ONLINE EXCLUSIVE

Systematic Review of Nonpharmacologic Approaches for the Management of Gastrointestinal Symptoms

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PROBLEM IDENTIFICATION: To summarize and critique the literature for nonpharmacologic complementary approaches to manage gastrointestinal (GI) symptoms attributed to chemotherapy.

LITERATURE SEARCH: A literature search was conducted using CINAHL®, MEDLINE®, and PsycINFO® from database inception through January 2018.

DATA EVALUATION: Studies were independently appraised by each author regarding inclusion eligibility and summary of GI symptom outcomes and the nonpharmacologic complementary intervention.

SYNTHESIS: 57 studies met inclusion criteria. GI symptoms most commonly evaluated as a chemotherapy outcome were nausea and vomiting and nausea alone. GI symptoms infrequently evaluated as outcomes included diarrhea, anticipatory nausea, and dysgeusia. Ten GI symptoms associated with chemotherapy were not evaluated by any study. Nonpharmacologic interventions included 15 different interventions.

IMPLICATIONS FOR RESEARCH: Studies evaluating nonpharmacologic interventions for managing chemotherapy-related GI symptoms have been growing but tend to focus on nausea and vomiting to the exclusion of other relevant GI symptoms. Studies evaluating nonpharmacologic effects on other GI symptoms may make great strides in reducing patient symptom burden.

KEYWORDS gastrointestinal symptoms; chemotherapy; nonpharmacologic therapies; symptom burden
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Patients with cancer receiving chemotherapy experience as many as 14 treatment-related symptoms, with each additional symptom resulting in an increase in symptom distress (Spichiger et al., 2011; Thiagarajan et al., 2016). Symptom management studies tend to focus on the more prevalent symptoms related to cancer chemotherapy, which include pain, fatigue, and sleep disturbance, but gastrointestinal (GI) symptoms have been shown to contribute to high symptom burden in this population. Although 19 GI symptoms are related to chemotherapy (i.e., oral mucositis, xerostomia, dysphagia, dysgeusia, anticipatory nausea, anticipatory vomiting, nausea, vomiting, anorexia, early satiety, pyrosis, bloating, eructation, flatulence, retching, diarrhea, constipation, rectal burning, and rectal itching) (see Table 1), symptom management literature predominantly focuses on nausea and vomiting. A study by Cherwin and Kwekkeboom (2016) demonstrated that, despite pharmacologic intervention, people with a hematologic cancer receiving chemotherapy experience as many as five concurrent GI symptoms, and 11 of 19 GI symptoms assessed met criteria to be considered clinically relevant (i.e., greater than 15% prevalence and moderate to severe duration, severity, or distress). Unrelieved GI symptoms contribute to depression, shortened survival, and poor quality of life (QOL) in people with cancer (Goodell & Nail, 2005). High symptom burden from GI symptoms, despite pharmacologic intervention, may indicate the need for novel methods of symptom management.

Modern health care is increasingly merging mainstream medicine with scientifically evaluated complementary therapies in a way that treats a person's mind, body, and spirit (National Center for Complementary and Integrative Health, 2017). The National Institutes of Health Office of Cancer Complementary and Alternative Medicine has assigned classifications to the different forms of

complementary therapies. These classifications include alternative medical systems (e.g., acupuncture, homeopathy), energy therapies (e.g., Qigong, Reiki, therapeutic touch), exercise therapies (e.g., tai chi, yoga), manipulative and body-based methods (e.g., chiropractic, massage), mind–body interventions (e.g., meditation, hypnosis, imagery), nutritional therapeutics (e.g., macrobiotic diet, vitamins), pharmacologic and biologic treatments (e.g., herbal therapies, off-label drugs), and spiritual therapies (e.g., prayer).

TABLE 1. Definition of Gastrointestinal Symptoms

Symptom	Definition
Anorexia	Lack or loss of appetite
Anticipatory nausea	Conditioned or learned response to chemotherapy resulting in nausea as long as 24 hours prior to administration of chemotherapy
Anticipatory vomiting	Conditioned or learned response to chemotherapy resulting in vomiting as long as 24 hours prior to administration of chemotherapy
Bloating	Stomach swelling as a result of the gastrointestinal tract filling with gas
Constipation	Infrequent or hard to pass bowel movements
Diarrhea	Loose, watery stools
Dysgeusia	Altered taste sensation
Dysphagia	Difficulty swallowing
Early satiety	Sensation of fullness that can limit food intake
Eructation	Belching or burping
Flatulence	Increased frequency of passing gas
Nausea	Sensation of unease with an inclination to vomit
Oral mucositis	Inflammation of the oral mucosa that results in redness and ulcerative lesions
Pyrosis	Heartburn; painful, burning feeling in the chest caused by stomach acid flowing back into the esophagus
Rectal burning	Sensation of burning at the rectum, often when having a bowel movement
Rectal itching	Sensation of itching at the rectum
Retching	Dry heaves; sensation of needing to vomit without expelling gastric contents
Vomiting	Emesis; expelling gastric contents
Xerostomia	Dry mouth; underfunctioning of oral saliva glands

Note. Based on information from Lewis et al., 2017.

Although mainstream medicine is the most commonly used medical therapy for people in the United States, many Americans choose to use complementary therapy to supplement their medical care. As many as 33% of adults in the United States report using some form of complementary therapy (Clarke, Black, Stussman, Barnes, & Nahin, 2015). Most people who report using a complementary approach do so to support general wellness or to prevent disease (Stussman, Black, Barnes, Clarke, & Nahin, 2015). The general population reports a relatively high use of complementary therapies, but people with a diagnosis of cancer use complementary therapies in far greater numbers. A meta-analysis of complementary therapy application showed that 50% of people with cancer in the United States reported using some form of complementary or alternative therapy (Horneber et al., 2012). This higher use of complementary therapy may be attributed to the high symptom burden in cancer. People with cancer in need of additional symptom relief may benefit from adding a complementary approach to their pharmacologic regimens.

