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ORIGINAL ARTICLE

Defining optimal control of chemotherapy-induced nausea and vomiting—based on patients' experience

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Abstract
Purpose A considerable challenge when comparing antiemetic trials for chemotherapy-induced nausea and vomiting (CINV) is the large number of outcome measures for nausea and vomiting. The objective of this study is to determine the optimal definition of CINV control from the patients' perspective.
Methods Patients with early-stage breast cancer who had received anthracycline-cyclophosphamide-based chemotherapy were surveyed. They were asked about their experiences of CINV and perceptions of different CINV assessment tools.
Results Of 201 patients approached, 168 (83 %) completed the survey. Patients consistently ranked nausea over vomiting as the "worst side effect from chemotherapy." Despite the use of multi-agent antiemetic regimens, 71 % of patients experienced nausea and 26 % vomiting. Only 57 % of patients with any nausea or vomiting took rescue medications and only then when the symptom was severe. Most (76 %) patients believed that the primary end point of antiemetic trials should include the absence of both nausea and vomiting. Patients felt that CINV should be evaluated for the overall period post chemotherapy (i.e., days 1–5) and not simply the acute (the first 24 h) or delayed (days 2–5) periods.
Conclusions Patients strongly favored a CINV end point that includes the absence of both nausea and vomiting. Patients' experience with CINV is underestimated when nausea is not included in composite end points. "Use of rescue medication," a commonly used surrogate for emesis control, is inappropriate as it underestimates nausea. A standardized primary end point that includes nausea is essential if CINV control is to be improved.

Keywords CINV · Patient · Perception · Breast cancer · End points

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Introduction

Advances in the management of chemotherapy-induced nausea and vomiting (CINV) have been driven by both the advent of new antiemetic regimens [1] and the widespread availability of local [2], national [3, 4], and international [5] treatment guidelines. Despite this, control of CINV in breast cancer patients remains suboptimal, with nausea in particular remaining a critical issue for those receiving anthracycline-cyclophosphamide combination regimens [6–8]. One of the major challenges for guideline developers is that many randomized trials use different composite end points for CINV. These typically consist of various combinations of nausea, vomiting, and the use of rescue antiemetics as their primary study end point [9]. For trials involving single-day chemotherapy regimens, CINV outcomes are also reported over varying time points, the acute period (the first 24 h), the delayed period (days 2–5), and the overall period (days 1–5) after chemotherapy. A recent systematic review and network meta-analysis of randomized controlled trials comparing antiemetic regimens found over 15 reported CINV end points [10] (Table 1).

Variability in study end points has important implications for patient care as it makes cross-trial comparisons of antiemetic regimens challenging. In addition, full study results are rarely freely available, reducing the ability to assess CINV control using different end points [9]. An additional concern is that these end points do not represent patient experiences

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accurately. We were unable to find any published evidence that patient experience of CINV had been used to define optimal emesis control. As we have recently completed a large randomized antiemetic study [12], this provided an excellent opportunity to survey patients regarding their perspectives as to the most representative way to define CINV control.

Subjects and methods

Target population

The EPIC trial (NCT01913990) [12] was a multi-center randomized study comparing CINV in patients with newly diagnosed, early-stage breast cancer, receiving anthracycline- and cyclophosphamide-based chemotherapy. Patients were randomized to receive antiemetics either based on their oncologists' choice (any combination of 5HT3, dexamethasone, and NK1) or based on their personal emesis risk (low risk—5HT3 and dexamethasone, high risk—addition of NK1) which was estimated using the mathematical decision aid (emesis risk calculator) [7]. The latter was used to decide if aprepitant was necessary (low-risk patients did not receive aprepitant); otherwise, treatment was based on provincial antiemetic guidelines [2]. Patients were ineligible for the study if they had received prior chemotherapy, if they had symptoms of nausea or vomiting at baseline related to disease, or if they were taking chronic antiemetic therapy/daily corticosteroids prior to initiation of chemotherapy. Patients who had completed the anthracycline and cyclophosphamide component of the trial were eligible for the current survey.

Survey design and distribution

The survey was developed collaboratively by clinicians and researchers with expertise in breast cancer and CINV trials. The survey consisted of 23 multiple choice and 3 ranking questions (Appendix 1). These questions assessed personal ranking of all chemotherapy side effects and personal CINV experiences and allowed patients to rate their own experience of CINV from commonly used clinical trial CINV scoring tools for nausea (n=5) and vomiting (n=3). For nausea assessment, the five scores included visual analogue scale 0–100 (100-mm VAS) [13–22], 5-point Likert scales [23], 4-point Likert scales [24–27], and a 7-point semantic differential scale [24, 25]. For the assessment of vomiting, there are three main assessment scales [26] for measuring vomiting episodes. There were 4-point Likert scales differing slightly on the description associated with each score, based on the Common Terminology Criteria for Adverse Events v4.0. Scales also included quantitative (i.e., defined by episodes of vomiting) and qualitative (i.e., none, mild, moderate and severe) assessments of vomiting. The survey also included questions about use of rescue antiemetic medications. Finally, patients were asked for their perspective on defining optimal CINV control by ranking the importance of various commonly used end points in clinical trials (Table 1). The study received local research ethics board approval and the survey was piloted on four patients prior to broad dissemination. Individual survey completion took between 10 and 15 min. Patients were approached either during a routine clinic visit, or if they were not due for clinic visit during the study period, a

