Chapter 10
Chemotherapy and Medication Safety

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Background/Overview

The use of antineoplastic agents provides substantial benefits to pediatric patients with cancer, but also come with significant risk as these medications have high toxicity profiles and narrow therapeutic indexes. The pediatric population is at particular risk due to the complexity of regimens, need for frequent dose changes, and age- and weight-based dosing. Although the literature regarding chemotherapy error rates in the outpatient pediatric oncology setting is limited, one study reported that 18.8% of pediatric visits were associated with a medication error, and 4.3 (95% CI, 2.3–4.2) per 100 visits were associated with a chemotherapy error specifically [1].

Causes for medication errors are multifactorial and can be attributed to communication defects; information gaps; confusion related to drug names, labels, directions, and packaging; competency; and education (staff and patients) among others. They can occur at any step of the medication use process of prescribing, preparing, dispensing, and administration. The medication use process is complex, involving multiple interacting clinical systems, staff from different disciplines, and work environments that are stressful with many interruptions. When determining what changes should be implemented to improve the safety of the medication use process, it is important to utilize a systems approach and look at the entire process instead of responding only to single events. The analysis of patterns/trends and vulnerabilities in the medication use process are essential to eliminate or minimize

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risks of errors reaching the patient. This chapter will outline strategies for measurement, improvement strategies, and sustainability to ensure safe chemotherapy and medication practices and processes.

Measurement

Introduction

Quality expert H. James Harrington stated that "measurement is the first step that leads to control and eventually to improvement. If you can't measure something, you can't understand it. If you can't understand it, you can't control it. If you can't control it, you can't improve it" [2]. In all forms of quality improvement, it is extremely difficult to create solutions to a problem until you truly understand its scope. Measuring medication errors as they relate to chemotherapy is critical in identifying areas that are in need of safety improvements. The measurement of these errors, however, remains a difficult field that is clouded by issues of nomenclature and the nature of reporting systems. This section of the chapter will focus on outlining the components that contribute to a medication error and how these components can be captured in order to allow for analysis and appropriate implementation of safe practices. All of the reviewed methods have distinct advantages and disadvantages, and no study has shown the clear advantage of one stand-alone system. The impetus is then placed on each hospital and patient care setting to find the best combination of these methods that maximize identifying serious preventable medication events while efficiently allocating resources. Ensuring proper measurement techniques will ultimately allow for trending medication errors after implementation of system changes and aid in creating sustainability for patient safety regarding chemotherapy and other medications.

Classification of Severity of Medication Errors

The World Health Organization (WHO) has adopted the definition of a medication error as "a failure in the treatment process that leads to, or has the potential to lead to, harm to the patient" [3]. An adverse drug event (ADE) is defined as any injury resulting from medical interventions related to a drug [4]. A key component in understanding medication errors is identifying the severity of the incident [5]. For the most efficient use of resources, many organizations focus their efforts on identifying those errors with the greatest potential harm to the patient as the most important to drill down and understand processes that could be improved. This can be accomplished by designating categories of severity for chemotherapy errors. The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) has established an index that helps better define the severity of medication errors (Fig. 10.1) [6]. This severity index can be applied to all medication

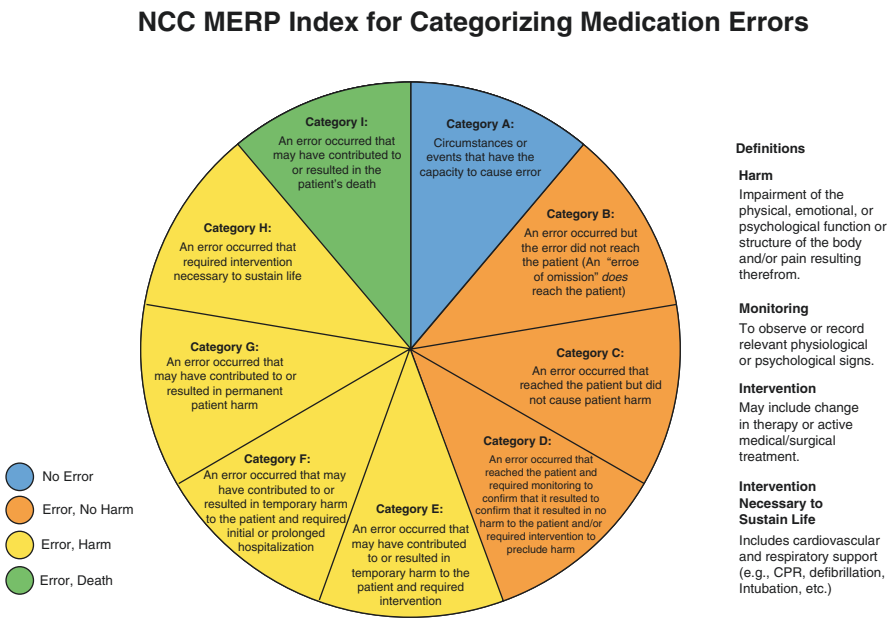

Fig. 10.1 Severity index for categorizing medication errors from NCC MERP (Used with permission. © 2001 National Coordinating Council for Medication Error Reporting and Prevention)

errors involved in the care of hematology and oncology patients including both chemotherapy and supportive care medications. Many other severity indexes are available, and institutions can tailor which index helps them discover and address their ADEs in the most efficient manner.