Despite the advancements in pharmacotherapy, GI symptoms in people with cancer remain prevalent and severe. Complementary therapies used in conjunction with mainstream medicine may offer additional relief from GI symptoms. Evidence has shown promising results for the use of complementary approaches to manage non-GI symptoms in people with cancer, including pain (Bardia, Barton, Prokop, Bauer, & Moynihan, 2006), fatigue (Finnegan-John, Molassiotis, Richardson, & Ream, 2013), and sleep disturbance (Langford, Lee, & Miaskowski, 2012). Other reviews have focused on examining the evidence for complementary therapies managing individual GI symptoms, such as oral mucositis (Clarkson et al., 2010), xerostomia (Furness, Bryan, McMillan, & Worthington, 2013), or nausea (Tipton et al., 2007), but there has yet to be a review of literature examining complementary approaches to manage GI symptoms as a whole. Because 19 different GI symptoms are associated with chemotherapy, clinicians should understand the available research on complementary management of these symptoms. However, it remains unclear which complementary therapies might be beneficial to offer to a patient with cancer experiencing GI symptoms. The purpose of this review is to summarize the evidence surrounding

complementary therapy use for the management of GI symptoms in people receiving chemotherapy and to offer practice recommendations based on a critical appraisal of available research.

Methods

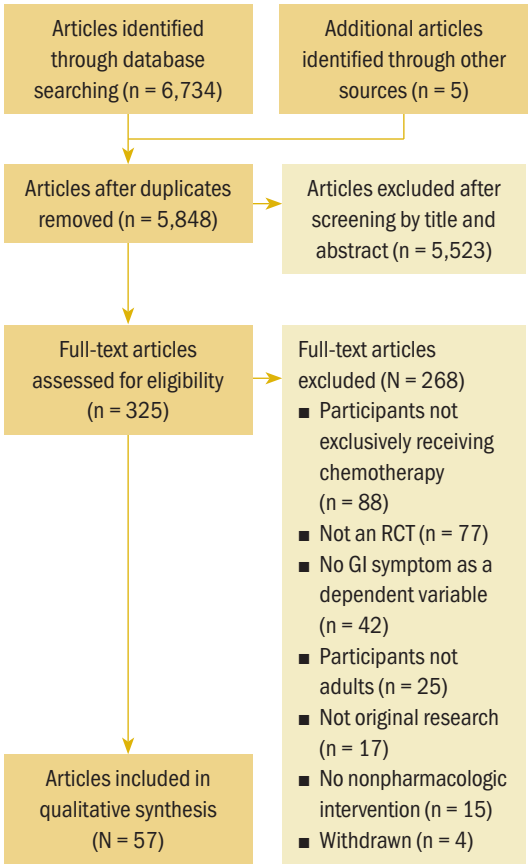
Literature Search

This systematic review was performed using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009). Three databases (i.e., CINAHL®, MEDLINE®, and PsycINFO®) were searched from database inception through January 2018. Inclusion criteria for studies involved adult (aged 18 years or older) participants with a cancer diagnosis who were receiving chemotherapy exclusively, reported the effect of a nonpharmacologic intervention, and experienced at least one GI-related symptom as a chemotherapy outcome.

This literature review focuses on nonpharmacologic complementary therapies. Because ingested therapies can elicit a pharmacologic-like effect in the body, nutritional therapeutics (e.g., diet therapy, vitamins) and pharmacologic and biologic treatments (e.g., herbal therapies, off-label drugs) were excluded, as well as any remedies that were ingested (e.g., a mouthwash that is swallowed). The authors also excluded complementary approaches that required extensive medical intervention, such as intubation for the use of esophageal laser treatments. When searching MEDLINE and CINAHL, to limit the search to studies with an experimental design, the authors used a search filter by Haynes, McKibbon, Wilczynski, Walter, and Werre (2005). When searching PsycINFO, the authors adapted the experimental design filter reported by Cochrane for use with the ProQuest platform of PsycINFO to enable it to work with the American Psychology Association platform (Cochrane Work, n.d.).

Search strategies were developed with the assistance of a health sciences librarian with expertise in conducting systematic reviews. Comprehensive strategies, including index and keyword methods, were devised for the databases used. The English-language filter was applied for CINAHL and PubMed. No other pre-established filters were used in an effort to maximize sensitivity. Searches were conducted from December 2016 to January 2017 and rerun in January 2018 to capture new records that became available during the screening process. To capture publications not indexed in the databases, reference lists and articles cited in the included studies were also reviewed.

FIGURE 1. PRISMA Flow Diagram



GI—gastrointestinal; PRISMA—Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT—randomized, controlled trial

Data Evaluation

Three reviewers individually assessed articles for eligibility, and each article included for full review was evaluated for risk of bias using the Cochrane Collaboration Tool for Assessing Risk of Bias (Higgins & Greene, 2011). The Cochrane Collaboration Tool for Assessing Risk of Bias evaluates each study based on the following criteria: adequate sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. Each domain is rated as high, low, or unclear risk of bias. Assessing the source of bias in a study allows the reviewer to identify how strong the presented evidence is and how reliable the conclusions are. Randomized, controlled trials with limited source of bias offer the highest grade of evidence for influencing practice.

Results

Selection of Articles

A total of 6,734 potentially relevant studies were identified through three databases and other sources (e.g., reference lists). Of these, 891 duplicates were excluded. After screening by title and abstract, an additional 5,523 articles were excluded. A total of 325 articles were included for a full-text review for eligibility. Of these, 268 articles were excluded for not meeting eligibility criteria (i.e., not original research, not adults, no nonpharmacologic intervention, no GI symptom measured, no randomization, participants not exclusively receiving chemotherapy, or withdrawn). A total of 57 studies were included for qualitative synthesis (see Figure 1).

Nausea and Vomiting

Most studies included in this review (n = 31) investigated the use of a nonpharmacologic complementary approach for nausea and vomiting (see Tables 2 and 3). The most common nonpharmacologic complementary interventions for nausea and vomiting included progressive muscle relaxation and acupressure. A handful of studies investigated acupuncture, acustimulation, distraction, education, guided imagery, transcutaneous electroacupuncture, transdermal electrical nerve stimulation, and aromatherapy. A majority of the studies found that the intervention had some effect on reducing nausea and vomiting.

