Danish were excluded. The intervention was a structured, supervised exercise program, consisting of resistance-fitness training, massage, relaxation, and body-awareness training held in a workout room within the hospital, two to three times per week for a six-week period. Participants trained in mixed groups of seven to nine. Physiotherapists and a specially trained nurse, who participated in the physical training, supervised the program. Participants selected a total package of high or low intensity physical activity. They were not able select one activity over another.</p>		<p>patients were simultaneously receiving chemotherapy can lead to reduction in symptoms.</p>	<p>hospital setting accessible to inpatients and outpatients may be an issue for some centers.</p> <p>Each symptom was given equal weight whereas some symptoms may be perceived as more problematic for patients.</p> <p>High level of knowledge and skill set of the person training and supervising patients</p>
Winningham & MacVicar, 1988	Subjects were randomized to an experimental exercise group (10-week supervised program with a cycle ergometer and aerobic and interval training three times per week), a placebo group (subjects met with exercise leaders on a weekly basis for conversational	<p>N = 42 women with breast cancer who had a mean age of 46 years No race or ethnicity data were recorded.</p> <p>All patients were receiving chemotherapy (no doxorubicin), had had surgical treatment</p>	Pre-test to post-test nausea responses were coded as improved, no change, or worsened as reported on the Derogatis Symptom Checklist-90-Revised, a 5 –point distress/somatization scale. 12 item somatization scale,	The differences among the experimental, control, and placebo groups were statistically significant, with the experimental group showing marked improvement in nausea compared to the control and placebo groups.	The study was restricted to women with breast cancer who are on a specific aerobic exercise protocol; therefore, the study is not generalizable to other groups with cancer. It cannot be assumed that other exercise techniques will generate the same results.

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	<p>interaction and the mild stretching and flexibility exercises that the experimental group performed during warm-up and cool down), or a control group (received no treatment but were instructed to continue normal activities and notify study personnel if they began exercising).</p>	<p>(mastectomy or lumpectomy), did not have uncontrolled cardiac disease or hypertension were within the first six months of chemotherapy, and had had three treatments before entering the program.</p> <p>Functional capacity at baseline was Zubrod 0–2 or Karnofsky 60%–100%.</p> <p>No participants were in an exercise program, and all were medically cleared by an oncologist.</p> <p>Participants were from a large Midwestern city and were recruited from outpatient clinics, private practices, and a university medical center.</p> <p>The design was randomized, with three groups and pre- and post-test measures.</p>	<p>includes a variety of symptoms common to medical patients</p>	<p>The experimental group showed significant improvements in the Somatization scale scores (i.e., perceptions of autonomically mediated symptoms) over the control and placebo groups.</p>	<p>Patients with a history of hypertension or cardiac disease were excluded. No patients receiving doxorubicin were admitted into the study.</p> <p>Researchers recommended that patients abstain from exercise several hours prior to blood testing and on days of treatment.</p> <p>Exercise testing was monitored by a physician.</p>
Guided Imagery, Progressive Muscle Relaxation, Music Therapy: PEP Weight of Evidence Category: Likely to Be Effective					
<p>Arakawa, 1997</p>	<p>Progressive muscle relaxation training was given to reduce nausea, vomiting, and anxiety induced by chemotherapy.</p> <p>Experimental group received training that consisted of tensing and releasing 16 muscle groups and breathing deeply for a total of 25 minutes. Each subject was provided with an audiotape and instructed to practice independently twice daily before meals or two hours afterward.</p>	<p>N = 60 Japanese patients with cancer (30 subjects in experimental group, 30 subjects in control group) actively receiving chemotherapy in a 415 bed hospital-based cancer center in Japan</p> <p>Ages ranged from 21–75 years; patients did not practice progressive muscle relaxation in their daily lives.</p> <p>The study was a randomized pretest, post-test control group design with repeated measures.</p>	<p>Rhodes Index of Nausea and Vomiting-Form 2 (Japanese version), Spielberger State-Trait Anxiety Inventory</p> <p>Reliability and validity were described in depth.</p>	<p>Progressive muscle relaxation decreased the total index of nausea and vomiting scores of the experimental group.</p> <p>Index of nausea and vomiting scores for the control group increased to their highest level 60–72 hours after chemotherapy.</p> <p>Progressive muscle relaxation may contribute to a reduction in delayed nausea and vomiting. This study did confirm the</p>	<p>The number, type, and dosage of chemotherapy and antiemetics were not controlled.</p> <p>Vomiting scores were very low for the experimental and control groups.</p> <p>Only one investigator conducted the study (investigator bias). The study included only one population (i.e., Japanese).</p>

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	Investigator met with the control group for 15 minutes per day to discuss concerns.			usefulness of progressive muscle relaxation in decreasing the incidence of vomiting. Progressive muscle relaxation decreased subjective feelings of anxiety.	
Borjeson et al., 2002	<p>Study I: A combined antiemetic strategy including a nursing intervention program (increased access to support and increased information and antiemetics based on high-dose metoclopramide and dexamethasone) was compared to standard antiemetic treatment in the 1980s. Patients also were offered progressive muscle relaxation training.</p> <p>Study II: Ondansetron plus dexamethasone or placebo was evaluated.</p> <p>Measures: well-being, nausea and vomiting, anxiety, pain</p>	<p>N = 162 chemotherapy-naive patients with ovarian cancer. All patients received similar combination chemotherapy, including cisplatin (50 mg/m²).</p> <p>Study I included 80 subjects; 46 were in the treatment group (mean age = 57.7 years), and 34 were in the control group (mean age = 55.6 years).</p> <p>Study II included 102 subjects; 53 were in treatment group (mean age = 52.3 years), and 48 were in the control group (mean age = 56.8 years).</p> <p>Setting was in the greater Stockholm, Sweden, area, with two gynecologic oncology wards.</p> <p>Patients were randomly admitted to one of the two hospital wards for the study. Study II was a randomized, double-blind trial on the same hospital wards.</p>	<p>Self-assessment questionnaires were completed by patients the day after and two weeks after chemotherapy.</p> <p>Frequency of nausea and vomiting: yes or no, any episode of emesis, intensity (0–100 VAS)</p> <p>Duration: acute nausea, time of onset of nausea, and number of hours until relieved</p> <p>Delayed nausea, number of days with any symptoms for two weeks after chemotherapy</p> <p>Questionnaires were given regarding well-being before, during, and after chemotherapy. A 0–100 VAS was used to measure aspects of quality of life and well-being.</p>	<p>Relief from delayed symptoms was highest with the antiemetic regimen consisting of high-dose metoclopramide (2.5 mg/kg x 2), dexamethasone (20 mg x 1), lorazepam (1 mg x 2), and biperiden (1-2 mg x 3). After chemotherapy, they received low dose metoclopramide (20 mg x 3) orally for 3 days.</p> <p>Nausea intensity was lowest in ondansetron (8 mg x 3) and dexamethasone (20 mg x 1) IV during the chemotherapy day and ondansetron orally (8 mg x 3) for 5 days after chemotherapy group.</p> <p>Duration of acute nausea was shortest in the high dose metoclopramide group.</p> <p>High dose metoclopramide and ondansetron and dexamethasone groups had better well-being.</p> <p>Duration of acute nausea was the only variable that was significantly related to well-being in both samples.</p> <p>Relaxation training was offered to 20 patients in the ondansetron</p>	<p>Some patients received a benzodiazepine, but no comparison regarding effect can be made.</p> <p>All patients had ovarian cancer, were on the same department, and were treated with similar chemotherapy.</p>