Table 1 Summary of chemotherapy-induced nausea and vomiting (CINV) outcomes across randomized controlled trials [11]

Outcomes from 0–120 h	Overall response measures	Total control %	No vomiting+no rescue+no nausea
		Complete protection %	No vomiting+no rescue+minimal nausea
		Complete response %	No vomiting+no rescue
		No vomiting %	
		No nausea %	VAS <5 mm
Outcomes from 0–24 h	Acute response measures	Total control %	No vomiting+no rescue+no nausea
		Complete protection %	No vomiting+no rescue+minimal nausea
		Complete response %	No vomiting+no rescue
		No vomiting %	
		No nausea %	
Outcomes from 24–120 h	Delayed response measures	Total control %	No vomiting+no rescue+no nausea
		Complete protection %	No vomiting+no rescue+minimal nausea
		Complete response %	No vomiting+no rescue
		No vomiting %	
		No nausea %	

telephone call was made to obtain permission to send a survey by mail.

Statistical analysis

Data was recorded in Excel (Microsoft). Age and specific chemotherapy data were collected in the survey and were corroborated from preliminary data collected in the EPIC trial.

Statistical analysis was completed using Stata 12.0 (StataCorp. 2011. *Stata Statistical Software: Release 12*. College Station, TX: StataCorp LP) by tabulating frequencies of multiple choice questions and ranking questions in the survey. Pearson's correlation coefficient and Spearman's rank correlation coefficient were used to compare commonly used scales for nausea and vomiting. Point estimates with 95 % confidence intervals (CI) are reported to summarize findings for ranking question.

Results

Between February and August 2014, 201 patients were approached and 168 (83 %) completed the survey. Patient demographics are shown in Table 2. The median patient age was 54 (range 29 to 76) and the most commonly received anthracycline-cyclophosphamide regimen was fluorouracil, epirubicin, and cyclophosphamide (FEC) (n=111, 66 %). Most patients (96 %) were surveyed within 1 year of starting their chemotherapy. Patients received either an aprepitant/5HT3 antagonist/dexamethasone combination antiemetic regimen (96/168; 57 %) or a 5HT3 antagonist/dexamethasone combination (72/168; 43 %).

Table 2 Patient characteristics

Variable	N=168
Women, *n* (%)	168 (100 %)
Age (years±SD)	54.3±10.61
Chemotherapy (%)	
AC	12
FEC-docetaxel	66
AC-paclitaxel	11
AC-docetaxel	7
Time from first chemotherapy cycle to completion of survey (%)	
Less than 3 month	23
Less than 6 months	13
6 months to 1 year	25
Over a year	34
Over 2 years	4
Antiemetic regimen (%)	
Aprepitant/ondansetron/dexamethasone	57
Ondansetron/dexamethasone	43

SD standard deviation; *AC* Anthracycline-cyclophosphamide; *FEC* fluorouracil, epirubicin, and cyclophosphamide

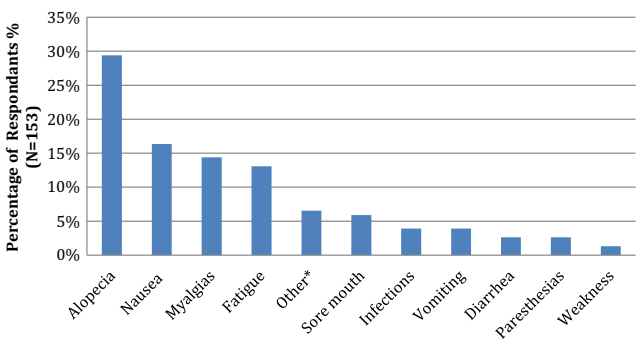
Patients' experience with CINV

Patients were asked to rank their "worst side effect of chemotherapy." The three most commonly reported symptoms were alopecia (29 %), nausea (16 %), and aching muscles and joints (14 %) (Fig. 1). Vomiting was the seventh most common side effect (4 %). The control of nausea during chemotherapy was considered very important to 87 % and the control of vomiting was considered very important to 89 % of patients. Nevertheless, when asked, "based on your experience with chemotherapy-induced nausea and vomiting, which of these was worse for you?," 44 % chose nausea and 2 % chose vomiting. Of note, 34 % of respondents did not experience any nausea or vomiting, 14 % experienced equally mild nausea and vomiting, and 6 % experienced equally severe nausea and vomiting (Fig. 2).