Nausea

Thirteen studies investigated the use of nonpharmacologic complementary approaches for nausea alone. These interventions included massage, education, exercise, acustimulation, therapeutic touch, and distraction. A majority of these studies demonstrated a positive effect of the intervention for reducing nausea.

Anorexia

Five studies investigated the use of nonpharmacologic complementary approaches for anorexia. These interventions included education, distraction, progressive muscle relaxation, and transcutaneous electroacupuncture. Less than half of these studies demonstrated an effect of the intervention of reducing anorexia.

Constipation

Five studies investigated the use of nonpharmacologic complementary approaches for constipation. Interventions investigated included acupuncture,

TABLE 2. Frequency of Nonpharmacologic Intervention Use for Gastrointestinal Symptoms

Symptom	n
Nausea and vomiting (N = 31)	
Progressive muscle relaxation	8
Acupressure	7
Acupuncture	3
Acustimulation	2
Distraction	2
Education	2
Guided imagery	2
Transcutaneous electroacupuncture	2
Transdermal electrical nerve stimulation	2
Aromatherapy	1
Nausea (N = 13)	
Education	3
Massage	3
Acustimulation	2
Exercise	2
Therapeutic touch	2
Distraction	1
Anorexia (N = 5)	
Education	2
Distraction	1
Progressive muscle relaxation	1
Transcutaneous electroacupuncture	1
Constipation (N = 5)	
Acupuncture	2
Education	2
Acupressure	1
Oral mucositis (N = 5)	
Education	2
Mouthwash	2
Exercise	1
Anticipatory nausea and vomiting (N = 4)	
Systematic desensitization	3
Progressive muscle relaxation	1
Vomiting (N = 4)	
Electroacupuncture	1
Distraction	1
Progressive muscle relaxation	1
Therapeutic touch	1

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TABLE 2. Frequency of Nonpharmacologic Intervention Use for Gastrointestinal Symptoms *(Continued)*

Symptom	n
Anticipatory nausea (N = 2)	
Distraction	1
Progressive muscle relaxation	1
Diarrhea (N = 2)	
Education	1
Exercise	1
Dysgeusia (N = 1)	
Education	1

education, and acupressure. A majority of these studies demonstrated a positive effect of the intervention for reducing constipation.

Oral Mucositis

Five studies investigated the use of nonpharmacologic complementary approaches for oral mucositis. Interventions included education, mouthwash, and exercise. Fewer than half of these studies demonstrated an effect of the intervention on reducing oral mucositis.

Anticipatory Nausea and Vomiting

Four studies investigated the use of nonpharmacologic complementary approaches for anticipatory nausea and vomiting. These interventions included systematic desensitization and progressive muscle relaxation. All of the studies demonstrated an effect on reducing anticipatory nausea and anticipatory vomiting.

Vomiting

Four studies investigated the use of nonpharmacologic complementary approaches for vomiting. These interventions included electroacupuncture, distraction, therapeutic touch, and progressive muscle relaxation. A majority demonstrated an effect of the intervention on reducing vomiting.

Diarrhea

Two studies investigated the use of nonpharmacologic complementary approaches for diarrhea. These interventions included education and exercise. One of the two studies demonstrated an effect of the intervention on reducing diarrhea.

Anticipatory Nausea

Two studies investigated the use of nonpharmacologic complementary approaches for anticipatory nausea alone. These interventions included distraction and progressive muscle relaxation. Both studies demonstrated an effect of the intervention on reducing anticipatory nausea.

Dysgeusia

One study investigated the use of a nonpharmacologic complementary approach for dysgeusia, which was education. This intervention was not shown to have an effect on reducing dysgeusia.

Nonpharmacologic Complementary Interventions

Most studies used a single intervention (e.g., acupuncture only), and few studies offered an intervention that combined more than one complementary approach (i.e., progressive muscle relaxation plus guided imagery). Overall, certain interventions were found to be more or less successful in having an effect on chemotherapy-associated GI symptoms. Of the studies using acupressure, progressive muscle relaxation, and acupuncture, 22 of 26 cases found a statistically significant effect of the intervention on GI symptoms. However, of the studies using an education-based intervention, the intervention was found to significantly affect GI symptoms in only 3 of 12 cases. Across all reviewed studies, sources of bias were low, but many reports lacked sufficient detail to assess source of bias. Sources of bias most consistently reported included not blinding participants and personnel and not blinding the outcome assessment.

Discussion

Complementary therapy use has been growing, and many people find it to be a welcome addition to mainstream therapy. This is particularly true for patients with cancer because cancer treatments often produce many severe and distressing symptoms. Although pharmacologic therapy can reduce GI symptom severity, many GI symptoms remain problematic. Therefore, complementary nonpharmacologic therapies can offer additional relief where pharmacologic therapy cannot. New evidence is emerging demonstrating the effectiveness of nonpharmacologic complementary approaches to managing GI symptoms; however, to date, no summary has collected and critiqued that evidence. This review of the literature addresses this gap by summarizing the evidence provided by randomized, controlled trials investigating nonpharmacologic complementary therapy to manage GI symptoms.

