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ORIGINAL ARTICLE

# Evaluation of antiemetic practices for prevention of chemotherapy-induced nausea and vomiting (CINV): results of a European oncology nurse survey

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## Abstract

**Introduction** Preventing CINV is possible when guideline-recommended antiemetics are used. Because oncology nurses play a critical role in risk assessment and management of CINV, a survey of European nurses was conducted to evaluate antiemetic practices, assess awareness of and adherence to current guideline recommendations, and explore barriers to adherence.

**Methods** From March 2016 to Feb 2017, 212 oncology nurses in 16 European countries completed a 20-question online survey.

**Results** Respondents had 15-year (median) oncology nursing experience, and most (75%) were able to suggest or prescribe antiemetics. Most (80%) worked in the public not-for-profit hospital setting. Guideline awareness was generally low with nurses most familiar with ASCO (46%) and MASCC/ESMO (40%) guidelines; individual institution guidelines were most commonly used (47%). Key discrepancies between reported antiemetic use and guideline recommendations in the highly emetogenic chemotherapy (HEC) setting were underutilization of the recommended $NK_1RA$ + 5-$HT_3RA$ + steroid combination on day 1 (55%) and high use of 5-$HT_3RAs$ (50%) on days 2–5 when a steroid (63% use) should be used. Metoclopramide use was high in both HEC and moderately emetogenic settings, with ~ 30% and ~ 50% reporting use on day 1 and days 2–5, respectively. The most common reported barrier to use of guideline-recommended agents was physician preference (40%). The most common challenges in managing CINV were "controlling nausea/vomiting in the delayed phase" (64%) and "reducing the impact of CINV on patients' quality-of-life" (61%).

**Conclusions** This survey highlights opportunities to improve utilization of guideline-recommended antiemetics, thereby optimizing prevention of CINV and QoL for patients receiving emetogenic chemotherapy.

**Keywords** Chemotherapy-induced nausea and vomiting (CINV) · Emesis · Antiemetics · Guidelines · Adherence · Oncology nurses

## Introduction

The European Society for Medical Oncology (ESMO) recently acknowledged that the varying needs of patients with cancer are not being adequately met as part of routine cancer care [1]. Consequently, they issued a position paper advocating for supportive and palliative care to be personalized and integrated with anticancer treatment by a multidisciplinary

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team, from the time of diagnosis and throughout the continuum of disease [1].

Chemotherapy-induced nausea and vomiting (CINV) is distressing for patients [2] and can significantly affect their quality of life during chemotherapy. It can lead to dehydration, electrolyte imbalances, malnutrition, weight loss, or even cachexia, sometimes resulting in hospitalization, thereby increasing the overall cost of cancer care [3]. In addition, for some patients, dose reductions or delays in chemotherapy may be necessary as a result of CINV; this could negatively impact patient outcomes [4, 5].

Fortunately, CINV (especially vomiting) can be prevented in the majority of patients [6, 7] with the use of guideline-recommended antiemetic regimens [8–10] and attentive monitoring of these symptoms. In a recent study, Basch and colleagues demonstrated that diligent Web-based monitoring of side effects such as nausea and vomiting improved health-related quality of life, decreased emergency room (ER) visits and hospitalizations, and improved survival for adult patients undergoing chemotherapy [11]. The development of a variety of antiemetics targeting different molecular pathways involved in the development of CINV has offered substantial improvements in the prevention of CINV for patients undergoing emetogenic chemotherapy [6, 7]. The American Society of Clinical Oncology (ASCO) recently acknowledged the development of effective antiemetics among the top 5 advances in oncology since ASCO's founding in 1964 [12].

Established international evidence-based guidelines include those of the Multinational Association of Supportive Care in Cancer/European Society of Medical Oncology (MASCC/ESMO) [8], ASCO [9], and the National Comprehensive Cancer Network (NCCN) [10]. Despite evidence suggesting that administration of guideline-recommended antiemetic prophylaxis correlates with improved CINV control, studies have suggested that adherence to antiemetic guidelines is poor, with patients frequently not receiving recommended antiemetic combinations [13–16]. In a recent 2017 evaluation of European (EU) oncology practices through the Global Oncology Monitor, antiemetic utilization was evaluated for 46,503 patients [17]. Only 18%, 20%, and 11% of patients receiving cisplatin-, anthracycline-cyclophosphamide (AC)-, and carboplatin-based chemotherapy, respectively, received the guideline-recommended $NK_1$ RA + 5-$HT_3$ RA + dexamethasone (DEX) triplet combination; 17% of all patients received no antiemetics.