Patients were asked to identify the chemotherapy cycle when their CINV was worst. For those patients who experience nausea, 31 % of patients experienced the worst nausea in the first cycle and 16 % experienced the same nausea during subsequent cycles (Appendix 2). In regard to vomiting, 11 % experienced their worst vomiting during the first cycle and 4 % experienced the same level of vomiting during each cycle (Appendix 2). When asked about which day after chemotherapy patients experienced the worst nausea or vomiting, the largest proportion of patients experienced their worst nausea either 1 day after chemotherapy (24 %) or the second day after chemotherapy (24 %). The majority of patients did not experience vomiting (73 %), and of those who did, vomiting episodes occurred most commonly on day 1 post chemotherapy (15 %) (Appendix 3). Some patients considered stopping chemotherapy either due to poorly controlled nausea (6 %) or vomiting (3 %). Of all surveyed patients, 5 % discontinued chemotherapy secondary to CINV.

Tools for assessment of nausea

Using the visual analogue scale for nausea (scale 1), the mean response was 32 out of 100 (where 100 is "nausea is as bad as



*Other: e.g. constipation, hypotension

Fig. 1 Patient ranking for worst side effects from anthracycline-cyclophosphamide-based chemotherapy. *Other: e.g., constipation, hypotension

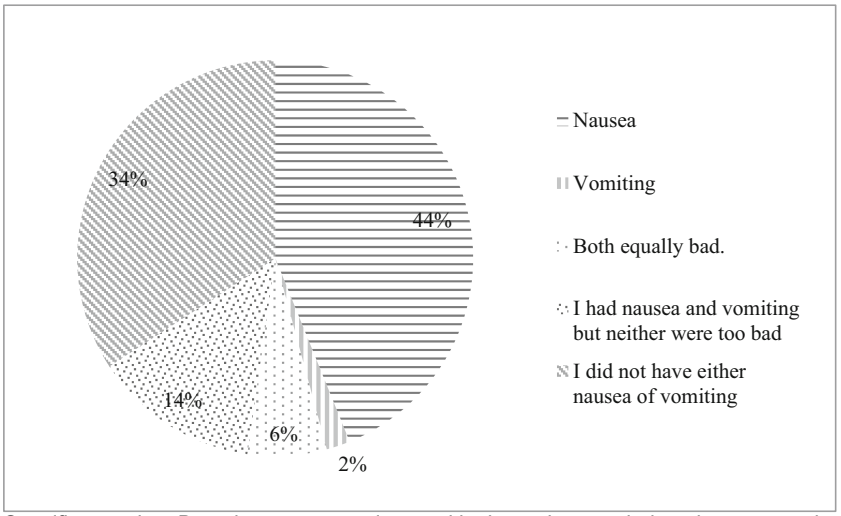


Fig. 2 Worse chemotherapy side effect when comparing nausea versus vomiting. Specific question: Based on your experience with chemotherapy-induced nausea and vomiting, which of these was worse for you?

it could be"). When evaluating nausea on the Likert scales, the percent of patients reporting no nausea was 27 % (45/165), 29 % (45/156), and 29 % (47/164) for scales 2, 3, and 4, respectively. The percent of patients reporting severe nausea was 18 % (29/165), 15 % (24/156), and 15 % (25/164) for scales 2, 3, and 4, respectively. Scale 5 divides nausea into 7 scores of severity and the mean response was 3 (Table 3). Using both parametric and nonparametric correlational analysis, all the scales were moderately to highly correlated. The lowest parametric correlation coefficient was between scale 1 and scale 2 ($r(151)=0.5$, $p<0.01$) and the highest correlation was between scores 4 and 5 ($r(151)=0.94$, $p<0.01$).

Tools for assessment of vomiting

We asked patients to quantify their experience with chemotherapy-induced vomiting using three previously reported scoring systems. Using rating scales with descriptions of vomiting severity (scales 1, 2, and 3), 74 % (122/164), 74 % (113/152), and 74 % (117/158) did not have any vomiting, respectively. According to scales 1, 2, and 3, 6 % (10/164), 9 % (14/152), and 10 % (16/152) experienced the most severe category of vomiting, respectively. Both parametric and nonparametric correlational analyses for all of the scales measuring vomiting are correlated (Table 3).