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				and placebo group and 18 in the ondansetron and dexamethasone group; no differences were found in the studied variables.	
Ezzone et al., 1998	<p>Patients were randomly assigned to the control group (usual antiemetic protocol) or experimental group (usual antiemetic protocol plus music intervention during the 48 hours of high-dose cyclophosphamide administered as part of the preparative regimen for autologous or allogeneic bone marrow transplantation).</p> <p>The experimental group listened to self-selected music (by portable compact disc players and headphones) for 45 minutes at 6, 9, and 12 hours after the start of each infusion as an adjunct to antiemetic therapy.</p>	<p>N = 39, but 33 were included in data analysis.</p> <p>Experimental group had 11 males and 5 females; the control group had 8 males and 9 females.</p> <p>The median age was 40.3 years for males and 36.9 years for females.</p> <p>Race and ethnicity were not mentioned.</p> <p>Treatment was autologous or allogeneic bone marrow transplantation, with high-dose preparative regimens.</p> <p>Participants were inpatients at a comprehensive cancer center in the midwestern United States.</p> <p>The study design was a randomized, controlled clinical trial.</p>	<p>Nausea was measured at baseline and every eight hours using a VAS in the form of a thermometer (0–100 in five-degree increments).</p> <p>Nausea was measured the with “feel bad” scale, a five-point Likert scale describing how bad the nausea felt or how sick to the stomach the patient was.</p> <p>Subjective feelings of nausea and all episodes of vomiting were recorded.</p>	<p>Significant differences were found between scores on the VAS for nausea and number of episodes of vomiting; less nausea and fewer instances of vomiting were reported in the experimental group.</p> <p>Music as an adjunct to antiemetic therapy for chemotherapy-induced nausea and vomiting with high-dose chemotherapy can be effective.</p>	<p>Only bone marrow transplant recipients were included, one site was used, and the sample size was small.</p> <p>The study was longitudinal study; therefore, problems existed with multiple data collection points, resulting in some missing data.</p> <p>Compliance issues existed regarding the music intervention.</p> <p>Patients did not always want to listen to music at designated times because they did not feel well or visitors were present.</p>
Molassiotis et al., 2002	Progressive muscle relaxation and guided imagery training were conducted to assess their effectiveness as an adjuvant intervention and accompanying antiemetics (metoclopramide, dexamethasone) in managing acute and delayed nausea and	N = 71 Chinese chemotherapy-naïve women with breast cancer who were older than 30 years and receiving doxorubicin and cyclophosphamide. Patients were receiving treatment at a university hospital outpatient treatment center in	Profile of Mood States, State-Trait Anxiety Index, and Morrow Assessment of Nausea and Vomiting were translated into Chinese and back-translation. Measures were piloted on 25 patients prior to use in the study.	Progressive muscle relaxation therapy with guided imagery was superior to standard antiemetic treatment alone in managing acute and delayed chemotherapy-induced nausea and vomiting.	Pharmacologic agents prescribed were Reglan and dexamethasone for doxorubicin and cyclophosphamide treatment; 5-HT ₃ was not given despite publication in 2002. Only one population was

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	vomiting, anxiety, and depression. For the experimental group, progressive muscle relaxation was initiated for 25 minutes and guided imagery for 5 minutes one hour before chemotherapy was administered.	Hong Kong. Randomized, controlled clinical trial	Demographic data and vital signs measures were used.	<p>The effects of progressive muscle relaxation therapy and guided imagery were more pronounced at the initial stage of treatment when patients did not know what to expect. The effects were less beginning with the 4th day and beyond.</p> <p>The study did not show a significant reduction in the intensity of nausea and vomiting after chemotherapy; the baseline nausea and vomiting values show that the patients in the present study began with considerably lower levels of nausea and vomiting than in previous studies.</p> <p>The combination of progressive muscle relaxation and guided imagery was beneficial for cognitive distraction and relaxation, components that reduce stress and anxiety. The physiologic benefit to these techniques was discussed. Noted differences in Chinese and Western cultures related to expression of emotions.</p>	included: Chinese.
Sahler et al., 2003	A 45-minute music-assisted intervention with relaxation imagery sessions was provided	N = 19 patients aged 5–65 years old	Patient self-reported pre- and post-intervention nausea and pain on a 0–10 scale.	Nausea, pain, and time to engraftment decreased from pre- to post-intervention.	Subjects were not randomized; the study did not inventory personality and other factors that

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	<p>twice a week by a trained therapist from the date of enrollment in the study to discharge.</p>	<p>Bone marrow transplant recipients older than four years undergoing active treatment in a university bone marrow transplant center</p> <p>The study had a case-controlled, nonrandomized convenience sample design.</p>	<p>Time to engraftment also was measured.</p>	<p>The intervention was implemented successfully with a very ill population (i.e., transplant environment).</p>	<p>influence bone marrow transplant outcomes.</p> <p>The intervention was delayed until after transplantation.</p> <p>The frequency of the intervention was lower than planned because of staff perceptions that patients were too sick to participate.</p> <p>Time and attention control condition was not provided to the control subjects.</p>
<p>Troesch et al., 1993</p>	<p>Guided imagery was added to a standard antiemetic regimen; subjects in the experimental group listened to a 20-minute audiotape during chemotherapy administration, and the control group received standard antiemetic regimen alone.</p> <p>The intervention was done over three cycles of chemotherapy. The 20-minute tape was listened to 60 minutes prior to cisplatin, the following morning before breakfast, and the following evening at bedtime.</p>	<p>N = 28 newly diagnosed chemotherapy naive- patients with cancer, who were receiving cisplatin; subjects ages ranged from 33–80 years, and the mean age was 63 years for the control and experimental groups.</p> <p>Patients with gastric cancer, malignancies in the upper gastrointestinal system, or pre-existing disease states of gastrointestinal tract were excluded.</p> <p>Subjects were recruited from one oncologist's practice (inpatients and outpatients) in a large Midwestern teaching center.</p> <p>The study included a convenience sample and was nonrandomized. The conceptual framework used was Orem's Self-Care Deficit Theory of Nursing.</p>	<p>Rhodes Index of Nausea and Vomiting, form 2 (eight-item, five-point, Likert-type, self-report tool): The total score provides the patient's total experience score.</p> <p>The Chemotherapy Experience Survey was used to evaluate overall perceptions of the chemotherapy experience (designed by researchers). It has two parts: The first is a five-point, Likert-type tool with eight word pairs ranging from negative to positive, and the second is a rating of overall chemotherapy experience (10 = most negative, 100 = most positive).</p>	<p>No statistical significance was demonstrated with symptom occurrence and distress.</p> <p>Guided imagery did not have a statistically significant effect on patients' perceptions of the frequency of nausea, vomiting, and retching, and associated distress.</p> <p>Patients who participated in the guided imagery felt significantly more in control, powerful, relaxed, and prepared than the control group.</p> <p>The guided imagery group described their overall experience more positively than the control group.</p>	<p>Only adult patients receiving cisplatin were included; in addition, one physician office was used for sample (could control antiemetic regimen). The scope was limited, and the study had a small sample size.</p> <p>Complex monitoring over three cycles, communication difficult, inability to control hospital setting and activities were limitations of the study.</p>

Oral Dissolving Tablet Ondansetron for Prevention of CINV With Highly Emetogenic Chemotherapy: PEP Weight-of-Evidence Category: Likely to Be Effective

