Patient-reported outcomes in daily clinical oncology practice: a tool for patient monitoring and quality of care assessment

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Summary and Discussion
**Introduction**

The profession of pharmacy has experienced significant growth and development over the past 40 years. Historically, pharmacy entered the twentieth century performing the social role of apothecary – preparing and selling medicinal drugs. During this traditional stage the pharmacist’s function was procuring, preparing, and evaluating drug products. His primary obligation was to ensure that the drugs he sold were pure, unadulterated, and leges artis. The traditional role began to wane as the preparation of pharmaceuticals was gradually taken over by the pharmaceutical industry and as the choice of therapeutic agents passed to the physician.

Clinical pharmacy practice was born in the mid 1960’s. There began a period of professional transition in which pharmacists sought the full achievement of their professional potential. The transitional stage was a time of rapid expansion of functions and of increased professional diversity. During this period, new pharmaceutical services evolved, which, while moving pharmacy closer to the patient, continued to focus on the drug and its delivery to abstract biological systems rather than to individual patients.

In the 1990’s, the concept of pharmaceutical care was launched, with the goal of restoring something that had been missing for years in pharmaceutical practice, a clear emphasis on the patient’s welfare, a patient advocacy role with a clear ethical mandate to protect the patient from the harmful effects, termed as drug misadventuring. Pharmaceutical care is the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient’s health-related quality of life (HRQL). These outcomes are (1) cure of a disease, (2) resolution or reduction of a patient’s symptomatology, (3) arresting or slowing the disease process, or (4) preventing a disease or symptomatology.

In daily clinical oncology practice, the role of hospital pharmacists in the care of patients is evolving. Traditionally, hospital pharmacists are not only responsible for every day preparation of chemotherapy, but also participate as a member of hospital drug admission committees.

Beginning in the 1990’s, hospitals have been continually confronted with new and an ever increasing number of costly treatments for cancer patients. For hospital pharmacists, a new dimension was added to their work, namely, helping to weigh the costs and benefits of these new drugs.

Anticancer drug regimens are administered following established protocols that have been developed on the basis of data from clinical trials. However, the administration of supportive medication is not as controlled as is the case with chemotherapy itself. Each treatment setting may define and practice...
supportive care in a different manner. Furthermore, in supportive care, evidence-based therapy is not as yet usual practice. Additionally, much of the supportive therapy may be administered or supervised in the primary care setting rather than in the oncology clinic. This can result in less effective protection against adverse drug events and thus potentially a decrease in patients’ HRQoL. In the community setting, the pharmacist can play an important role in ensuring that the patients (and her family) are well informed about the dosing schedule of their medications, and the potential side effects involved.

Whether working in the hospital or community context, it is important for health care providers, including pharmacists, to deliver care that takes the HRQoL of the individual patient into consideration. To achieve this goal, health care providers need to have access to reliable information about patients’ HRQoL. For the pharmacist, this can be important in providing appropriate advice and counseling, and in assisting clinicians and nurses in managing patients’ care and ultimately, in improving patients’ health and well-being.

Especially for patients receiving chemotherapy in an outpatient setting, the monitoring of patients’ HRQoL requires more attention and active questioning by the health care professionals involved. This includes the oncology nurses who play a central role in the support of patients treated on an outpatient basis. In addition to their responsibility for the proper administration of chemotherapy, they increasingly bear the responsibility for obtaining patient histories and performing physical examinations, and as such have more in-depth, day-to-day patient contact. If therapy-related toxicity occurs, the nurse may well be the first professional that the patient contacts. Their close contact with patients allows nurses to focus on patients’ HRQoL concerns and priorities. Additionally, in their role as liaison between the oncologist and patient, nurses can help to ensure that HRQoL needs are being addressed.6, 7, 8

Individual PRO data used in daily clinical practice
In order to better understand the HRQoL issues confronting patients with cancer at various points in their disease and treatment trajectory, it is essential that valid and reliable measures are available, and that practical procedures are available for systematically assessing HRQoL on a regular basis in daily clinical practice. The primary objective of the first part of this thesis was to investigate the value (and limitations) of standardized HRQoL information in daily clinical oncology practice.