Rescue medication use

Use of rescue medication was assessed by asking specifically, "Did you ever have to take "rescue" medications (extra medications over and above the regular anti-sickness medication you were given) for nausea or vomiting?," and 42 % of patients reported taking rescue medication at least once. The most common reason for taking rescue medications was because nausea and vomiting were "really bad" (57 %). If patients did not take rescue medications, it was because they never had nausea or vomiting (46 %); did experience nausea and/or vomiting, but did not want to take more medications (29 %); or for other reasons (25 %).

Optimal CINV end points from the patient's perspective

Patients were asked which end point should be the most important when comparing antiemetic medications (Fig. 3). Patients thought the primary end point should be no CINV (absence of both nausea and vomiting) (45 %) or total control (absence of nausea and vomiting with no need for rescue medication) (32 %). When asked to rank the importance of which time period CINV should be evaluated, 46 % (71/155) chose the overall period (i.e., days 1 to 5 after chemotherapy), 27 % (42/155) chose the acute period (day 1 after chemotherapy), and 23 % (35/155) chose the delayed period (days 2–5 after chemotherapy).

Discussion

Despite the widespread availability of treatment guidelines [2–5], CINV continues to be one of the most common side effects of chemotherapy [27, 28]. Control of CINV in breast cancer patients remains suboptimal, with nausea in particular remaining a critical issue for those receiving anthracycline-cyclophosphamide combination regimens [6, 7]. One of the major challenges for clinicians and guideline developers is that many randomized antiemetic trials use different composite end points of vomiting, nausea, and the use of rescue antiemetics without reporting all permutations of these end points (Table 1). This makes identification of an optimal antiemetic regimen challenging as it is impossible to make comparisons across trials if the clinical end

Table 3 Comparison of commonly used nausea and vomiting scores

	Type	Description	Results
Nausea			
Scale 1 (N=114)	VAS scale[a]	0–100 graphic scale. 0=no nausea and 100=nausea as bad as it can be	Mean±SD=32±35
Scale 2 (N=165)	Qualitative description[b]	I did not have nausea	27 %
		I had nausea but I could still eat as I normally do	22 %
		I had nausea and had to change my diet/eat less than I would normally	29 %
		I had nausea and was unable to eat	17 %
		I had nausea, was unable to eat, and had to have intravenous fluids/be hospitalized	3 %
Scale 3 (N=157)	Qualitative with description and assigned score[c]	0=none, absence of nausea	28 %
		1=mild, induced by certain odors or flavors, mild nausea that does not interfere with daily life, but slight decrease in appetite	27 %
		2=moderate, food intake compromised, moderate nausea that does interfere with daily life and experience decrease in appetite	29 %
		3=severe, food intake impeded, severe nausea requiring bed rest	15 %
Scale 4 (N=165)	Qualitative with score[c]	1=None	28 %
		2=Mild	28 %
		3=Moderate	28 %
		4=Severe	15 %
Scale 5 (N=164)	VAS Scale[d]	0–7 graphic scale. 1=not at all nauseated, 4=moderately nauseated, 7=extremely nauseated	Mean±SD=3.28±2.09
Vomiting			
Scale 1 (N=164)	Quantitative[c]	1–2 episodes in 24 h	13 %
		3–5 episodes in 24 h	6 %
		More than 6 episodes in 24 h	6 %
		I did not have vomiting	74 %
Scale 2 (N=152)	Quantitative with score[c]	1=mild, 1–2 vomiting episodes in 24 h	12 %
		2=moderate, 3–4 vomiting episodes in 24 h	4 %
		3=severe, ≥5 vomiting episodes in 24 h	21 %
		0=none, 0 vomiting episodes in a 24-h period	74 %
Scale 3 (N=158)	Qualitative with score[c]	1=None	74 %
		2=Mild	9 %
		3=Moderate	7 %
		4=Severe	10 %

[a] References [13–22]

[b] Reference [23]

[c] References [24–27]

[d] References [24, 25]

points are not identical. In addition, we were unable to find any studies in the literature that addressed what patients themselves perceived as the most important definitions for control of CINV.

The current survey confirmed that with the use of guideline-based antiemetic regimens, control of chemotherapy-induced vomiting is much better than control of nausea [29, 30]. However, a number of patients still considered discontinuing their therapy because of nausea (6 %) and vomiting (3 %). Overall, 5 % of the patient population who answered the survey discontinued chemotherapy due to emesis. Clearly, if patient care is to be improved, there needs to be a greater emphasis on antiemetic regimens that will also improve nausea control.

Many different tools and time points are available to measure nausea and vomiting, but it is uncertain which best reflects the patient's experience of CINV. Nausea can be particularly challenging to measure, and therefore, multiple scoring tools have been developed to assess both chemotherapy-induced nausea and vomiting [31]. It is clearly reassuring that the scales compared in our study correlated with each other for nausea and vomiting independently. Nevertheless, a validated standardized tool to measure CINV will make easier to compare data from different trials in the future.

