Controlling Chemotherapy Induced Nausea and Vomiting Through Guideline Adherence

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Abstract

Background

Thirty to fifty percent of cancer patients undergoing chemotherapy will experience chemotherapy induced nausea and or vomiting (CINV) despite the use of antiemetic prophylaxis Uncontrollable CINV can lead to complications that add extra stress to patients, increase in healthcare costs, and utilization of resources. CINV can lead to chemotherapy dose reductions, treatment delays, chemotherapy changes, or discontinuation of treatment. Guidelines exist to better prevent and treat CINV. Evidence supports the use of guidelines to prevent CINV, however patients still suffer from CINV often due to a lack of guideline adherence.

Objectives

The purpose of this project was to increase CINV guideline adherence by increasing knowledge of antiemetic guidelines utilizing an educational intervention for providers and nurses at an outpatient oncology office.

Methods

A brief educational intervention on CINV and recommended NCCN guidelines was conducted with providers and nurse (n=6) at an oncology practice in Southwestern United States. An evaluation to assess change in knowledge was performed using a pre and post test format. Statistical analysis was performed using descriptive statistics, McNemar tests and Wicoxan Signed Rank Test.

Findings

There was a significant effect on knowledge of NCCN antiemetic guidelines (Z=-1.89, p=0.059, mean 2.5) post intervention. There also was a significant impact on likelihood to use guidelines in practice (Z=-1.89, p=0.059, mean 2.5). Increasing awareness and likelihood to

follow recommended guidelines may improve CINV symptoms in patients undergoing chemotherapy and improve the treatment outcomes for these patients.

Keywords: CINV, Chemotherapy, Symptoms management, guideline adherence

Chemotherapy Induced Nausea and Vomiting Guideline Adherence

One of the most distressing side effects of cancer treatment is chemotherapy induced nausea and vomiting (CINV). CINV is difficult to assess and treat because it is subjective and often underreported by patients and its impact is often under estimated by providers.

Problem Statement

Chemotherapy induced nausea and vomiting adds extra stress to patients and causes an increase in healthcare costs and utilization of resources. CINV can lead to chemotherapy dose reductions, treatment delays, chemotherapy changes, or discontinuation of treatment. Van Lear, Desai, and Jatoi (2015) found 32% of oncologists surveyed needed to delay or dose reduce chemotherapy due to CINV. Guidelines exist to better prevent and treat CINV (American Society of Clinical Oncology [ASCO], 2017; National Comprehensive Cancer Network [NCCN], 2017). Evidence supports the use of guidelines to prevent CINV, however patients still suffer CINV often due to a lack of guideline adherence (Caracuel, Munoz, Banos, & Ramirez, 2015).

Purpose and Rationale

Chemotherapy induced nausea and vomiting is one of the most distressing and severe side effects of chemotherapy for patients (Hernandez Torrez et al., 2015; Inoue et al., 2015). Uncontrolled CINV negatively impacts patients' lives and can lead to decreased quality of life, dehydration, and poor treatment outcomes. There is an extensive body of evidence to guide providers in effectively preventing and managing CINV. The purpose of this project is to create more knowledge and awareness of these guidelines in an effort to increase their use in practice.

Background and Significance

The National Cancer Institute (NCI) (2016) estimates one million people are diagnosed with cancer each year and for many of these people chemotherapy is a treatment option. It is estimated 30-50% of patients undergoing chemotherapy experience CINV (Hu et al., 2016; Moradian & Howell, 2015). It is a major concern because if left uncontrolled it can lead to dose reductions, treatment delays, and unanticipated stoppage of treatments which can affect overall treatment outcomes. Improving treatment outcomes and improving supportive and palliative therapy are major initiatives of the NCI (National Cancer Institute [NCI], 2016).

CINV is a major area of concern for both patients and providers. Hernandez Torres et al. (2015) suggest many providers consider adequate treatment of CINV to be the absence of emesis. However, patients report nausea just as distressing as vomiting (Hernandez Torres et al., 2015; Vidall et al., 2015). Patients have also suggested providers underestimated the impact nausea has on daily life (Vidall et al., 2015). Van Lear et al. (2015) found 88%-92% of providers felt they could adequately control CINV but 38% of providers admitted to delaying, stopping, or changing chemotherapy due to uncontrolled CINV. This gap in patient provider perception of the impact of CINV suggests room for improvement in understanding and managing symptoms.

Treating CINV can be a difficult undertaking as there are many risk factors and multiple mechanisms of actions. CINV usually occurs in the first 5 days following chemotherapy administration and poorly controlled nausea and vomiting during this time can cause anticipatory nausea and vomiting in following cycles of chemotherapy (Hopkins &Donovan, 2014; NCCN, 2017; Tegeja &Groning, 2016).

Another complexity in the management of CINV is the emetogenic potential of certain chemotherapies meaning the likelihood of a chemotherapy to cause nausea and vomiting. Different chemotherapies and regimens have different emetogenic potentials which creates the

need for varying medications to control CINV. Tageja and Groninger (2016) as well as Boccia (2013) indicate multiday regimens for IV chemotherapy and oral chemotherapy agents further add to the emetogenic potential of medications.

The different types of CINV, multiple mechanisms of action, individual risk factors and the different emetogenic potential of chemotherapeutic agents require a complex assessment and multipronged approach to successfully manage CINV. This complexity has led to the importance of guidelines for the management CINV.

To help manage the effects of CINV, professional organizations have created guidelines to help providers to adequately prescribe the correct prophylaxis and treatment needed. Three main organizations – the Multinational Association for Supportive Care in Cancer/ European Society for Medical Oncology (MASCC/ESMO), ASCO, and NCCN have all issued guidelines for the management of CINV. These guidelines were based on research and evidence in antiemetic agents, as well as consensus of experts. The Oncology Nursing Society (ONS), the major certifying agency for chemotherapy administration, recommends the utilization of guidelines.

Despite the evidence and consensus behind the guidelines, there is a lack of adherence to guideline recommendations. Guideline adherence is the responsibility of providers and patients. Providers must be aware of guideline recommendations to prescribe and educate the patients. Gilmore et al. (2014) found patients were less likely to experience CINV when guidelines were followed.