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Pectasides et al., 2007	Compare oral ondansetron to oral dissolving tablet (ODT) ondansetron at same dose (8 mg twice daily for three days)	Patients (N = 134) with breast cancer receiving first doses of highly emetogenic, phase II randomized trial, 66 in the ODT arm and 68 in the oral arm	Diary to record emesis and nausea episodes Intensity of nausea measured with a four-point Likert scale	Inferior emesis control in the ODT arm (52% for ODT versus 72% for oral arm, p = 0.020) and more patients in the ODT arm required rescue medication Patients in the ODT arm also had significantly higher nausea intensity (p = 0.036); as such, the ODT arm was found to be inferior for emesis control than oral arm.	
Psychoeducational (Support and Education): PEP Weight-of-Evidence Category: Likely to Be Effective					
Williams & Schreier, 2004	<p>To determine the effectiveness of audiotapes on self-care behaviors, state anxiety, and the use of self-care behaviors</p> <p>To describe the occurrence and intensity of common side effects in patients with breast cancer</p> <p>Two 20-minute audiotapes provided information on nutritional management of side effects, exercise, and relaxation techniques along with written transcripts that were professionally developed at a fifth-grade reading level.</p> <p>All subjects received standard education for the clinic but not standardized education. The experimental group received audiotapes and transcripts via mail and were provided with a cassette player if they did not</p>	<p>N = 70 women with newly diagnosed stage I or II breast cancer starting the first cycle of chemotherapy treatment; most women received docorubicin and cyclophosphamide.</p> <p>43% of the population was African American population, and half were younger than age 50.</p> <p>The setting was outpatient chemotherapy clinics operated by a university center in satellite clinics in rural areas of southeastern United States that covered 29 counties.</p> <p>The design was an experimental, randomized, clinical trial.</p> <p>The conceptual framework was Orem's Self-Care Deficit Theory (1995)</p>	<p>Spielberger State-Trait Anxiety Instrument</p> <p>Nail Self-Care Dairy (modified)</p> <p>Measures: anxiety, self-care measures in diary (nausea, fatigue, taste change, difficulty sleeping)</p>	<p>Informational audiotapes are effective teaching tools.</p> <p>Self-care behaviors can be taught and be effective in managing side effects.</p> <p>Women who used the audiotapes demonstrated effective self-care behaviors over time, whereas the control group appeared to experiment to find effective self-care behaviors.</p> <p>Anxiety was high in both groups, but the symptoms decreased among women who received audiotapes and telephone calls.</p> <p>The most frequently experienced side effects were fatigue, nausea and vomiting, and taste changes.</p> <p>The number of women reporting nausea and vomiting decreased by half from the first and second self-care diary.</p> <p>More self-care behaviors were</p>	<p>The amount and type of information received in clinics and from community was not controlled.</p> <p>A limitation of the study was a small sample size. In addition, the telephone intervention may have had a substantial effect on patients' behaviors. The questions asked during the phone interview reinforced self care behaviors in the experimental group and provided information to women in the control group that they may not have had otherwise.</p> <p>The age of the population (half were younger than the age of 50) should be considered.</p> <p>The intervention was expensive; costs were incurred when developing the audiotapes in a studio with a professional</p>

Nausea and Vomiting

Evidence Table

(Literature search completed through May 2008)

Author and Year	Characteristics of the Intervention	Sample Characteristics, Setting Characteristics, Study Design, and Conceptual Model	Measures	Results and Conclusions	Limitations, Major and Minor Flaws, Cautions and/or Contraindications, Special Training Needs, and Costs
	<p>have one at home. All subjects were interviewed three times via telephone.</p>			<p>used for nausea and vomiting than any other side effect experienced by the subjects.</p> <p>Prescription medications were the most frequently used self-care behavior and were effective over time.</p>	<p>speaker.</p>
<p>Intervention: Virtual Reality: PEP Weight-of-Evidence Category: Benefits Balanced With Harms</p>					
<p>Oyama et al., 2000</p>	<p>The purpose of the study was to develop a new treatment using virtual reality technology as an intervention to decrease chemotherapy-related side effects in patients with cancer.</p> <p>Patients chose a preferred aromatic essential oil, sound system (headphone or speakers), and content. Three virtual worlds (lake, forest, and country town) were available, and each lasted about 20 minutes.</p> <p>The length of the intervention was dependent on the length of chemotherapy. If chemotherapy was long, patients could rest and restart the intervention.</p>	<p>N = 30 (6 males, 24 females) who had an average age of 53.5 years (range = 18–70 years)</p> <p>The setting was an outpatient clinic at a national cancer center hospital in Japan.</p> <p>The study had a randomized, controlled design.</p>	<p>Hospital Anxiety and Depression Scale</p> <p>Cancer Fatigue Scale</p> <p>Face Visual Analogue Scale</p> <p>Emesis was measured using a VAS after the experience.</p>	<p>Fatigue and emesis scores decreased three to five days after chemotherapy.</p> <p>The decreases in fatigue and emesis score 3-5 days after chemotherapy were statistically significant (both $p < 0.05$)</p> <p>Carry-over effects were detected.</p> <p>Emesis was strongly related to psychological state.</p> <p>The intervention decreased postinfusion emesis.</p> <p>Virtual reality may be a new way to treat emesis.</p>	<p>Nausea was not measured, only the number of time a patient vomited was measured. The VAS was used postemesis as a measure of vomiting.</p> <p>The study did not use available tools to measure nausea, vomiting and retching.</p> <p>The fatigue scale was developed by an institution.</p> <p>Motion sickness is a potential side effect when using virtual reality.</p> <p>The cost of the virtual reality system and set-up must be considered.</p>
<p>Pharmacologic Intervention: Mirtazapine: PEP Weight-of-Evidence Category: Effectiveness Not Established</p>					
<p>Kim et al., 2008</p>	<p>Evaluate the effectiveness of mirtazapine for nausea and insomnia in patients with cancer with depression</p>	<p>Four-week, prospective, open-label study of 28 patients with cancer with depression to evaluate the effectiveness of</p>	<p>Clinical Global Impression Scale for Nausea and Vomiting</p> <p>Chonnam National University</p>	<p>Most patients (26/28) experienced significantly improved nausea from day 1 without increasing dosages or</p>	<p>There is a possibility that a placebo effect influenced the results. It was not a controlled trial. The sample size was small</p>

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		<p>mirtazapine in reducing nausea and insomnia. Patients were eligible if they had a malignant cancer with nausea or insomnia and met <i>Diagnostic and Statistical Manual for Mental Disorders VI</i> diagnostic criteria for major depression. Participants were excluded if they were taking other antidepressants to control depressive symptoms. Participants were recruited from a university cancer center in Korea. Assessments were conducted at baseline, days 1, 3, 5, 7, 14, and 28 by trained psychiatrists in an outpatient clinic. In addition, side effects were assessed with each visit.</p>	<p>Hospital-Leeds Sleep Evaluation Questionnaire</p> <p>Montgomery-Asberg Depression Rating Scale (MADRS)</p> <p>Euro-Qol (EQ-5D)</p> <p>Short Form Health Survey (SF-36)</p>	<p>adding antiemetics.</p> <p>The subjects were divided into two groups: patients undergoing chemotherapy (n = 11) and those who were not (n = 17) The improvement was sustained in both groups; however, changes in nausea were greater for patients receiving chemotherapy.</p> <p>Total night sleep time improved from days 1-5.</p> <p>A reduction in scores for pain and anxiety on the MADRS and the VAS of EQ-5D</p> <p>Mirtazapine rapidly improved nausea, sleep disturbance, pain, depression, and quality of life for patients with cancer.</p>	<p>with a large number of variables. The physical status, symptom of depression, frequency and length of assessments, and outpatient clinic visits for the assessment may have contributed to a high drop out rate by participants.</p>
<p>Pharmacologic Intervention: Skipping Day 2 Antiemetics: PEP Weight-of-Evidence Category: Effectiveness Not Established</p>					
<p>Lajolo & del Giglio, 2007</p>	<p>Evaluating a hypothesis that skipping day 2 antiemetic medications may improve delayed CINV through two pilot trials. Hypothesis: Repeated consecutive doses of antiemetics may lead to increased accumulation of 5HT₃ at the presynaptic level in the gastrointestinal tract, decreasing the activity of the next dose of a 5HT₃ receptor antagonist (tachyphylaxis).</p>	<p>42 chemotherapy-naïve patients, > 18 years old and receiving MEC to HEC participated in two pilot studies while receiving care in hematology and oncology department in a School of Medicine in Brazil. Patients were excluded with an abnormally high serum creatinine, bilirubin, or SGPT, If pregnant, and if who reported vomiting or used antiemetics 24 hours before the administration of chemotherapy, or who receiving radiation therapy. Patients with brain metastasis, gastrointestinal</p>	<p>Functional Living Index of Vomiting (FLIE)</p>	<p>21 patients were on each study with no significant differences between the two populations in terms of clinical characteristics or chemotherapy emetogenicity. Patients who received no antiemetic medications on day 2 had statistically significant complete control of their nausea and vomiting. Skipping day 2 antiemetic medications does not seem to worsen delayed CINV and may reduce CINV.</p>	<p>The limitations are: non-randomized design small sample size</p>

