SYSTEMATIC REVIEW

Effects of Guideline-based Computerized Provider Order Entry Systems on the Chemotherapy Order Process: a Systematic Review

Sougand Setareh[1], Reza Rabiei[1], Hamid Reza Mirzaei[2], Arash Roshanpoor[3], Mahtab Shaabani[4]

[1]Department of Health Information Technology and Management, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[2]Cancer Research Center, Shohadae Tajrish Hospital, Department of Radiation Oncology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[3]Department of Computer Science, Sama Technical and Vocational Training College, Tehran Branch (Tehran), Islamic Azad University (IAU), Tehran, Iran

[4]Private Gastroenterologist, Tehran, Iran

Corresponding author: Reza Rabiei, PhD, Department of Health Information Technology and Management, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences. P.O. 19395, Tehran, Iran. Phone: +989122195276. E-mail: r.rabiei@sbmu.ac.ir . ORCID ID: https:/orcid.org/0000-0003-0771-7306.

doi: 10.5455/aim.2022.30.61-68

ACTA INFORM MED. 2022 MAR 30(1): 61-68

Received: Jan 03, 2022

Accepted: Feb 10, 2022

ABSTRACT

Background: Computerized Provider Order Entry (CPOE) systems developed based on clinical guidelines are believed to greatly reduce chemotherapy medication prescription errors. **Objective:** The present study reviewed the effects of guideline-based CPOEs on the chemotherapy order process. **Methods:** PubMed, Scopus, Embase, Web of Science, and IEEE Xplore databases published up to 1 June 2020 were systematically searched for studies investigating the effect of guideline-based CPOEs on the chemotherapy order process. Moreover, the bibliography of relevant retrieved publications was also checked. **Results:** Nineteen articles from the five databases met the eligibility criteria and were reviewed. Eleven out of 19 (58%) articles investigated the effect of CPOEs on medication errors, and other studies examined other aspects of CPOE efficacy, including time required for chemotherapy prescriptions; Safety, policy compliance and communication between health care providers; physicians prescribing behavior; quality and safety of treatment; workflow; direct patient care time; and adherence to guidelines. In addition, 15 out of 19 mentioned the use of specific clinical guidelines. **Conclusion:** Evidence indicates CPOEs can positively affect the quality of healthcare service delivery for cancer patients, but there is still a dearth of clinical outcome evaluation data about the effects of these systems on patients undergoing chemotherapy. Moreover, there is limited information about guideline compliance errors, which highlights the needs for further research in this area.

Keywords: Clinical Decision-Support Systems, Computerized Physician Order Entry, Clinical Practice Guideline, Chemotherapy Prescription, Medication errors.

1. BACKGROUND

Cancer treatment remains a major challenge for health systems all over the world. GLOBOCAN's 2021 report estimated a global cancer prevalence of 19.3 million new cases, with 10.0 million deaths by 2020 (1). Cancer treatment methods differ depending on disease stage, patients' age and physical condition. Radiation, surgery, and chemotherapy are among the available options for treatment. Cancer therapy is complex and error prone and the adjustment of chemotherapy drugs dose is essential due to their toxicity and narrow therapeutic windows. Optimizing the provision of care to cancer patients often requires complex decisions, and coordination between care team (2).

Research indicates that dose adjustment is not error-free; it ranks second among pharmacotherapy errors resulted in death (3). The chemotherapy-related medication errors are reported 7.1% among adults and 18.8% among children (4). Research reported the errors in prescribing chemotherapy and its related harm confirming that the process is not error-free (5). The chemotherapy-related errors might be experienced in different stages including prescription, preparation, administration, and monitoring and its requires a high degree of precision due to the complexities associated with medication type and dose, diluents, injection sequences and durations, and dose modification based on laboratory findings or toxicity assessments (6).

Limitations	Time Limitation	up to June 2020
#1	"medical order entry system* " OR "Order Entry System*" OR "medication alert system*" OR "Alert System*" OR "Medication Alert*" OR "computerized physician order entry system*" OR " computerized physician order entry" OR "computerized provider order entry" OR "computerized provider order entry" OR "computerized provider order entry system*" OR "CPOE" OR "Computerized prescriber order entry" OR "electronic prescribing" OR "e prescribing" OR "clinical decision support system*" OR "clinical decision support*" OR "Medication Systems Drug Distribution System*" OR "computer-assisted therapy Medication Assistance Program*" OR "Computer-Assisted Drug Therapy"	
#2	"drug therapy" OR "chemotherap*" OR "Pharmacotherap*" OR "Polychemotherap*"	
Search	#1 AND #2	

Box 1: Search strategy in scientific databases.

Motivated by the significance of this issue and for patient safety, chemotherapy guidelines have been developed to help oncologists in treatment management and reducing therapeutic errors (7). The complex, multi-dimensional, and prolonged nature of the treatment process and the wide range of recommended doses make it difficult for physicians to comply with paper-based protocols, leading to a variety of medical errors (8, 9).

The clinical practice guidelines play a significant role in prescribing the correct chemotherapy regimen, and may become more significant depending on the stage of the disease and factors such as age, weight, and body surface area (10, 11). The chemotherapy regimens determined accurately and based on guidelines can decrease prescription errors by about 50% annually (12, 13).

As the clinical practice guidelines change over time, having access to computer-interpretable guidelines may facilitate and improve the drug prescribing process by updating regimens and reducing guideline complexity (12), automatic dose calculation, and creating automatic drugs interaction alerts (14, 15).