Classification of Processes Involved in Medication Errors

The processes that lead to medication errors related to chemotherapy mimic those involved in general medication errors. With the unique complexity and toxicity of these medications, however, the risk to the patient can increase greatly when an error does occur [7]. The areas in which chemotherapy medication errors can occur include the time of prescribing, preparing, dispensing, administering, and monitoring a medication (e.g., see Table 10.1). In many chemotherapy errors, there are numerous processes at play that contribute to the ultimate error taking place. Even within one location, there may be many issues that contribute to an error. With respect to prescribing errors, many medical facilities continue the practice of ordering chemotherapy via paper utilizing handwritten orders as opposed to computerized physician order entry (CPOE). This process can lead to numerous potential errors that may have been caught and otherwise eliminated by utilizing the process checks built into CPOE such as elimination of hand-writing interpretation errors

Table 10.1 The processes where errors can occur while a patient receives chemotherapy and common errors associated with each procedure

Error location	Examples of errors
Prescribing	Wrong dosing weight and height are used while calculating chemotherapy dose (mg/m^2 vs. mg/kg) Wrong unit of measure utilized (milligram vs. microgram) Incorrect or absent dose adjustment based on prior toxicity
Preparing	Incorrect diluent selected Prepared with wrong volume
Dispensing	Product labeled incorrectly (wrong patient, wrong drug) Lack of verification that correct drug, diluent, and dose have been prepared by chemotherapy pharmacist
Administration	Administered to wrong patient Infused over incorrect time (IV push vs. 3-h infusion) Administered via inappropriate route (IV vs. IT) Infusion pump is programmed incorrectly
Monitoring	Failure to identify toxic levels of a drug Inappropriate monitoring for acute toxicities after administration of a drug (e.g., anaphylaxis)

and utilities such as dose calculators [8]. Coupled with severity classification, identifying and appropriately labeling the various processes involved in each error can help ensure accurate measurement and subsequent interpretation of the events that lead to a chemotherapy error.

Medication Error Measuring Systems

In 1999, the Institute of Medicine published a report that outlined significant patient safety concerns through the medical system in the United States and outlined recommendations on how to measure and address these concerns [9]. The report elucidated that voluntary reporting systems have the best means to focus on patient safety improvement in the field of medication safety. These types of systems usually evaluate errors that resulted in minimal or no harm to patients, and analyzing these errors can lead institutions to identify and address vulnerabilities in their systems before harm occurs [9, 10]. Following the release of this report, there was a large growth and advancement in medication error reporting systems. One recent review cited over 12 various types of medication error reporting systems available [11]. Since that time with the help of technological advances within electronic medical record (EMR) information systems, automated medication event reporting systems have been implemented as well. With the many variations on measuring and reporting systems, medical institutions are now burdened with identifying which systems can help provide a balance between resources available and identifying patient safety concerns. Outlined in the following sections are the most commonly used reporting systems and analysis of the benefits and potential concerns of each.

Incident Reporting Systems

Incident reporting systems utilize structured data collection to input medication error information. These systems are all confidential and can vary from anonymous to non-anonymous reporting strategies. [12] Incident reporting systems are the most commonly utilized measurement system, and numerous reporting systems exist in healthcare in both local hospital systems and nationally [13]. Several countries have developed national adverse medication event systems, such as the UK's National Reporting and Learning System (NRLS), which have allowed findings to be applied to a wider system and have a national affect [14]. On average over 1.5 million incident reports are submitted each year to the NRLS. In the United States, the Patient Safety and Quality Improvement Act of 2005 established a voluntary reporting system that utilizes patient safety organizations through the Agency for Healthcare Research and Quality in an attempt to standardize and nationalize incident reporting [15]. The benefits and concerns of these varied reporting systems can be applied fairly universally. These systems have been identified as being relatively easy to implement and are generally of low cost to a health system [11]. This system allows frontline staff who were directly involved in the incident to input data in a structured format that is submitted to be reviewed via the hospital systems' designated review structure. Examples of standardized systems include MEDMARX and the MedWatch program from the US Food and Drug Administration (FDA) [16, 17]. Table 10.2 outlines the components required for documentation of an incident report using the MedWatch system from the FDA.

While this type of measurement system may be easily implemented at relatively low cost, there exist several concerns regarding its stand-alone efficacy. Volunteer incident reporting systems can be impacted significantly by reporter bias [12, 18, 19]. They have been shown to identify only a small percentage of target problems

Table 10.2 Components required in documentation of incident report as outlined from MedWatch from the US FDA

Category	Details
Patient information	Patient identifier (MRN/FIN), age, sex, height, weight, ethnicity/race
Type of event	Adverse event, product defect
Outcome	Death, life-threatening, hospitalization—initial or prolonged, other serious, required intervention to prevent permanent impairment/damage, disability or permanent damage, congenital anomaly/birth defects
Chronology/location	Date, time, location/hospital unit
Event description	Free text area for thorough event description
Relevant tests/laboratory data	Any additional testing necessary secondary to the event that would not have been obtained otherwise
Suspected medication	Name, dose, route, frequency, length of infusion time
Indication for use	Diagnosis or problem indicated for use of medication

and are dependent upon the involved parties accurately filling out details that are critical for analysis of the event [19]. An additional concern is that physicians have relatively low error reporting rates. One study which surveyed over 1600 hospitals reported that at 86% of hospitals, physicians submitted few or no incident reports [18]. With the complexities of chemotherapy and biotherapies in the practice of pediatric hematology/oncology and bone marrow transplant, physician contribution to error reporting is critical. While these concerns can overlap with many of the other reporting systems, a more specific concern is that events are reported without clearly identifying the total numbers of patients at risk for such an event [19]. This may allow for analysis of trends of error types over time, but does not allow for assessment of which populations are at most risk and who would benefit the most from intervention based on incident report review. Medication error measurement via incident report submission and review involves having a structured review process. Often multidisciplinary teams are involved in the review process, identification of potential preventable errors, and creation of subsequent system changes. This system of a review and subsequent feedback loop to correct and prevent errors is a critical element of all measurement systems.

Chart Review

Utilizing chart review as a form of medication error measurement builds upon many of the processes involved with incident report creation. Chart review does this in a retrospective manner in surveying patient's medical records prior to an error being reported and attempting to identify issues in a timely manner [11, 20]. The process of chart review often involves evaluating many components of the medical record including medication administration record (MAR) review and identifying any specific signals or triggers that might be concerning for an error. While reviewing the patient's MAR, the orders are screened for the appropriate inclusion of important details such as legibility, medication name, dosage form, route of administration, dose, dosage unit, frequency of administration, duration of therapy, number of doses to be dispensed, and directions or warnings for use [21, 22]. Data reviewers are vigilant for certain changes in patient status (e.g., transfer to the intensive care unit), and new diagnostic or laboratory tests that can indicate where errors may have occurred (e.g., abnormal echocardiogram, elevated liver enzymes). The data is collected on forms, and when errors are identified, further drill down occurs. This is a labor- and resource-intensive process that requires dedicated teams for review and usually necessitates daily review of charts to have effective real-time identification of errors and interventions.