Oncology nurses, as part of a multidisciplinary team, play a critical role in the risk assessment and management of CINV and are therefore in a good position to promote and reinforce guideline-recommended antiemetic prophylaxis. Many are able to influence the choice of or prescribe antiemetics, thereby having the opportunity to improve adherence to evidence-based guideline recommendations. A recently published survey administered to approximately 500 oncology nurses in the United States (US) evaluated antiemetic practices and adherence to antiemetic guideline recommendations in US-based practices [18]. Consistent with the prior formal studies that have shown poor adherence with antiemetic guidelines [13–15], the survey revealed inconsistencies between practice patterns of antiemetic use and what antiemetic guidelines recommend [18].

To assess whether these same practice patterns existed in Europe (EU), a subsequent survey was conducted with European oncology nurses. As was the case with the US-based survey, the primary aim of this European survey was to explore practice patterns of antiemetic use by asking nurses to report on antiemetic agents being used in their hospitals/clinics and then to determine whether practice patterns were consistent with antiemetic guideline recommendations. Additional objectives of the survey were to assess oncology nurses' awareness of antiemetic guideline recommendations for the prevention of CINV, evaluate their perception of CINV control within their practices, and explore their perceptions of barriers to guideline adherence.

## Methods

Between March 2016 and February 2017, a sample of oncology nurses across 16 countries in Europe (Austria, Belgium, Denmark, Finland, France, Germany, Ireland, Italy, Norway, Portugal, Spain, Sweden, Switzerland, Turkey, Ukraine, and UK) were recruited to participate in a 20-question online survey. The survey (Supplementary File) was the same survey as that administered to oncology nurses in the US [18], with slight modifications made to a few questions to improve clarity. The survey questions asked of nurses' awareness of antiemetic guidelines, their confidence in the knowledge of chemotherapy emetogenicity, the antiemetic agents being used in their hospitals/practices for patients receiving highly (HEC) or moderately emetogenic chemotherapy (MEC), barriers that may prevent their hospital staff from using guideline-recommended antiemetics, how adherence to guidelines could be improved, perceptions of their greatest challenges/unmet needs in preventing/managing CINV in their practice, and perceived CINV control (i.e., complete response rates, percentage of patients with chemotherapy altered because of CINV, and emergency visits or hospitalization due to CINV).

Cogora, an independent European market access and customer intelligence agency, managed the conduct of the survey and summarized the findings. A combination of recruitment methods were used to channel respondents to the surveys including but not limited to utilizing connections and contacts within the Cogora database and with professional societies,

snowball recruiting via LinkedIn, Facebook, and Twitter, and having the authors asking their national societies to forward the survey questionnaire to their members via e-mail. The survey was translated and administered in the local language in each country.

Results are reported for all nurses who opted in by completing the survey. All survey questions offered multiple answer options with no open-ended-type questions. The proportion of the total respondents was calculated for each of the survey responses for the overall survey population and separately for individual participating countries. Data were summarized in a descriptive manner; all statistical analyses were done in IBM SPSS version 24. The data were not normally distributed and therefore analyzed using a non-parametric Kruskal–Wallis test. In instances where a significant main effect was found, post hoc pairwise comparisons with a Bonferroni correction were used to identify what groups differed significantly from each other. However, because the sample of nurses was small in each individual country aside from the UK (which comprised 38% of the total group), the results are presented predominantly as a single sample of respondents in Europe.

For responses to the survey question on the greatest challenges in the prevention or management of CINV, respondents were requested to select the top 3 from a list of 8 items. Proportions of respondents ranking each option in the top 3 were calculated for each.