We carried out an intervention study to investigate the efficacy of incorporating standardized HRQoL assessments as a routine part of the outpatient treatment of cancer patients being treated with chemotherapy in a
community hospital setting. Efficacy was evaluated in terms of two primary outcomes: (1) facilitating nurse-patient communication; (2) increasing nurses' awareness of patients' HRQoL. Additional outcomes were patients' and nurses' satisfaction with their interactions, patient management activities, and patients' HRQoL over time.

Prior to conducting the intervention study, we needed to perform some methodological work to validate a checklist used by patients to report which HRQoL topics had been discussed during the consultation with their nurse. This preparatory work was necessary because, in the setting in which the intervention study took place, it was not possible (for logistical reasons) to audio- or videotape the patient-nurse interactions. Thus we were dependent on self-report data, and that data needed to be valid and reliable.

**Summary of the results**

*Chapter 2* describes the work that we carried out to validate a checklist designed to assess the HRQoL topics discussed during patient-nurse contacts. Specifically, we examined the level of agreement between patients and observers regarding the frequency with which HRQoL topics were discussed during outpatient clinical oncology visits.

A total of 50 cancer patients undergoing chemotherapy were asked to complete a checklist, indicating which HRQoL topics had been discussed during a recent conversation with their oncology nurse. To ensure that the checklist included the most salient aspects of HRQoL for cancer patients, it was designed to parallel the content areas of the EORTC QLQ-C30, a well-known, cancer-specific HRQoL questionnaire developed on the basis of both patient and health care professional input.

Observers (i.e., research assistants) also completed the checklist, based on either direct observation of the encounters that took place on the hospital ward, or on audiotaped information of encounters that took place in private hospital rooms. Level of agreement was assessed by determining the percentage of agreement, kappa and prevalence-adjusted kappa statistics.

The percentage of agreement between patients’ and observers’ ratings was generally high, ranging from 74% for fatigue to 96% for sleep problems and cognitive functioning. The average percentage of agreement over the 13 HRQoL topics rated was 86%. Cohen's kappa varied between 0.41 (for pain) and 0.78 (for sleep problems). Prevalence-adjusted kappa's were generally higher, ranging from 0.48 (for fatigue) to 0.92 (for sleep problems and social functioning). The average Cohen's kappa and prevalence-adjusted kappa over the 13 HRQoL topics were 0.56 and 0.71, respectively. Level of agreement was not found to vary significantly as a function of patients’ background characteristics. It was concluded that oncology patients’ self-reports of the HRQoL-related topics discussed during outpatient chemotherapy
visits are in reasonably close agreement with those provided by observers. The results indicate that the patient is a legitimate source of information about the HRQL-related content of medical encounters, and thus can be used in communication studies where the collection of observational data (e.g., via audio- or videotaping) is either too costly or logistically impractical.

Chapter 3 describes the results of a prospective, sequential, cohort study, with repeated measures, evaluating the efficacy of incorporating standardized HRQL assessments as a routine part of the outpatient chemotherapy treatment of cancer patients in a community hospital. The outcomes were: 1) facilitating nurse-patient communication, 2) increasing nurses’ awareness of patients’ HRQL, 3) patient management, 4) patients’ satisfaction and 5) patients’ HRQL.

Ten nurses and 219 patients participated in this community hospital-based study. The intervention involved patients’ completing standardized HRQL questionnaires via a touch screen computer, the results of which were provided to nurses and patients in a graphic summary. Questionnaire and medical record data were used to assess outcomes.

HRQL-related topics were discussed significantly more frequently in the intervention than in the control group (mean = 4.8 vs. 3.8 topics, respectively; \( p = 0.02 \)). Nurses’ awareness of patients’ levels of daily activity, pain, and overall quality of life was significantly better in the intervention than the control group. The mean number of HRQL-related notations in the medical records was significantly higher in the intervention group (24 versus 20; \( p < 0.05 \)). Only modest effects were observed in patient management (counseling behaviour), and no significant effects were found in patient satisfaction or changes in HRQL over time.

It was concluded that incorporating standardized HRQL assessments in daily clinical oncology nursing practice primarily facilitates the discussion of HRQL issues, and increases nurses’ awareness. Additional efforts are needed to enhance the effect of routine HRQL assessments on patient management and HRQL.