Guideline nonadherence can take many shapes and forms such as prescribing incorrect classes of medications, not prescribing corticosteroids in the delayed phase, and the over dosing of some medications. All of the guidelines take into account the emetogenic potential of the

chemotherapy agents used. The emetogenic potential of chemotherapy agents are classified as highly emetogenic (HEC), moderately emetogenic (MEC), low emetogenic (LEC), and minimally emetogenic. Some providers are less likely to adhere to guidelines with LEC, mostly by over prescribing medications with LEC regimens (Franca et al., 2015; Vidall et al., 2015). Other studies have found that guideline nonadherence was due to the lack of prescribing corticosteroids during the delayed phase of CINV (Burmeister, Aebi, Studer, Fey, & Gautschi, (2012).

Another aspect of guideline adherence is patient compliance with medications. Patients must comply with the guideline recommendations and take medications as prescribed to achieve optimal results. Patient compliance is easier to manage in the hospital setting as nurses are often administering medications, however this is difficult to control in the outpatient setting when the patient must take medications independently at home in the days following chemotherapy administration. Caracuel et al. (2015) found only 61% of patients were compliant with their oral antiemetics. In another survey, only 38% of patients remembered taking their antiemetics as instructed (Vidall et al., 2015). Reasons patients did not want to take medications included not wanting to taking medications when not feeling nauseous, not wanting to take any additional medications, and being afraid taking medications may lead to vomiting (Vidall et al., 2015). Educating both providers and patients may be a way to help improve guideline adherence and better control CINV.

In an oncology practice in the Southwestern United States, patients are usually given their chemotherapy education on a day prior to starting chemotherapy. On this day, the patient often receives all the information needed for their entire chemotherapy course, including information for managing CINV. This amount of information is overwhelming and often forgotten. There is

no system currently set up to track the incidence of CINV or dehydration related to CINV in this practice.

Providers will often follow some of the NCCN guideline recommendations to insure insurance approval; however, there are often inappropriate exceptions or omissions. For example, patients receiving HEC will often be written for a prescription for an NK-1 receptor antagonist (NK-1RA), 5-HT3RA, and corticosteroids per NCCN guidelines. Some patients are not able to afford the high cost associated with the NK-1RA and often this gets removed from the treatment plan. NCCN also recommends the use of olanzapine, an atypical antipsychotic, and corticosteroids orally as antiemetic prophylaxis prior to HEC but this option is rarely utilized.

The severity of CINV experienced by patients and the lack of guideline adherence raise the following PICO question: In adults undergoing chemotherapy, how does guideline adherence compare to nonadherence affect CINV?

Search Process

A search of the literature was done using 3 databases - CINHAL, PubMed, and the Cochrane library. Search terms included *chemotherapy, antiemesis, nausea, vomiting, guidelines, protocols, adherence,* and *compliance*. Variations of these terms were also searched. The results were limited to the last 5 years to make sure current evidence was being used. All of the studies considered needed to include the use of chemotherapy guidelines. The results were also limited to adults over the age of 18. Ancestry was also used during the literature search (Appendix A).

Critical Appraisal and Synthesis

Following the literature search, 10 high quality studies were used for critical appraisal and analysis. Most of the studies were level three cohort studies but two of the studies were level 2 randomized control trials (RCTs) according to the hierarchy of evidence (Melnyk &Fineout-

Overholt, 2015). The eight other studies reviewed were observational studies, retrospective and prospective studies (Appendix B). There was homogeneity as all the studies showed better CINV outcomes with guideline adherence as a result, but only one study looked at patient adherence to prescription medication (Caracuel, et al., 2015). The samples all included cancer patients undergoing chemotherapy. Three studies looked at breast cancer patients and one study looked at glioma patients. There was some heterogeneity in the guidelines. Some studies used a combination of guidelines and some used independent institutional protocols.

The studies took place all over the world, Europe, Japan, Singapore, Canada, and the United States. Most of the studies followed international guidelines except for two studies which followed institutional guidelines. The most common guideline used was MASCC/ESMO guideline (Appendix C).

The consensus of results from the critical analysis shows guideline adherence when prescribing antiemetics has better outcomes. Antiemetic guidelines are evidenced based and have been shown to decrease CINV incidence. Decreased incidence of CINV improves the overall treatment experience and treatment outcomes of patients. Improving guideline adherence in both patients and providers can reduce the overall incidence of CINV. Controlling CINV in early chemotherapy cycles also improves the rates of anticipatory CINV in following cycles. Guideline consistent prescribing leads to less office and emergency room visits for dehydration secondary to CINV, lowering health care costs. Ensuring guideline adherence can reduce health care costs and decrease the incidences of CINV.

Conceptual/Theoretical Model and Evidence Based Practice Model

The theory of symptom management depicts the three main components, symptom experience, the components of symptoms management, and the outcome, as being interrelated

and affecting each other (Linder, 2010). The symptoms experience and symptom management strategies are encompassed in the outcomes (Appendix D). The symptom experience, CINV, includes the perception, evaluation, and response to symptoms; symptoms management strategies includes the providers who deliver care, what is being done to improve the symptoms, how much and when the intervention is being delivered (Linder, 2010). The symptoms management strategy utilized for the intervention is CINV guideline adherence. The symptom may or may not be present but may be a threat to the individual's overall outcome. Adherence also plays a role in maintaining the balance of wellbeing and has the power to disrupt the outcome. Adherence or nonadherence to symptom management strategies may cause a worsening of symptoms and put an individual at risk for poor outcomes (Linder, 2010).

The evidence based practice model that drove this project was the Ottawa Model for Research Use (OMRU) (Graham & Logan, 2004). This model is a dynamic and fluid model for evidenced based practice. OMRU identifies who is responsible for making change decisions and key stakeholders for change (Appendix E). After key individuals are assessed, it is important to clearly state and know the intervention being implemented. The next step is to identify potential barriers and potential adopters and facilitators to the change. After implementation, evaluation of knowledge translation and situational assessment are important to monitor the change. Another key aspect of monitoring change is the evaluation of the change and the impact it has on key stakeholders. Due to the dynamic nature of this model, there is a constant evaluation, assessment and monitoring of change and adaptations needed (Graham & Logan, 2004). The dynamic nature of this model allows for post intervention changes, which may be important to any change. The fluid nature of the OMRU allows for constant adaptation and change during the implementation process and helps to aid with sustainability.

Using OMRU, the practice environment was assessed first. The patient flow and education were noted, and key individuals were identified. Potential adopters were also identified, as were those who could be resistant to change. Also, the evidence was analyzed and synthesized during the initial stages. The evidence transfer strategy chosen was dissemination, and an evidence based educational intervention was the tool used to disseminate the evidence. Following the interview, the staff chose to adopt the change and outcomes were assessed for providers.