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		<p>obstruction, or who used regularly corticosteroids or benzodiazepines before the initiation of chemotherapy. Patients were given day 1 antiemetics according to ASCO guidelines. Patients on Study 1 received metochlopramide 10 mg po q 8 hours, granisetron 0.5 mg po QD, and dexamethasone 8 mg QD on days 2 and 3. On Study 2, patients received the same medications, but no drugs were given on day 2. Patients recorded emetic episodes in a diary and responded to QOL questionnaire at baseline and day 6.</p>			
<p>Pharmacologic Intervention: Topical ABH Gel: PEP Weight-of-Evidence Category: Effectiveness Not Established</p>					
<p>Bleicher et al., 2008</p>	<p>The results of two pilot trials on the efficacy of a topical gel containing lorazepam, diphenhydramine, and haloperidol (ABH), in reducing CINV among patients with cancer were described.</p>	<p>Trial 1: 23 adult patients with a cancer diagnosis (solid tumor or hematology) receiving chemotherapy in an outpatient clinic of a university in the midwestern United States; they were prescribed prophylactic antiemetics standard guidelines. This method was initiated in one physician practice. Patients were given a prescription for six, prefilled, capped tuberculin syringes of ABH gel when they received emetogenic chemotherapy. The same gel formulation was used in both trials. The patients were instructed to use the ABH gel when they developed significant nausea and/or vomiting in the</p>	<p>Trial 1: standardized questionnaire developed for the study</p> <p>Trial 2: numeric rating scale, ranging 0 (no nausea or vomiting) to 10 (worst imaginable nausea or vomiting)</p>	<p>Trial 1: 74% of patients believed the gel decreased their nausea, and 70% of patients experienced relief from vomiting. Seventy percent of patients reported relief within 30 minutes of applying the gel. Thirteen percent of patients reported fatigue after using the gel. No patients reported skin irritation or muscle spasms.</p> <p>Trial 2: Nausea scored significantly decreased at 30 minutes. No significant side effects were reported.</p> <p>Transdermal ABH gel decreases the severity of CINV with minimal side effects, only slight sedation reported.</p>	<p>Small sample size</p> <p>Heterogeneous population</p> <p>No control for disease, chemotherapy agents, cycle, or antiemetic agents</p> <p>Trial 1 was retrospective asking participants to recall symptom experience.</p> <p>Convenient and easily taught to patients; however, availability of this combination topical agent may be a challenge in community settings because hospital pharmacies are less likely to compound products.</p>

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Evidence Table

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		<p>days that followed chemotherapy and the option to repeat it at six-hour intervals. They were instructed to place 0.5 ml of the gel on the palmar aspects of their wrist using the prefilled syringe. After applying the gel, the participants were instructed to rub their wrist together gently for one to three minutes to facilitate transdermal absorption. Patients were contacted by telephone within one month by the investigator. Patients provided verbal informed consent when called to answer questions about their progress with ABH gels using a standard questionnaire, developed for the pilot. They were asked to rate their CINV and if they believed the gel to cause sedation, skin irritation, or muscle spasms.</p> <p>Trial 2: 10 adult patients with a cancer diagnosis; no control for diagnosis or chemotherapy treatment; following verbal consent, an investigator used a structured interview by telephone or in person to rate the severity of their CINV on a combined scale at 30 minutes and four hours after applying ABH gel.</p>			
<p>Alternative Dosing Regimen: Palonosetron on Days 1, 3, and 5 for Prevention of CINV With Highly Emetogenic Chemotherapy: PEP Weight-of-Evidence Category: Effectiveness Not Established</p>					
Einhorn et al., 2007	Patients received 0.25 mg IV palonosetron as a	Study design to evaluate safety and efficacy of palonosetron plus	Number of emetic episodes (vomiting and retching)	Descriptive analysis shows rates of CR	Small sample size

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	<p>infusion 30 minutes before chemotherapy on days 1, 3, and 5 plus dexamethasone 20 mg IV on days 1 and 2, 8 mg orally twice daily on days 6 and 7, and 4 mg orally twice daily on day 8.</p>	<p>dexamethasone for patients receiving multiple day HEC. Patients (N = 41) with germ cell tumors were enrolled. Given the high receptor binding affinity and prolonged half-life of palonosetron, this study did alternate day dosing (days 1, 3, and 5 rather than days 1-3) combined with a standard dexamethasone regimen for multiple-day cisplatin-based chemotherapy.</p>	<p>Use of rescue medication</p> <p>Intensity and duration of nausea (four-point Likert scale used for nausea intensity).</p> <p>Osoba nausea module, which assesses five patient-rated items using a four-point scale was used to evaluate the effect of nausea on patients' quality of life.</p> <p>Pharmacokinetic data (PK) also was collected.</p>	<p>The protocol prevented vomiting for most subjects at all timepoints of the study (days 1-9) (the lowest percentage came at day 4 when 68% of patients reported no vomiting).</p> <p>Some protection against nausea provided, with 59% or more of patients reporting no, or, at maximum, mild nausea at any time on each study day.</p> <p>No severe adverse events noted; most common were headache and constipation, no evidence of cumulative toxicity</p> <p>PK data reported.</p>	<p>No control arm</p> <p>Nonrandomized trial</p>
<p>Acustimulation: PEP Weight-of-Evidence Category: Effectiveness Not Established</p>					
<p>Roscoe et al., 2002</p>	<p>Patients who had previously experienced moderate or more severe nausea following their first chemotherapy treatment were screened for the study.</p> <p>Patients were scheduled to receive at least three more chemotherapy treatments without radiotherapy or interferon.</p> <p>This randomized controlled trial used a 3 level crossover design (active acustimulation, sham acustimulation, and no acustimulation). All patients received standard antiemetics</p>	<p>N = 27 (25 women, 2 men) patients with a mean age of 49.7 years</p> <p>Most were Caucasian, but one was African American and one was Asian.</p> <p>Cancers types: Breast (81%) Colorectal (11%) Ovarian (4%) Lung (4%)</p> <p>Setting was three outpatient oncology clinics in the northeastern United States.</p> <p>The study design was a randomized clinical trial using a</p>	<p>A patient report diary was used. Patients reported on the severity of nausea for each period (morning, afternoon, evening, night) on the day of treatment and on the following four days. Severity of nausea was assessed on a seven-point rating scale. Patients also reported on the type and total number of antiemetic pills taken on days 1–5.</p>	<p>No statistical differences in average severity of nausea were observed between the interventions.</p> <p>A nearly significant difference was found in the severity of delayed nausea reported during active acustimulation compared to no acustimulation.</p> <p>Findings were positive but not conclusive.</p>	<p>The sample size was small, and data were missing.</p> <p>The study did not account for medication changes (antiemetics).</p> <p>The wristband may cause a placebo effect; mood elevation may be possible with nerve stimulation and the release of endorphins.</p> <p>Caution should be used in patients with pacemakers.</p>