In addition to the above, the CPOEs developed based on clinical practice guidelines could improve the patient safety through minimizing the chemotherapy errors (16-18). Systematic reviews on drug dose monitoring and determination (19) and drug prescription and management (20) have demonstrated that the CPOEs supported with clinical decision support systems (CDSSs) improve drug order registration and reduce medication errors in the treatment process.

Some of the benefits of these systems include: updating guidelines and approved regimens; automatically calculating the drug dose and scheduling multiple-day treatments (21, 22). and oncologists will no longer need to recall complex equations for Body Surface Area (BSA) calculation, creatinine clearance, and drug concentration dose on the time curve, and this facilitates cumulative dose tracking (23). We appreciate that almost all of the recent COPEs utilize a form of clinical decision support system, so the focus of this review was the utilization of guidelines in the development of COPEs.

Limited research has been conducted on the effectiveness of guideline-based CPOE systems. A study by Pawloski et al. in 2019 aimed to examine decision support systems in oncology processes. Twelve out of 24 studies reviewed were related to the positive effect of CPOE on reducing prescribing errors, increasing safety, and improving work processes (21). Another study by Rahimi et al. (2019) conducted with the aim of investigating the impact of CPOE systems showed that CPOEs reduced drug-related errors, especially dose errors, and also reduced the time of the chemotherapy order process. However, there was insufficient evidence with respect to compliance with protocols and reduction of chemotherapy costs (24). Owing to the significance of guidelines as the most frequently used reference by oncologists in cancer treatment, the present study aimed to review the effects of guideline-based CPOE systems on chemotherapy order processes.

2. OBJECTIVE

The aim of study was to present review effects of guideline-based CPOEs on the chemotherapy order process.

3. METHODS

3.1. Information sources and search strategy

All stages of this systematic review were based on the 2009 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis). The search strategy was set for each database based on aims of research and the author's opinions by combining two groups of relevant keywords: keywords describing CPOE systems, and those describing chemotherapy (medical subject heading [MeSH], Truncation symbols and Boolean Operators). The search was then performed in PubMed, Scopus, Embase, Web of Science, and IEEE Xplore databases. The keywords used for searching the literature are listed in Box 1.

3.2. Eligibility criteria and study selection

Inclusion criteria: studies examining the effect of guideline-based CPOEs on the chemotherapy order process were included. Exclusion criteria: studies that examined CPOE systems, but did not use of guidelines were excluded. Moreover, studies on the technical evaluation of CPOE systems, and those that did not investigate the effects of CPOE on the chemotherapy order process were excluded. Non-original articles (e.g., review articles, editorials, poster papers, and protocols) were also excluded. In addition, we exclude articles that were not available in full text.

In the screening phase, three authors independently reviewed the titles and abstracts of the retrieved articles and excluded irrelevant studies based on inclusion and exclusion criteria. In the eligibility phase, three authors independently read the full text of all the pre-selected articles. Eventually, articles meeting the inclusion criteria were selected. Cases of disagreement on article selection were resolved by the fourth independent researcher. The bibliography of the included articles was also checked to identify other eligible articles.

Hand-searching was also performed in the Journal of

Study	Country	Study Design	Sample Size	Guideline	Study Setting	Study Population	CPOE
Lichtner et.al (2019)	Australia	Observational	827 voluntarily reported incidents relating to oncology patients	Not-specified	Inpatient and outpatient and home-based care	Pediatric	EMM
Reinhardt et.al (2019)	Germany	Observational	18,823 prescriptions	Not-specified	Inpatient and outpatient	Adult	CPOE tool for chemotherapy ordering
Chung et.al (2018)	USA	Pre-Post	100 prescriptions	NCCN	Inpatient and outpatient	Adult	Beacon EPIC systems
Aziz et.al (2015)	Pakistan	Pre-Post	9,279 chemotherapy orders	ISMP	Not-specified	Adult	Inbuilt system with CDSS
Cuervo et.al (2015)	Spain	Pre-post	207	ASHP guidelines	Inpatient and outpatient	Not-specified	ONCOWIN version 8.0
Martin et.al (2015)	USA	Observational	Not-specified	ASCO/ONS	Inpatient	Adult	CPOE for inpatient chemotherapy
Gandhi et.al (2014)	Canada	Observational	Not Available	ASCO, COSA, and CCO	Not-specified	Not-specified	OPIS (Oncology Patient Information System)
Meisenberg et.al (2014)	USA	Pre-Post	9,838 chemotherapy order sets	ASCO/ONS and ASHP	Inpatient and outpatient	Not-specified	Beacon system
Elsaid et.al (2013)	USA	Pre-post	1,192 chemotherapy orders	ASHP ASCO NCCN	Inpatient and outpatient	Pediatric and Adult	Siemens Medical Solutions' + (CDSSs) + (EDDSs), + barcode point-of-care medication administration system
Hanauer et al (2013)	USA	Pre-post	228 clinician hours	Not-specified	Inpatient	Not-specified	commercial CPOE system
Chen et.al (2011)	USA	Pre-Post	212 medication-related events	ASCO	Inpatient	Pediatric	MLM programming
Hoffman et.al (2011)	USA	Observational	Not Available	ASHP ASCO/ONS	Inpatient and outpatient	Pediatric	CPOE for chemotherapy at a children's cancer center
Markert et.al (2008)	Germany	Observational	22,216 chemotherapy orders	CSC-Blue Book	Inpatient and outpatient	Adult	Electronic chemotherapy ordering and prescription (eCOP) system
Small et.al (2008)	UK	Pre-Post	1941 prescriptions for chemotherapy	ASHP	Outpatient	Not-specified	VARIS MedOnc system
Crossno et.al (2007)	USA	Observational	Not Available	Pediatric Antiemetic Guidelines.	Outpatient	Pediatric	Ordering Pediatric Chemotherapy
DuBeshter et.al (2006)	USA	Pre-post	2,558 drug administrations in 235 patients treated with 26 different chemotherapy regimens.	ISMP	Outpatient	Pediatric and Adult	IntelliDose
Huertas Fernandez et.al (2006)	Spain	Cross-sectional	60 chemotherapy orders	ASHP	Not-specified	Not-specified	ONCOWIN
Voeffray et.al (2006)	Switzerland	Pre-Post	2,445 chemotherapy orders	Not-specified	Inpatient and outpatient	Adult	Inbuilt system (File Maker Pro)
Bouaud et al (2001)	France	Cross-sectional	127 decisions	Not-specified	Not-specified	Adult	OncoDoc