With respect to the choice of composite end point, landmark CINV trials that have led to recommendation and approval of contemporary antiemetic regimens have largely adopted "overall complete response" (no vomiting and no rescue medications during days 1–5 post chemotherapy) as the primary end point. Fifteen out of 30 studies identified in a systematic review of CINV regimens in breast cancer patients receiving an anthracycline and cyclophosphamide combination reported an

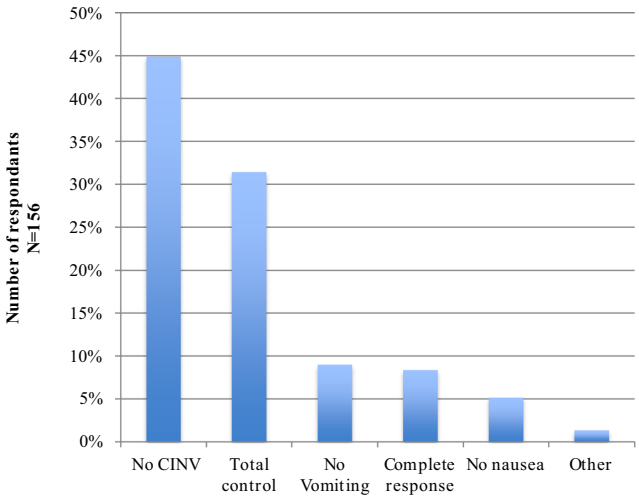


Fig. 3 Most important outcome from patient perspective when comparing antiemetic medication in CINV. *No CINV* no nausea and no vomiting, *total control* no vomiting and nausea and no need to use rescue medications, *complete response* no vomiting and no need to use rescue medications

overall complete response [10]. Overall complete response does not truly account for nausea control, but is consistently being used as the benchmark measure for antiemetic efficacy when making cross-trial comparisons. Our survey demonstrated that despite 72 % of patients having some degree of nausea, only 42 % took any rescue medications. Even when they did take rescue medications, it was only when they had "severe nausea or vomiting." This is consistent with the literature, in randomized studies that report both overall complete response and overall total control (i.e., no vomiting, no nausea, and no rescue antiemetic use); the total control rate is much lower than complete response rate [14, 15]. Therefore, using overall complete response as the primary measure of antiemetic efficacy by licensing boards [32] and guideline groups [2–5] likely overestimates the efficacy of CINV treatments. While most trials report some measure of nausea control separately, the method of reporting is inconsistent, which again makes it difficult to compare antiemetic treatments across trials. It is therefore not surprising that when patients themselves were asked to rate different antiemetic outcomes, they consistently chose "overall total control" (i.e., no vomiting, no rescue antiemetic use, and no nausea) and "no CINV" over "complete response" as the most representative outcome measure.

This study adds the patient's perspective to validate the need of measuring an end point in antiemetic trials that incorporates complete or total control of nausea and vomiting as a primary end point, a position shared by expert opinion [33]. The standard inclusion of nausea as an end point in CINV is even more relevant today when control of vomiting has markedly improved compared to control of nausea. As per our observations from this survey, recent guidelines from the European Society for Medical Oncology (ESMO) [5, 33] suggest that even though nausea and vomiting are related, patients may respond differently to different antiemetic medications. This aspect needs to be further characterized in future trials and reflected in guideline documents. Of interest is the level of agreement across studies for the absence of nausea as an outcome. In the current study, "0" was used on the VAS for the absence of nausea while most studies use <5 mm. The limitations of this study include the relatively small sample size and the fact that the patients were chosen from a clinical trial population. However, the results have internal validity in relation to what is commonly observed in clinical practice. Patients who experience CINV more commonly endure their worst symptomatology on the first day of the first cycle with an increased incidence of nausea over vomiting.

There is also the possibility of recall bias that is inherent to retrospective questionnaires. We plan to compare the findings from this survey with patient diaries completed in the EPIC study in a future analysis. It is also possible that many patients did not receive "optimal" guideline-based antiemetic therapy. However, all patients received combination antiemetic therapy, and aprepitant was used in over half of the patient population. Nausea continues to be a major clinical problem, even in the subgroup of patients that received aprepitant. This is in keeping with the randomized trial data [14, 34, 35].

In conclusion, as Hesketh et al. reported in 1998 when discussing the methodology of antiemetic trials [33], the gold standard for antiemetic response should include complete prevention of both nausea and vomiting. Trials that do not account for a patient's nausea present results from antiemetic trials that are overly optimistic and do not represent patients' experience accurately. As CINV tends to be at its worst during the first cycle of chemotherapy, strategies are needed to optimize control when treatments are initiated. These strategies include the development of regimens with more emphasis on nausea control; encouraging published trials and future trials to make all components of their data that comprise these composite end points freely available so that objective comparisons can be made, and the data can be translated into a common framework for evidence synthesis; and the use of standardized study end points that reflect total control of both nausea and vomiting to identify more optimal regimens. Using a personalized approach that assesses an individual patient's risk of emesis may be a further step forward in reducing the side effect of CINV [7, 36, 37]. Hopefully, with these strategies we will be able to remove CINV from the list of the most common side effects for our patients.