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Evidence Table

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	<p>ordered by the physician. Patients wore a wristband before chemotherapy and as needed.</p> <p>Patients could adjust the stimulation intensity.</p>	<p>three-level crossover design (active acustimulation, sham acustimulation, and no acustimulation)</p>			
Roscoe et al., 2003	<p>Patients were randomized to</p> <ol style="list-style-type: none"> 1. Acupressure bands (Seabands®) 2. Acustimulation band (ReliefBand®) 3. No band control. <p>The intervention or lack of intervention was used in combination with standard antiemetics for chemotherapy-induced nausea and vomiting.</p> <p>Patients wore devices (if any) continuously for five days, and those in the acustimulation band group could adjust the intensity of stimulation.</p>	<p>N = 739 chemotherapy-naïve patients 85% had breast cancer, and 10% had hematologic neoplasms.</p> <p>88% were white, and 92% were female.</p> <p>Patients about to begin cancer treatment, with regimens containing cisplatin or doxorubicin, without concurrent radiation therapy or interferon.</p> <p>The setting was outpatient clinics at 17 geographically diverse member sites of the University of Rochester Clinical Oncology Program.</p> <p>The study design was a randomized controlled trial.</p>	<p>Patient report diary (morning, afternoon, evening, night)</p> <p>Patients reported on the severity of nausea and number of vomiting episodes for each period on the day of treatment and the following four days on a seven-point scale.</p> <p>Quality of Life was measured using the Functional Assessment of Cancer Therapy Scale-General.</p> <p>Demographic data, chemotherapy information, and antiemetics</p> <p>Efficacy reports of wristband(s) were assessed on a five-point scale prior to treatment.</p>	<p>Patients in the acupressure condition experienced less nausea on the day of treatment compared to controls.</p> <p>No significant differences existed in delayed nausea and vomiting among the three groups.</p> <p>Pronounced gender differences existed: Men in the acustimulation group had less nausea and vomiting compared to controls.</p> <p>No significant differences existed in women among the three groups, although the reduction in nausea on the day of treatment in the acupressure group approached clinical significance.</p>	<p>A possible placebo effect existed.</p> <p>Patients with pacemakers excluded, bowel obstruction, or symptomatic brain metastases were excluded.</p>
Roscoe et al., 2005	<p>96 women with breast cancer who received doxorubicin and cyclophosphamide were randomized to</p> <ol style="list-style-type: none"> 1. Active acustimulation 2. Sham acustimulation 3. No acustimulation. <p>Participants were told to wear the assigned band and adjust the acustimulation dial to</p>	<p>N = 96 of 107 women with breast cancer on the second cycle of chemotherapy who were randomized provided evaluable data. Patients' mean age was 49.5 years</p> <p>87 were white, and 8 were African American.</p> <p>89 of 96 took some type of antiemetic following treatment.</p>	<p>Demographic information and details of prior nausea and vomiting experience</p> <p>Five-point Likert-type questions were assessed at the time of randomization following a one-minute trial of the band.</p> <p>Nausea and emesis were measured by a patient report diary that was completed over</p>	<p>No significant differences were found in any study measures among the three treatment conditions.</p> <p>The study does not support the use of acustimulation bands as an adjunct to antiemetics in female patients with breast cancer.</p>	<p>Only women were included in the study.</p> <p>The band could be viewed as a reinforcer (negative conditioning effect) and reminder of an unpleasant state.</p> <p>Patients with brain metastases, bowel obstructions, or cardiac pacemakers, or those</p>

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	increase or decrease the acustimulation; they could wear the band as frequently as desired over five days.	All participants were treated at outpatient centers at one of four Rochester, NY, area cancer centers The study design was a randomized, three-arm trial.	the five-day period. The severity of nausea and vomiting episodes, as well as antiemetics, were recorded. Other measures: quality of life with the Functional Assessment of Cancer Therapy Scale-General		undergoing concurrent radiation therapy or interferon therapy were excluded.
Treish et al., 2003	Adult cancer patients receiving MEC or HEC were randomized to receive the active Reliefband © or an inactive device. All patients received scheduled and as-needed antiemetics. Patients wore devices continuously for 5 days, except during showering and hand washing.	N = 49 men and women with a median age of 45 years Diagnoses included leukemia, non-Hodgkin lymphoma, sarcoma, and breast, head and neck, lung, and other cancers. A variety of chemotherapy regimens were reported that met criteria for MEC or HEC. Many subjects had three to four prior chemotherapy cycles. All were inpatients at the University of North Carolina Hospitals (single site). All received single- or multiday chemotherapy, including myeloablative chemotherapy for bone marrow transplant. The study design was a randomized, prospective, double-blind, placebo-controlled trial.	Daily diary of nausea, vomiting, retching episodes, and antiemetic medications taken Functional Living Index Emesis and tolerability survey at the conclusion of the study	Patients wearing the Reliefband experienced less vomiting, retching, and nausea severity over the five-day period than patients wearing the inactive device. Vomiting was statistically and significantly reduced during the delayed period, and nausea was significantly reduced during the acute and delayed periods. Functional Living Index Emesis scores did not differ between the two groups.	Differences existed in risk factors for emesis, chemotherapy, and antiemetic regimens. The sample size was small. Patients with pacemakers, a low life expectancy, and poor performance status (greater than three) were excluded.
Exercise: PEP Weight-of-Evidence Category: Effectiveness Not Established					
Andersen et al., 2006	Effect of multidimensional exercise program on symptoms in patients with cancer	This prospective, exploratory study to evaluate the effectiveness of a six-week	Semi-Structured Diary with 12 symptoms, including lack of appetite, nausea and vomiting,	During the intervention, there was a decrease in 10 of 12 symptoms.	The use of daily diaries is time consuming for patients.