In comparison to incident reports alone, more detailed data is generally gathered from prospective chart review [11, 23]. This system can be an effective tool at identifying errors during the prescribing, administration, and monitoring of medications [11, 22, 23]. As chart review identifies errors that have not yet been voluntarily reported, there have been concerns that the seriousness of problems detected via this

method is often associated with lower clinical significance [23]. While a higher number of errors may be identified, fewer error reviews that would lead to system changes have been observed in some studies [22, 23]. The significant time and resources needed to have a large-scale prospective chart review for medication error must also be considered when evaluating this as a medication error measurement tool and often preclude this from being a viable solution for most institutions.

Trigger Tools

In 1999, the Institute for Healthcare Improvement's expert panel on patient safety devised a trigger tool methodology that utilizes identifying key triggers in patient records during review that prompt medication error detection [24].The IHI Global Trigger Tool is incorporated by utilizing a team of three or more reviewers evaluating randomly selected charts and searching for triggers to adverse events in six modules: cares, medication, surgical, intensive care, perinatal, and emergency department [25].Within the medication module, triggers have been identified that are often included when a medication error occurs such as diphenhydramine administration, partial thromboplastin time (PTT) greater than 100 s, and vitamin K administration. The use of this trigger-focused review expands on the concept of chart review and allows for a more streamlined approach that has been shown to be an effective and reproducible form of medication error detection [24, 25]. Many of the components that are manually evaluated in trigger tool-focused chart review can be automated by utilizing the ever-expanding technology of the EMR information systems. Automated adverse event detection or trigger tools have been developed to allow the prospective gathering of data via specific signals or triggers. Several EMR trigger tools have been implemented and reviewed in the general pediatric setting [26–28] and in the pediatric hematology and oncology subspecialty setting as well [29]. These trigger tools focus on discrete events that occur in the EMR, and reports can be created that prompt further investigation into potential medication errors. Several multi-institutional collaborations have been formed, such as the Automated Adverse Event Detection Collaborative (AAEDC), with the goal of improving the detection, collection, and analysis of medication events among groups of academic pediatric hospitals [26]. The triggers utilized by the AAEDC cover a wide range of medication and laboratory values and are summarized in Table 10.3.

These triggers can be utilized in a wide variety of EMR information systems and utilized as both retrospective auditing tools and real-time interventions to prevent an error before it occurs. A more specific tool for the automated detection of medication errors in pediatric hematology oncology has been developed and evaluated at St. Jude Children's Research Hospital (SJCRH) with a focus on supportive care and chemotherapy-related medications including protamine, vitamin K, sodium polystyrene, naloxone, flumazenil, and hyaluronidase [29]. This trigger tool noted that when one of the listed medications was ordered and administered

Table 10.3 Triggers utilized by the Automated Adverse Event Detection Collaborative

Medication administration	Laboratory results
Digoxin immune fab	Anti-Xa > 1.5
Flumazenil	aPTT > 100 s
Hyaluronidase	Bilirubin > 25 mg/dL
Sodium polystyrene	Creatinine doubling
Naloxone	Glucose < 50 mg/dL
Protamine	INR > 4.0
Acetylcysteine	Potassium > 6 mmol/L
Glucagon	
Vitamin K	

to a patient, it was logged and the data could be extracted into a report. These triggers for potential medication errors were reviewed by both a pharmacist and physician. After review, if a medication event was truly linked to the trigger, data was collected regarding the event similar to that of an incident report. Trigger tools like the one developed at SJCRH can be developed within most existing EMR information systems and help automate the process of medication error detection. As with chart review and other forms of measurement, the data from these triggers must be then reviewed and classified in order to identify interventions to prevent future errors [26, 29].

Electronic trigger tools build upon the medication error capturing of a chart review in a quicker and automated process. This tool can allow for decreased sampling bias that can be seen with manual trigger identification via chart review. As with chart review, it allows for near real-time detection of medication errors which can help facilitate timelier investigations. Several studies have shown this tool to be a valuable addition to traditional measurement options as it has shown minimal overlap (1.9–7.8%) with voluntary incident reporting systems [26–28]. A major limitation in automated trigger tools are the lack of fully validated trigger events specifically related to chemotherapy, such as the use of methylene blue in ifosfamide neurotoxicity or timing of leucovorin administration following high-dose methotrexate infusion. Many of the validated trigger tools focus on identifying errors of supportive care medicines or hematology-related medications such as anticoagulants. As institutions continue to evaluate new chemotherapy-related triggers, it is important that these triggers proceed through an important validation phase. If the trigger tool has been validated appropriately, it can be as sensitive as chart review and more sensitive than incident report review at identifying medication errors [11].

During the validation process, it is important for hospital systems to evaluate the positive predictive value of each medication trigger. For example, during the validation study of the SJCRH trigger tool, no events were detected associated with the use of vitamin K. The study concluded that if the tool had been restricted to the use of patients only with known concurrent use of warfarin, that data may have been more helpful for review. It is therefore important that when a trigger

tool is implemented, that there be a process of internal review to identify the predictive value of errors based on trigger to ensure continued measurement will be beneficial. There can be significant financial investments in the development and implementation of a trigger tool, but once implemented many studies have shown trigger tools to require the least resources to continually review medication errors [20, 30, 31]. As more tools are developed and validated, this field will continue to expand as a complimentary and potentially primary medication error measurement tool.

Direct Observation

Direct observation refers to real-time evaluation techniques throughout the medication process. This technique is one of the oldest methods of detecting medication errors and has been studied since the 1960s [32]. This measurement technique involves real-time auditing of the practices of prescribing, preparing, dispensing, administration, and monitoring of medications [11, 33]. Direct observation of nursing by review teams has been the backbone of direct observation, and over time this has been expanded to include both provider and pharmacist observation as well. Examples of observations include on the prescriber level of ensuring double provider signatures for chemotherapy ordering, on the pharmacy level by selecting correct diluents for medications, and on the nursing level of appropriate administration rates and times. Errors are noted in real time and data is collected for analysis.