Table 1. Study Characteristics

National Comprehensive Cancer Network and Google Scholar. The most prominent authors were contacted with a request for grey literature, including conference papers having a full text, unpublished studies, and reports.

3.3. Data collection process

One author extracted the data from the articles, while the second and the third authors checked the extracted data. Cases of disagreement were resolved by discussions

between four authors.

3.4. Quality assessment

Quality assessment was performed for all included articles using 12 criteria selected based on the objectives of the study and the consensus of the research team.

Quality scores showed the overall application and effect of the studies. None of the studies met all the 12 criteria, but their total scores were moderate to high and, thus, acceptable for inclusion in the study.

4. RESULTS

4.1. Study selection

In the preliminary examination of the five databases, 9225 articles were retrieved and exported to Mendeley 1.19.4. In this stage, 4248 duplicates and 4957 irrelevant cases were detected based on checking the titles, abstracts, full texts, and the list of selected articles, and finally, 19 articles remained.

4.2. Source of studies

Of the 4977 retrieved articles, 19 articles met the eligibility criteria (Figure 1). The US had published the most papers (n=9) (5, 14, 25–31), followed by Germany (n=2) (8, 13), Spain (n=2) (32, 33), Canada (n=1) (34), Australia (n=1) (35), the UK (n=1) (36), Switzerland (n=1) (37), France (n=1) (38), and Pakistan (n=1) (39). The studies had pre-post (n=10) (5, 14, 26, 27, 29, 30, 32, 37–39), observational (n=7) (8, 13, 25, 28, 31, 34, 35), and cross-sectional designs (n=2) (33, 38).

4.3. Study characteristics

All of these studies were published between 2001 and 2019 and examined different aspects of CPOE systems discussed below. The extracted data on the efficacy dimensions and study parameters are listed in Table 1.

Medication errors from different perspectives

In two studies, after CPOE system implementation, chemotherapy drug prescription errors generally decreased by 75% (29). Moreover, the prescription errors reduced drastically from 30.6% to 2.2% when traditional handwritten method was replaced by a CPOE, and the incidence of errors that could harm the patient was reduced from 4.2% (with handwritten prescription) to 0.1% (with the CPOE system) (5). In a study by Small, computerized prescription decreased the errors by 42%. Moreover, errors occurred in 12% of the computerized prescriptions and 20% of spreadsheet prescriptions (36).

Two studies examined different dimensions of error reduction. One study was conducted on prescriptions issued five years after the system implementation. Before the implementation, 270 errors (37.5% of the total prescriptions) were detected from 143 prescriptions for 114 patients, and after implementation, 9 errors were detected from 134 prescriptions for 82 patients. These findings indicate that the CPOE's implementation significantly decreased medication errors (32). Another study compared the incidence of errors in CPOE and in manual prescriptions. The findings showed that at least one error was detected in 100% of the manual prescriptions and 13% of the computerized prescriptions. False-negative errors were dominant in the manual approach. Errors in interpretation, the use of abbreviations, and illegible handwriting were frequent in handwritten prescriptions but were not identified in computerized prescriptions (33).

Eleven studies investigated the effect of COPE on medication errors (5, 8, 14, 26, 29, 32, 33, 36–39), while other studies examined other aspects of CPOE efficacy.

The incidence and severity of chemotherapy protocol errors and the time of the chemotherapy order process

Two studies compared the incidence and severity of chemotherapy protocol errors between manual and CPOE in an adult setting. The first study reported a decrease in the number of medication errors in the manual system compared to the computerized system (2.43 vs. 0.26), as well as a reduction in the chemotherapy duration while dispensing in chemotherapy protocols. Drug intervention acceptance was higher with CPOE (85.3 vs. 91.1%), demonstrating a higher accuracy. Therefore, the chemotherapy CPOEs significantly decreased the incidence and severity of medication errors, improved the chemotherapy order process during dispensing, reduced the chemotherapy time, and decreased the chemotherapy costs (39).

Another study evaluated the effect of the CPOEs on the number of prescription errors recorded by the pharmacy service. Before the CPOE implementation, 141 errors were recorded for 940 prescribed chemotherapy regimens (15%), after launching the system, 75 errors were recorded for 1505 prescribed chemotherapy regimens (5%). Of these errors, 69 cases (92%) were recorded in prescriptions that did not follow the computer protocol. A remarkable reduction in the number of errors was observed when 50% of chemotherapy protocols were prescribed by the CPOE system (37).