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	<p>undergoing chemotherapy as measured by semistructured diaries.</p>	<p>structured physical activity, relaxation, and body awareness training techniques as well as massage on self-reported symptoms of patients concurrently undergoing chemotherapy in university outpatient and inpatient settings in Denmark. Participants (N = 54) were aged 18-65 years with a diagnosis of cancer given at least one month prior receiving chemotherapy for adjuvant or advanced disease with a performance status of 0-1 (WHO). Patients with documented brain metastases; who received anticoagulation treatment or treatment for arrhythmia or myocardial infarction within the past three months; who had dementia and psychotic conditions; or who were unable to read and write in Danish were excluded. The intervention was a structured, supervised exercise program, consisting of resistance-fitness training, massage, relaxation, and body-awareness training held in a workout room within the hospital, two to three times per week for a six-week period. Participants trained in mixed groups of seven to nine. Physiotherapists and a specially trained nurse, who participated in the physical training, supervised the program. Participants selected a total</p>	<p>diarrhea, paraesthesia, constipation, physical fatigue, treatment-related fatigue, muscle pain, arthralgia, and other pain, defined by CTC (Cancer Therapy Evaluation Program, 1999).</p> <p>Participants completed daily logs, scoring (0-4) each symptom.</p>	<p>Patients with evidence of disease scored higher in symptoms than those without evidence of disease.</p> <p>Both groups responded positively to the intervention based on sum of symptom scores.</p> <p>A six-week, multidimensional exercise intervention while patients were simultaneously receiving chemotherapy can lead to reduction in symptoms.</p>	<p>There was missing data.</p> <p>Because this continued over time, participants may have recorded the previous score just to fill it in.</p> <p>The exercise program does take commitment-length of time for classes varied from high- and low-intensity groups.</p> <p>Space for workout room in hospital setting accessible to inpatients and outpatients may be an issue for some centers.</p> <p>Each symptom was given equal weight whereas some symptoms may be perceived as more problematic for patients.</p> <p>High level of knowledge and skill set of the person training and supervising patients</p>

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		package of high or low intensity physical activity. They were not able select one activity over another.			
Ginger: PEP Weight-of-Evidence Category: Effectiveness Not Established					
Manusirivithay et al., 2004	Regimen A: 1 g of ginger per day for five days starting on the first day of chemotherapy Regimen B: placebo given on day 1 and metoclopramide on days 2–5	N = 48 females being treated for a gynecologic cancer who were receiving cisplatin chemotherapy in Bangkok, Thailand	Number of emetic episodes	Regimen A: No effect was found in acute or delayed treatment. Regimen B: For delayed nausea, ginger had same control as metoclopramide 40 mg.	The sample size was small; comparing antiemetics was difficult because the study did not use 5-HT ₃ antiemetics.
Hypnosis: PEP Weight-of-Evidence Category: Effectiveness Not Established					
Marchioro et al., 2000	The use of hypnosis in anticipatory nausea and vomiting Two-hour training of progressive relaxation, followed by a one-hour hypnosis program No drugs were given in association with the hypnotherapy. After the intervention, patients immediately went to their scheduled chemotherapy.	N = 16 (14 females, 2 males) adults with anticipatory nausea and vomiting from at least four previous courses of chemotherapy; median age was 44 years. Patients did not have metastatic disease to the brain or gastrointestinal tract. Cancer types included were ovarian, Hodgkin, testicular, lung, and breast. Chemotherapy received included cisplatin, carboplatin, cyclophosphamide, dacarbazine, doxorubicin, and epirubicin. All patients were from an outpatient setting. The sample was a convenience sample. All patients had to have previously undergone four cycles of 5-HT ₃ and developed nausea and vomiting.	VAS CR (mild nausea with no vomiting), major response (moderate to severe nausea and one vomiting episode), or no response (none of the above)	In all of the 16 patients in the study, anticipatory nausea and vomiting disappeared. There were major responses (moderate to severe nausea, with 1 vomiting episode) to chemotherapy induced emesis control in 14 of the 16 patients.	The study included a very small population. No interrater reliability was reported. No control group was used. Patients with brain metastasis or cognitive disabilities were excluded. Caution should be used regarding patient selection; some patients should not be hypnotized.
Massage/Aromatherapy: PEP Weight-of-Evidence Category: Effectiveness Not Established					

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Ahles et al., 1999	<p>Patients scheduled to undergo bone marrow transplant were randomly assigned to</p> <ol style="list-style-type: none"> 1) Massage therapy, consisting of 20-minute sessions of shoulder, neck, head, and facial massage. As many as nine sessions were reported during patients' hospital stay. The average length of stay was three weeks; therefore, three massages were slated per week. Massages were performed by a trained, healing arts specialist with more than 10 years of experience. <p>Standard treatment.</p>	<p>N = 34 patients with a mean age of 41 years \pm 9.3</p> <p>Race and ethnicity were not evaluated.</p> <p>All patients were bone marrow transplant recipients; The majority of the patients had breast cancer (22 of 34), and the remaining patients had acute myelogenous leukemia, non-Hodgkin's lymphoma, Hodgkin's lymphoma, and other (ovarian cancer or acute promyelocytic leukemia).</p> <p>Participants were inpatients and were scheduled for bone marrow transplant at Dartmouth-Hitchcock Medical Center in New Hampshire.</p> <p>The study design was a randomized, controlled clinical trial.</p>	<p>Numeric scales for nausea (0–10), with 0 representing an absence of the symptom and 10 representing an extreme level of the symptom</p> <p>Total dosages of opioids, anxiolytics, and/or antiemetics were recorded because of confounding effects of the drugs on anxiety, nausea, and emotional distress.</p> <p>Data were collected prior to and following the patients' first, fifth, and final massages (on day 7 and at mid-treatment and pre-discharge)</p>	<p>Patients in the massage group experienced significantly larger reductions in nausea than the standard group at day 7.</p> <p>The strongest effects were seen immediately after massage when patients experienced a reduction in diastolic blood pressure, nausea, distress, and anxiety.</p> <p>How long the positive effects were maintained is difficult to evaluate.</p>	<p>A small sample size was used from one institution.</p> <p>The timing of massage was variable.</p>
Billhult et al., 2007	<p>Intervention consisted of five massage sessions (effleurage), lasting about 20 minutes. Control group received visit by hospital staff member (attention control).</p>	<p>Prospective trial with random assignment to one of two groups: the intervention group (n = 19) and the control group (n = 20). Patients had breast cancer, were enrolled prior to start of third cycle of chemotherapy, and were assigned to groups randomly.</p>	<p>100 mm VAS for nausea and anxiety was completed before and immediately after the massage intervention or after the staff visit for the control group.</p> <p>Hospital Anxiety and Depression Scale (HAD) was completed before the first and last massage session.</p>	<p>No differences in anxiety (as measured by the VAS) between groups.</p> <p>No differences between groups or within groups over time in anxiety or depression as measured by HAD.</p> <p>Authors stated that nausea was significantly reduced in the massage group, as measured by the VAS; they do not report raw scores, but as "percentage improved."</p>	<p>Massage intervention delivered by hospital staff (nurses and nurse's aid) after one day of training</p> <p>No control for consistency or adequacy of the intervention</p> <p>Assessed nausea only, not vomiting.</p> <p>Assessed nausea (by VAS) immediately before and after the massage, but the massage was delivered during the chemotherapy infusion and</p>

Nausea and Vomiting

Evidence Table

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				Difficult to interpret or understand the findings as written?	<p>nausea measured right after.</p> <p>Seems erroneous to conclude that "massage reduces nausea" when nausea was not assessed at the points when one might expect it to be a problem (e.g., patients received antiemetic prophylaxis with 5HT3 and steroid, would one expect severe nausea 30 minutes into the chemo infusion?)</p> <p>Measurement/sampling period does not coincide with when one would expect nausea to be most severe or occur at all? Measured nausea prior to start of massage, but why expect nausea to be present or severe at this point??</p>
Cassileth & Vickers, 2004	Patients with cancer received massage (i.e., light touch, Swedish, or foot).	<p>N = 1,290 (1,255 reported on the nausea question.)</p> <p>Researchers were unable to ascertain which patients were receiving chemotherapy.</p> <p>Inpatients and outpatients</p> <p>No control group was included. Patients were self-referred or referred by a physician.</p>	VAS measured nausea and vomiting, pain, fatigue, stress, anxiety, and depression.	51% experienced decreased nausea.	Bias exists for nontraditional treatment.
Grealish et al., 2000	Patients were given a 10-minute foot massage (five minutes per foot). Inpatients received the massage on three consecutive days from 7–8 pm. Massage was slow and firm, or gentle strokes toward the heart were used, from the base of	<p>N = 87 (52 women, 35 men) aged 18–88 years</p> <p>Inclusion criteria were a diagnosis of cancer, age 18 years or older, reported pain and/or nausea, and no recent surgery in the past six weeks.</p> <p>Primary cancer sites varied, and</p>	<p>100 mm VAS (0 mm = no nausea, 100 mm = vomiting or dry retching)</p> <p>Heart rate and subjective data were measured at two intervals: before the massage and 10–20 minutes after completion of the</p>	<p>Evidence exists that massage reduces feelings of nausea.</p> <p>No significant difference was found between the control session pretest mean nausea score and post-test score.</p> <p>In contrast, the mean nausea</p>	<p>The study did not control for medications, although they were recorded.</p> <p>Findings were not correlated with diagnosis, type of cancer, metastases, or treatment schedules.</p>