Reported use of antiemetic agents is presented in the context of antiemetic guideline recommendations at the time the survey was conducted [8–10]. Practice patterns viewed as consistent with guideline recommendations were as follows:

- Highly emetogenic chemotherapy (HEC):
  - Acute phase (0–24 h after chemotherapy initiation [day 1]): neurokinin-1 receptor antagonist ($NK_1$ RA) + serotonin receptor antagonist ($5HT_3$ RA) + dexamethasone (DEX); delayed phase (25–120 h [day 2–5]): DEX + $NK_1$ RA (if oral $NK_1$ RA used on day 1)
- Moderately emetogenic chemotherapy (MEC): acute phase: 5-$HT_3$ RA + DEX or $NK_1$ RA + 5-$HT_3$ RA + DEX; delayed phase: 5-$HT_3$ RA or DEX.

## Results

Two hundred twelve nurses participated in the survey. Respondents had 15-year (median) experience as an oncology nurse, and most (80%) worked in the public not-for-profit hospital setting, seeing both inpatients and outpatients (50%) (Table 1). Most nurses (75%) were able to suggest or prescribe antiemetics.

**Table 1** Respondent demographics

| Characteristic | Respondents | |
|---|---|---|
| | *N* = 212 | % |
| Country of origin | | |
| UK | 81 | 38% |
| France | 33 | 16% |
| Portugal | 25 | 12% |
| Italy | 19 | 9% |
| Spain | 17 | 8% |
| Switzerland | 10 | 5% |
| Germany | 6 | 3% |
| Scandinavia | 11 | 5% |
| Other | 10 | 5% |
| Office type | | |
| Inpatient | 37 | 17% |
| Outpatient | 68 | 32% |
| Both inpatient and outpatient | 107 | 50% |
| Work setting | | |
| Public/not-for-profit hospital | 169 | 80% |
| Private hospital | 17 | 8% |
| Bone marrow transplant center | 7 | 3% |
| Community-based healthcare | 4 | 2% |
| Other | 15 | 7% |
| Antiemetic prescribing role | | |
| Can prescribe antiemetics | 32 | 15% |
| Can suggest antiemetics | 127 | 60% |
| None | 65 | 31% |

### Awareness and use of antiemetic guidelines

The majority of nurses reported being either confident (42%) or very confident (34%) in their knowledge of the emetogenic potential of various chemotherapies/regimens.

Respondents were most familiar with the ASCO antiemetic guidelines (46%) and slightly less familiar with those developed by their own institutions (41%) and those by MASCC (40%) and NCCN (34%). Approximately half (47%) of respondents were utilizing their own institutional guidelines in practice, while around a quarter were using those of ASCO or MASCC.

### Antiemetic agents administered in practice and consistency with antiemetic guidelines

In the HEC setting where guidelines recommend the triplet combination of $NK_1$ RA + 5-$HT_3$ RA + DEX in all patients, the most commonly reported antiemetics being administered on day 1 were the guideline-consistent agents of DEX (82%), a 5-$HT_3$ RA (81%), and $NK_1$ RA (61%)