Safety, policy compliance and communication between health care providers

Four studies examined the effects of CPOEs in pediatric settings. In the one study, over nine months, 30 medical logic modules and 110 prescription sets were developed for pediatric oncology support. The ratio of chemotherapy orders submitted using a specific research protocol or a set of standard care prescriptions was increased from 57 to 84%. The number of drug-related patient safety events was reduced by 39% after CPOE system (30).

A study of the four studies examined the use of a CPOE for improving safety, accordance with policies, and the communication between healthcare providers during chemotherapy prescription. According to the findings, the system could promote a safe chemotherapy prescription process, the accordance with policies, communication between physicians, pharmacists, and healthcare personnel. Indeed, it could help automatic calculations and could standardize the chemotherapy prescriptions.

Another study demonstrated that with careful planning, CPOEs could be safely used for chemotherapy. Moreover, the extensive use of electronic prescription sets, re-designing the official process and system analysis, accurate and strategic use of CDSS, a stepwise implementation approach, and interactions with software providers are essential for a safe and usable CPOE or chemotherapy (28). An analysis of patient safety event reports revealed that, of 827 candidate events related to pediatric

oncology patients, 79% (n = 651) were drug-related, of which 45% (n = 294) were Electronic Medication Management system related. The drug-related events included: prescription, dispensing, management, administration, forgetting the chemotherapy protocol and current treatment stage information, chemotherapy management coordination, and medication handling.

Physicians prescribing behavior

A study was conducted on therapeutic decisions for breast cancer patients before and after the use of a CPOE to assess the system's effect on the physician prescribing behavior. After four months, 127 decisions were recorded, and the physicians' compliance with the system was significantly improved to 85.03%. A comparison of the initial and final decisions revealed that physicians modified their prescriptions in 31% of cases, most of which were based on system recommendations (62% of the cases). In the clinical trial, the adherence rate was enhanced by 50%. This study was conducted on a small sample, and a larger-scale assessment was suggested for further analysis (38).

Errors related to the dose and time required for chemotherapy prescriptions

Some studies evaluated the medication dose errors and the time required for chemotherapy order preparation. These studies also identified medication errors and the potential rate of adverse drug effects (ADE) in the chemotherapy setting. Out of 2558 prescriptions for 235 patients treated with 26 chemotherapy regimens, no errors occurred in dose calculation, decimal places, or medication choice. The dose alarm level exceeded the limit in 152 cases of prescription (6%) but the users were not allowed to override the alarm. The mean time saved per prescription was 10 minutes (26).

Quality and safety of treatment

In a study by Markert et al. conducted to improve cancer treatment quality and safety using a CPOEs, over two years, 22216 chemotherapy prescriptions were sequentially analyzed, of which 83.5% were completely error-free. Moreover, 17.1% of medical and administrative errors were detected and refined, 3.8% of which dealt with chemotherapy, 4.5% of which with patient data, and 8.7% with a lack of informed consent form. The chemotherapy errors were fewer in outpatients than inpatients (3.3 vs. 4.5%). In outpatients, the chemotherapy errors were reduced from 4% in 2005 to 2.8% in 2006; however, no change was reported for inpatients (4.4% in 2005 vs. 4.7% in 2006). Only three out of 3,792 identified errors were patient related (0.079%) (13).

Effect of CPOE on prevention of chemotherapy prescription errors

In 2019, Reinhardt et al. studied the reasons, potential consequences, and prevention of chemotherapy prescription errors. Within 24 months, 406 chemotherapy prescription errors were tracked which affected 375 cases (2%) of all prescriptions. In 279 cases (1.5%), the errors were categorized as clinical. In these cases, some potential consequences, e.g., reduced therapeutic efficacy (0.44%), the need for enhanced monitoring (0.48%), prolonged hospitalization (0.55%), and mortality (0.02%), were prevented. The most efficient common measures to prevent errors include examining the prescription history and the patient's medical records, and having accurate knowledge about chemotherapy protocols. The findings showed that 61% of errors were prevented following further software development. The identified improvements were implemented through the next generation of the CPOE system (8). One study explored the effects of standardized electronic chemotherapy prescription models on the incidence of prescription errors in an ambulatory cancer center before and after implementing a CPOEs. The results showed a 30% reduction in prescription errors after the intervention. Implementing standardized chemotherapy-prescribing templates significantly reduced all types of prescribing errors and improved chemotherapy safety (14).

Workflow, direct patient care time

Two studies were designed only for inpatients, aiming to quantify the effect of CPOE implementation on hospital workflow, with an emphasis on prescription and direct patient care time. A chemotherapy prescribing system was developed and implemented in an academic institute via a commercial CPOE system. The participants were observed for 228 hours during 53 sessions. A slight change was found in the proportion of census-adjusted time for prescription (10.2% before and 11.4% after the prescription) and direct patient care (50.7% before and 47.8% after).