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	<p>the toes up the foot and lower leg to the knee.</p> <p>A short foot massage was done before enrolling in the study to reduce the possibility of anticipatory anxiety.</p>	<p>32 had metastatic disease.</p> <p>All were inpatients, and no further setting description was provided.</p> <p>The convenience sample was randomly assigned to one of three groups.</p>	<p>massage.</p> <p>On control nights, participants stayed quietly in bed and did a quiet activity with the same measurements.</p>	<p>score for massage sessions 1 and 2 decreased.</p> <p>t = 3.117, p = 0.0012, difference of 6.4 mm</p> <p>t = 3.178, p= 0.0011, difference of 4.9 mm</p>	<p>Long-term effects are unknown.</p> <p>Pain and relaxation were measured as well as nausea and vomiting</p>
<p>Olanzapine for Prevention of CINV With Highly and Moderately Emetogenic Chemotherapy: PEP Weight-of-Evidence Category: Effectiveness Not Established</p>					
<p>Navari et al., 2007</p>	<p>Olanzapine 10 mg orally every day four times a day; olanzapine as prevention (rather than as agent for breakthrough N/V); attempt to examine effectiveness of olanzapine and to avoid use of dexamethasone on days 2-4.</p>	<p>Chemotherapy-naïve patients (N = 40) receiving HEC or MEC. On day 1 of chemotherapy, patients received palonosetron 0.25 mg IV and dexamethasone (8 mg for MEC, 20 mg for HEC) as well as olanzapine 10 mg orally. On days 2-4, patients received only olanzapine 10 mg daily. The same antiemetic regimen was continued for as many cycles as the patient completed (1-6 cycles). Patients received no other anti-emetics on days 2-4. Patients were permitted to take rescue therapy. Prospective, nonrandomized trial with no control or comparison group; descriptive analysis only (percentage of patients with response described).</p>	<p>M.D. Anderson Symptom Inventory (MDASI)</p> <p>Patient recording of daily episodes of vomiting and retching</p>	<p>CR defined as no emesis and no rescue medications administered and no nausea) in 100% of HEC patients and 97% of MEC patients in the acute period (0-24 hours after chemotherapy).</p> <p>Responses for the delayed period (24-120 hours) decreased</p> <p>Seventy-five percent of patients with CR in delayed and overall period for emesis and even less for control of nausea (50% of HEC patients with CR for nausea and 78% of MEC patients had CR for nausea in the delayed and overall period)</p> <p>No adverse events to study drugs noted (no grade 3 or 4 toxicities).</p> <p>Olanzapine was not associated with sedation, weight gain, or hyperglycemia.</p>	<p>Sample size small</p> <p>Investigators state that olanzapine, dexamethasone, and palonosetron combination was effective in controlling acute and delayed CINV in patients receiving both HEC and MEC; however, there was no control or comparison group.</p> <p>Difficult to compare effectiveness as compared to what treatment? (Although investigators do state as compared to studies using triple drug regimen, but there is no head-to head comparison in this study.) Especially given that aprepitant was not used and is now recommended per guidelines. Furthermore, 50% of the patients in the HEC group (n = 8 only) still experienced nausea in the delayed and overall study period (0-120 hours after chemotherapy).</p> <p>Twenty-two percent of patients</p>

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					<p>receiving MEC still experienced nausea in the delayed and overall period.</p> <p>Use of rescue medications not described, although it is stated that these were allowed and patients were permitted to continue in the study even if rescue medications used.</p>
<p>Progressive Muscle Relaxation: PEP Weight-of-Evidence Category: Effectiveness Not Established</p>					
<p>de Carvalho et al., 2007</p>	<p>Effect of progressive muscle Relaxation on CINV</p>	<p>A pilot study of 30 hematology patients who were aged 18 years or older, had diagnosis of cancer, were receiving a cycle of chemotherapy and experiencing nausea and vomiting at the time of data collection, and hospitalized in a large hospital in Brazil. Participants were capable of maintaining a logical conversation and had not received antiemetics five hours before relaxation intervention. Patients with evolving multiple myeloma and suspected bone fractures were excluded. Pre- and post-test study tested the efficacy of progressive muscle relaxation on patients receiving chemotherapy by measuring specific physiologic and self-report variables before and after a progressive muscle relaxation intervention. An RN trained on how to measure physiologic alterations and muscle reactions collected data. Patients were asked to consider the presence</p>	<p>Physiologic indicators of nausea (i.e., vital signs, perspiration, pupil dilatation, salivation, and skin color)</p> <p>Muscle reactions (e.g. forearm, leg, forehead, and eye tension)</p> <p>Huskisson's VAS (adapted version) for nausea and vomiting intensity levels</p>	<p>Progressive muscle relaxation decreases physiologic conditions, muscle reactions, and statistically significant reduction in the intensity of nausea and vomiting levels. This relaxation technique may be an effective intervention to reduce nausea in patients receiving chemotherapy.</p>	<p>Lack of a control group</p> <p>Heterogeneous population</p> <p>Types of chemotherapeutic and antiemetic agents were not controlled.</p> <p>Patient included with any cycle of chemotherapy treatment</p> <p>Low cost</p> <p>Easily teachable to patients</p> <p>RN training required</p>

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		<p>of nausea one hour before and after the intervention. The progressive relaxation technique was progressive muscle group relaxation (tensing-releasing) and control of respiration in an environment characterized by little artificial illumination and adequate music, without interruptions. The duration of each session was 25 minutes.</p>			
<p>SC Granisetron for Prevention of CINV With Highly Emetogenic Chemotherapy: PEP Weight-of-Evidence Category: Effectiveness Not Established</p>					
<p>Guripide et al., 2007</p>	<p>Aim of the study was to assess bioavailability of s.c. granisetron; clinical efficacy was not an endpoint of the study.</p>	<p>Patients (N = 25) receiving platinum-based chemotherapy. Patients were randomized to receive either 3 mg subcutaneous granisetron or 3 mg IV granisetron during cycle 1 and then crossover to the alternative route during cycle 2</p>	<p>Frequent blood sampling (13 samples over 24 hours) to obtain pharmacokinetic parameters to assess bioequivalence between the two routes (IV vs. s.c.) Urine collection as well</p>	<p>s.c. granisetron did not produce local reactions. Bioavailability of s.c. granisetron determined to be similar to that of IV, suggesting that this might be a viable alternative route of delivery; however clinical efficacy still needs to be determined.</p>	
<p>Single Day Aprepitant Versus 3 Day Regimen for Prevention of CINV With Highly Emetogenic Chemotherapy: PEP Weight-of-Evidence Category: Effectiveness Not Established</p>					
<p>Herrington et al., 2008</p>	<p>study designed to evaluate the effectiveness of single-dose aprepitant on Day 1 of chemotherapy versus 3-day aprepitant in combination with palonosetron and dexamethasone in patients receiving HEC.</p>	<p>pilot, single-institution, randomized, double-blind, placebo-controlled comparative trial. N+75 patients randomized to 1 of 3 treatment arms: group 1 received palonosetron .25 mg, dex 12 mg and aprepitant 125 mg on day 1 and 80 mg on days 2,3. group 2 received the same except for placebo on days 2 and 3 instead of aprepitant, and group 3 received palonosetron</p>	<p>VAS for nausea Diary to record emetic episodes and use of rescue medications</p>	<p>Group 3 was removed after early interim analysis because of severe emesis (this was the group with no aprepitant). Groups 1 and 2 did not differ with respect to emesis control (proportion of patients without emesis during the first 24 hours was similar between groups 1 and 2,</p>	