This measurement tool has been considered the gold standard of identifying medication errors. A systematic review of medication safety assessment practices showed that direct observation revealed the highest number of error reports, in some studies up to 400-fold the number of reports compared with incident report review, chart review, or trigger tool [11]. As with any scientific study, there are concerns as that observer influence can be involved and significant [11, 29, 33]. The review teams often include representatives from physician, pharmacy, and nursing staffs and can be resource demanding regarding the time needed for this ongoing observation [11, 33]. Some of the limitations of other measurement techniques are avoided as knowledge of the errors by subjects is not needed and willingness to report the errors is not required. As with all other measurement techniques reviewed, once the errors have been measured, an infrastructure must be in place to review and analyze the errors.

The measurement of medication errors is key to understanding the processes involved with the error and subsequently creating system changes to ensure prevention of future errors. Many studies have evaluated the costs and benefits of the individual measurement techniques. While the reviewed methods have distinct advantages and disadvantages, no study has shown the clear advantage of one standalone system. It is critical to understand that a multifaceted approach to measurement will be key when a healthcare organization approaches improvement strategies for patient safety regarding chemotherapy and other medications.

Improvement Strategies

Introduction

Organizational strategies for improving chemotherapy and medication safety should focus on the overall chemotherapy process including chemotherapy prescription, preparation, and administration [1, 7, 34, 35]. Institutions must ensure that safeguards are in place at each step and should place these strategically within the chemotherapy use process. A successful system design should account for psychological precursors and human factors and incorporate standardization, technology, patient input, and double checks to ensure that errors are prevented [1, 36].

Standardization

One of the most effective ways to minimize error is to standardize the process and tools used to prescribe, dispense, and administer chemotherapy. A lack of standardization can create an environment of confusion, misinterpretation, and variability in these processes. One way to improve the chemotherapy process is to evaluate each of these steps and implement evidence-based strategies that can minimize errors [7, 34, 37].

Prescribing

It is well known that incomplete, illegible, or incorrect chemotherapy orders can lead to ambiguity and misinterpretation, thereby putting patients at significant risks [1]. Patient care facilities should utilize standardized pre-printed or electronic order sets whenever possible and at least for commonly used regimens and treatments. This tool helps to simplify the ordering process in that much of the basic information is prefilled [7, 37, 38].

Best practice recommendations suggest that the basic elements of all chemotherapy orders should include patient demographic information and treatment plan, hydration orders if applicable, supportive care medications, and chemotherapy medications. The orders should be presented in a standard format, in the order which they will be administered and incorporate general medication safety principles (Table 10.4). Specific recommendations for each component of the order template include the following [1, 7, 38–42]:

1. Patient demographics:
   (a) At least two patient identifiers, including the patient's name
   (b) Patient-specific dosing parameters: Height (cm), weight (kg), and BSA (m^2)
   (c) Diagnosis

Table 10.4 General medication order safety principles

	Do	Correct example	Don't	Incorrect example
Drug name	Generic name Brand name in parenthesis (when appropriate) Tallman lettering	CISplatin Fluorouracil	Do not use unapproved abbreviations for drug names	CDDP SFU
Dosage	Planned treatment dose as function of patient-specific parameters and calculated dose Place a space between the dose and units Use commas when expressing numbers >999 Doses less than 1 should be preceded by a zero	CISplatin 36 mg = 20 mg/m^2 × 1.8 m^2 Fluorouracil 1800 mg = 1000 mg/m^2 × 1.8 m^2	Avoid trailing zeros	CISplatin 36.0 mg = 80 mg/m^2 × 1.8 m^2 Fluorouracil 1800.0 mg = 80 mg/m^2 × 1.8 m^2
Route	Clearly define administration routes and durations	IV over 30 min	Do not use bolus as administration instruction	IV Bolus
Schedule of administration	Frequency Number of doses Days to be taken Include total daily dose and total dose over total length of time for continuous infusions	CISplatin **Q24 h for** three doses on days **1, 2, 3** Fluorouracil 1000 mg/m^2/day IV continuous over 24 h on days 1, 2, 3, 4 (total 4000 mg/m^2 continuous IV over 96 h)	Do not use hyphens used to express dosing schedules Avoid unapproved abbreviations, such as QD Avoid unclear expression of timing and frequency of administration	Oplatia **days 1–3** Fluorouracil 4000 mg/m^2 IV over 96 h 1000 mg/m^2 OD × 4 days

2. Treatment plan:
   (a) Name of treatment regimen and protocol number for research regimens
   (b) Treatment intent (optional)
   (c) Current day and cycle, cycle length, and total number of anticipated cycles
3. Hydration orders:
   (a) Solution type
   (b) Volume of solution
   (c) Route of administration
   (d) Duration of infusion
4. Supportive care medications (pre-chemotherapy)
   (a) Include default medication choices. These should be customized to the regimen given and meet evidence-based practice guidelines
   (b) Alternative or add-on options should be available for situations in which the patient does not respond appropriately to default medication choices. These options should also be based on clinical practice guidelines
   (c) Standardized full generic name, dose, route of administration, duration of infusion as applicable, and time of administration in relation to chemotherapy should be included.
5. Chemotherapy medications
   (a) Standardized full generic name of the chemotherapy agent.
   (b) Brand names should be included in situations of look-alike-sound-alike medication names.
   (c) Dosing unit (mg/m^2, mg/kg, etc.) and patient calculated dose.
   (d) Reasons for dose modifications.
   (e) IV solution and volume and duration of infusion as applicable.
   (f) Drug dosages and calculated doses should be expressed according to the "container" rule (i.e., the calculated dose is the amount prepared and administered from a single container).
   (g) Chemotherapy medications infused over multiple days (continuous infusions) should include total daily dose and total dose over total length of time (i.e., 1200 mg/m^2/day IV continuous over 24 h on days 1 and 2 (2400 mg/m^2 IV over 48 h).
   (h) Solution types, volume, and duration of infusion should be standardized for each chemotherapy medication.
   (i) The administration schedule, including frequency of administration and days on which each dose is to be given within a treatment cycle or course, should be specified.
6. Supportive care medications (post chemotherapy)
   (a) Growth factor support
   (b) Anaphylaxis control
   (c) Prescriptions for post chemotherapy emesis control