The fragmentation in the workflow was reduced, and the time spent by providers on a continuous task was 131.2 seconds before and 218.3 seconds after the implementation of system. Moreover, an eightfold reduction was observed in the number of pages. The workflow was enabled to obtain the provider's confirmation status in real-time during dispensing. A prescription display system in the EMR showed the chemotherapy dose-related parameters, including previous height and weight measurements, dose adjustments, provider confirmation, previous chemotherapy regimens, and a summary of the standard regimen for reference. This system was activated with 127 chemotherapy programs, which were then expanded to 189 programs. The staff reported that, in the second year of system use, safety events were reduced, especially in terms of prescription and transcription. Implementation findings demonstrated that the CPOE can be safely used in inpatient chemotherapy, even in a very complex setting (27,31).

Adherence to guidelines

There were 15 studies that clearly employed a guideline for system design (5, 13, 14, 25, 26, 28–34, 36, 37, 39), while four studies did not clearly state this use (8, 27, 35, 38).

5. DISCUSSION

This systematic review investigated the effects of guideline-based CPOEs in the chemotherapy order process. Based on the review of articles included in this study, it is inferred that in the design of CPOEs, the guidelines were either not considered or, if used, were not explicitly mentioned in the studies. The results showed that most CPOEs lead to a significant reduction in chemotherapy-related

errors (11 out of 19) (5, 8, 39, 14, 26, 29, 32, 33, 36-38). Although chemotherapy improvement and error reduction were reported by all these studies, and most of them only used systems with a basic CDSS (29).

The use of computer systems in healthcare has played an important role in improving service delivery to patients (40, 41). In the treatment of cancer patients, there is evidence of the effectiveness of using CPOEs in the chemotherapy orders process (34). Studies exploring the effect of CPOE on the chemotherapy order process revealed that, during dispensing, the incidence and severity of medication errors (39), the rate of medication errors (29, 34) and especially chemotherapy-related medication errors (32, 33), the number of errors during prescription, and the number of errors recorded by the pharmacist (37) were considerably reduced after computerizing only 10% of the protocols in CPOE compared to the manual system (39), However, according to Meisenberg et al., although CPOE reduced the number of problematic and erroneous chemotherapy prescriptions, it did not completely resolve all the errors (5).

Based on these findings, a reduction in prescription errors in chemotherapy led to optimal outcomes, including patient safety. Based on the literature, a reduction in chemotherapy errors by using CPOE can contribute to a safe chemotherapy prescription process (25). It can also improve chemotherapy safety by implementing standard chemotherapy prescription models and significantly reducing prescription and dose calculation errors (14).

Medication prescription errors have the potential for adverse outcomes for patient care. The use of CPOE in medication prescription directly affects the reduction in medication errors, the number of prescribing errors, and patient safety; this effect is long-term and improves patient safety indices (34, 37). Thus, by CPOE implementation, it is possible to ensure that chemotherapy orders processes are followed safely (33). If CPOE is updated and popularized in various treatment centers, the level of safety standards will increase, thereby benefiting more patients (8). Cooperation and giving feedback to software vendors is critical to a safe and usable CPOEs for chemotherapy (28).

In addition to decreasing medication errors, CPOEs can improve chemotherapy dispensing time, reduce chemotherapy costs (39), and provide a cost-effective treatment approach (14). Moreover, by using error analysis algorithms, several chemotherapy prescription errors can be resolved without loss of system efficiency (26). CPOE can also have other important functions, e.g., clinical decision support, improvement of adherence to clinical practice guidelines, and data collection (34). Planning for the extensive use of electronic prescription sets, re-designing processes and system analysis, accuracy and strategic use of clinical decision support, and a stepwise implementation approach are critical to safe CPOE implementation for chemotherapy (28). Other advantages of CPOEs for institutes include user satisfaction (29); improved communication between physicians, pharmacists, and the nursing staff; automatic calculations and standardization of chemotherapy prescriptions based on institution policies (25); compatibility with healthcare institutes of various scales (14); qualitative support for nurses (42); the use of standard prescribing templates, ongoing medicinal control and nursing to reduce prescription defects (43). CPOEs can also eliminate safety issues with the chemotherapy dose through creating a chemotherapy dose summary for the physicians and pharmacists. A customized display system was embedded in the EMR to provide a single screen view of the relevant parameters of chemotherapy doses including current and previous patient measurements of height and weight, dose adjustments, provider verifications, prior chemotherapy regimens, and a synopsis of the standard regimen for reference (31).

In addition to the benefits of CPOE, there are other points to consider First, the appropriate design and ease of use for physicians can minimize human errors and, eventually, promote patient safety (32). Second, according to Reinhardt et al., 30-40% of the electronic errors cannot be prevented; therefore, medication monitoring practices are still necessary (8). Third, the automatic nature of CPOEs has contributed to the occurrence of some incidents. Considering the effects of high-risk settings on patient safety, the users should be aware of the automatic system capabilities and receive training for troubleshooting (36). The use of multidisciplinary teams can potentially influence patient care (44), but therapeutic protocols for chemotherapy prescription should not be neglected in the design of the system. Comprehensive evaluation of system performance with appropriate user interfaces and staff training to ensure the optimal use of such systems are also essential (36). The automatic rounding off in these systems can reduce the time of chemotherapy prescription and dose fragmentation (45). Still, the presence of oncology pharmacists is crucial to ensuring safe and appropriate chemotherapy prescription (46) because, in some CPOE systems, the computer cannot evaluate the chemotherapy protocols or adjust antineoplastic drug dosage based on patient conditions. Based on the review of the studies, their limitations, and the diversity in CPOEs, it appears that no definitive conclusion of the findings can be made. Some of these limitations include:

a) The system evaluation results are not generalizable due to implementation in a specific setting or a center with few patients or prescriptions or data collection in a single university center with fully standard procedures;

b) The clinical outcomes related to medication errors have not been examined, such that the clinical outcomes of reduced medication error cannot be used. Additionally, it is impossible to assess why there are so few medication errors with CPOE implemented;

c) Error classifications in some studies reflect only the pharmacist's opinion and belongs to the prescribing stage only;

d) The evaluations are biased, e.g., conducting a survey six months after implementation and during major system progress, uncontrolled evaluation in which the increase/decrease in the recorded safety events cannot be attributed to the interventions. Furthermore, the actual side-effect incidence rates might differ from what the re-

porting systems show because these systems may not detect the actual rate of medication side effects;

e) Inferential statistics have not been calculated and the prescribing system has not been integrated with therapeutic program documents;

f) Management has been disrupted, indicating that workflow issues following CPOE implementation;

g) The benefits and effectiveness of such systems in relation to errors events were not reported by users.

Considering the evaluation of different studies on CPOE and the sharing of experiences with other institutions, it is expected that any institute will be able to achieve a safe and successful system implementation with maximum efficiency.

6. CONCLUSION

There is still a dearth of clinical outcome evaluation data about CPOEs in relation to patient care and safety during chemotherapy. Evidence indicates that these systems can positively affect the quality of care for patient with cancer. Most of them merely discussed improved patient care quality and reduced rate of medication errors; however, these systems cannot decrease all types of errors, and new sources of errors can emerge after implementation and process alteration. Nevertheless, the sources of new errors are not mentioned in any of the studies

Finally, there has been limited research concerning the design of CPOEs based on guidelines there is little information in this regard; Therefore, further studies are required to determine the advantages or disadvantages of these systems.

- **Author's contribution:** S.S., R.R. and Hr.M contributed to the conception and design of the work. S.S. drafted the manuscript, performed data collection and conducted the analysis in collaboration with R.R. and Hr.M. A.R. analyzed the data in collaboration with R.R. and S.S. and revised the manuscript critically. Hr.M. contributed to the interpretation of data and revised the manuscript critically. M.Sh. revised the manuscript critically. All authors approved the final version of the submitted manuscript.
- **Conflicts of interest:** There are no conflicts of interest.
- **Financial support and sponsorship:** None.

REFERENCES

1. Ferlay J, Colombet M, Soerjomataram I, Parkin DM, Piñeros M, Znaor A, et al. Cancer statistics for the year 2020: an overview. International Journal of Cancer. 2021;
2. Clauser S, Wagner E, Bowles E, … LT-A journal of, 2011 undefined. Improving modern cancer care through information technology. Elsevier [Internet]. [cited 2022 Jan 5]; Available from: https://www.sciencedirect.com/science/article/pii/S074937971100095X
3. Bryant-Bova JN. Improving Chemotherapy Ordering Process. Journal of oncology practice. 2016; 12(2): e248–56.
4. Walsh K, Dodd K, … KS-J of C, 2009 undefined. Medication errors among adults and children with cancer in the outpatient setting. academia.edu [Internet]. 2008 [cited 2022 Jan 5]; Available from: https://www.academia.edu/download/39833209/891.pdf
5. Meisenberg BR, Wright RR, Brady-Copertino CJ. Reduction in chemotherapy order errors with computerized physician order entry. J Oncol Pract. 2013/09/05. 2014; 10(1): e5-9.
6. Pirnejad H, Gao C, Reddingius R, Rijneveld A, Bal R. Improving chemotherapy processes with a protocol-based information system: A pre and post-implementation study. International journal of medical informatics. 2013; 82(4): 220–229.
7. Goldspiel B, Hoffman J, … NG-AJ of, 2015 undefined. ASHP guidelines on preventing medication errors with chemotherapy and biotherapy. academic.oup.com [Internet]. [cited 2022 Jan 5]; Available from: https://academic.oup.com/ajhp/article-abstract/72/8/e6/5111768
8. Reinhardt H, Otte P, Eggleton AG, Ruch M, Wohrl S, Ajayi S, et al. Avoiding chemotherapy prescribing errors: Analysis and innovative strategies. Cancer [Internet]. 2019 May; 125(9): 1547–1557. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L626180232
9. Weingart S, Zhang L, Sweeney M, Oncology MH-TL, 2018 undefined. Chemotherapy medication errors. Elsevier [Internet]. [cited 2022 Jan 5]; Available from: https://www.sciencedirect.com/science/article/pii/S1470204518300949
10. Teich JM, Schmiz JL, O'Connell EM, Fanikos J, Marks PW, Shulman LN. An information system to improve the safety and efficiency of chemotherapy ordering. In: Proceedings of the AMIA Annual Fall Symposium. American Medical Informatics Association; 1996: 498.
11. Kim GR, Chen AR, Arceci RJ, Mitchell SH, Kokoszka KM, Daniel D, et al. Error reduction in pediatric chemotherapy: computerized order entry and failure modes and effects analysis. Archives of pediatrics & adolescent medicine [Internet]. 2006 May; 160(5): 495–498. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L43708183
12. Barreto J, Griffith N. Standardizing Chemotherapy Orders for CPOE.
13. Markert A, Eronique Thierry V, Kleber M, Behrens M, Engelhardt M. Chemotherapy safety and severe adverse events in cancer patients: Strategies to efficiently avoid chemotherapy errors in in-and outpatient treatment. 2008 [cited 2021 May 14]; Available from: www.interscience.
14. Elsaid K, Truong T, Monckeberg M, McCarthy H, Butera J, Collins C. Impact of electronic chemotherapy order forms on prescribing errors at an urban medical center: results from an interrupted time-series analysis. International journal for quality in health care : Journal of the International Society for Quality in Health Care. 2013/10/18. 2013 Dec; 25(6): 656–663.
15. Levy MA, Giuse DA, Eck C, Holder G, Lippard G, Cartwright J, et al. Integrated information systems for electronic chemotherapy medication administration. Journal of Oncology Practice [Internet]. 2011 Jul [cited 2022 Jan 5];7(4): 226–230. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L362971653
16. Seidling HM, Stutzle M, Hoppe-Tichy T, Allenet B, Bedouch P, Bonnabry P, et al. Best practice strategies to safeguard drug prescribing and drug administration: an anthology of expert views and opinions. International Journal of Clinical Pharmacy [Internet]. 2016 Apr; 38(2): 362–373. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L608975374
17. Wolfstadt JI, Gurwitz JH, Field TS, Lee M, Kalkar S, Wu W, et al. The effect of computerized physician order entry with clinical decision support on the rates of adverse drug events: A systematic review. Journal of General Internal Medicine. 2008 Apr; 23(4): 451–458.
18. Kaushal R, Shojania KG, Bates DW. Effects of computerized physician order entry and clinical decision support systems on medication safety: A systematic review. Archives of Internal Medicine [Internet]. 2003 Jun; 163(12): 1409–1416. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L36758913
19. Nieuwlaat R, Connolly SJ, Mackay JA, Weise-Kelly L, Navarro T, Wilczynski NL, et al. Computerized clinical decision support systems for therapeutic drug monitoring and dosing: a decision-maker-researcher partnership systematic review. Implementation Science. 2011; 6(1): 90.
20. Hemens BJ, Holbrook A, Tonkin M, Mackay JA, Weise-Kelly L, Navarro T, et al. Computerized clinical decision support systems for drug prescribing and management: a decision-maker-researcher partnership systematic review. Implementation science : IS [Internet]. 2011 Aug; 6: 89. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L560064114