TABLE 3. Summary of Findings

Study	Sample and Design	Results	Risk of Bias
Acupressure for nausea and vomiting			
Avc et al., 2016	Three-group study of 90 patients with leukemia using manual acupressure on bilateral wrists at P6 acupoint, acupressure band on bilateral wrists at P6 acupoint, or usual care	Acupressure band reduced occurrence and severity of nausea and vomiting compared to the manual acupressure and control groups.	■ RSG: H ■ BPP: H ■ BOA: L ■ IOD: L
Hughes et al., 2012	Three-group study of 500 patients with cancer using acupressure bands, sham acupressure bands, or usual care	No significant difference between groups for nausea and vomiting	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: L ■ IOD: L
Molassiotis et al., 2007	Two-group study of 36 women with breast cancer using acupressure bands worn bilaterally at the P6 acupoint or usual care	Acupressure group reported less nausea and distress compared to the control group; no significant difference between groups for vomiting	■ RSG: L ■ BPP: H ■ BOA: L ■ IOD: L ■ SR: L
Molassiotis et al., 2014	Three-group study of 500 patients with cancer using acupressure bands worn bilaterally at the P6 acupoint, sham acupressure, or usual care	No significant difference between groups for nausea and vomiting	■ RSG: L ■ AC: L ■ BOA: L ■ IOD: L
Roscoe et al., 2010	Two-group study with 74 women with breast cancer using acupressure band plus nausea expectancy–enhancing handout and CD or acupressure band plus nausea expectancy–neutral handout and CD	The group receiving acupressure plus expectancy-enhancing materials reported reduced nausea when participants were screened as high nausea expectancy but reported more nausea when screened as low nausea expectancy compared to the acupressure plus neutral materials group.	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: L
Shen & Yang, 2017	Two-group study of 70 patients with lung cancer using acupressure on PC6 and SP4 acupoints or sham acupressure on SI3 acupoint	Acupressure group reported less severe nausea and vomiting compared to sham acupressure group.	■ RSG: L ■ AC: H ■ BPP: L ■ BOA: H ■ IOD: L ■ SR: L
Suh, 2012	Four-group study of 120 women with breast cancer using acupressure bands, counseling, acupressure bands plus counseling, or sham acupressure bands	Acupressure plus counseling group reported less nausea and vomiting compared to the other groups.	■ RSG: L ■ IOD: L
Acupuncture for nausea and vomiting			
Liu et al., 2015	Two-group study of 60 women with gynecologic cancer using wrist/ankle acupuncture combined with ginger moxibustion or usual care	Acupuncture group reported less nausea and constipation compared to the control group.	■ RSG: L ■ AC: L ■ BPP: H ■ BOA: H ■ IOD: L

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TABLE 3. Summary of Findings *(Continued)*

Study	Sample and Design	Results	Risk of Bias
Acupuncture for nausea and vomiting *(continued)*			
Rithirangsriroj et al., 2015	Two-group study of 70 women with gynecologic cancer using acupuncture on bilateral wrists at P6 acupoint or usual care	Acupuncture group reported less nausea, vomiting, and constipation compared to the control group.	■ RSG: L ■ BOA: L ■ IOD: L
Streitberger et al., 2003	Two-group study of 80 patients with cancer using acupuncture to bilateral wrists at P6 acupoint or sham acupuncture	No significant difference between groups for nausea and vomiting	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: L ■ IOD: L
Acustimulation for nausea and vomiting			
Roscoe et al., 2003	Three-group study of 739 patients with cancer using acustimulation band, acupressure band, or usual care	Acupressure band group experienced less nausea compared to the control group. Patients in the acustimulation group reported less nausea and vomiting compared to the control group.	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: L ■ IOD: L
Roscoe et al., 2005	Three-group study of 96 women with breast cancer using acustimulation band at P6 acupoint, sham acustimulation at a nontherapeutic location, or usual care	No significant difference between groups for nausea and vomiting	■ RSG: L ■ BOA: L ■ IOD: L
Aromatherapy for nausea and vomiting			
Lua et al., 2015	Two-group study of 60 women with breast cancer using a necklace infuser with ginger essential oil or a necklace infuser with fragrance-matched artificial placebo	Ginger oil aromatherapy group reported less nausea compared to the control group. No significant difference was found between groups for vomiting.	■ RSG: L ■ BPP: L ■ BOA: L ■ IOD: L ■ SR: L
Distraction for nausea and vomiting			
Ezzone et al., 1998	Two-group study of 33 patients undergoing stem cell transplantation using music therapy or usual care	Music therapy group reported less nausea and vomiting compared to the control group.	■ RSG: L ■ BOA: L ■ IOD: L
Vasterling et al., 1993	Three-group study of 60 patients with cancer using video games, progressive muscle relaxation, or usual care	Intervention groups reported less anticipatory nausea compared to the control group. No significant difference between groups for acute or delayed nausea or vomiting	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: L ■ IOD: L
Education for nausea and vomiting			
Jahn et al., 2009	Two-group study of 208 patients with cancer using the Improvement Through Oncology Nursing multimodular nursing-administered program focusing on self-care or usual care	No significant difference between groups for nausea, vomiting, or anorexia	■ RSG: L ■ BPP: H ■ BOA: H ■ IOD: L

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TABLE 3. Summary of Findings *(Continued)*

Study	Sample and Design	Results	Risk of Bias
Education for nausea and vomiting *(continued)*			
Williams & Schreier, 2004	Two-group study of 70 women with breast cancer using educational audio recordings about nutritional and symptom management or usual care	No significant difference between groups for nausea, vomiting, anorexia, diarrhea, dysgeusia, oral mucositis, or constipation	■ RSG: L ■ BOA: L ■ IOD: L
Guided imagery for nausea and vomiting			
Syrjala et al., 1992	Four-group study of 67 patients with cancer using self-hypnosis training, coping skills training, attention, or usual care	No significant difference between groups for nausea or vomiting; guided imagery group reported less oral pain compared to the coping skill training group and the two control groups.	■ RSG: L ■ BOA: L ■ IOD: L
Troesch et al., 1993	Two-group study of 28 patients with cancer using guided imagery or usual care	No significant difference between groups for nausea and vomiting	■ RSG: L ■ BOA: L ■ IOD: L
Progressive muscle relaxation for nausea and vomiting			
Arakawa, 1997	Two-group study of 60 patients with cancer using progressive muscle relaxation plus focused breathing or usual care	Progressive muscle relaxation group reported less nausea compared to the control group. No significant difference between groups for vomiting	■ RSG: L ■ BPP: H ■ BOA: L ■ IOD: L ■ SR: L
Burish & Jenkins, 1992	Six-group study of 81 patients with cancer using electromyographic biofeedback plus progressive muscle relaxation, electromyographic biofeedback alone, skin temperature biofeedback plus progressive muscle relaxation, skin temperature biofeedback alone, progressive muscle relaxation, or usual care	All three progressive muscle relaxation groups reported less nausea compared to the three groups not receiving progressive muscle relaxation. No significant difference between groups for vomiting	■ RSG: L ■ BOA: L ■ IOD: L ■ SR: L
Burish & Lyles, 1981	Two-group study of 16 patients with cancer using progressive muscle relaxation training plus guided imagery or usual care	Progressive muscle relaxation group reported less nausea compared to the control group. No significant difference between groups for vomiting	■ RSG: L ■ BOA: L ■ IOD: L ■ SR: L
Burish et al., 1987	Two-group study of 24 patients with cancer using progressive muscle relaxation training plus guided imagery or usual care	Progressive muscle relaxation group reported less nausea compared to control group. Vomiting in the control group increased compared to the intervention group.	■ RSG: L ■ BOA: L ■ IOD: L
Cotanch & Strom, 1987	Three-group study of 60 patients with cancer using progressive muscle relaxation plus hypnosis, relaxing music attention, or usual care	Progressive muscle relaxation plus hypnosis group reported less vomiting and more caloric intake compared to the two control groups. No significant difference between groups for nausea	■ RSG: L ■ BOA: L ■ IOD: L

