

Development and Proof of Concept of an Audit Toolkit for the Safe Handling of Cytotoxic Drugs in Low- and Middle-Income Countries

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PURPOSE Chemotherapies are considered high-risk drugs for patient and staff safety. Considering the rising burden of cancer and the increasing use of chemotherapy drugs in low- and middle-income countries (LMICs), promoting continuous improvements in the safety and quality of practices in these settings is essential. This paper describes the development and proof of concept of a toolkit to audit chemotherapy handling practices in the health care facilities of LMICs.

METHODS A steering committee defined the audit method and the toolkit content. Several checklists were developed to facilitate the audit and data collection. Items included in checklists were derived from key reference works on safe handling. Different tools were validated using Delphi surveys and expert reviews. Audits of pilot sites were performed to test the toolkit's applicability and relevance.

RESULTS The toolkit contains a 134-item global assessment tool for the different processes at each step of the medication pathway and three step-specific observation checklists to assess different health workers' practices during the prescription, preparation, and administration of chemotherapies. The toolkit also proposes using a surface-wipe sampling method to measure any cytotoxic contamination of the immediate environment. The toolkit was tested in three teaching hospitals in Africa.

CONCLUSION The toolkit developed was successfully implemented in a variety of LMIC settings, providing a comprehensive evaluation of the quality and safety of the chemotherapy drug handling practices in participating health care facilities. This toolkit can help facilities in LMICs to implement a new approach to continuously improving the quality and safety of their practices and ultimately ensure patient and staff safety.

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INTRODUCTION

Chemotherapies are considered high-risk drugs, not only for patients but also for the staff handling them. The risks related to occupational exposure were first described in the literature in the late seventies in the study by Falck et al¹ that reported mutagenic activity in the urine of nurses handling chemotherapy drugs without specific protection. Over the years, the risks of this ongoing challenge were studied and addressed by many experts, from professional organizations, national authorities, and even insurance companies.²⁻⁷ As a result, several recommendations, guidelines, and regulations on safe handling practices were developed. In high-income countries, implementing preventive and control measures wherever chemotherapy drugs were transported, received, stored, prepared, administered, and disposed of became standard professional practice or a legal obligation.

The use of chemotherapy drugs in low- and middle-income countries (LMICs) is much more recent. For

many years, LMICs shouldered a great burden of infectious diseases and little attention was given to noncommunicable diseases. But recently, the increase in premature cancer deaths in LMICs can no longer be ignored and the burden of cancer has become a public health issue in these countries as well.⁸⁻¹⁰ In 2020, GLOBOCAN statistics produced by the International Agency for Research on Cancer estimated 2,977,172 new cases of cancer, 5,720,384 cases of 5-year prevalence, and 1,953,071 cancer-related deaths in countries with medium- and low-human development indexes.^{11,12} The economic impact and human development challenges resulting from this rising burden have led the WHO and other stakeholders to take action.^{8,13} Substantial efforts have been made to prevent and manage cancer in LMICs, notably by expanding access to affordable, high-quality chemotherapy drugs.

In the coming years, increasing numbers of patients, combined with improved access to chemotherapy, will

ASSOCIATED CONTENT

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

How to evaluate and promote continuous improvement of safe handling of chemotherapy drugs through a quality-oriented approach in low- and middle-income countries (LMICs)?

Knowledge Generated

The audit method and the different tools developed via this project enabled a comprehensive assessment of the safety of chemotherapy handling in three health care institutions in LMICs. Its implementation in a variety of settings enabled us to verify its applicability by future users.

Relevance

The audit toolkit offers health care facilities in LMICs ready-to-use tools and checklists to assess their safe handling of cytotoxic medicines and ensure patient and staff safety.

increase the use of these hazardous drugs. A recent survey on handling practices in LMICs showed that unsafe practices remained a significant safety risk to patients and staff in many places.¹⁴ Strategies to remedy and improve this situation are needed, therefore, especially in lower-income countries.

Introducing a quality-oriented approach to the handling of chemotherapies is essential for ensuring patient and staff safety. The Deming cycle describes four iterative steps (plan, do, study, and act) and has been widely used as a quality improvement model.^{15,16} In our context, the assessment or evaluation step consists of ensuring that the good practices that the cycle defines are implemented. Simply disseminating these recommendations is insufficient: their implementation must be ensured. Indeed, several works have highlighted the gap between current scientific knowledge and actual practices, as well as the significant variability in those practices.^{14,17-19} There are currently few tools available to assess safe practices in LMICs. Their availability would facilitate the implementation of a continuous quality approach within LMIC institutions. This paper describes the development and proof of concept of a toolkit to audit chemotherapy handling practices in LMIC health care facilities.