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Conflict of interest Brian Hutton received Honoraria for attendances at advisory boards from Amgen Canada. Catalina Hernandez-Torres, Sasha Mazzarello, Terry Ng, George Dranitsaris, Stephanie Smith, Amy Munro, Carmel Jacobs, and Mark Clemons have no conflicts to declare.

Appendix 1 EPIC ER 11-02 sub study survey

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Dear Participant, Study # _____

The EPIC study was looking at nausea and vomiting in patients receiving specific types of chemotherapy for breast cancer. You will remember completing diaries that asked you to rate how much nausea and vomiting you had after each chemotherapy cycle.

Research groups across the world score these diaries in many different ways. However, no one has asked patients what they think is the best way of scoring chemotherapy induced nausea and vomiting.

As an EPIC study participant, we would like to invite you to participate in a brief survey to find out what you think are the most important areas that we should focus on when trying to assess chemotherapy-induced nausea and vomiting.

The participation in this survey is completely voluntary. This questionnaire will take approximately 10-15 minutes of your time.

Thank you for participating in this survey.

1. How old are you?

2. What type of chemotherapy did you receive?

   a. AC
   b. FEC-D
   c. AC-Taxol
   d. AC-taxotere
   e. Other – please state _____
   f. Unsure

3. How long ago did you receive your first cycle of chemotherapy?

   a. Less than 3 months ago
   b. Less than 6 months ago
   c. 6 months to a year ago
   d. Over a year ago
   e. Over 2 years ago

4. Looking back, now that your chemotherapy is complete, what do you remember as being the worst overall side effects of chemotherapy – please choose your top 3 side effects only (where 1 is the worst side effect, 2 is the second worst etc.): Please enter 1, 2, 3 in the box beside the side effect that best describes the worst top 3.

☐ Loss of hair

☐ Diarrhea

☐ Tiredness

☐ Infections

☐ Weakness

☐ Aching muscles and joints

☐ Nausea (The feeling that you might vomit)

☐ Numbness and tingling in your fingers and toes

☐ Sore mouth

☐ Vomiting (the bringing up of stomach contents)

☐ Other – please state

_____

_____

_____

5. In your opinion, how important is control of nausea during chemotherapy?

    a. Not at all
    b. A little bit
    c. Somewhat
    d. Quite a bit
    e. Very much

6. In your opinion, how important is control of vomiting during chemotherapy?

    a. Not at all
    b. A little bit
    c. Somewhat
    d. Quite a bit
    e. Very much

Now we are going to ask specific questions about YOUR experiences with chemotherapy-induced nausea (feeling like you might vomit) and vomiting (bringing up of stomach contents).

We are specifically talking about the chemotherapy you received while you were participating in the EPIC study (usually the first half of your chemotherapy when you were receiving a drug called adriamycin or epirubicin)

7. Based on your experience with chemotherapy-induced nausea and vomiting, which of these was worse for you?

    a. Nausea
    b. Vomiting
    c. Both equally bad.
    d. I had nausea and vomiting but neither were too bad
    e. I did not have either nausea of vomiting
    f. Other – please state

_____
_____
_____

8. Which cycle of chemotherapy was your worst one in terms of nausea control?

a. Cycle 1
b. Cycle 2
c. Cycle3
d. Cycle 4
e. The same in all the cycles
f. I did not have nausea
g. Other – please state

_____
_____
_____

9.Which cycle of chemotherapy was your worst one in terms of vomiting control?

a. Cycle 1
b. Cycle 2
c. Cycle3
d. Cycle 4
e. The same in all the cycles
f. I did not have vomiting.
g. Other – please state

_____
_____
_____

10.During your anthracycline-cyclophosphamide part of chemotherapy (i.e. the FEC or AC part), on which day did you have the worst NAUSEA?

a. Before chemotherapy was given
b. During the 1st day (24 hours) after chemotherapy
c. During the 2nd day after chemotherapy
d. During the 3rd day after chemotherapy
e. During the 4th day after chemotherapy
f. During the 5th day after chemotherapy
g. After the 5^{th} day
h. Other – please state _____

11. During your anthracycline-cyclophosphamide part of chemotherapy (i.e. the FEC or AC part), on which day did you have the worst VOMITING?

    a. Before chemotherapy was given
    b. During the 1st day after chemotherapy
    c. During the 2nd day after chemotherapy
    d. During the 3rd day after chemotherapy
    e. During the 4th day after chemotherapy
    f. During the 5th day after chemotherapy
    g. After the 5th day
    h. Other – please state _____

12. In the next few questions we are going to present several different ways of measuring NAUSEA. We are asking you to rate your WORST nausea with each of these tools. It may seem repetitive but we are trying to see which are the most useful types of measures.