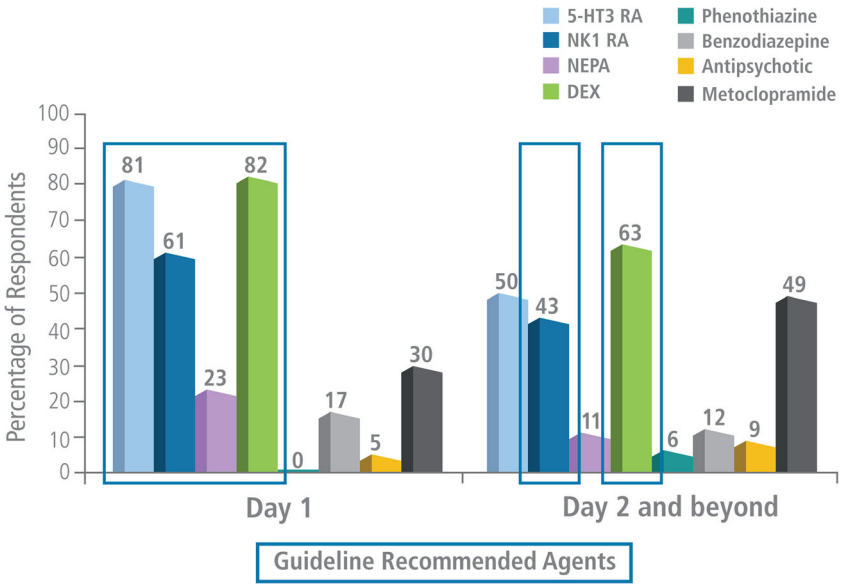


**Fig. 1** Classes of antiemetics used to prevent CINV (HEC setting)

or NEPA (the fixed $NK_1$ RA + 5-$HT_3$ RA combination agent) (23%) (Fig. 1); however, only 55% of respondents reported administering a minimum of all three of these agents comprising this triplet combination. This is a key discrepancy compared with the guideline recommendations for patients receiving HEC. During the delayed phase, the most commonly used agents were DEX (63%), 5-$HT_3$ RAs (50%) and metoclopramide (49%) (Fig. 1). The use of 5-$HT_3$ RAs and metoclopramide during the delayed phase is inconsistent with the guideline-recommendations of using DEX ± an $NK_1$ RA (if an oral $NK_1$ RA had been administered on day 1).

In the MEC setting on day 1 where guidelines recommend administration of a 5-$HT_3$ RA + DEX in all patients (and in higher risk patients the addition of an $NK_1$ RA), 5-$HT_3$ RAs and DEX were the most commonly used agents as reported by 86% and 77% of respondents, respectively (Fig. 2). However, reported use of these in combination (either alone or also with an $NK_1$ RA) was only 72%. While appropriate use of 5-$HT_3$ RAs (47%) or DEX (58%) was reported by respondents during the delayed phase, substantial guideline-inconsistent use of metoclopramide was reported by 51% of respondents (Fig. 2).

## Barriers interfering with utilizing recommended antiemetic regimens and approaches for improving adherence to antiemetic guidelines

"Physician preference" was perceived by respondents as the predominant barrier (39%) preventing staff from using guideline-recommended antiemetic prophylaxis (Fig. 3).