METHODS

A steering committee was created within Geneva University Hospitals' Pharmacy Department to lead the project and define the audit method and toolkit. It was composed of the department head, the pharmacist in charge of the cytotoxic drug preparation unit, and the study's principal investigator. Toolkit design was guided by the objectives that it should first provide an overview of the processes and practices implemented throughout the chemotherapy circuit (eg, receiving drugs, storage, transport, prescription, preparation, administration, waste management, disposal, etc) and then compare them with existing best practices and guidelines. Various audit evaluation methods were chosen, such as interviews with key informants, structured observations, and surface-wipe sampling.

Instrument Design

Several tools were developed to facilitate the audit and data collection.

Assessment tool. The kit's first tool makes a full assessment of every step involved in the processes and practices of handling chemotherapy drugs (eg, receipt, storage, transport, prescription, preparation, administration, waste management, cleaning, and patient counseling). Items addressing aspects of quality and safety were derived from key sources (Table 1) and underwent a first review by the steering committee. A panel of 27 pharmaceutical experts in oncology practices from 13 low-, middle-, and high-income countries subsequently validated those items via a two-round online Delphi survey. A previous publication described the development of this tool in detail.²⁶

Structured observation checklists. Additionally, we developed three structured observation checklists for noting how different staff applied safety and quality practices during the three main steps of the cytotoxic treatment process: prescription, chemotherapy preparation, and administration. Each checklist was based on professional guidelines and best practices but was adapted to the contexts existing in LMICs (Table 1); each item was reviewed and validated by two or three experts from within our institution.

Surface-Wipe Sampling

Surface-wipe sampling has been widely used in health care settings handling hazardous drugs.²⁷ This methodology has been recommended for evaluating contamination trends, implementing corrective measures, and increasing workers' awareness about the risks related to handling chemotherapy drugs.^{22,27} A variety of surfaces should be selected depending on the setting and how the health care facility works (eg, preparation workbenches and adjacent areas, drug administration areas, etc). For this section of the toolkit, we chose to use methods previously developed and validated by Guichard et al.²⁸⁻³⁰

Sampling was performed by wiping polyester swabs (TX716, Texwipe, Kernersville, NC) moistened with

TABLE 1. Toolkit Design References

Document	Authors	Year	Region or Country	Document Type
ISOPP Standards ⁴	International Society of Oncology Pharmacy Practitioners	2007	International	Scientific society's recommendations
QuapoS 4: Quality Standard for Oncology Pharmacy Services, With Commentary ²⁰	German Society of Oncology Pharmacy and European Society of Oncology Pharmacy	2009	Europe	Quality standards from a scientific society
ASHP Guidelines on Handling of Hazardous Drugs ²¹	American Society of Health-System Pharmacists	2006	United States	Scientific society's recommendations
USP (United States Pharmacopeia), Chapter 800: Hazardous Drugs—Handling in Healthcare Settings ²²	The Compounding Expert Committee	2015 (draft)	United States	Regulatory framework
Good Preparation Practices ²³	Afssaps (Agence française de sécurité sanitaire de produits de santé)	2007	France	Regulatory framework
Mesures de protection relatives à la manipulation de médicaments (Protective measures related to the handling of medicines) ²⁴	Swiss Accident Insurance Fund	2018	Switzerland	Occupational safety recommendations
WHO Good Manufacturing Practices, Annex 3 ²⁵	WHO Expert Committee on Specifications for Pharmaceutical Preparations	2010	International	Regulatory framework
Chemotherapy Administration Safety Standards ⁷	American Society of Clinical Oncology/ Oncology Nursing Society	2016	United States	Scientific society's quality standards
OSHA: Controlling Occupational Exposure to Hazardous Drugs ³	Occupational Safety and Health Administration (US Department of Labor)	Consulted 2016	United States	Occupational safety recommendations
NIOSH Alert: Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings ²	National Institute for Occupational Safety and Health	2004	United States	Occupational safety recommendations
Safe Handling of Hazardous Chemotherapy Drugs in Limited-Resource Settings ⁵	Pan American Health Organization (PAHO)	2013	PAHO	Recommendations

isopropanol 75% over a surface of 100 cm². After sampling, each swab was preserved separately in a small closed glass container. Samples were transported in insulated envelopes, with ice packs (for < 24 hours), and then frozen to < -20°C until analysis. Samples were analyzed in Switzerland by CytoLab³¹ using an ultrahigh pressure liquid chromatography coupled with mass spectrometry method, enabling the simultaneous identification of 23 antineoplastic drugs.²⁹

Proof of Concept

The principal investigator organized audits in several hospitals in LMICs to test the toolkit's applicability and relevance. Facilities were chosen through professional networks, and participation was voluntary. The same investigator performed audits at the different sites during 4-day visits (Table 2). Data were collected through observations, interviews, and surface-wipe sampling.