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TABLE 3. Summary of Findings *(Continued)*

Study	Sample and Design	Results	Risk of Bias
Progressive muscle relaxation for nausea and vomiting *(continued)*			
Lyles et al., 1982	Three-group study of 50 patients with cancer using progressive muscle relaxation plus guided imagery, therapist support attention, or usual care	Progressive muscle relaxation group reported less nausea compared to the two control groups. No significant difference between groups for nausea	■ RSG: L ■ BOA: L ■ IOD: L
Molassiotis et al., 2002	Two-group study of 71 women with breast cancer using progressive muscle relaxation, focused breathing, and guided imagery or usual care	Progressive muscle relaxation group reported less nausea and vomiting compared to the control group	■ RSG: L ■ AC: L ■ BOA: L ■ IOD: L
Yoo et al., 2005	Two-group study of 30 women with breast cancer using progressive muscle relaxation plus guided imagery or usual care	Progressive muscle relaxation group reported less nausea and vomiting compared to the control group.	■ RSG: L ■ BPP: L ■ BOA: L ■ IOD: L
Transdermal electrical nerve stimulation for nausea and vomiting			
Pearl et al., 1999	Two-group study of 32 women with gynecologic cancer using transdermal electrical nerve stimulation or sham transdermal electrical nerve stimulation	Transdermal electrical nerve stimulation group reported less nausea compared to the sham transdermal electrical nerve stimulation group. No significant difference between groups for nausea	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: L ■ IOD: L ■ SR: L
Saller et al., 1986	Two-group study of 22 patients with head and neck or lung cancer using transdermal electrical nerve stimulation or sham transdermal electrical nerve stimulation	Transdermal electrical nerve stimulation group reported less nausea compared to sham transdermal electrical nerve stimulation group. No significant difference between groups for vomiting	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: L ■ IOD: L
Transcutaneous electroacupuncture for nausea and vomiting			
Xie et al., 2017	Two-group study of 142 patients with liver cancer using transcutaneous electroacupuncture to LI4, P6, and ST36 acupoints or sham transcutaneous electroacupuncture without electrical stimulation	No significant difference between groups for nausea, vomiting, or anorexia	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: H ■ IOD: L ■ SR: L
Zhang et al., 2014	Two-group study of 72 patients with cancer using needleless transcutaneous electroacupuncture at PC6 and PC5 acupoints or sham transcutaneous electroacupuncture done at non-acupoints	Transcutaneous electroacupuncture group reported less nausea and vomiting compared to the sham transcutaneous electroacupuncture.	■ RSG: L ■ IOD: L
Acustimulation for nausea			
Roscoe et al., 2002	Three-group study of 27 patients with cancer using acustimulation worn at P6 acupoint, sham acustimulation at a non-therapeutic location, or usual care	No significant difference between groups for nausea	■ RSG: L ■ BOA: L

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TABLE 3. Summary of Findings *(Continued)*

Study	Sample and Design	Results	Risk of Bias
Acustimulation for nausea *(continued)*			
Roscoe et al., 2006	Three-group study of 86 women with breast cancer using acustimulation band, acupressure bands worn bilaterally, or usual care	Acupressure band group reported less severe nausea compared to the acustimulation band and control groups.	■ RSG: L ■ BOA: L ■ IOD: L
Distraction for nausea			
Bilgic & Acaroglu, 2017	Two-group study of 70 patients with cancer using a relaxing music CD or usual care	Distraction group reported less nausea and anorexia after chemotherapy compared to the control group.	■ RSG: H ■ AC: H ■ BPP: H ■ BOA: H
Education for nausea			
Gaston-Johansson et al., 2000	Two-group study of 110 women with breast cancer using education about pain management, positive coping, and guided imagery or usual care	Education group reported less nausea compared to the control group.	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: L ■ IOD: L
Lerman et al., 1990	Two-group study of 48 patients with cancer using education about chemotherapy, relaxation, deep breathing, and progressive muscle relaxation or usual care	Education group reported less nausea after chemotherapy compared to the control group.	■ RSG: L ■ BOA: L ■ IOD: L
Shelke et al., 2008	Two-group study of 358 patients with cancer using education about cancer, nausea expectancy, and efficacy of antiemetics or education about cancer only	No significant difference between groups for nausea occurrence	■ RSG: L ■ AC: L ■ BOA: L ■ IOD: L
Exercise for nausea			
Hornsby et al., 2014	Two-group study of 20 women with breast cancer using aerobic training at a moderate-to-high intensity or usual care	No significant difference between groups for nausea	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: L ■ IOD: L
Jacobsen et al., 2014	Four-group study of 711 patients undergoing stem cell transplantation using exercise training, stress management training, exercise plus stress management training, or usual care	No significant difference between groups for nausea	■ RSG: L ■ BOA: L ■ IOD: L
Massage for nausea			
Ahles et al., 1999	Two-group study of 35 patients undergoing stem cell transplantation using massage or usual care	Massage group reported less nausea compared to the control group.	■ RSG: L ■ SR: L

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TABLE 3. Summary of Findings *(Continued)*