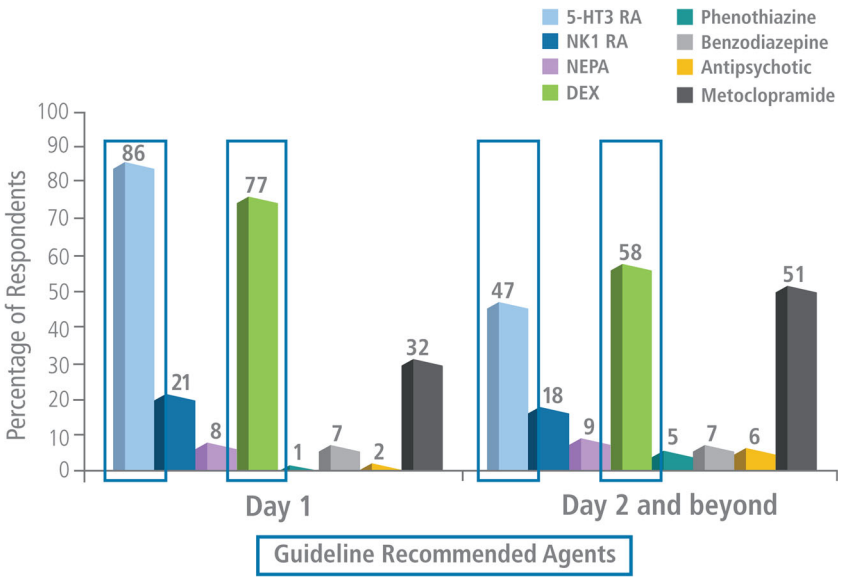


**Fig. 2** Classes of antiemetics used to prevent CINV (MEC setting)

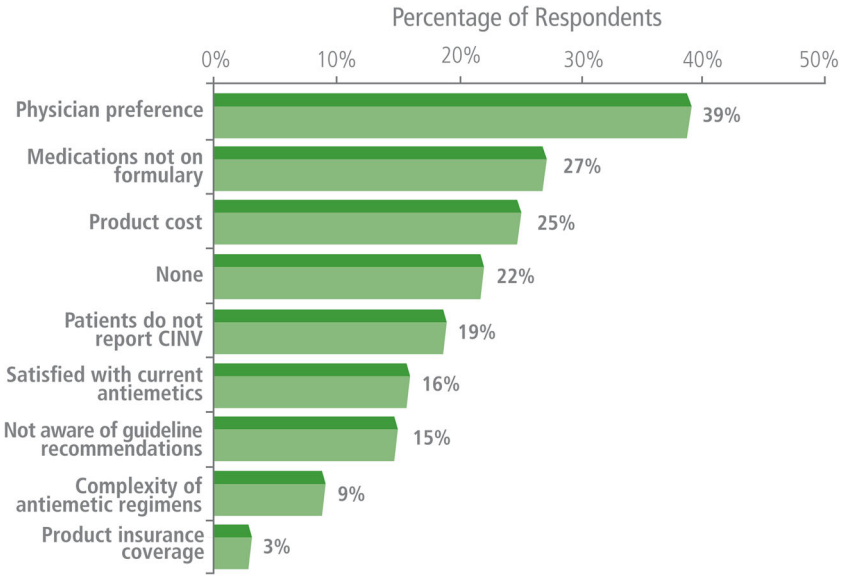


**Fig. 3** Barriers/reasons interfering with use of guideline-recommended antiemetics (HEC setting)

Medications not on formulary and product cost were also selected as main barriers by respectively 27% and 25% of respondents. It is noteworthy that 19% of nurses reported that patients do not report CINV if they experience it.

Solutions suggested by nurses to potentially improve guideline adherence in the HEC setting included increasing health care provider education (78% of respondents suggested this) and patient education (52%), as well as addressing cost/formulary/insurance barriers (28%), and enhancing ordering tools (8%). A small proportion (8%) of nurses did not feel that adherence could be improved.

## CINV control and impact of CINV on chemotherapy regimen/schedule, ED visits, and hospitalizations

Only 19% of respondents reported that CINV was prevented (i.e., experienced no emesis/no use of rescue antiemetics) in most (> 75%) of their patients (Fig. 4).

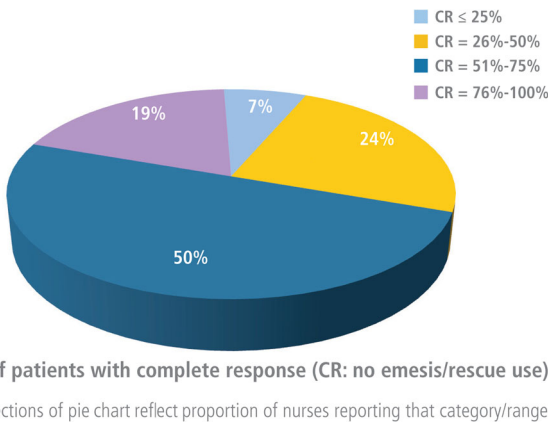


**Fig. 4** Nurses' perceptions of CINV control rates of their patients with currently administered antiemetics

Respondents reported that approximately 5% (median) of their patients have their chemotherapy postponed, stopped or delayed due to CINV. A total of 21% of all respondents reported that > 10 of their patients required emergency visits or hospitalization due to suboptimal control of CINV in the last year (Fig. 5).

## Challenges managing CINV

The greatest perceived challenges or unmet needs in preventing and managing CINV within the respondents' practices were reported as controlling CINV in the delayed phase (64%) and the impact of CINV on patients' quality-of-life (QOL) (61%). Others included controlling acute CINV (42%), increasing patient adherence (23%), and increasing access to better antiemetics (21%).