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		and dex on day 1 and placebo on days 1-3 instead of aprepitant.		indicating that single dose of aprepitant was as effective as three-day regimen.	
Yoga: PEP Weight-of-Evidence Category: Effectiveness Not Established					
Raghavendra et al., 2007	Effects of an integrated yoga program in reducing frequency and intensity of nausea and vomiting chemotherapy naïve early stage breast cancer patients	62 chemotherapy naïve patients with breast cancer (stage II and III) were randomly assigned to receive yoga intervention (n = 28) or supportive therapy intervention (n = 34). The patients were recruited from a comprehensive cancer care center in India following recently diagnosed operable breast cancer. The women were aged 30-70 years, Zubrod's performance status of 0-2, high school education, with a treatment plan including surgery followed by adjuvant chemotherapy or both adjuvant chemotherapy and radiation therapy. Patients were excluded if they had a medical condition that was likely to interfere with treatment, major psychiatric, neurologic illness or autoimmune disorders, known metastases, a history of intestinal obstruction, or known sensitivity to antiemetics. The subjects in the yoga group received both supervised and home practice of yoga sessions for 60 minutes daily, starting prior to chemotherapy. These subjects had supervised initial training, audio and videocassettes for	Morrow Assessment of Nausea and Emesis (MANE) State Trait Anxiety Inventory (STAI) Beck's Depression Inventory (BDI) Functional Living Index for Cancer (FLIC) Symptom checklist	The severity of post-chemotherapy vomiting was mild to moderate in both groups. The nausea severity was moderate to severe for the control group and mild to moderate in the yoga group. The frequency and intensity of nausea were reduced in the yoga group. In addition, intensity of anticipatory nausea and vomiting was also decreased in the yoga group compared to the control group. There was a positive correlation between MANE scores and anxiety, depression, and distressful symptoms. The intervention of yoga was effective in reducing the frequency and intensity of nausea and the intensity of anticipatory nausea and vomiting in women with early stage breast cancer.	The antiemetics for the management of delayed emesis were not based on guidelines or consensus statements. The subjects in the control group were offered supportive therapy and coping less frequently than the yoga intervention group. In addition, the yoga group started the intervention earlier than the control group, closer to the time of surgery and radiation than chemotherapy. With the overlap of physical symptoms of cancer, the BDI and STAI in cancer populations have limitations.

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		<p>home, and supervised home visit. For the control group, supportive therapy and coping preparation during the hospital visits over a complete course of chemotherapy was provided. Both groups started before first chemotherapy cycle. The yoga instructor was trained in counseling and facilitated both groups. Subjects maintained diaries to record episodes of vomiting and duration of nausea, and at the fourth cycle, they completed MANE, STAI, BDI, FLIC, and a symptom checklist questionnaire.</p>			
<p>Metopimazine (as Monotherapy) for Prevention of Delayed CINV With Highly Emetogenic Chemotherapy: PEP Weight-of-Evidence Category: Not Recommended for Practice</p>					
<p>Khamales et al., 2006</p>	<p>Compare efficacy and safety of sublingual metopimazine to ODT ondansetron in patients receiving HEC for the treatment of delayed CINV. This regimen was NOT used for prevention of acute CINV, but as an adjunct for prevention of delayed CINV.</p>	<p>Participants (N = 210) were randomized to one of two treatment arms: sublingual metopimazine (n = 103) versus ODT ondansetron (n = 97). Patients received metopimazine 7.5 mg sublingual every 8 hours on days 2-6 or ODT ondansetron * mg orally on days 2-6.</p>	<p>Daily diary and FLIE</p>	<p>No significant differences between groups in control of delayed CINV, QOL, or safety; however, control of delayed CINV was inferior as compared to other studies.</p>	<p>Evaluation of an "old" regimen that would now be considered sub-optimal care per consensus guidelines due to availability of newer, superior agents.</p> <p>Corticosteroids not allowed. Overall dose of metopimazine low (ineffective)</p>
<p>Ramosetron for Prevention of CINV With Highly Emetogenic Chemotherapy: PEP Weight-of-Evidence Category: Not Recommended for Practice (as Monotherapy)</p>					
<p>Shi et al., 2007</p>	<p>Compare the efficacy and safety of two different 5HT3 receptor antagonists</p>	<p>Prospective, randomized crossover trial that enrolled 50 patients (conducted in China only). In the first group, patients received ramosetron for prevention of CINV in cycle 1 of HEC and then ondansetron in cycle 2. Patients in group 2</p>	<p>Assessed nausea, emesis and loss of appetite, but it is not clear how this data was collected or who scored or rated the measures?</p> <p>Whether they were patient self-report or as observed by the</p>	<p>No significance reported for any measure between groups at any time point, but this is a poorly reported study.</p>	<p>Small sample</p> <p>Measures unclear</p> <p>No significant differences noted between the two groups on any measure at anytime point</p>

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		received ondansetron first, followed by ramosetron.	investigators is not known.		Triple drug regimen not recommended for prevention of CINV Not a single 5HT3 receptor antagonist
Tropisetron Plus Metopimazine for Prevention of CINV With Multiple Day, Multiple Cycle Highly Emetogenic Chemotherapy: PEP Weight-of-Evidence Category: Not Recommended for Practice					
Herrstedt et al., 2007	<p>Comparing two different treatments for CINV protection: tropisetron plus metopimazine versus tropisetron plus placebo for multiple-day cisplatin regimens</p> <p>Tropisetron is a 5HT3 receptor antagonist that is FDA approved for use in the United States. Metopimazine is a dopamine antagonist/phenothiazine that is also FDA approved for use in the United States.</p>	Randomized, double-blind trial that enrolled 82 patients with germ cell tumors scheduled to receive four cycles of cisplatin, given as a five-day treatment every three weeks.	Diary to record number of vomiting and retching episodes and nausea severity (four-point Likert), data on appetite also was evaluated on a four-point Likert scale. Satisfaction with antiemetic treatment was collected via a categorical question (satisfied versus not satisfied) and those who were not satisfied with the antiemetic treatment were withdrawn from the study, as they were requesting additional or other treatments.	Tropisetron plus metopimazine was superior to tropisetron plus placebo arm in the overall period (days 1-9) in terms of complete protection from vomiting as well as decreased nausea. The treatment arm also was superior over multiple cycles, providing cumulative emetic protection.	Issue that is addressed is appropriate and effective anti emetic prophylaxis for multiple-day chemotherapy regimens (usually these are cisplatin-based regimens). However, antiemetic control in both of these treatment arms was poor and since this study, newer agents (palonosetron and aprepitant) have proven efficacy that is superior to the treatments used in this study. Furthermore, these treatments are inferior to treatments that include a corticosteroid, and the rates of protection from CINV are not good.