Project Methods

Protections of human subjects was approved through the Institutional Review Board at Arizona State University. Recruitment was done by a team member familiar with the practice. Participants were provided with information of the intervention, including risks and benefits; consent was implied by participation in the educational intervention. Providers and nurses were asked to participate in a brief educational intervention. A pretest and posttest assessment was conducted before and immediately after the intervention (Appendix F). Unique identification numbers were assigned to the participants to maintain confidentiality. Content validity for the pre and posttest was assessed by review by content experts.

The educational session on CINV was prepared for both providers and nurses in the office using the evidence gathered from the literature search. The educational session discussed the underlying pathophysiology of CINV and risk factors for CINV; the educational session also included the 2017 NCCN guideline recommendations for HEC and MEC, patient education for CINV, and information the MASCC Antiemesis Tool (MAT) for objective CINV assessment.

Patient education material was created utilizing NCCN guidelines, ONS recommendations, and evidence gathered during the literature search and given to the

participants as part of the intervention. The educational sheets where written using plain language and clearly listed steps for patients to take to manage their CINV at home. Also included in the educational material was a blank calendar week for the patient to list when they needed to take their home corticosteroids and information on how to manage breakthrough medications as needed. Lastly, the patient education sheet listed who to call for questions or uncontrolled CINV.

Outcomes and Impact

Data gathered through the pretest and posttest was analyzed utilizing SPSS (IBM Corp, 2016) for statistical analysis. Demographic information was analyzed using descriptive statistics. The sample consisted of two doctors and four nurses who cared for patients undergoing chemotherapy (n=6). The years of oncology experience ranged from 3 years to 17 years with a mean of 9.08 years (SD= 5.43). The level of education of the participants included associate's degrees, bachelor's degrees, and MDs.

Pretest and posttest data were compared using the McNemar test and Wilcoxan Signed Rank test. Due to the pre-existing knowledge level of the participants about CINV, the McNemar test indicated this intervention failed to change the knowledge level and there was no change in the knowledge of CINV when comparing the pretest and the posttest.

Participants were asked to rate their familiarity with NCCN guidelines for antiemesis on a scale of zero to five before and after the intervention. Using the Wilcoxan Signed Rank test and a 90% confidence interval (α=0.1), there was a significant change in familiarity of the guidelines (Z= -1.89, p=0.059). Similar results were found when participants were asked to rate their likelihood to use the guidelines in practice (Z= -1.89, p=0.059). These results indicate the

intervention was effective in increasing knowledge of the guidelines and increasing the likelihood the participants would use them in practice.

Discussion

CINV is very distressing for many patients undergoing chemotherapy and is a side effect that most patients are concerned about. Recommended guidelines are consensus and evidence based, making them the standard of practice. The results for both familiarity of NCCN guidelines and likelihood to use these guidelines in practice showed significant change following the educational intervention (Z= -1.89, p=0.059). The significance of these results indicates the educational intervention was effective at increasing familiarity and awareness of the guidelines. Improving the awareness of the guidelines and the options offered for treating CINV may improve patient symptoms and outcomes if applied to practice.

The intervention also caused a significant result in participants' likelihood to use guidelines in practice (Z= -1.89, p=0.059). Increasing awareness of the recommended guidelines may increase provider adherence when writing antiemetic prophylaxis. Properly medicating patients before chemotherapy will have a positive effect on overall treatment outcomes because there will be an expected decrease in the treatment changes, stoppages, and delays. It may also decrease the cost to the healthcare system in general as there will likely to be less costs for additional medications and hydration treatments.

Strengths and Limitations

One of the biggest strengths was this project did increase providers knowledge of the guidelines and providers reported an increase in likelihood to utilize the guidelines in practice. Another strength of this project was that it gave providers resources to use in future practice. This helps to aid in the sustainability as it creates a simpler way for assessing and educating

patient on CINV. Participants were able to keep the patient education designed from current evidence and a copy of the MAT tool for assessing CINV. Another strength of this intervention was it worked with the current practice environment and strengthened it with the current evidence.

This intervention did have some weaknesses as well as strengths. The first limitation was the timeframe for the intervention. Due to the limited time to perform the intervention, the original plan needed to be changed and excluded implementing the MAT tool and performing chart audits for outcome measures addressing compliance with guidelines and assessing whether there was an improvement in the management of CINV. Also, all of the educational sessions were held in one day and one participant did not finish the post test, making it difficult to compare the data. The condensed timeframe also did not allow for the measurement of long term outcomes associated with the educational intervention.

Another limitation was the small sample size (n=6). While the sample was a sample of convenience by including participants who were in the office on that day, the small sample size may have affected the validity of the results and limited the transferability of the intervention.

Conclusion

The purpose of this project was to increase knowledge regarding CINV guideline recommendations in an effort to increase guideline adherence. The educational intervention was designed specifically for the practice environment in which the project took place, limiting its transferability. The timeframe was also a large limitation of this intervention. Despite its limitations, this intervention demonstrated a significant change on familiarity with NCCN recommended guidelines for CINV. Participants also indicated a significantly higher likelihood to use the guidelines in future practice. This project provided the practice with additional patient

education tools which may help to improve patient adherence to prescribed treatment for the management of CINV.