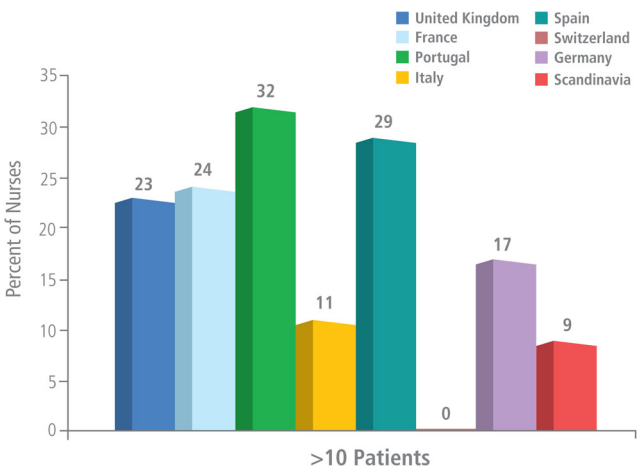


**Fig. 5** Nurses reporting > 10 patients with emergency visits/hospitalizations in the past year

## Discussion

This survey revealed several opportunities to enhance knowledge and improve inconsistencies with practice versus guideline-based antiemetic prophylaxis for patients. Disappointingly, < 50% of nurses were familiar with each of the antiemetic guidelines, including those of their own institution. Use of international antiemetic guidelines was generally low [ASCO (27%), MASCC (25%)] while approximately half of the practices use their own institutional guidelines. As 60% of nurses reported having an influence on antiemetic treatment prescription and 15% indicated they can prescribe, their education and awareness of guidelines is essential. Adherence to guidelines can lead to better treatment outcomes for patients and reduce follow-up patient care and resources (including hospitalizations).

Practice patterns of antiemetic use revealed some inconsistencies with guideline recommendations in both HEC and MEC settings. $NK_1$ RAs, 5-$HT_3$ RAs, and DEX are all underutilized in the HEC setting, and just 55% of nurses reported using all three of these agents on day 1 as recommended by guidelines. Guideline adherence was seemingly greater in the MEC setting with 72% of nurses reporting use of both 5-$HT_3$ RAs and DEX on day 1. Inappropriate use of metoclopramide during the delayed phase was common in both HEC and MEC settings.

"Physician preference" was the leading perceived barrier interfering with administration of guideline-recommended prophylactic treatment, while others, such as product cost, formulary/insurance inclusion/coverage, and complexity of antiemetic regimens, also play a role. Correspondingly, increasing healthcare provider and patient education as well as addressing cost/formulary/insurance barriers were suggested key solutions to potentially improving guideline adherence.

CINV does not appear to be optimally controlled in these practices as reflected in nurses' reports of control rates as well as the proportions of patients with ED visits/hospitalizations due to CINV. In addition, some patients have chemotherapy alterations made due to CINV which has the potential to lead to decreased tumor response. Controlling CINV in the delayed phase and managing its impact on patients' QOL were the greatest reported challenges for nurses. It is difficult to know if this is a reflection of nurses not effectively supporting patients once home, not being aware of breakthrough symptoms, or not sufficiently intervening in the prevention phase. In a recently published survey, European oncologists suggested that patient administration mistakes at home (occurring in a third of their patients) may play a role in breakthrough CINV and suggested that simplification of antiemetic regimens may be another means of improving CINV [19]. In another survey of physicians, nurses, and patients in five countries in Europe, only 38% of patients reported full compliance with physicians'/oncology nurses' instructions when self-administering antiemetic medication. Leading factors for poor compliance included patients' "not accepting the need to take medication until actually feeling sick" and reluctance to add to a pill burden and fear that swallowing itself would induce nausea/vomiting [20]. This highlights not only the need for education and reassurance to patients about antiemetics to be taken after leaving the hospital/clinic but also the value of additional follow-up with patients during this time.

As this survey mimicked that conducted in the US [18], it is interesting to note the similarities and differences in the findings. Unsurprisingly, there were differences in familiarity and use of antiemetic guidelines, with the US-based nurses using those of NCCN, while EU nurses were using their own institutions' or those of ASCO or MASCC. Practice patterns of antiemetic use were similar for both, with use of guideline-compliant agents somewhat lower in Europe vs the US. Disappointingly, both groups continue to utilize older less-effective agents such as benzodiazepines or metoclopramide, particularly in the delayed phase, rather than optimizing use of evidence-based guideline-recommended agents for HEC and MEC. The introduction of 5-$HT_3$ RAs in the 1990s and palonosetron and aprepitant in 2003 radically altered the antiemetic treatment landscape [21]. These older agents which were the only antiemetics in the 1970s and 1980s were removed from antiemetic guidelines for use in HEC and MEC settings and should have become obsolete. Metoclopramide remains an acceptable guideline-recommended agent for patients receiving chemotherapy of low emetic risk. Interestingly, in a recently published retrospective analysis of the Adverse Event Reporting System Database (from 2006 to 2014) of the Food and Drug Administration (FDA), metoclopramide was among the top 10 drugs (listed as no. 1) with the highest reports of associated serious adverse drug reactions/disabilities [22].