Score 1:

If you had nausea during your chemotherapy, how bad was the nausea at its worst?

On the line below please place a vertical mark to indicate how bad your WORST nausea was during chemotherapy -- where 0 is no nausea and 100 is nausea as bad as it could be.

0_____100
(No Nausea) (Nausea as bad as it could be)

Score 2:

If you had nausea during your chemotherapy, how bad was the nausea at its worst (please tick one)?

a. I did not have nausea
b. I had nausea but I could still eat as I normally do
c. I had nausea and had to change my diet / eat less than I would normally
d. I had nausea and was unable to eat
e. I had nausea, was unable to eat and had to have intravenous fluids / be hospitalized

Score 3:

If you had nausea during your chemotherapy, how bad was the nausea at its worst?

0 = none, absence of nausea

1 = mild, induced by certain odors or flavours , mild nausea that does not interfere with daily life, but slight decrease in appetite

2 = moderate, food intake compromised, moderate nausea that does interfere with daily life and experience decrease in appetite

3 = severe, food intake impeded, severe nausea requiring bed rest

Score 4:

If you had nausea during your chemotherapy, how bad was the nausea at its worst?

1	2	3	4
None	Mild	Moderate	Severe

Score 5:

If you had nausea during your chemotherapy, how bad was the nausea at its worst?

On the line below please place a vertical mark to indicate how bad your WORST nausea was during chemotherapy -- where 0 is not at all nauseated and 7 is extremely nauseated.

1	2	3	4	5	6	7
Not at all nauseated			Moderately nauseated			Extremely nauseated

13. In the next few questions we are going to present several different ways of measuring VOMITING. We are asking you to rate your WORST vomiting with each of these tools. It may seem repetitive but we are trying to see which are the most useful types of measures.

Score 1:

If you had vomiting during your chemotherapy, how bad was it at its worst?

a. 1 -2 episodes in 24 hours
b. 3 – 5 episodes in 24 hours
c. More than 6 episodes in 24 hours
d. I did not have vomiting

Score 2:

If you had vomiting during your chemotherapy, how bad was it at its worst?

0 = none, 0 vomiting episodes in a 24 hour period
1 = mild, 1-2 vomiting episodes in 24 hours
2 = moderate, 3-4 vomiting episodes in 24 hours
3 = severe, >=5 vomiting episodes in 24 hours

Score 3:
If you had vomiting during your chemotherapy, how bad was it at its worst?

1	2	3	4
None	Mild	Moderate	Severe

14. If nausea was poorly controlled, did you ever consider stopping chemotherapy?

a. No
b. My nausea was not poorly controlled
c. Yes

15. If vomiting was poorly controlled, did you ever consider stopping chemotherapy?

a. No
b. My vomiting was not poorly controlled
c. Yes

16. If you did consider stopping chemotherapy because of nausea or vomiting, why did you not stop?

a. I considered it an acceptable side effect
b. I expected it
c. I did stop chemotherapy
d. Other – please state:

_____
_____
_____

17. Did you ever have to take “rescue” medications (extra medications over and above the regular anti-sickness medication you were given) for nausea or vomiting?

    a. Yes
    b. No

18. If you did take “rescue” medications, you took them because:

    a. I took them whenever I had ANY nausea and / or vomiting
    b. I took them only when the nausea or vomiting was really bad
    c. I thought that I was supposed to take them regularly regardless

19. On average, how often did you take rescue medication during each cycle of chemotherapy?

    a. Only once or twice during each cycle of chemotherapy
    b. Three or more times during each cycle of chemotherapy
    c. Other -- please state:

_____
_____
_____

20. On average, how often did you take rescue medication during a given 24 hour period after you received chemotherapy?

    a. Only once or twice during each 24 hour period
    b. Three or more times during each 24 hour period
    c. Other -- please state:

_____
_____
_____

21. On average, when did you have to take your first dose of rescue medication after receiving chemotherapy?

    a. Within the first 24 hours after receiving chemotherapy
    b. On the second day after receiving chemotherapy
    c. On the third day after receiving chemotherapy
    d. On the fourth day after receiving chemotherapy
    e. On the fifth day after receiving chemotherapy
    f. On the sixth day after receiving chemotherapy

22. If you did not take “rescue” medications, it was because:

    a. I never had nausea or vomiting
    b. I had nausea and/or vomiting, but did not want to take more medications
    c. Other -- please state:

_____
_____
_____

23. Did you buy medication or other treatments (i.e. herbal remedies) on your own to help control your nausea and vomiting following chemotherapy?
    a. Yes
    b. NO

If yes,
what did you purchase? _____
Please indicate how much money you spent. _____

Research groups use different ways of assessing chemotherapy-induced nausea and vomiting. We would like to know what you think the most important measures are.