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Appendix A

CINHAL Search Strategy

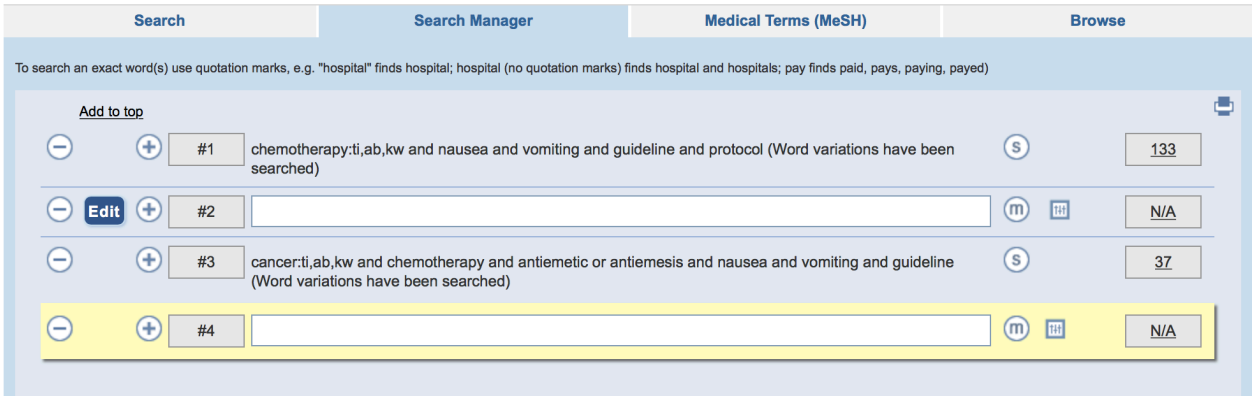
	Search ID#	Search Terms	Search Options	Actions
☐	S14	S12 AND S13	**Search modes** - Boolean/Phrase	View Results (23) | View Details | Edit
☐	S13	adherence	**Search modes** - Boolean/Phrase	Rerun | View Details | Edit
☐	S12	(Cancer OR Neoplastic OR Neoplasm OR Malignant) AND (antiemesis OR anti-emesis OR antiemetic OR anti-emetic) AND ((nausea and vomiting) OR nausea OR vomiting) AND (guideline OR protocol)	**Search modes** - Boolean/Phrase	Rerun | View Details | Edit
☐	S11	(guideline OR protocols) AND (S10)	**Search modes** - Boolean/Phrase	Rerun | View Details | Edit
☐	S10	(Cancer OR Neoplastic OR malignant) AND (Chemotherapy OR Antineoplastic) AND ((nausea and Vomiting) OR nausea OR Vomiting)	**Search modes** - Boolean/Phrase	Rerun | View Details | Edit
☐	S9	(cancer) AND (S8)	**Search modes** - Boolean/Phrase	Rerun | View Details | Edit
☐	S8	Chemotherapy AND (Nausea and vomiting) AND (guidelines OR protocols)	**Search modes** - Boolean/Phrase	Rerun | View Details | Edit
☐	S7	S5 AND S6	**Search modes** - Boolean/Phrase	View Results (23) | View Details | Edit
☐	S6	adherence	**Search modes** - Boolean/Phrase	View Results (34,166) | View Details | Edit
☐	S5	(Cancer OR Neoplastic OR Neoplasm OR Malignant) AND (antiemesis OR anti-emesis OR antiemetic OR anti-emetic) AND ((nausea and vomiting) OR nausea OR vomiting) AND (guideline OR protocol)	**Search modes** - Boolean/Phrase	View Results (160) | View Details | Edit
☐	S4	(guideline OR protocols) AND (S3)	**Search modes** - Boolean/Phrase	View Results (252) | View Details | Edit
☐	S3	(Cancer OR Neoplastic OR malignant) AND (Chemotherapy OR Antineoplastic) AND ((nausea and Vomiting) OR nausea OR Vomiting)	**Search modes** - Boolean/Phrase	View Results (2,341) | View Details | Edit
☐	S2	(cancer) AND (S1)	**Search modes** - Boolean/Phrase	View Results (177) | View Details | Edit
☐	S1	Chemotherapy AND (Nausea and vomiting) AND (guidelines OR protocols)	**Search modes** - Boolean/Phrase	View Results (255) | View Details | Edit

PubMed Search Strategy

History Download history Clear history

Search	Add to builder	Query	Items found	Time
#11	Add	Search (((((cancer OR neoplastic OR malignant)) AND (chemotherapy OR antineoplastic)) AND ((nausea and vomiting) OR nausea OR vomiting)) AND (guideline OR protocols)) AND adherence Filters: **Humans; Adult: 19+ years**	32	23:12:26
#10	Add	Search (((((cancer OR neoplastic or malignant)) AND (chemotherapy OR antineoplastic)) AND ((nausea and vominting) OR nausea OR Vomting)) AND (guideline OR protocols)) AND adherence Filters: **Humans; Adult: 19+ years**	28	23:07:31
#9	Add	Search (((((cancer OR neoplastic OR malignant)) AND (chemotherapy OR antineoplastic)) AND ((nausea and vomiting) OR nausea OR vomiting)) AND (guideline OR protocols)) AND adherence Filters: **Humans**	59	23:07:05
#8	Add	Search (((((cancer OR neoplastic or malignant)) AND (chemotherapy OR antineoplastic)) AND ((nausea and vominting) OR nausea OR Vomting)) AND (guideline OR protocols)) AND adherence Filters: **Humans**	53	23:07:05
#7	Add	Search (((((cancer OR neoplastic OR malignant)) AND (chemotherapy OR antineoplastic)) AND ((nausea and vomiting) OR nausea OR vomiting)) AND (guideline OR protocols)) AND adherence Filters: **Other Animals; Humans**	59	23:06:57
#6	Add	Search (((((cancer OR neoplastic or malignant)) AND (chemotherapy OR antineoplastic)) AND ((nausea and vominting) OR nausea OR Vomting)) AND (guideline OR protocols)) AND adherence Filters: **Other Animals; Humans**	53	23:06:57
#5	Add	Search (((((cancer OR neoplastic OR malignant)) AND (chemotherapy OR antineoplastic)) AND ((nausea and vomiting) OR nausea OR vomiting)) AND (guideline OR protocols)) AND adherence Schema: **all** Filters: **Other Animals**	0	23:06:47
#4	Add	Search (((((cancer OR neoplastic OR malignant)) AND (chemotherapy OR antineoplastic)) AND ((nausea and vomiting) OR nausea OR vomiting)) AND (guideline OR protocols)) AND adherence Filters: **Other Animals**	0	23:06:46
#3	Add	Search (((((cancer OR neoplastic or malignant)) AND (chemotherapy OR antineoplastic)) AND ((nausea and vominting) OR nausea OR Vomting)) AND (guideline OR protocols)) AND adherence Filters: **Other Animals**	0	23:06:46
#2	Add	Search (((((cancer OR neoplastic OR malignant)) AND (chemotherapy OR antineoplastic)) AND ((nausea and vomiting) OR nausea OR vomiting)) AND (guideline OR protocols)) AND adherence	60	23:06:13
#1	Add	Search (((((cancer OR neoplastic or malignant)) AND (chemotherapy OR antineoplastic)) AND ((nausea and vominting) OR nausea OR Vomting)) AND (guideline OR protocols)) AND adherence	54	23:06:12