Methodological reflections

Chapter 2 describes a study designed to determine the level of agreement between patients and observers regarding the frequency with which health-related quality of life topics are discussed during outpatient clinical oncology visits. This study was conducted in the outpatient oncology clinic. Given the physical layout of the clinic (i.e., open waiting room areas, multi-patient treatment rooms), audiotaping or videotaping conversations was not feasible for either technical or privacy reasons, and would likely lead to confusion or between-patient contamination. For this reason patient self-report data are frequently used to evaluate patient–health care provider...
communication. The study was premised on the increasing recognition that communication between health care providers and patients may not always be optimal, although it is often critical for effective treatment.

To “set the stage” for this study, essentially an argument had to be built that: (1) there is evidence that patient-caregiver communication about HRQoL-related issues is suboptimal; (2) that studies have been conducted (and are on-going) to investigate ways of improving such communication; (3) in order to evaluate the effect of such interventions, the actual patterns and content of communication between patients and health care providers have to be evaluated systematically; (4) that the preferred method of evaluating the content of such communication is to use audiotapes, videotapes, or external observations; (5) that these techniques are sometimes not feasible in practice settings; and thus (6) it needs to be evaluated whether one can rely on patients to provide information about what has been discussed with them in medical/nursing encounters.

This study was not concerned with the value of proxy raters in evaluating the HRQoL of patients with cancer. Although this is an important issue, it has been investigated in a number of previous studies. Rather, the focus of the study was on assessing whether patients can provide accurate feedback on what was actually discussed during a session with their nurse. Because patient self-report data may also be subject to problems of recall and may be distorted when sensitive topics are at issue, it is interesting to determine whether, in studies of patient-health care provider communication, it is possible (i.e. valid) to rely on patients’ self-reports of what actually was discussed during medical consultations.

The checklist that patients and raters filled out was dichotomous (yes/no). This checklist did not, however, assess how much or how well any particular HRQoL-related issue was discussed. By simply asking a yes/no question, the assessment misses this type of information.

In the EORTC QLQ-C30, which was used as a model for designing the content of the checklist, a 4-point scale is used. A possible way to study how thoroughly a topic was addressed is to use this type of 4-point scale. However as stated above, as the key issue for this study was whether patients could provide accurate information on whether various HRQoL-related topics were actually discussed, the use of a 4-point scale did not seem feasible. The checklist was designed to confirm, in essence, factual information that can be confirmed or disconfirmed by comparing it with observer ratings. That is why a dichotomous response format was used (i.e., each HRQoL topic was discussed or not). In contrast, ratings of the perceived quality of
communication are much more subjective in nature, and reliance on patient self-report raises fewer issues of accuracy or validity.

The important “practice implication” of this study (actually, an implication for conducting communication research in this area) is that patients can provide accurate feedback about the hrqol-related content of medical encounters in communication studies where the collection of observational data is either too costly or logistically impractical.

In chapter 3 a prospective, sequential, cohort study, with repeated measures, evaluating the efficacy of incorporating standardized health-related quality of life (hrqol) assessments as a routine part of the outpatient chemotherapy treatment of cancer patients is described. The study employed a pretest-posttest cohort design with repeated measures. An initial cohort of 100 consecutive patients formed the control arm of the study. These patients were asked to participate in the study at the time of their initial outpatient visit with the oncology nurse. After providing informed consent, they were followed for 4 consecutive outpatient visits. Following a “wash out” period of approximately 2 months, a second cohort of consecutive patients was recruited into the study, and formed the experimental arm of the study. This 2nd cohort was similarly followed for 4 consecutive outpatient visits.

We considered this to be the optimal research design, given the practical and ethical constraints involved. A classical, randomized, control group design would require that the participating nurses and patients be randomly assigned to either the control or experimental group. For several reasons, this was not deemed feasible nor acceptable in the outpatient clinic setting in which the study would be carried out. First, it would require that the participating nurses be exposed to the experimental intervention (i.e., receive the hrqol profiles) for some patients, but not for others. In such a situation, the risk of a carry-over or contamination effect is too great. Additionally, it would require that, during the same outpatient clinic sessions, some patients would be exposed to the intervention while others would not. Given the physical layout of the clinic (i.e., open waiting room areas, multi-patient treatment rooms), this would likely lead to confusion and between-patient contamination.