Remarkably, physician preference was the reported predominant barrier interfering with administration of guideline-compliant antiemetics by both groups, suggesting that perhaps nurses are not optimally using their influence to change physician practice. Perceptions of CINV control rates were very comparable with only 19% of European and 17% of US-based nurses reporting that the majority (> 75%) of their patients had their CINV optimally controlled. While the survey questions varied regarding patients requiring ED visits/hospitalizations or having their chemotherapy altered due to CINV, the findings were similar. Considering the similar practice patterns and perception of CINV control within European and US practices, it is not unexpected that the reported key challenges for nurses (i.e., controlling delayed CINV and managing the impact of CINV on patients' QOL) were the same.

It is interesting to also consider these survey findings in the context of those from a prospective PEER study in Europe

exploring actual antiemetic use and adherence with guidelines and the effect of guideline-consistent prophylaxis on patient outcomes [13]. In that study, only 43% of patients in the HEC setting received guideline-consistent prophylaxis of an $NK_1$ RA + $5HT_3$ RA + corticosteroid on day of chemotherapy; our survey revealed 55% of nurses reporting using a minimum of a $NK_1$ RA + $5HT_3$ RA + DEX in the HEC setting. In the MEC setting, guideline compliance is much better; the PEER study showed 91% of patients receiving guideline-consistent prophylaxis of a 5-$HT_3$ RA + corticosteroid on the day of chemotherapy, while this survey indicated that 72% of nurses reported using a minimum of 5-$HT_3$ RA + DEX. The study also showed that guideline-consistent use of antiemetics resulted in higher complete response rates and reduced ER visits and hospitalizations.

It is important to address the limitations of this survey. The sample was based on a convenience strategy and the size of this survey population is relatively small and it is impossible to know whether the demographics of the respondents reasonably reflect a broad range of clinical practices within Europe; therefore, caution should be used when extrapolating these conclusions to the whole of Europe. It is also important to highlight that the findings of this survey reflect nurses' perceptions of antiemetic practices in their hospitals and not an actual practice analysis, such as the PEER study. As the questions posed to nurses exploring practice patterns asked specifically about classes of individual antiemetic agents being used, calculations pertaining to utilization of specific guideline-recommended combinations make some assumptions; however, if anything rates of adherence reflect a conservative calculation.

As was the case with the US survey, these findings elicit follow-up questions such as *why* older agents such as metoclopramide continue to be frequently used when more effective antiemetics are available, or *why* physician preference is the predominant barrier to administration of guideline-recommended agents. However, the consistency of these findings and those from the US-based nurse survey as well as the recent formal studies in Europe [13] and the US [14] exploring guideline adherence emphasize the critical need to increase awareness and education of evidence-based antiemetic guidelines. Practical multi-faceted approaches for overcoming barriers that interfere with the selection and administration of guideline-recommended antiemetics are essential and aligned with ESMO's recent holistic patient-centered position [1]. Adherence with guideline recommendations will inevitably improve CINV control and QOL for all patients receiving emetogenic chemotherapy, thereby decreasing ED visits/hospitalizations due to CINV and allowing patients to complete their chemotherapy as planned. Nurses should take advantage of the opportunity to show leadership qualities and challenge practice to do what is best for their patients and caregivers—now.

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## Compliance with ethical standards

**Conflict of interest** The authors have the following conflicts of interest to disclose:

*Dielenseger*: Advisory boards: Helsinn, Roche, Shire, Tesaro, BMS, Pfizzer, Janssen Cilag, Bayer Healthcare, IPSEN.

*Börjeson*: None.

*Vidall*: None.

*Young*: Honoraria from Helsinn, Bayer, Leo Pharma; Educational grant from Bayer.

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