Cochrane Library Search Strategy



Appendix B

Evaluation Table

Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis (stats used)	Findings/ Results	Level/Quality of Evidence; Decision for practice/ application to practice
Aapro et al., (2012). The effect of guideline-consistent antemetic therapy on chemotherapy-induced nausea and vomiting.	Physiological framework	Prospective Observational Multicenter Study	n=1128 Pt initiating HEC or MEC C1=991 C2=888 C3=769 **Setting:** 8 European Countries, Infn clinic	IV- GCP DV-GIP **g/l:** MASCC	Daily Diary Rx information VAS	Pearson X^2 Student *t*-test Multivariate logistic regression	Adh increased in MEC. g/l Rx higher in AP MEC or HEC. CR higher in GCP. Desired outcomes higher GCP.	**Lvl of Evidence:** Lvl 3 **Decision for Practice:** GCP improves CINV for pts and decreases HCC. **Application to Practice:**

Key: **AE**-Antiemetic; **Adh**- Adherence; **An/v**- Anticipatory nausea and vomiting; **AP**- Acute Phase; **b/t**- breakthrough; **C1**-Cycle one; **C2**- Cycle 2; **C3**-Cycle 3; **C4**-Cycle 4; **Ca**-Cancer; **CINV**- Chemotherapy induced nausea and vomiting; **CR**- Complete response; **CT**- Chemotherapy; **d/t**- due to; **dex**-dexamethasone; **DP**- delayed phase; **DS**- Descriptive Statistics; **DV**-dependent variable; **ER**-Emergency Room; **FACIT**-Functional Assessment of Chronic Illness Therapy Fatigue; **FACT-BR**- Functional assessment of cancer therapy-brain; **FLIE**- Functional living index-emesis; **f/u**- follow up; **g/l**-guideline; **GCP**- guideline consistent prescribing; **GEE**-generalized equation estimates; **GIC**-guideline inconsistent prescribing; **grp**-group; **HCC**-Health Care Costs; **HEC**- Highly Emetogenic Chemotherapy; **HP**- Hospital Protocol; **IG**- Intervention group; **inc**-increase; **Infn**- Infusion; **IV**- independent variable; **LEC**- Low emetogenic chemotherapy; **Lvl**- level; **MASCC**- Multinational Association of Supportive Care in Cancer; **MAT**-MASCC Antiemetic Tool; **MEC**- Moderately emetogenic chemotherapy; **med**- medication; **N**-number of studies; **n**- number of participants; **n/v**- nausea and/or vomiting; **NCCN**-National Comprehensive Cancer Network; **NK-1**- Neurokinin receptor antagonist; **outpt**-outpatient; **OV**- Office visit; **PC**- physicians choice; **Pt**- Patient; **Pts**- Patients; **QOL**- quality of life; **RF**-Risk Factors; **RMG**-Risk model guided; **Rx**- Prescribing/prescription; **std**- Standard; **VAS**- visual analog scale; **X^2**- Chi Squared

Country: 8 European Countries **Funding:** Merck Sharp & Dohme Corp. **Bias**: None Stated. ESMO guideline study.							GCP grp had less OV and ER visit follow tx	Encourage GCP to decrease HCC and improve Pt outcomes.

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Affronti et al. (2014). Adherence to antiemetic guideline in patients with malignant glioma: A quality improvement project to translate evidence into practice. **Country:** US (Duke University) **Bias:** None Stated.	Change Theory	Single arm quasi experimental study	n= 61 pt order sets for MEC n= 32 pts surveyed for QOL	Pts of providers who received intervention	Chart Review of Rx Osoba Survey FACT-BR FACIT-fatigue	DS Cronbach's Alpha Wilcoxan Sign Rank test	Post intervention adh increased from 58% to 92% with edu and EMR; CR 75% with adh	**Lvl of evidence:** Lvl 3 **Decision for Practice:** g/l adh increases CR of CINV. **Application to practice:** Provider edu increase adh. **Limitations:** One center Specialty practice.
Burmeister et al. (2012). Adherence to ESMO clinical recommendations		Retrospective observational	n= 299 charts	New CT pts	Chart Review of Regimen	DS Logistic Regression	61% g/l adh Overuse of triple AE	**Lvl of Evidence:** Lvl 3

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for prophylaxis of chemotherapy-induced nausea and vomiting **Country:** Switzerland **Bias:** None stated							11% g/l adh in LEC No Dex DR with NK-1	**Decision for Practice:** Over use of antiemetics reason for low g/l adh. **Application to Practice:** Provider edu on g/l… **Limitations:** Does not look at CINV CR outcomes. Does not include personal risk factors for low adh.
Caracuel et al. (2015). Adherence to antiemetic guidelines and	Medication adherence?	Observational Study	n= 102 Rx n= 10 Rx providers	New CT pts	Chart Review Daily Diary	DS X^2	No sig between g/l adh and CR	**Lvl of Evidence:** Lvl 3 **Decision for practice:**

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control of chemotherapy-induced nausea and vomiting (CINV) in a large hospital. **Country**: Spain **Bias:** None Stated							Adh to HP which was different the g/l	Pt adh plays role in CINV and g/l adh **Application for Practice:** Need intervention to increase pt adherence. **Limitations:** Follow HP not std g/l.
Chan et al. (2012). Assessment between adherence with antiemetic drug therapy and control of nausea and vomiting in breast cancer patients receiving anthracycline-based chemotherapy.	Physiological	Prospective Observational study	n=519 123 excluded d/t loss of f/u or refused participation outpt clinic	Cohort: Adult Breast Ca pts receiving anthracycline CT	Diary Likert Scale for n/v f/u phone call	DS X^2 Fisher's exact test Linear association	62% took b/t med 57.9% adh to outpt med Low adh to dex Rx 58.6% adh had CR in DP	**Lvl of Evidence:** Lvl 3 **Decision for practice:** g/l adh increases CR or CINV **Application:** Better adh decreases CINV. **Limitations:**

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Country: Singapore **Bias**: None stated.								NK-1 not used d/t cost. Used Independent g/l.
Clemons et al. (2016). Risk Model guided antiemetic prophylaxis vs physcians choice in patients receiving chemotherapy for early-stage breast cancer: A randomized trial **Country:** Canada **Funding**: Canadian Breast Cancer Research Foundation **Bias**: None stated.	Physiological	RCT	n= 324 newly dx breast ca	IV- RMG n=154 DV- PC n=170 RMG grp AE adjusted after each cycle	FLIE index Likert scale f/u phone call	DS Repeated measures	6% in each grp An/v; 4.1% in PC grp used NK-1; More med to inc control added to RMG grp than PC grp; Fewer pt in RMG required b/t med	**Lvl of Evidence:** Lvl 2 **Decision for practice:** Triple AE improve HEC CINV (g/l recommendation) **Application:** AE should be eval with each cycle of CT. **Limitations:** Did not use g/l but followed some recommendations. At one facility.