Study	Sample and Design	Results	Risk of Bias
Massage for nausea *(continued)*			
Billhult et al., 2007	Two-group study of 39 women with breast cancer using massage of foot/lower leg or hand/lower arm or usual care	Massage group reported less nausea compared to the control group.	■ RSG: L ■ BOA: L ■ IOD: L
Post-White et al., 2003	Four-group study of 230 patients with cancer using massage, healing touch, attention control, or usual care	No significant difference between groups for nausea	■ RSG: L ■ BPP: H ■ BOA: L ■ IOD: L
Therapeutic touch for nausea			
Matourypour et al., 2015	Three-group study of 108 women with breast cancer using therapeutic touch, sham therapeutic touch, or usual care	Therapeutic touch group reported less nausea compared to the sham therapeutic touch and control groups.	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: L ■ IOD: L
Vanaki et al., 2016	Three-group study of 108 women with breast cancer using therapeutic touch with energy transfer, sham therapeutic touch, or usual care	Therapeutic touch group reported less nausea compared to the sham therapeutic touch and control groups.	■ RSG: L ■ BOA: L
Distraction for anorexia			
Bilgic & Acaroglu, 2017	Two-group study of 70 patients using a relaxing music CD or usual care	Distraction group reported less nausea and anorexia after chemotherapy compared to the control group.	■ RSG: H ■ AC: H ■ BPP: H ■ BOA: H
Education for anorexia			
Jahn et al., 2009	Two-group study of 208 patients with cancer using the Improvement Through Oncology Nursing multimodular nursing-administered program focusing on self-care or usual care	No significant difference between groups for nausea, vomiting, or anorexia	■ RSG: L ■ BPP: H ■ BOA: H ■ IOD: L
Williams & Schreier, 2004	Two-group study of 70 women with breast cancer using educational audio recordings about nutritional and symptom management or usual care	No significant difference between two groups for nausea, vomiting, anorexia, diarrhea, dysgeusia, oral mucositis, or constipation	■ RSG: L ■ BOA: L ■ IOD: L
Progressive muscle relaxation for anorexia			
Cotanch & Strom, 1987	Three-group study of 60 patients with cancer using progressive muscle relaxation plus hypnosis, relaxing music attention, or usual care	Progressive muscle relaxation plus hypnosis group reported less vomiting and more caloric intake compared to the two control groups. No significant difference between groups for nausea	■ RSG: L ■ BOA: L ■ IOD: L

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TABLE 3. Summary of Findings *(Continued)*

Study	Sample and Design	Results	Risk of Bias
Transcutaneous electroacupuncture for anorexia			
Xie et al., 2017	Two-group study of 142 patients with liver cancer using transcutaneous electroacupuncture to LI4, P6, and ST36 acupoints or sham transcutaneous electroacupuncture without electrical stimulation	No significant difference between groups for nausea, vomiting, or anorexia	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: H ■ IOD: L ■ SR: L
Acupressure for constipation			
Shin & Park, 2018	Two-group study of 52 women with breast cancer using acupressure (viccaria seeds applied to auricular acupoints) or usual care	Acupressure group reported less constipation compared to the control group.	■ RSG: L ■ AC: L ■ BOA: L ■ IOD: L
Acupuncture for constipation			
Liu et al., 2015	Two-group study of 60 women with gynecologic cancer using wrist/ankle acupuncture combined with ginger moxibustion or usual care	Acupuncture group reported less nausea and constipation compared to the control group.	■ RSG: L ■ AC: L ■ BPP: H ■ BOA: H ■ IOD: L
Rithirangsriroj et al., 2015	Two-group study of 70 women with gynecologic cancer using acupuncture on bilateral wrists at P6 acupoint or usual care	Acupuncture group reported less nausea, vomiting, and constipation compared to the control group.	■ RSG: L ■ BOA: L ■ IOD: L
Education for constipation			
Hanai et al., 2016	Two-group study of 30 women with breast cancer using education about self-management or usual care	Education group reported less constipation compared to the control group.	■ RSG: L ■ BPP: L ■ BOA: L ■ IOD: L ■ SR: L
Williams & Schreier, 2004	Two-group study of 70 women with breast cancer using educational audio recordings about nutritional and symptom management or usual care	No significant difference between groups for nausea, vomiting, anorexia, diarrhea, dysgeusia, oral mucositis, or constipation	■ RSG: L ■ BOA: L ■ IOD: L
Education for oral mucositis			
Syrjala et al., 1992	Four-group study of 67 patients with cancer using self-hypnosis training, coping skills training, attention, or usual care	No significant difference between groups for nausea or vomiting; guided imagery group reported less oral pain compared to the coping skill training group and the two control groups.	■ RSG: L ■ BOA: L ■ IOD: L
Williams & Schreier, 2004	Two-group study of 70 women with breast cancer using educational audio recordings about nutritional and symptom management or usual care	No significant difference between groups for nausea, vomiting, anorexia, diarrhea, dysgeusia, oral mucositis, or constipation	■ RSG: L ■ BOA: L ■ IOD: L

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TABLE 3. Summary of Findings *(Continued)*

Study	Sample and Design	Results	Risk of Bias
Exercise for oral mucositis			
Dimeo et al., 1997	Two-group study of 70 patients with cancer using exercise (bed-based stationary bicycle) or usual care	Exercise group reported less diarrhea severity compared to the control group. No significant difference between groups for oral mucositis	■ RSG: L ■ BOA: H ■ IOD: L ■ SR: L
Mouthwash for oral mucositis			
Fidler et al., 1996	Two-group study of 164 patients with cancer using mouthwash (chamomile; swish and spit) or placebo mouthwash	No significant difference between groups for oral mucositis	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: L ■ IOD: L ■ SR: L
Tavakoli Ardakani et al., 2016	Two-group study of 60 patients with cancer using mouthwash (chamomile and peppermint oil; swish and spit) or placebo mouthwash	Mouthwash group reported less oral mucositis compared to the control group.	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: L ■ IOD: L
Progressive muscle relaxation for anticipatory nausea and vomiting			
Yoo et al., 2005	Two-group study of 30 women with breast cancer using progressive muscle relaxation plus guided imagery or usual care	Progressive muscle relaxation group reported less anticipatory nausea and anticipatory vomiting compared to the control group.	■ RSG: L ■ BPP: L ■ BOA: L ■ IOD: L
Systematic desensitization for anticipatory nausea and vomiting			
Morrow, 1986	Four-group study of 92 patients with cancer using systematic desensitization, relaxation, counseling, or usual care	Systematic desensitization group reported less anticipatory nausea compared to the other groups. Systematic desensitization and relaxation groups reported less post-treatment nausea compared to the other groups.	■ RSG: L ■ BOA: L ■ IOD: L
Morrow & Morrell, 1982	Three-group study of 60 patients with cancer using systematic desensitization and progressive muscle relaxation, counseling, or usual care	Systematic desensitization group reported less anticipatory nausea and anticipatory vomiting compared to the counseling and control groups.	■ RSG: L ■ BOA: L ■ IOD: L
Morrow et al., 1992	Three-group study of 72 patients with cancer using systematic desensitization delivered by medical personnel, systematic desensitization delivered by clinical psychologists, or usual care	Systematic desensitization groups reported less anticipatory nausea, anticipatory vomiting, post-treatment nausea, and post-treatment vomiting compared to the control group.	■ RSG: L ■ BOA: L ■ IOD: L