21. Pawloski PA, Brooks GA, Nielsen ME, Olson-Bullis BA, P.A. P, G.A. B, et al. A Systematic Review of Clinical Decision Support Systems for Clinical Oncology Practice. Journal of the National Comprehensive Cancer Network : JNCCN [Internet]. 2019 Apr; 17(4): 331–338. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L2001810836
22. Page N, Baysari MT, medical JW-I journal of, 2017 undefined, Westbrook JI. A systematic review of the effectiveness of interruptive medication prescribing alerts in hospital CPOE systems to change prescriber behavior and improve patient safety. International journal of medical informatics [Internet]. 2017 Sep [cited 2022 Jan 5]; 105: 22–30. Available from: https://www.sciencedirect.com/science/article/pii/S1386505617301600
23. Devine E, Hansen RN, Wilson-Norton JL, Lawless NM, Fisk AW, Blough DK, et al. The impact of computerized provider order entry on medication errors in a multispecialty group practice. Journal of the American Medical Informatics Association : JAMIA. 2010; 17(1): 78–84.
24. Rahimi R, Moghaddasi H, Rafsanjani KA, Bahoush G, Kazemi A. Effects of chemotherapy prescription clinical decision-support systems on the chemotherapy process: A systematic review. International journal of medical informatics. 2019 Feb; 122: 20–26.
25. Crossno CL, Cartwright JA, Hargrove FR, C.L. C, J.A. C, F.R. H, et al. Using CPOE to improve communication, safety, and policy compliance when ordering pediatric chemotherapy. Hospital Pharmacy [Internet]. 2007; 42(4): 368–373. Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-34247358270&partnerID=40&md5=1f88174b23ffeaaccee2b962147afaa7
26. Dubeshter B, Walsh CJ, Altobelli K, Loughner J, Angel C. Experience with computerized chemotherapy order entry. J Oncol Pract. 2006/03/01. 2006 Mar; 2(2): 49–52.
27. Hanauer DA, Zheng K, Choi SW, Beasley R, Schumacher J, Duck M, et al. Impact of CPOE on workflow and direct patient care time in an inpatient hematology/oncology service. Journal of Clinical Oncology [Internet]. 2010; 28(15). Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L70260365
28. Hoffman JM, Baker DK, Howard SC, Laver JH, Shenep JL, J.M. H, et al. Safe and successful implementation of CPOE for chemotherapy at a children's cancer center. JNCCN Journal of the National Comprehensive Cancer Network [Internet]. 2011/05/20. 2011 Feb; 9 Suppl 3(SUPPL. 3): S36-50. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L361450612
29. Chung C, Patel S, Lee R, Fu L, Reilly S, Ho T, et al. Implementation of an integrated computerized prescriber order-entry system for chemotherapy in a multisite safety-net health system. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists [Internet]. 2018/03/11. 2018 Mar; 75(6): 398–406. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L621177329
30. Chen AR, Lehmann CU. Computerized provider order entry in pediatric oncology: Design, implementation, and outcomes. Journal of oncology practice [Internet]. 2011/11/02. 2011 Jul; 7(4): 218–222. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L362971649
31. Martin DB, Kaemingk D, Frieze D, Hendrie P, Payne TH, D.B M, et al. Safe Implementation of Computerized Provider Order Entry for Adult Oncology. Applied clinical informatics [Internet]. 2015 [cited 2021 Mar 8]; 6(4): 638–649. Available from: /pmc/articles/PMC4704034/
32. Cuervo MS, Sanchis AR, Lopez CP, de Silanes E, Caro TG, Vicedo TB, et al. The impact of a computerized physician order entry system on medical errors with antineoplastic drugs 5years after its implementation. J Clin Pharm Ther [Internet]. 2015; 40(5): 550–554. Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-84940994364&doi=10.1111%2Fjcpt.12305&partnerID=40&md5=2f11cad5567c9f97597f50b1379f736f
33. Huertas Fernández MJ, Baena-Cañada JM, Martínez Bautista MJ, Arriola Arellano E, García Palacios M V, Huertas Fernandez MJ, et al. Impact of computerised chemotherapy prescriptions on the prevention of medication errors. Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico. 2006/12/01. 2006 Nov;8(11):821–5.