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Dranitsaris et al. (2016). Measuring the impact of guideline-based antiemetic therapy on nausea and vomiting control in breast cancer patients with multiple risk factors. **Country:** Canada **Funding:** Canadian Breast Cancer Research Foundation **Bias:** None Stated. Same sample from Clemons et al.		Exploratory analysis	n=152 Newly dx breast Ca pt. (same sample as clemons et al.)	Newly dx breast Ca pt in RMG utilizing personal RF	FLIE index Diary Telephone call f/u	Repeated Measures	Pts with inc RF for CINV had higher instances of CINV despite prophylaxis. RMG decreased CINV from C1 to C4.	**Lvl of Evidence:** Lvl 3 **Decision For Practice:** Personal RF needs to be considered despite adequate prophylaxis. **Application for practice:** Consider personal RF for CINV when Rx for AE. **Limitations:** Missing data on 3-6% of participants. Sample used in previous study. Don't clearly identify g/l following.

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Gilmore et al. (2014). Antiemetic guideline consistency and incidence of chemotherapy-induced nausea and vomiting in US community practice: INSPIRE study. **Country:** US **Funding:** Merck Sharp & Dohme Corp	Physiological	Prospective Observational Study	n= 1295 C1 new chemo for HEC or MEC per NCCN g/l	IV- GCP n= 742 DV-GIP n= 553	MAT f/u phone call	DS X^2 t-test Multivariate logistical regression	Main reason for lack of g/l adh no dex Rx for DP. GCP had less CINV than GIP.	**Lvl of Evidence:** Lvl 3 **Decision for Practice:** GCP inc CR in CINV **Application:** g/l Rx to decrease CINV. **Limitation:** Assumed pts adh to home AE med. Research funded by pharmaceutical company. Data collected in one f/u phone call 5-8 days after CT
Inoue et al. (2015). Cohort study of consistency between the compliance with guidelines for	Physiological	Retrospective design	n=73 Outpt CT clinic	CT pts in outpt setting monitored for g/l adh.	MAT Chart Review	DS Relative risk	Inc g/l adh in AP, less g/l adh HEC in DP, CINV not prevented in 22.2% in AP	**Lvl of Evidence:** Lvl 3 **Decision for Practice:** Evaluation of CINV and g/l adh

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chemotherapy-induced nausea and vomiting and patient outcome. **Country:** Japan **Bias:** None stated								**Application:** Encourages use of g/l adherence in practice. **Limitations:** Used 3 g/l in practice, used HEC, MEC, and LEC pts.
Molassiotis et al. (2014). Evaluation of risk factors predicting chemotherapy related nausea and vomiting: Results from a European Prospective observational study.	Physiological	Prospective Observational Study	n=1128 137 excluded for no diary or CT change MASCC g/l	n=991 CT naïve pts receiving HEC or MEC with GCP	Diary VAS	DS Multivariate Logistic Regression GEE	Lack of CR from C1 to C2 increased risk for CINV 6.6 time; lack of CR in C2 caused 8 times inc in RF for CINV in C3.	**Lvl of Evidence:** Lvl 3 **Decision for practice:** g/l adh shows decreased rates of CINV but personal RF need to be considered **Applications for Practice:** An/v plays large role in CINV management.

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Country: 8 European Countries **Funding:** Merck Sharp & Dohme Corp **Bias:** Authors speakers and have received compensation from Merck Sharp & Dohme Corp.								**Limitations:** Does not consider outpt adh as part of study.
Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis (stats used)	Findings/ Results	Level/Quality of Evidence; Decision for practice/ application to practice
			N= n=	IV- DV-				

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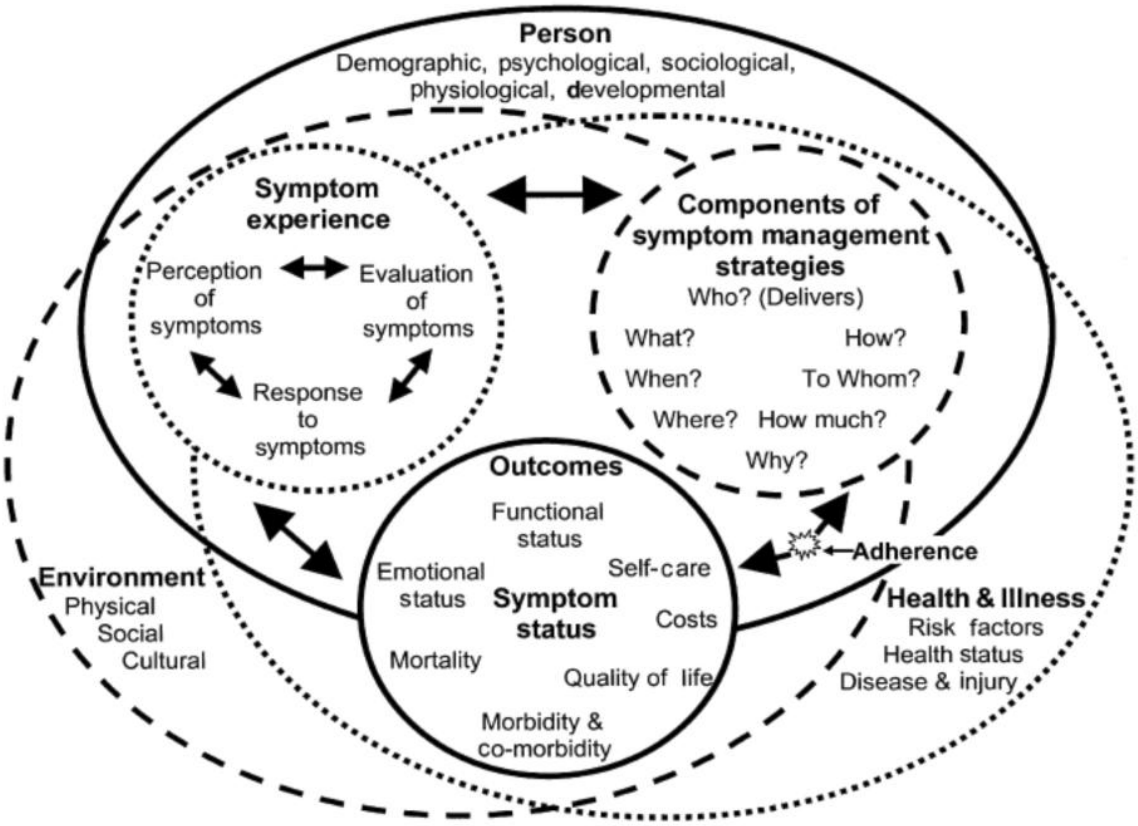
Appendix C