7. Provider signature, date, and time

Standardized chemotherapy order forms and electronic templates should be developed by designated multidisciplinary teams who prescribe, prepare, and administer chemotherapy medications. Practitioners involved in this process should draft the template content which should then undergo formal independent review and approval by each discipline (a physician, advanced practice providers, pharmacist, and nurses). Review and approvals should be completed in a quiet area. The information from the creation, review, and approval process should be retained for future reference. The standardized order set templates should be reviewed on a regular basis. A maintenance schedule should also be established. Reviewing the templates on a standard frequency (i.e., annually or every 2 or 3 years) will help ensure that the templates are up-to-date in terms of evidence-based clinical practice guidelines and formulary changes [7, 38, 40].

The institution should consider restricting who is allowed to order chemotherapy. Be sure to consider all situations. For example, you may want an emergency room physician to be able to order chemotherapy for a patient who is admitted into the emergency room with blast crisis; however, you may not want a fellow or other trainee ordering chemotherapy without an attending co-signature.

Preparation/Dispensing

Chemotherapy orders should be reviewed by an oncology pharmacist. The value of a pharmacist's review has been well documented in playing a pivotal role in identifying prescribing errors. Although the use of standardized order templates minimizes the need to reverify predefined elements of medication orders, certain treatment aspects are not captured by order templates. A pharmacist's review should consist of the following [7, 38]

(1) Patient-specific parameters: including height (cm), weight (kg), BSA (m^2), and significant changes in these parameters.
(2) Drug allergies and current medications for potential drug interactions.
(3) Treatment plan is appropriate for the patient and treatment indication (i.e., evidence supports the use of the regimen in the disease being treated).
(4) Relevant laboratory test and physical assessment values have been taken, and results are within appropriate limits for treatment.
(5) Dose and dose calculations are correct according to patient-specific parameters.
(6) Doses, cycle number, and day of treatment are consistent with treatment history, and the appropriate treatment interval has elapsed.

Orders should be compared with a primary reference, and if an investigational agent is used, the research protocol should be referenced to verify the appropriateness of the orders for the patient. Tools such as checklists or chemotherapy

Pt_____ MRN:_____ Appt time_____ RN:_____

◆Verify the following:
Height:_____cm Weight:_____kg BSA_____m2
Allergies_____ □ Consent Diagnosis:_____

□ The following are appropriate per protocol #_____, standard, or exception order:
- □ Drug
- □ Dose
- □ Schedule

□ Review patient's treatment history and verify:
- □ Drugs and doses Cycle_____ Day_____ Time elapsed since last dose:_____

□ Criteria to treat has been assessed
Labs: ANC:_____ PLTs:_____ T.Bill:_____ Scr:_____ Others:

□ Hydration is appropriate

□ Supportive Care is appropriate:

Dexamethasone	Palonosetron	Famotidine	Others:
Ondansetron	Acetaminophen	Hydrocortisone	
Aprepitant/Fosaprepitant	Diphenhydramine	Methylprednisolone	

Notes:

Fig. 10.2 Chemotherapy order checklist example

drug work cards can be used to help ensure that all elements of chemotherapy orders have been verified. An example of a chemotherapy order checklist is provided (Fig. 10.2).

Standardizing the preparation process is another component of minimizing medication errors. Standardized guidelines for the reconstitution, dilution, packaging, and labeling of chemotherapy admixtures [7, 37] should be established. These guidelines should be readily available to all practitioners involved in verification, drug preparation, and drug preparation checking processes. Commercially available products should also be used whenever possible but are often not available for chemotherapy. Thus, when admixing these medications, it has been recommended that direct observation of product preparation be used whenever possible. Ideally, two individuals should independently verify the drug, diluents, administration containers, and volume measurements before the drug dose is transferred into the final administration container. Other post hoc verification methods, such as the syringe pull-back method, in which the syringe plunger is pulled back to demonstrate the volume of drug that was injected into the container, have been described. However, it is recommended that this should not be used alone as a verification method. Other practices include drawing up the volume to be administered and marking the syringe before transferring the medication into the final container, using specific gravity information to confirm doses [7]. At the completion of preparation, all original medication vials,

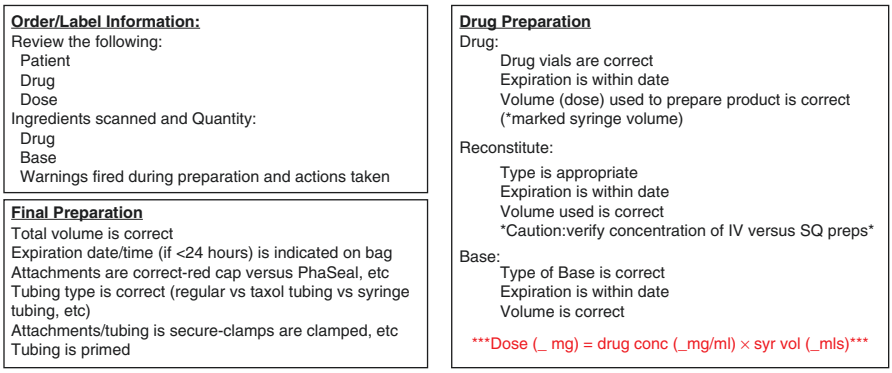

Fig. 10.3 Pharmacy preparation checklist example

diluents, syringes, and transfer devices should be presented for final product verification. At this point, a pharmacist should verify label/order information, drug reconstitution, and final product preparation. Checklists or chemotherapy drug work cards can serve as useful tools to aid in these processes as well (Fig. 10.3).