34. Gandhi S, Tyono I, Pasetka M, Trudeau M, S G, I T, et al. Evaluating an oncology systemic therapy computerized physician order entry system using international guidelines. Journal of Oncology Practice [Internet]. 2014 Mar [cited 2020 Jul 2];10(2):e14–25. Available from: https://pubmed.ncbi.nlm.nih.gov/24254406/
35. Lichtner V, Baysari M, Gates P, Dalla-Pozza L, Westbrook JI. Medication safety incidents in paediatric oncology after electronic medication management system implementation. Eur J Cancer Care (Engl). 2019/08/23. 2019;28(6):e13152.
36. Small MDC, Barrett A, Price GM. The impact of computerized prescribing on error rate in a department of Oncology/Hematology. J Oncol Pharm Pract. 2008/08/30. 2008 Dec;14(4):181–7.
37. Voeffray M, Pannatier A, Stupp R, Fucina N, Leyvraz S, Wasserfallen J-BB, et al. Effect of computerisation on the quality and safety of chemotherapy prescription. Quality and Safety in Health Care [Internet]. 2006/12/05. 2006 Dec;15(6):418–21. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L46025153
38. Bouaud J, Séroussi B, Antoine ÉC, Zelek L, Spielmann M. A before-after study using oncodoc, a guideline-based decision support-system on breast cancer management: Impact upon physician prescribing behaviour. In: Studies in Health Technology and Informatics [Internet]. IOS Press; 2001 [cited 2021 Jun 1]. p. 420–4. Available from: https://ebooks.iospress.nl/doi/10.3233/978-1-60750-928-8-420
39. Aziz MT, Ur-Rehman T, Qureshi S, Bukhari NI. Reduction in chemotherapy order errors with computerised physician order entry and clinical decision support systems. The HIM journal [Internet]. 2015/10/16. 2015;44(3):13–22. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L614593866
40. Garavand A, Rabiei R, Emami H, Pishgahi M, Vahidi-Asl M. The attributes of hospital-based coronary artery diseases registries with a focus on key registry processes: A systematic review. Health information management : journal of the Health Information Management Association of Australia [Internet]. 2020 [cited 2021 Oct 7]; Available from: https://pubmed.ncbi.nlm.nih.gov/32677480/
41. Tabrizi AT, Moghaddasi H, Rabiei R, Sharif-Kashani B, Nazemi and E. Development of a Catheterization and Percutaneous Coronary Intervention Registry with a Data Management Approach: A Systematic Review. Perspectives in Health Information Management [Internet]. 2019 Dec 1 [cited 2021 Oct 7];16(Winter). Available from: /pmc/articles/PMC6341417/
42. Lopes VJ, Shmeil MAH. Evaluation of computer-generated guidelines for companions of paediatric patients undergoing chemotherapy. Revista gaucha de enfermagem. 2017 Apr;37(spe):e67407.
43. Mertens WC, Brown DE, Parisi R, Cassells LJ, Naglieri-Prescod D, Higby DJ. Detection, classification, and correction of defective chemotherapy orders through nursing and pharmacy oversight. Journal of Patient Safety [Internet]. 2008;4(3):195–200. Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-67650245399&doi=10.1097%2FPTS.0b013e3181858370&partnerID=40&md5=e4d3b853452762bf2fd15d94f90da42a
44. Valencia FS, Ruiz R, Neciosup SP, Mas LA, Aliaga KM, Huaman F, et al. Implementation of Computerized Physician Order Entry for Chemotherapy: A Latin American Experience. JCO clinical cancer informatics. 2019/01/18. 2018 Dec;2:1–12.
45. Tsuda K, Kimura YN, Tanimoto T, Takaba Y, Okubo K, Ishii T, et al. Impact of the automatic rounding-off function of the computerized physician order entry system on the ordering time and dose dispersion of chemotherapeutic drugs in regimens for hematologic malignancies. International Journal of Medical Informatics. 2016 Jan; 85(1): 76–79. Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-84951320598&doi=10.1016%2Fj.ijmedinf.2015.10.006&partnerID=40&md5=e4bc39ea93907b19fc3150700d2054f0
46. Suzuki S, Chan A, Nomura H, Johnson PE, Endo K, Saito S. Chemotherapy regimen checks performed by pharmacists contribute to safe administration of chemotherapy. Journal of Oncology Pharmacy Practice [Internet]. 2015/11/13. 2017 Jan;23(1):18–25. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L613785406