Synthesis Table

Citation	Guideline	Tool	Diary	Phone	Emetogenic Potential	Emesis w/ g/l adherence
Aapro et al. (2012)	MASCC	VAS; Precribing Inforomation	X		HEC/MEC	↓
Affronti et al. (2014)	MASCC/ESMO, NCCN, ASCO	Chart Audit; Osoba			MEC	↓
Burmeister et al. (2012)	MASCC/ESMO	Chart Audt			HEC/MEC/LEC	———
Caracuel et al. (2015)	Indep/ASCO	Chart Audit	X		HEC/MEC/LEC/ Min	↔
Chan et al. (2012).	Independent	Likert Scale	X	X	HEC/MEC	↓
Clemons et al. (2016)	ASCO	FLIE index		X	HEC/MEC	↓
Dranitsaris et al, (2016).	ASCO	FLIE index	X	X	HEC/MEC	↓
Gilmore et al. (2014)	NCCN	MAT		X	HEC/MEC	↓
Inoue et al. (2015)	Independent	MAT/Chart Audit			HEC/MEC/LEC/Min	↓
Molasiotis et al. (2014).	MASCC	VAS	X		HEC/MEC	↓

Appendix D

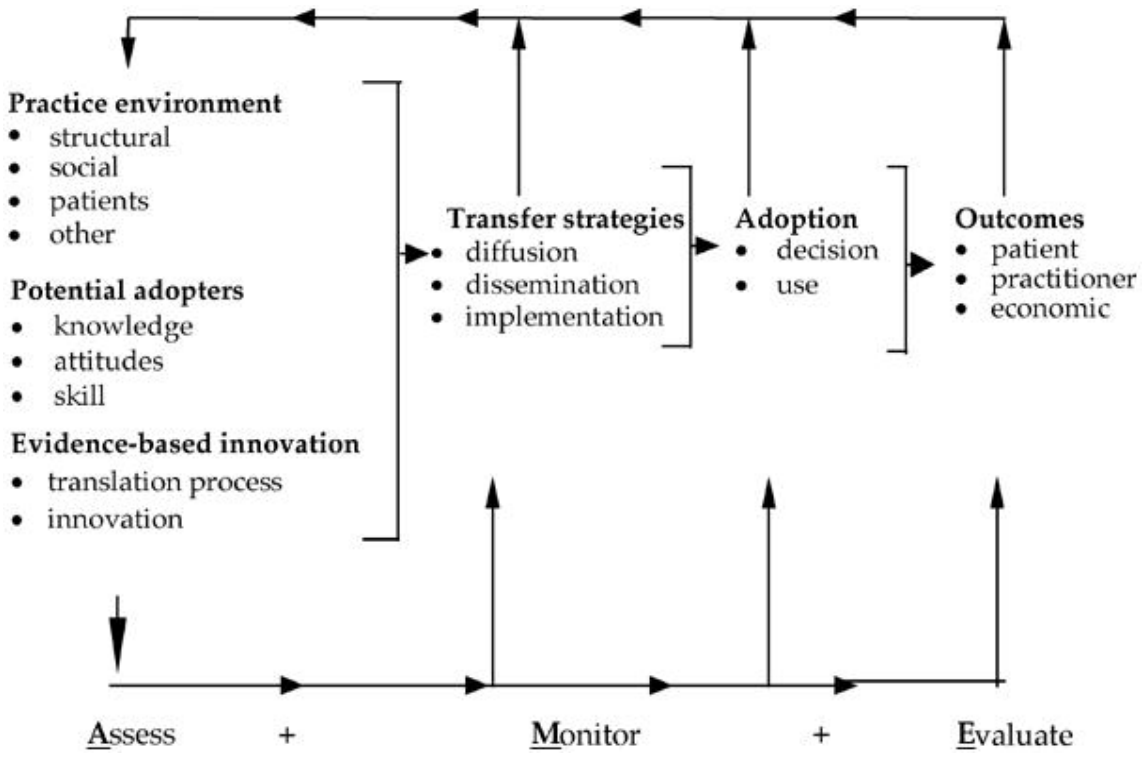
Symptom Management Theory



(Linder, 2010)