A potential risk involved in the chosen design is a so-called “history effect” (i.e., that changes might occur in the outpatient clinic unrelated to the intervention that might provide an alternative explanation for any observed, between-cohort differences). In the context of this study, the greatest potential “history effect” was that, during the course of the study, there would be changes in the nursing personnel within the hospital. However, this history effect, a major potential threat to the
internal validity of the study, did not materialize. The nursing staff remained stable throughout the entire period of the study. Also, it is important to emphasize that the baseline characteristics in the two cohorts were well balanced to confirm the validity of this non-randomized cohort study.

Abstracting reliable/valid data from nursing and medical records is challenging. The nursing and medical records were handwritten. To maximize reliability, data were abstracted from these records using a structured checklist covering all topics of the QLQ-C30 and condition specific HRQL modules for breast, lung and colon cancer. The medical records audit determined (yes/no) if any information on a given HRQL topic was noted and, if so, whether it had led to a specific patient management activity. However, notes in the nursing and medical records may not have captured all of the care potentially occurring, which might have led to an underestimation of the amount of patient management activities actually undertaken. However, if such underreporting did occur, there was no reason to believe that it would have been more prevalent in the usual care than in the intervention group.

Prior to our study, almost all studies of the use of HRQL assessments in clinical practice had been conducted in specialized cancer treatment centres. To our knowledge, our study was the first to be conducted among cancer patients being treated in a community hospital. This is important for the generalizability of the results, because a majority of cancer patients are treated in general hospitals. Patients treated in a community hospital often tend to be older and less highly educated than cancer patients treated in cancer centres. These patient characteristics may, in turn, influence communication behaviour. In addition, patients who choose to be treated in a specialized cancer centre may have different treatment preferences and might be more willing to accept limitations in their HRQL than patients treated elsewhere. Particularly in the community hospital setting, nurses carry a major responsibility for delivering the chemotherapy, and for monitoring patients’ physical and psychosocial health on a day-to-day basis. They also play an important role as liaison between patient and physician, and can help to ensure that the patients’ HRQL concerns are addressed.

**Future research**

Approximately one-third of the patients recruited into our intervention trial did not complete the study due primarily to disease progression or death. This is not uncommon in clinical studies among cancer patients with a range of diagnoses and disease stages, including advanced disease. However, our study included a mix of patients, both those treated in the adjuvant setting and those who were receiving palliative chemotherapy. We did not include patients who were receiving
palliative care (i.e., supportive care, without active chemotherapy). It would be of interest to determine the usefulness of routine health-related quality of life (HRQL) assessments in facilitating communication and enhancing clinical decision-making and care in the palliative care setting. In this setting, symptom relief is often the primary focus of treatment and care, and thus continuous monitoring of symptoms and functioning may be particularly important. There are, of course, challenges in routinely collecting HRQL information via self-report from very ill patients. The use of routine HRQL assessment in the palliative care setting should be the focus of future research.

Recently, the Dutch Association of Integral Cancer Centres (Integrale Kankercentra Nederland, iKCNL), published a guideline on detecting psychosocial distress in cancer patients. In this guideline it is strongly recommended that the Distress Thermometer be used to identify distress in cancer patients. To measure distress, the definition of the NCCN has been used. The Distress Thermometer measures the severity of distress in cancer patients using a single item; a thermometer that is scored from 0 - 10. In addition, a ‘problem list’ is used. On this list, the patient can indicate in which areas he/she is experiencing problems. The domains are: physical problems, emotional problems, philosophical problems, social problems and practical problems. The list can be completed by patients themselves.

The Distress Thermometer has been validated in the Netherlands under the name ‘Lastmeter’ in patients with different types of cancer. A cut-off point of 5 was chosen for the distress thermometer to detect clinically relevant levels of distress. The percentage of patients with a score of 5 or higher who wanted to be referred (14%) or possibly referred (29%) was significantly higher than the percentage of patients with a score lower than 5 who wanted to be referred (5% and 13%, respectively).

The introduction of the Distress Thermometer in daily clinical practice is noteworthy as it reflects our recommendations, based on the results of our study on the use of HRQL related information. The use of the Distress Thermometer as well as the intervention used in our study can be seen as a tool for use during conversations with the patient; it offers structure and a starting point to discuss the issues together with the patient, to determine if there is a need for extra care in any area and who would be the best provider of this care.