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TABLE 3. Summary of Findings *(Continued)*

Study	Sample and Design	Results	Risk of Bias
Electroacupuncture for vomiting			
Shen et al., 2000	Three-group study of 104 women with breast cancer using electroacupuncture, minimal needling/sham electroacupuncture, or usual care	Electroacupuncture group reported less vomiting compared to the sham electroacupuncture and control groups. The sham acupuncture group reported less vomiting compared to the control group.	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: L ■ IOD: L
Distraction for vomiting			
Oyama et al., 2000	Two-group study of 30 patients with cancer using virtual reality or usual care	The distraction group reported less vomiting compared to the control group.	■ RSG: L ■ BOA: L
Progressive muscle relaxation for vomiting			
Holli, 1993	Two-group study of 67 patients with cancer using progressive muscle relaxation or usual care	No significant difference in vomiting between groups	■ RSG: L ■ BOA: L ■ IOD: L
Therapeutic touch for vomiting			
Matourypour et al., 2016	Three-group study of 108 women with breast cancer using therapeutic touch, sham therapeutic touch, or usual care	Therapeutic touch group reported less vomiting compared to the control group. No significant difference between groups for vomiting	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: L ■ IOD: L
Education for diarrhea			
Williams & Schreier, 2004	Two-group study of 70 women with breast cancer using educational audio recordings about nutritional and symptom management or usual care	No significant difference between groups for nausea, vomiting, anorexia, diarrhea, dysgeusia, oral mucositis, or constipation	■ RSG: L ■ BOA: L ■ IOD: L
Exercise for diarrhea			
Dimeo et al., 1997	Two-group study of 70 patients with cancer using exercise (bed-based stationary bicycle) or usual care	Exercise group reported less diarrhea severity compared to the control group. No significant difference between groups for oral mucositis	■ RSG: L ■ BOA: H ■ IOD: L ■ SR: L
Distraction for anticipatory nausea			
Vasterling et al., 1993	Three-group study of 60 patients with cancer using video games, progressive muscle relaxation, or usual care	Progressive muscle relaxation and distraction groups reported less anticipatory nausea compared to the control group. No significant differences between groups for nausea or vomiting after chemotherapy	■ RSG: L ■ AC: L ■ BPP: L ■ BOA: L ■ IOD: L

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TABLE 3. Summary of Findings *(Continued)*

Study	Sample and Design	Results	Risk of Bias
Progressive muscle relaxation for anticipatory nausea			
Burish et al., 1991	Four-group study of 60 patients with cancer using progressive muscle relaxation plus guided imagery, coping preparation, progressive muscle relaxation plus coping preparation, or usual care	Coping preparation and progressive muscle relaxation plus coping preparation groups reported less nausea and anticipatory vomiting compared to the two groups that did not receive coping preparation.	■ RSG: L ■ BOA: L ■ IOD: L
Education for dysgeusia			
Williams & Schreier, 2004	Two-group study of 70 women with breast cancer using educational audio recordings about nutritional and symptom management or usual care	No significant difference between groups for nausea, vomiting, anorexia, diarrhea, dysgeusia, oral mucositis, or constipation	■ RSG: L ■ BOA: L ■ IOD: L

AC—allocation concealment; BPP—blinding of participants and personnel; BOA—blinding of outcome assessment; H—high; IOD—incomplete outcome data; L—low; RSG—random sequence generation; SR—selective reporting
Note. Unless noted, risk of bias assessment was unknown.

This systematic review demonstrates that evidence supports the use of complementary approaches to manage certain GI symptoms. In total, 15 different complementary approaches were used to manage nine unique GI symptoms. Although this evidence is a meaningful step toward improved GI symptom management, many bothersome GI symptoms had little to no evidence to support the use of complementary approaches. Forty-eight of the 57 studies included in this review focused on nausea or vomiting, and only 19 studies focused on GI symptoms other than nausea or vomiting. Although nausea and vomiting are prevalent, severe, and distressing symptoms, they do not comprise the entirety of the chemotherapy symptom experience. Research has shown that GI symptoms like xerostomia, anorexia, bloating, and early satiety are prevalent, severe, and distressing in patients undergoing chemotherapy (Cherwin & Kwekkeboom, 2016; Thiagarajan et al., 2016). However, these symptoms are often overlooked in intervention studies. More research is needed investigating the effectiveness of nonpharmacologic therapies in preventing or relieving GI symptoms other than nausea and vomiting.

Although research on nonpharmacologic interventions has become more prevalent, more progress is needed. Thirty-three of 57 studies reviewed were published more than 10 years ago. Major advancements in chemotherapy have been made in that time, including the use of immunotherapy. Immunotherapy treatment regimens come with a different set of side effects as compared to the older, cytotoxic treatment regimens. Although this new class of cancer therapy tends to be better tolerated than older-generation cytotoxic therapies, it is still associated with many severe and distressing side effects, including a number of GI toxicities like dysgeusia, oral mucositis, xerostomia, and diarrhea (Rapoport et al., 2017). Studies need to account for the changing face of cancer treatment–related symptoms and evaluate how effective nonpharmacologic complementary therapies can be against these symptoms.