Administration

Nurses often have the last opportunity for error recognition and intervention in the medication use process. It is therefore necessary to institute administration practices that will allow nurses to easily identify and intercept errors to prevent potentially lethal consequences. Similar to a pharmacist's order review, nurses should also verify order and patient-specific elements prior to drug administration. They should assess the patient for previous chemotherapy-related toxicity, confirm treatment plans for the day, and counsel patients on expected toxicities and how to manage symptoms. Prior to drug administration, recommendations indicate that two nurses should compare the pharmacy product to the original order and assess the medication's integrity [7, 35, 37] Infusion pumps should be used to administer chemotherapy. The infusion rate and pump settings should be entered and then independently reviewed by another individual prior to the start of administration. Ideally, this should occur at the bedside where the two practitioners can also validate the patient's identity to ensure that the correct drug is given to the correct patient [7, 35].

Errors in administration have been documented to account for 13% of errors in one study of hospitalized pediatric patients [19]. Institutions can minimize the incidence of these errors by following recommended practices: chemotherapy should be administered on designated units or floors where chemotherapy competent nurses are located; cutoff times for nonurgent chemotherapy administration should be established to ensure adequate pharmacy and nursing staffing; the institution should determine whether chemotherapy agents should be infused as a primary or secondary infusion. Another important component to the medication administration process includes documentation of administration.

Treatment flow sheets can serve as a useful tool to outline information regarding a patient's treatment history, especially when a standardized format of documentation is employed, including patient's name; medical record number and/or date of birth (two patient identifiers); drug name, dosing unit, and calculated dose; administration rate, route, duration of infusion, time infusion started and ended, and date of administration; and information regarding tolerance.

Technology

Implementing the use of technology at various points in the medication use process can improve communication and structure workflow and aid in clinical decisions. By eliminating handwritten orders and providing clinical decision support, prescribers can gain significant ordering advantages through the use of computerized order entry. Bar code scanning technology can prevent medication mix-ups at the point of preparation, and infusion pump guardrails can ensure that medications are administered at the appropriate rates.

Computerized Order Entry

The Institute of Medicine recommends that all medication orders be written electronically [43]. Although the benefit of its use is well established, institutions should recognize that the implementation of these systems can introduce new errors. Experience from various institutions indicates that each step of the existing and proposed medication use process should be compared for potential gaps and failure points. Failure modes and effects analysis (FMEA; see also Chap. 20) and failure modes, effects, and critical analysis (FMECA) have been successfully used for this purpose [44–47]. These proactive risk assessment methods allow institutions to evaluate risks and design chemotherapy processes accordingly.

The positive impact of computerized physician order entry (CPOE) on error reduction serves as a primary motivation to implement its use in the pediatric chemotherapy setting. Depending on how CPOE is designed, it can reduce the likelihood of improper dosing, incorrect dosing calculations, and missing cumulative dose calculations, among others. To maximize the benefits of CPOE, several concepts should be considered [7, 37, 48–51]

1. Workflow: Display data in CPOE consistent with the chemotherapy use process. Chemotherapy orders should be entered first, followed by pharmacy verification, product preparation, nursing verification, medication administration, and documentation.
2. Verification: The number and type of checks should be placed strategically in the medication use process. Consider the capabilities of CPOE, which can restrict

provider privileges, automate calculations, apply forcing functions, and provide drug interaction checking.
3. Information access: Ensure that all providers have access to patient information including demographics, laboratory values, notes, treatment plans, consents, past medication administration history, etc. This information should display in a manner that encourages that appropriate clinical decisions and verifications are made during each step of the chemotherapy use process.
4. Clinical decision support: Automated safety checks should be instituted wherever possible. A few examples include:

(a) Automated dose calculations and dose rounding
(b) High-dose warnings
(c) Dose caps
(d) Cumulative dose calculations
(e) Interaction and allergy alerts

Bar Code Verification

Linking the manufacturer's bar code, the National Drug Code (NDC) number to respective medications ordered for a particular patient in a CPOE system can allow bar code verification to prevent wrong patient and medication mix-ups at the point of administration. During preparation, systems allow each ingredient of a preparation to be checked against the components of an order and can fire warnings or hard stops to guide drug selection. These systems have been particularly helpful in preventing look-alike-sound-alike drug errors. Some intelligent systems can also direct the amount of drug used to prepare the product, alerting the preparer if too many or too little drug packages have been scanned to complete the ordered dose.

"Smart" Pumps

Infusion pumps which incorporate medication safety software ("smart pumps") can prevent errors in administration rates. This software has a comprehensive drug dictionary with limits for dosing, dosing units, concentration, and duration of infusion. These dictionaries should be customized to the institution's established drug preparation and administration guidelines and utilize the following functions [7, 48]:

(1) Customize different profile settings for different patient populations and locations (pediatric vs. adult; NICU vs. general pediatric unit or clinic).
(2) Incorporate soft and hard limits strategically.
(3) Use nomenclature that mirrors medication orders in CPOE and pharmacy labels.
(4) Provide drug-specific clinical advisory alerts (i.e., infusion tubing or filter needs).

Patient and Family Involvement

Although a survey by the National Patient Safety Foundation revealed that only 10% of patients had taken an active role in ensuring their own safety, patients and families can play an integral part in the medication use process [51]. Healthcare providers, patients, and families share responsibility to ensure that this happens.

Healthcare providers should present patients and families with information important to their care including their treatment course, medications, expected side effects, and when to call the provider's office. They should do this with clear and complete instructions at a level that the patient and family can understand. Medical jargon should be avoided; pictures can be used if needed and information should be repeated. An underutilized method of teach-back is an effective practice to ensure that the information was received and interpreted in the manner intended. The pediatric setting offers additional intricacies to this task. Patients are often young and may have limited abilities to fully participate in their own care. Thus, patient and family dynamics need to be greatly considered since multiple people may be involved in the child's care. It is important that all family members involved receive education and are coordinated in their roles.