However, although the routine collection and dissemination of HRQL-related information in the outpatient chemotherapy setting in our study resulted in a significant increase in the frequency with which HRQL issues were discussed and significant improvement was observed in nurses’ awareness of the level of functioning, symptoms and the overall quality of life of their patients, the intervention had only a modest effect on patient management.
activities, primarily in terms of increased levels of patient counseling. This could be due, at least in part, to the fact that no explicit practice guidelines were provided or recommendations made that linked (changes in) patients’ self-reported HRQOL with patient management strategies. Also no significant between-group differences in patient satisfaction or HRQOL were detected. Satisfaction with the intervention itself was high, with most patients reporting that the HRQOL summary profile was useful in facilitating communication and in enhancing nurses’ awareness of patients’ problems. Most patients and all of the nurses also favored introducing such a procedure as a standard part of the outpatient clinic procedure. This finding supports the introduction of HRQOL assessment, such as the Distress Thermometer, in daily clinical practice. However implementation of such an instrument should be accompanied by research to determine whether such screening results in the referral of those cancer patients who need it, and whether the process of screening improves satisfaction with care, quality of care, and ultimately HRQOL. The introduction of clinical pathways and treatment guidelines as part of such an HRQOL assessment package may be particularly important, and should be the topic of future research.

PRO data at the aggregate level in daily clinical practice

In addition to the use of PRO data at the individual patient level, interest is increasing in using PRO data at the aggregate level as a part of outcomes research in daily clinical practice. Post-authorization research and surveillance, also known as outcomes research or comparative effectiveness research, has become more and more important. Outcomes research seeks to understand the end results of particular health care practices and interventions. End results include effects that people experience and care about, such as change in the ability to function. By linking the care people receive to the outcomes they experience, outcomes research has become the key to developing better ways of monitoring and improving the quality of care.

In 2007, the Dutch Health Care Insurance Board (cvz) expanded its guideline on pharmacoeconomic research for generating data relevant to the registration of new costly drugs to include guidelines on the conduct of outcomes research. The guidelines describe how the efficiency of new drugs needs to be established. During three years of provisional registration, a set of data, depending on the indication of the new drug, has to be aggregated. These data consist of patient characteristics, clinical data, costs and patient reported outcomes (PRO’s). PRO’s include, but are not limited to HRQOL data.

The second part of this thesis focuses on the use of PRO’s in monitoring the quality of care. Specifically, we carried out two observational studies on the role of PRO’s in evaluating important side effects of chemotherapy.
treatment, i.e. fatigue and chemotherapy-induced nausea and vomiting.

**Summary of the results**

*Chapter 4* presents the results of a study investigating the adherence to treatment guidelines on cancer-related anaemia and fatigue (cra/crf), and factors influencing the choice of intervention. In this prospective, observational study, 136 cancer patients being treated with chemotherapy in a large community hospital completed a questionnaire at consecutive outpatient visits assessing fatigue (the FACIT-f) and fatigue-related counseling and advice received. Data on administration of chemotherapy, and use of epoetin or blood transfusions were abstracted from the medical records.

Fifty-three percent of patients with severe anaemia (Hb < 10 g/dl) and 6% of patients with less severe anaemia (Hb levels 10–12 g/dl) received treatment (epoetin and/or blood transfusions). Half of the patients with less severe anaemia reported clinically relevant levels of fatigue. More than 50% of all patients received fatigue-related counseling, primarily at the start of chemotherapy. Most counseling was directed at energy conservation. Fatigue was not associated significantly with the use of epoetin or blood transfusion. Patients receiving palliative treatment (17%), male patients (16%) and patients with a low Hb-level (<10 g/dl, 38%) were treated significantly more often with epoetin.

It was concluded that, in daily clinical practice, guidelines concerning the use of epoetin or blood transfusion in severe cra are adhered to in about half of the cases. In patients with less severe anaemia, the level of fatigue did not play a significant role in the use of epoetin. According to current guidelines, counseling on crf should be directed primarily at activity enhancement. However, only a minority of patients received such counseling.