The available evidence has some methodologic limitations. Of the 326 full-text articles assessed for eligibility, about one-fourth had to be excluded because they were not randomized, controlled trails. There is a shortage of high-grade evidence describing the effectiveness of nonpharmacologic interventions for managing chemotherapy-related GI symptoms. In addition, of the 57 articles included for full review, a majority had a small sample size. The sample sizes for articles included for full review ranged from 16–739, but 42 of 57 studies had a sample size of less than 100. Although most of the studies reviewed showed a positive effect on GI symptoms as a result of a nonpharmacologic intervention, a number of studies did not show a difference in GI outcomes as a result of the intervention, or the intervention effect was not sustained. This may be a result of many of the studies not being powered appropriately to detect a difference caused by the intervention. More large-scale,

randomized, controlled trials are needed to determine which nonpharmacologic interventions elicit an effect on GI symptom outcomes. Of the sources of bias most commonly found in the articles reviewed, not blinding the participant/personnel and not blinding the outcome assessment were the most common. It is often difficult to blind a participant or interventionist to the intervention when it is a complementary therapy like acupuncture or transdermal electrical nerve stimulation. However, more randomized, controlled trials are employing sham interventions in an effort to blind the participants to the intervention. Blinding the outcome assessment can be more problematic because assessing symptoms most often requires the person to self-report, making concealment difficult.

The results of the current literature review mirror the results of a 2008 review of nonpharmacologic strategies for managing common chemotherapy side effects (Lotfi-Jam et al., 2008). Lofti-Jam et al. (2008) concluded that, although many nonpharmacologic strategies have evidence to support their use for managing chemotherapy-related symptoms, much of the evidence was of lower quality, calling their results into question and making clinical application difficult. Despite the limitations of the studies reviewed in the current article, nonpharmacologic complementary therapy use is supported by evidence, generally inexpensive, safe for use, and well-liked by participants. Some of the interventions need a trained practitioner or assistance from a healthcare provider (e.g., acupuncture, transcutaneous electrical stimulation), but many of these interventions are self-care strategies that can be used at any time. The Oncology Nursing Society ([ONS], 2017) Putting Evidence Into Practice (PEP) recommends certain complementary approaches for managing treatment-related GI symptoms, such as hypnosis, progressive muscle relaxation, and guided imagery for nausea and vomiting. Although many complementary approaches are not yet specifically recommended for practice, practice recommendations will change to reflect this as more high-grade evidence is produced.

Limitations

Although inclusion criteria limited studies to randomized, controlled trials, the review of bias revealed that many studies had a high risk of bias regarding blinding of personnel or outcome assessment. This knowledge of who had the active intervention on the part of the participants and interventionists may have artificially skewed the results of the intervention to have a larger effect size than may have been actually present. A second limitation relates to the large number of studies that needed to be excluded from this review. Many studies were not considered for this review because the study design did not employ random assignment, the participants were not receiving chemotherapy exclusively, or the complementary therapy was an ingestible herbal remedy. This means that the articles reviewed were a relatively small selection of the total available research on complementary therapies, and the results are only applicable to a small subset of people with solid tumors. Future reviews should summarize evidence for herbal therapies, using people with hematologic cancers and people receiving other treatment regimens, such as radiation therapy or stem cell transplantations.

KNOWLEDGE TRANSLATION

- Evidence supports a wide variety of nonpharmacologic interventions for the management of nausea and vomiting.
- Additional research is needed to evaluate nonpharmacologic interventions for gastrointestinal symptoms apart from nausea and vomiting.
- Oncology nurses should be familiar with current research on nonpharmacologic interventions to properly educate their patients.

Implications for Practice

This review of evidence suggests that nonpharmacologic complementary approaches are effective for managing chemotherapy-related GI symptoms in people with cancer. The National Center for Complementary and Integrative Health (2016) strategic plan has made care improvement for hard-to-manage symptoms a primary objective. GI symptoms can be classified as hard to manage because recent evidence has suggested that, despite the availability of pharmacologic interventions, more than 25% of patients with a hematologic cancer receiving chemotherapy experienced GI symptoms like nausea, xerostomia, anorexia, bloating, flatulence, dysgeusia, and constipation (Cherwin & Kwekkeboom, 2016). Complementary approaches can offer additional relief from GI symptoms when pharmacologic therapies are not sufficient. Oncology nurses should be aware of current practice recommendations to discuss complementary treatment approaches with their patients. ONS (2018) PEP committees review current literature on interventions and publish summaries of the strengths and limitations of that literature. Twenty symptom topics comprise the PEP summaries, five of which are GI symptoms (i.e.,

anorexia, chemotherapy-induced nausea and vomiting, constipation, diarrhea, and mucositis). Summaries like these are needed because a survey found that, although nurses like complementary therapy options for their patients, they feel unfamiliar with the research and are unsure of how to discuss these therapies with their patients (Hall, Leach, Brosnan, & Collins, 2017). Literature reviews, such as the one provided in the current article and the ONS PEP resources, are useful tools for practicing nurses to become familiar with evidence surrounding complementary therapy use in their patient population.

The further dissemination of high-grade research (i.e., randomized, controlled trials with large sample sizes) of complementary strategies to manage GI symptoms will help to strengthen the ONS PEP recommendations for use of these interventions. As of December 2018, only chemotherapy-induced nausea and vomiting has nonpharmacologic complementary therapies classified as Likely to be Effective, and only mucositis has nonpharmacologic complementary therapies classified as Recommended for Practice. For the other GI symptoms reviewed by the PEP committees, many of the interventions discussed in this review of literature are still classified as Effectiveness not Established, primarily because of the lack of high-grade evidence. A need exists for studies exploring GI symptoms beyond nausea and vomiting because treatment-related symptoms can be highly varied. Building the body of evidence will influence practice, which will in turn make more complementary approaches available to patients, ultimately reducing the treatment burden they face.

Conclusion

The purpose of this systematic review was to summarize and critique the literature reporting nonpharmacologic management of chemotherapy-related GI symptoms. In particular, this review focused on high-grade evidence; therefore, only randomized, controlled trials were included. The results of this systematic review demonstrate that evidence supports the use of nonpharmacologic management of GI symptoms in chemotherapy, but a wide variety of interventions can be used for several GI symptoms, primarily nausea and vomiting. More research is needed to evaluate nonpharmacologic interventions for GI symptoms beyond nausea and vomiting.

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