The first question is about the importance of the time after chemotherapy that nausea and vomiting occur.

24. I feel the most important time point to evaluate chemotherapy induced nausea and vomiting is: (Please rank them 1 to 3. Where 1 is the most important outcome to you as a patient and 3 is the least important.)

☐ In the first 24 hours after chemotherapy

☐ From 24 hours after chemotherapy until 5 days after chemotherapy

☐ _From immediately after chemotherapy until 5 days after chemotherapy

☐ _Other – please state:

_____
_____
_____

25. When comparing anti-sickness drugs given with chemotherapy for breast cancer, what do you think the most important nausea and vomiting outcome to measure is? Please rank them 1 to 5. Where 1 is the most important outcome to you as a patient and 5 is the least important

☐ Absence of nausea

☐ Absence of vomiting

☐ Absence of both nausea and no vomiting

☐ Absence of vomiting and minimal nausea, and no need to use rescue __medications

☐ Absence of vomiting and nausea, and also no need to use rescue medications

☐ Other

_____
_____
_____

26. Do you have any other comments about your experience with nausea and vomiting during chemotherapy

_____
_____
_____
_____
_____

THANK YOU FOR YOUR PARTICIPATION

Appendix 2

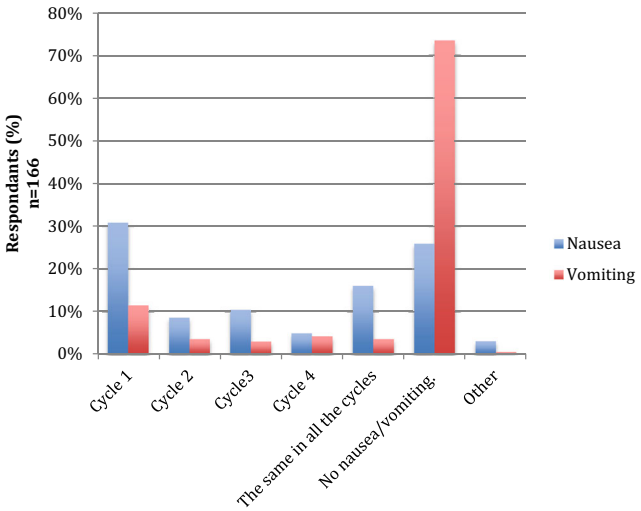
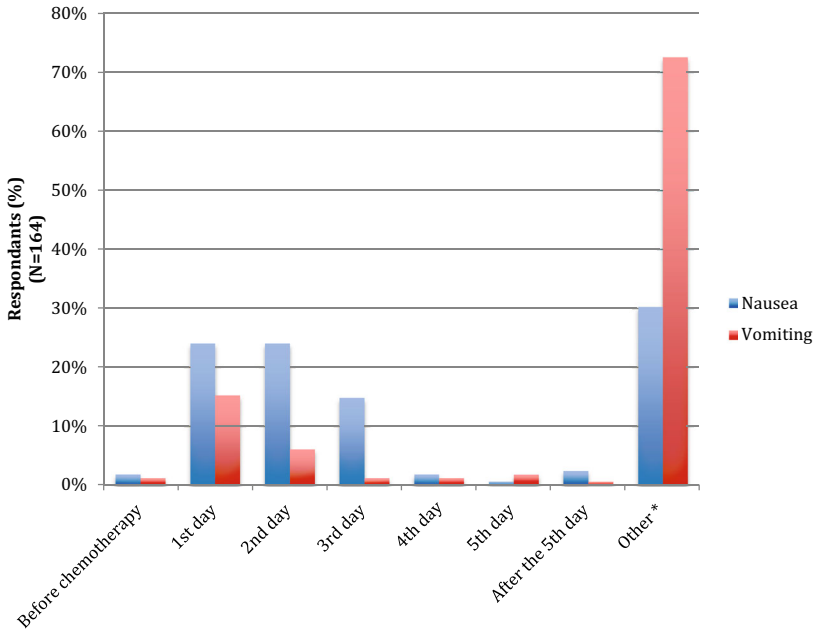


Fig. 4 Worst cycle for nausea and vomiting control from patients' experience

Appendix 3

Fig. 5 Day after AC chemotherapy cycle, when nausea and vomiting was worse



*Other: Most patient who chose other did not experience vomiting or nausea, respectively.

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