*Chapter 5* presents an observational study investigating: (1) the impact of chemotherapy induced nausea and vomiting (cinv) on patients’ health-related quality of life (hrql) in daily clinical practice; (2) the association between patient characteristics and type of antiemetics and cinv; and (3) the role of cinv in physicians’ decisions to modify antiemetic treatment. This prospective, multicenter study was conducted in 9 general hospitals in the Netherlands. During three consecutive chemotherapy cycles, patients used a diary to record episodes of nausea, vomiting and antiemetic use. For each cycle, these ratings were made one day prior to and 6 days after having received chemotherapy. The influence of cinv on patients’ hrql was evaluated with the Functional Living Index-Emesis (FLIE) questionnaire at day 6 of each treatment cycle. (Changes in) antiemetic use were recorded by the treating nurse. Patient inclusion took place between May 2005 and May 2007.
Two hundred seventy-seven patients were enrolled in the study. Acute and delayed nausea during the first treatment cycle was reported by 39% and 68% of the patients, respectively. The comparable figures for acute and delayed vomiting were 12% and 23%. During the first and subsequent treatment cycles, approximately one-third of the patients indicated that CINV had a substantial impact on their daily life. Female patients and younger patients reported significantly more CINV than male and older patients. At all treatment cycles, patients receiving treatment with moderately emetogenic chemotherapy containing anthracyclines reported more acute nausea than patients receiving highly emetogenic chemotherapy, containing platinum. Acute vomiting was associated significantly with change in (i.e., additional) antiemetic treatment. Delayed CINV did not influence antiemetic treatment.

It was concluded that CINV continues to be a problem that adversely affects the daily lives of patients. CINV is worse in women and in younger patients. In daily clinical practice, acute CINV, but not delayed CINV results in changes in antiemetic treatment. In view of the effects of not only acute- but also delayed CINV on daily life, more attention should be paid to adjustment of anti-emetic treatment to cover CINV complaints later during the chemotherapy cycle.

**Study limitations and discussion**

There are several ways in which one can assess the relationship between an intervention and an outcome. Randomized controlled trials (RCTs) are considered the gold standard for evaluating interventions. However, RCTs are resource intensive and focus on short-term effects of an intervention in a well-defined but often limited population. The generalizability of results from RCTs to the larger population of interest may be limited because of the strict inclusion and exclusion criteria applied: criteria that over result in an underrepresentation of vulnerable patient groups. Additionally, trial results typically provide information on how the “average” patient will respond to a treatment, although the average patient does not really exist.

Clinicians must therefore also draw upon the results of well designed observational studies to obtain additional information on how treatments work in everyday clinical practice. The studies on cancer-related fatigue and anaemia, and on chemotherapy-induced nausea and vomiting (CINV) presented in chapters 4 and 5 were observational in nature. In observational studies it is critical to minimize the effects of bias and confounding in order to generate credible results. The risk of confounding was limited in our studies, because patient and treatment characteristics most likely to be associated with the outcomes (fatigue and CINV) were predefined on the basis of the literature and were taken into account.
account in the regression analyses that were performed 15.

In both of the observational studies reported in this thesis, a majority of patients did not receive treatment according to published treatment guidelines. Clinical practice guidelines are intended to assist clinicians and patients in making decisions about appropriate treatment and care under specific clinical circumstances. Their successful implementation should, in theory, improve the quality of care by decreasing undesirable and inappropriate variations in daily clinical practice 16.

However, despite their wide availability, clinical practice guidelines have tended to have limited effect on physicians' behaviour 17. Physician adherence to guidelines may be hindered by a variety of barriers, including lack of awareness, lack of familiarity, lack of agreement, limited self-efficacy, low outcome expectancy, the inertia of previous practice, and various external barriers 18.

In our study on fatigue, a minority of patients received counseling according to the guidelines and about half of the patients with chemotherapy-related anaemia of sufficient severity to merit pharmacological treatment actually received it.

In the case of fatigue, numerous patient, professional and system barriers to effective symptom management have been documented. Patients may be reluctant to report fatigue and have little expectation that it can be relieved 19, 20. Patients frequently report that they have difficulty communicating with their health care providers about their fatigue 21. Neither patients nor their healthcare providers may understand the mechanism of cancer-related fatigue or how to prevent, minimize, or resolve this pervasive and distressing symptom 22, 23. This lack of knowledge stems from the complex nature of fatigue and the lack of agreement in the literature on its definition, causes, indicators, effects, or remedies. Cancer-related fatigue is a symptom that is not routinely assessed in the clinical setting and therefore often goes unreported, underdiagnosed, and undertreated.