It is imperative that patients and families ask questions about their care. They should speak up if something is unclear or does not seem right. Patients and parents should verify all medications given. When picking up a prescription from the pharmacy, they should read labels and compare the information on the bottles to what the doctor told them. Patients and families should be encouraged to review the prescription bottle for patient name, medication name, and directions for use and read about possible side effects. Since children's medications are often in liquid form, the pharmacist should be asked to demonstrate how to use the oral syringe to measure and administer the dose prescribed. Patients and parents should also keep records of all medications, including over-the-counter medications and record information regarding missed doses, side effects, etc. This information should be reported back to all providers so that treatment plans can be adapted accordingly.

Institutions should also incorporate patients and families into their chemotherapy use policies and processes. They can be involved at a global level, participating in institutional quality improvement and safety initiatives as well as granular levels and verifying their name and date of birth prior to medication administration. Their input is invaluable in identifying ways to ensure that care is tailored to patient needs.

Overall Chemotherapy Use Process and Double Checks

Evaluating the overall chemotherapy process in addition to the individual steps of the process is essential in determining if gaps persist. It is helpful to outline the overall chemotherapy use process and respective checks and balances used within

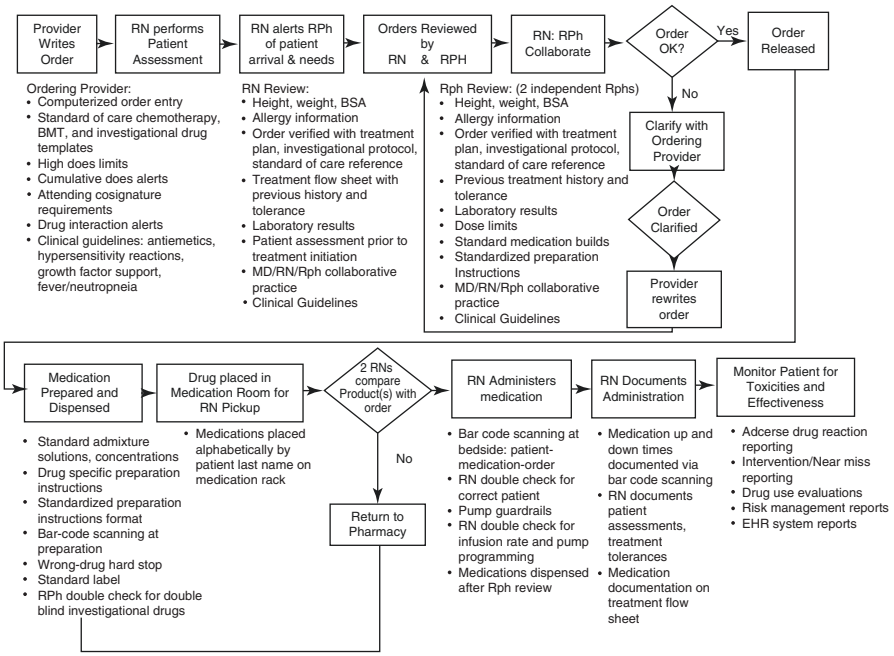

Fig. 10.4 Chemotherapy use process map example

each step [7, 34, 35, 37] (Fig. 10.4). It may be noted that technology is used in various process aspects and is successful in preventing errors; however, it cannot prevent all and can even introduce new issues. For example, the CPOE system may autocalculate doses based on height and weight, but if the incorrect parameter is entered into the system, then the dose will inevitably be wrong. It is imperative that everyone in the process asks themselves if the information at hand makes sense. The CPOE system may also be effective in alerting providers to drug allergy or drug-drug interaction checking, but if patient allergies are not entered or medications are not reconciled, these interactions may go unrecognized. In other cases, alert fatigue can cause significant interactions and contraindications to slip through. This speaks to the importance of carefully designed process double checks. One common strategy used is the double check.

Various studies have demonstrated the effectiveness of double checks when they are conducted appropriately [52, 53]. It is important to note that the double check must be performed independently, meaning that a second practitioner verifies the work process that a first practitioner has verified, but does this separately. This minimizes the risk of confirmation bias. When performed in this manner, double checks can detect up to 95% of errors [52]. Although this error prevention method can be quite effective, it should be used purposefully and should not replace system fixes when they are needed. Developing policies which standardize when double checks should be conducted will help ensure consistency. Additionally, tools to support double checks can

improve error detection rates by making it easier for practitioners to complete checks without relying on memory. One study showed that the use of a checklist increased the detection of wrong patient errors by 433% [54]. Tools should provide specific direction. For example, leave space to allow practitioners to enter information related to the aspect that should be checked. (Fig. 10.2) Maximizing the design can improve the effectiveness of the tool itself, increasing error detection rates from 45% to 60% [54]. Overall, their use can be quite successful. However, double checks should be layered among other risk reduction strategies to minimize error risks.

Clinical practice is a continuously evolving field in which new chemotherapies and treatment regimens are proven and new providers join the healthcare team regularly. Reassessment of the chemotherapy use process using methods to measure and sustain its effectiveness is an ongoing process.

Strategies for Sustainability

A systems approach should be utilized to drive improvements in the medication use process. As improvements are made, it is critical that these changes become integrated into daily workflow, processes, and systems. Sustainability of improvements in the medication use process is dependent on establishing and maintaining an organizational culture of safety, utilization of a quality improvement process including ongoing process monitoring, data collection and analysis, and the redesign of systems and workflow.

Culture of Safety

Establishing and maintaining an organizational culture of safety are the foundation for achieving improvements in medication safety as well as sustaining improvements [55, 56]. The American Society of Health-System Pharmacists (ASHP) definition of culture is as follows: “A just culture is one that has a clear and transparent process for evaluating errors and separating events arising from flawed system design or inadvertent human error from those caused by reckless behavior, defined as a behavioral choice to consciously disregard what is known to be a substantial or unjustifiable risk” [57]. An organizational culture of safety is one where leadership has prioritized safety, created an environment where weaknesses in the medication use process can be openly discussed through ongoing learning and education, promoted inclusion of frontline staff, and include the participation of patients and families (Fig. 10.5). The engagement of leadership, including the board of trustees, is critical in order to keep the organization focused on safety. Leadership must prioritize safety, establish specific safety culture principles, and make these visible to the frontline staff [58]. The prioritization of safety involves the inclusion of specific safety goals in the organization’s annual goals. The organizational safety goal can then be incorporated into the various departments’ goals and initiatives.