Appendix E

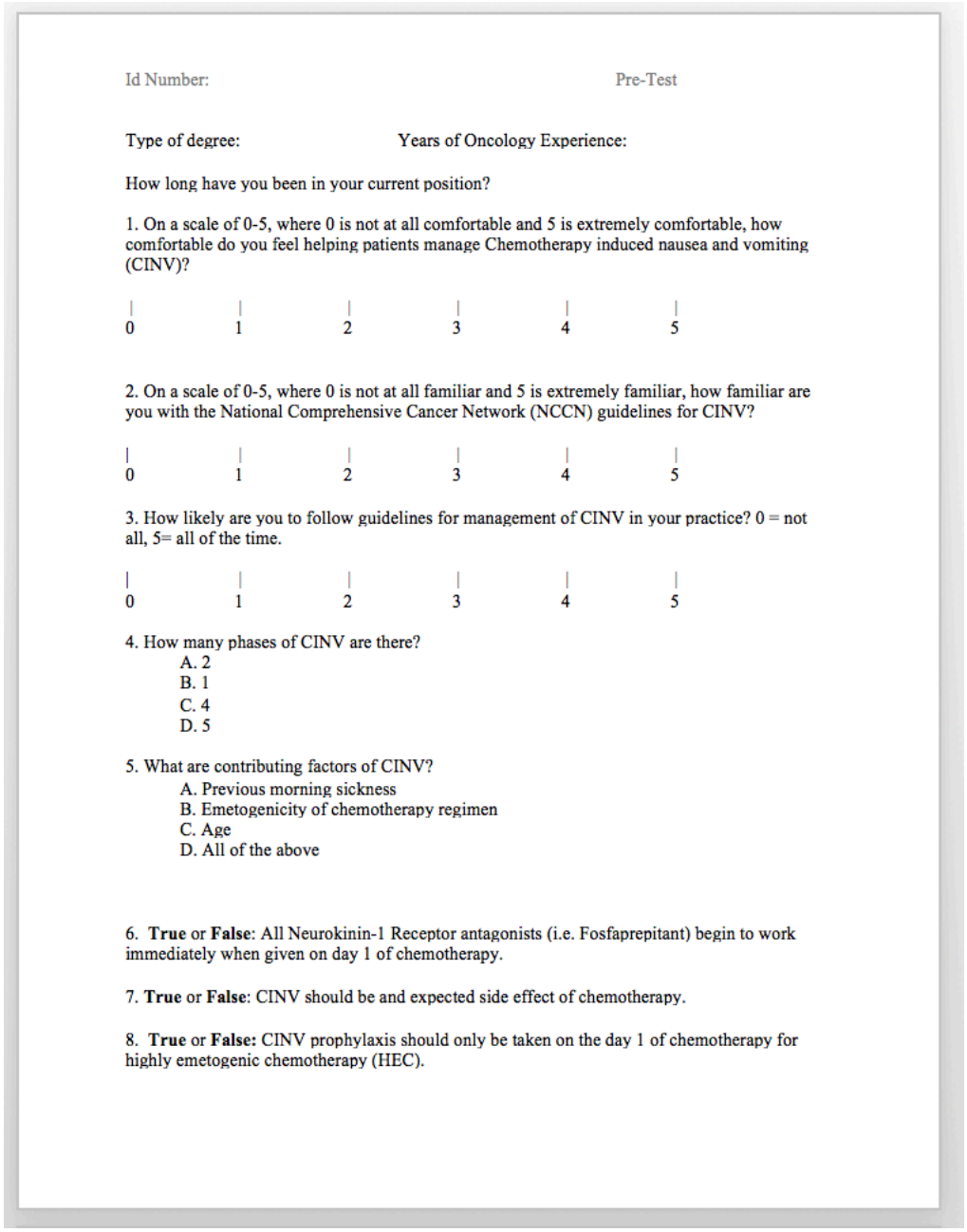
Ottawa Model for Research Use



(Hogan & Logan, 2004)

Appendix F

Pretest



Id Number: Pre-Test

Type of degree: Years of Oncology Experience:

How long have you been in your current position?

1. On a scale of 0-5, where 0 is not at all comfortable and 5 is extremely comfortable, how comfortable do you feel helping patients manage Chemotherapy induced nausea and vomiting (CINV)?

0	1	2	3	4	5

2. On a scale of 0-5, where 0 is not at all familiar and 5 is extremely familiar, how familiar are you with the National Comprehensive Cancer Network (NCCN) guidelines for CINV?

0	1	2	3	4	5

3. How likely are you to follow guidelines for management of CINV in your practice? 0 = not all, 5= all of the time.

0	1	2	3	4	5

4. How many phases of CINV are there?
   A. 2
   B. 1
   C. 4
   D. 5

5. What are contributing factors of CINV?
   A. Previous morning sickness
   B. Emetogenicity of chemotherapy regimen
   C. Age
   D. All of the above

6. **True** or **False**: All Neurokinin-1 Receptor antagonists (i.e. Fosfaprepitant) begin to work immediately when given on day 1 of chemotherapy.

7. **True** or **False**: CINV should be and expected side effect of chemotherapy.

8. **True** or **False:** CINV prophylaxis should only be taken on the day 1 of chemotherapy for highly emetogenic chemotherapy (HEC).

Id Number: Pre-Test

9. Which of the following interventions can be done for patients who experience breakthrough nausea and vomiting following chemotherapy? (select all that apply)

A. Instruct patients to take as needed medications (i.e. Zofran or Compazine) and continue on a schedule until symptoms resolve.
B. Modify prophylactic medication regimen for the next cycle of chemotherapy.
C. Encourage non-pharmacological interventions such as small meals frequently, bland foods, and food/nausea diary.
D. Nothing, nausea and vomiting are side effects that everyone experiences during chemotherapy.
E. Additional hydration if needed in patients with dehydration or impaired oral intake

10. Assessing CINV can be done best in which of the following ways:

A. Asking the patient if they experienced nausea and/or vomiting
B. Using a standardized tool (i.e. the MASCC Antiemesis Tool (MAT)
C. There is no way to assess CINV accurately because it is subjective.
D. A and B
E. None of the above

11. **True** or **False:** The MASCC Antiemesis Tool is a reliable tool for the patient to report and incidences of CINV in the 5 days following their last chemotherapy treatment.

Appendix G

Posttest

Id Number: Post Test

1. On a scale of 0-5, where 0 is not at all comfortable and 5 is extremely comfortable, how comfortable do you feel helping patients manage Chemotherapy induced nausea and vomiting (CINV)?

0	1	2	3	4	5

2. On a scale of 0-5, where 0 is not at all familiar and 5 is extremely familiar, how familiar are you with the National Comprehensive Cancer Network (NCCN) guidelines for CINV?

0	1	2	3	4	5

3. How likely are you to follow guidelines for management of CINV in your practice? 0 = not all, 5= all of the time.

0	1	2	3	4	5

4. How many phases of CINV are there?
   A. 2
   B. 1
   C. 4
   D. 5

5. What are contributing factors of CINV?
   A. Previous morning sickness
   B. Emetogenicity of chemotherapy regimen
   C. Age
   D. All of the above

6. **True** or **False**: All Neurokinin-1 Receptor antagonists (i.e. ~~Fosaprepitant~~) begin to work immediately when given on day 1 of chemotherapy.

7. **True** or **False**: CINV should be and expected side effect of chemotherapy.

8. **True** or **False:** CINV prophylaxis should only be taken on the day 1 of chemotherapy for highly emetogenic chemotherapy (HEC).

Id Number: Post Test

9. Which of the following interventions can be done for patients who experience breakthrough nausea and vomiting following chemotherapy? (select all that apply)

A. Instruct patients to take as needed medications (i.e. Zofran or Compazine) and continue on a schedule until symptoms resolve.
B. Modify prophylactic medication regimen for the next cycle of chemotherapy.
C. Encourage non-pharmacological interventions such as small meals frequently, bland foods, and food/nausea diary.
D. Nothing, nausea and vomiting are side effects that everyone experiences during chemotherapy.
E. Additional hydration if needed in patients with dehydration or impaired oral intake

10. Assessing CINV can be done best in which of the following ways:

A. Asking the patient if they experienced nausea and/or vomiting
B. Using a standardized tool (i.e. the MASCC Antiemesis Tool (MAT)
C. There is no way to assess CINV accurately because it is subjective.
D. A and B
E. None of the above

11. **True** or **False:** The MASCC Antiemesis Tool is a reliable tool for the patient to report and incidences of CINV in the 5 days following their last chemotherapy treatment.

12. How likely are you to use the MASCC Antiemesis Tool when assessing for CINV in your practice?

0	1	2	3	4	5