Documentation of fatigue assessment and management in the medical record is not common and is often not a priority, and there are few if any triggers to do so routinely 24.

Reducing patient, professional, and system barriers requires more than providing guidelines or staff education 25. Continued research is warranted to develop educational measures for both patients and providers that are effective in decreasing the barriers that exist to effective communication and treatment of fatigue. Additional research is needed to determine if these educational efforts make a difference in fatigue assessment, documentations, and patient outcomes.
In our study on cINV, a minority of patients receiving HEC was treated with the three drug combination of a NK-1 antagonist, a 5HT3 antagonist and dexamethason. Our study was conducted shortly after the introduction of NK-1 antagonists in the treatment guidelines. This may explain, at least in part, our finding that adherence to the guideline in daily clinical practice was relatively poor.

Dranitsaris et al. studied a multifaceted approach to promote adherence to guidelines on the prevention and treatment of cINV. Their six-step, multifaceted approach includes guideline dissemination, the use of opinion leaders, interactive educational workshops, therapeutic reminders in the form of pre-printed antiemetic orders, educational outreach using the pharmacist as the vehicle for communicating information, and physician audit and feedback. In their work, once the guidelines had been disseminated and the educational programs had been completed, the next step was to implement a prospective drug use evaluation study with the clinical pharmacist as the instrument for promoting change. Overall, 88.7% of prescriptions fulfilled the guidelines with respect to appropriate indication, dosage, and duration of therapy. Patients who received evidence-based antiemetic therapy experienced a significant reduction in the severity of acute nausea. In the Netherlands, a study on the implementation of distributing prefilled boxes with antiemetics, accompanied by extra written patient information, led to a 50% reduction of cINV and obstipation. At the same time, the intervention led to a reduction in the amount of time that physicians spent on writing prescriptions, and a reduction in drug spilling and costs.

Our studies on fatigue and cINV used standardized, validated condition-specific questionnaires. As guidelines in oncology treatment are rapidly evolving, such condition-specific questionnaires may not always reflect the most recent developments in and standards of treatment. In particular, the introduction of new drugs often carries with it new side-effects that may not yet be included in existing questionnaires. This suggests that available measures for assessing symptom burden need to be continually checked for relevance and completeness, and that amended versions need to be generated to keep pace with clinical developments.

**Conclusion**

The use and interpretation of pro’s to document the effect of treatments in daily clinical practice is an important development in optimizing pharmaceutical care. This patient-centered approach has been advocated as a means of assessing and monitoring the effectiveness of different interventions or health care policies in real world clinical practice, as opposed to clinical trials. Others have suggested that population-based pro data can be used as an indicator of the quality of
The outcomes of our studies may form a basis for evaluating new treatments intended to prevent or minimize fatigue and cinv. In the case of fatigue, use of clinically relevant thresholds for patient-reported fatigue could be tied to appropriate clinical pathways for the treatment of CRA and CRF. Any such future enhancements in counseling for CRF should be investigated, preferably in a RCT in order to establish a strong evidence base for such counseling.

In the case of cinv, special attention should be paid to patients receiving anthracyline containing chemotherapy, especially because the majority of patients receiving this chemotherapy are young women with breast cancer (female gender and younger age are two well known risk factors for developing cinv). As the guidelines for preventing cinv have been updated for patients receiving anthracyline containing chemotherapy, it is our strong recommendation to continue using PRO’s to evaluate these new guidelines.

Considering implementation of treatment guidelines, future studies should emphasize the use of multifaceted approaches to promoting adherence. When changes in drug-prescribing are promoted, pharmacist-driven intervention programs should be developed and investigated. Additional budget is required to finance this new role for hospital pharmacists.

Introduction of new drug treatments in daily clinical practice should be accompanied by an on-going program of outcomes research. Patients treated in daily clinical practice may have different characteristics than those studied in the context of clinical trials. Outcomes research is particularly important in oncology, where new treatments may be introduced rapidly without extensive use and experience in daily clinical practice. In this context, it is important to continually monitor and weigh the potential benefits of new therapies against their costs (i.e., side effects). Hospital pharmacist, as a part of the team of health care providers, should be intimately involved in such work to ensure that the treatments given to patients reflect an optimal balance between minimizing morbidity and mortality, and maintaining or enhancing HRQL.
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