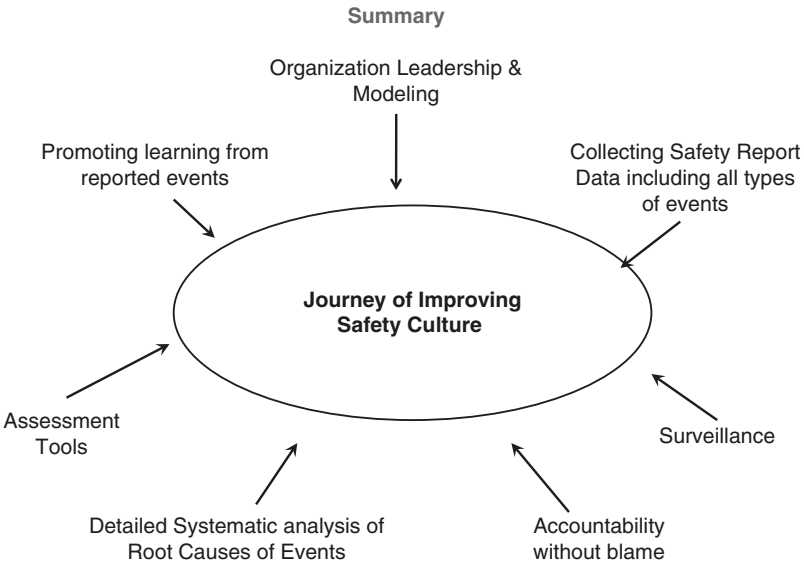

Fig. 10.5 Summary of components to improving safety culture and sustainability

It is equally important that leadership establish safety culture principles that address the balance between individual accountability and system failures, support transparent discussion of actual and potential safety issues and risks, support implementation of specific system or workflow changes, and include patients and families in open discussions of weaknesses in the medication use process [59]. These principles are important not only for creating an organizational safety culture but also serve as a guide during event and process evaluations and improvement initiatives. An additional principle that is important to integrate into the safety culture especially when guiding specific improvement initiatives is safety over convenience or efficiency. Leadership has a key role in communicating these principles to staff and modeling appropriate safety culture behavior in order to sustain safe medication use processes instead of focusing on short-term fixes in response to single events.

Data Collection, Surveillance, and Analysis

To identify the medication-related risks, it is important to collect data from a variety of sources. As discussed previously in the measurement section, these include voluntary staff incident reporting, detailed analysis of specific errors or events, proactive review of the medication use process, and health information record review. Data collection from the various measurement modalities allows for root cause analysis and failure mode effects analysis, which provide critical underlying reasons for the occurrence of the adverse event or near miss. These are analytical approaches based

on information provided by automated trigger tools or staff that have been involved in the event or workflow process. Based on the information that is gathered, there are specific recommended actions to ensure the event does not occur in the future.

An additional data collection tool is proactive risk assessments. This includes routine literature review from peer-reviewed journals and Institute for Safe Medication Practices Safety Alerts. The use of self-assessments, such as the ISMP International Medication Safety Self Assessment for Oncology [60], is another way to obtain proactive information regarding key components of an institution's medication use systems. Executive leadership walk-rounds and management meetings where staff are able to discuss safety concerns, policies/procedures that are challenging to adhere to, and technology or other system defects are very good sources of information about vulnerabilities or defects that are in the medication use process. The use of national guidelines, standards, and practice recommendations such as the ASCO/ONS Chemotherapy Administration Safety Standards, and the American Society of Health-System Pharmacists guidelines on preventing medication errors with chemotherapy and biotherapy can serve as a tool for organizations to review their current chemotherapy medication systems. These proactive risk assessments can be used as a starting point for organizations to prioritize current focus areas as well as serve as a road map for future initiatives.

An additional data source is from technology such as the computerized order entry system, pharmacy system, bar coding during drug preparation and administration, and smart pumps. This includes data on alerts clinicians receive during the drug ordering, preparation, and administration processes.

The ISMP has identified targeted medication safety best practices for 2014–2015 and now 2016–2017 [61, 62]. These are best practices of specific safety issues that continue to result in patient harm and should be adopted by hospitals. This is a way for hospitals to review their own practices and focus their medication safety efforts on strategies that have been successfully implemented in other organizations. Implementing these best practices allows organizations to reduce vulnerabilities and sustain improvements in reducing patient harm.

In 2016, the ISMP has identified selected safety risks that might not be identified as a risk unless an adverse event happens [63, 64]. These ten risks and their management can be used by organizations to review their associated workflows and processes, focus their efforts, and be proactive before an adverse event occurs. This approach is also important so that organizations can begin to look at the entire medication use process as a system instead of focusing on single-event improvements.

System Redesign

The sustainability of improvements in medication safety depends on the redesign of systems, workflows, and processes based on the data that has been gathered and its analysis. In order to accomplish the redesign, it is important to have the support of

leadership, a multidisciplinary team—including patients and/or families—and identified project managers and timeline. The system redesign includes technology and ensuring they contain specific safety features. These safety features include the appropriate and significant alerts and warnings, presentation of information on the computer screens and printed information, and the availability of information across disciplines or applications. Working with the technology vendors is critical in being able to achieve computer system changes.

The redesign of workflows and processes should include the utilization of techniques and principles such as Lean Six Sigma that have been successful in improving the safety in other industries. It is important to have a formal process improvement methodology that is utilized in an organization to ensure the new workflow or processes will have the best positive impact. Leadership is essential in supporting the redesign and assisting in the change management process.

The sustainability of the improvements in medication safety requires a culture of patient safety, an identified process improvement tool, current data on the risk areas in the medication use process, and a culture of transparency and continuing learning. It should be expected that institution's systems and workflows will be continuing to change and evolving as new systems and information and knowledge are gained. Therefore, it is essential to continue to keep medication safety as a top priority in our organizations and work.

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