RESULTS

The final toolkit consisted of one assessment tool, three observation checklists, and a surface-wipe sampling

method. The Cyto-SAT assessment tool encompasses 134 items in 10 domains and 28 subdomains covering the entire cytotoxic drug handling process in health care facilities (Table 3). A free online service was developed to allow any LMIC hospital to self-assess its practices.³²

Unlike Cyto-SAT, the three structured observation checklists focus on one process each.

The prescription checklist includes items evaluating whether the chemotherapy prescription is clear and unambiguous and includes all the necessary information to provide safe treatment. It addresses prescription format, prescriber identification, patient-related information, and the chemotherapy protocol (Data Supplement).

The preparation checklist items assess the preparation process and operators' practices to ensure traceability throughout chemotherapy preparation, thus maintaining product integrity, preventing potential medication errors, and limiting the risks of occupational exposure (Data Supplement). This checklist exists in three versions so as to cover every possible situation found in LMICs: (1) chemotherapy preparation in environments without biosafety cabinets

TABLE 2. Example of a 4-Day Audit Visit Program

Days of Visit	Morning	Afternoon	Remarks
Day 1	Meeting with the local audit coordinator Presentation and description of the local cancer patient management context Facility tour Introduction of the auditor to staff and presentation of the 4-day audit's objectives and program	Start of the audit Data collection according to the Cyto-SAT tool Review of different prescribers' prescription practices (checklist)	Before the visit, each pilot site had to appoint a local audit coordinator
Day 2	Structured observation of chemotherapy preparation practices (checklist) Structured observation of chemotherapy administration practices (checklist)	Data collection according to the Cyto-SAT tool (end) Prescription review of the different prescribers with the prescription observation checklist	Timetable for observing prescriptions, preparation, and administration according to the activity in the facility
Day 3	Structured observation of chemotherapy preparation practices (checklist)	Structured observation of the chemotherapy administration practices (checklist)	
Day 4	Feedback from the auditor to the medical representative, nurse, and pharmacist to discuss results	Collection of the surface-wipe samples Return to airport	An audit report would be sent a few days later (including results of the surface-wipe contamination tests)

(BSCs) and cleanrooms, (2) chemotherapy preparation under a BSC but without a cleanroom, and (3) chemotherapy preparation under a BSC inside a cleanroom.

The administration checklist considers the entire course of care, with items assessing practices before, during, and after chemotherapy administration. It addresses aspects related to hygiene measures, the protection of nurses, checking procedures to limit treatment errors, patient surveillance, and waste management (Data Supplement). This checklist was developed for peripheral intravenous administration (infusion or a direct intravenous route) solely, as this is by far the most common route of administration. Administration via a central venous catheter is very rarely used in LMIC public hospitals because of its high cost.

We tested the toolkit in three teaching hospitals in Africa (Yaoundé in Cameroon, Fès in Morocco, and Dakar in Senegal) between November 2019 and February 2020. All three hospitals treated inpatients and outpatients for cancer. One of the institutions had a centralized chemotherapy preparation unit with two isolators located in a nonclassified room inside the hospital pharmacy. At the other two hospitals, nurses prepared chemotherapies in patients' rooms just before administration, directly at the bedside in one and on a workbench in the other. In each hospital, the investigator used all four data collection tools and took 10-15 surface-wipe samples. The tools developed enabled measurement of how well standards of practice were applied (Table 3) and provided the levels of cytotoxic contamination in the real-world environments of all three sites (Fig 1). All 35 samples revealed some cytotoxic contamination, with a total contamination level of the different drugs tested ranging from 74 ng to 12,401 ng, with a median of 856 ng (first quartile: 255 ng-third quartile: 3,104 ng). The safety and procedural gaps and points requiring improvement that were identified enabled us to

draw up an action plan for implementing improvement measures in each hospital (Table 4).

DISCUSSION

The audit method and the different tools developed via this project enabled a comprehensive assessment of the safety of chemotherapy handling in three health care institutions in LMICs. The toolkit contains one 134-item global assessment tool to evaluate the different processes at each step of the medication pathway and three step-specific observation checklists to assess the practices of different health workers during the prescription, preparation, and administration of chemotherapies. The toolkit also proposes the use of a surface-wipe sampling method to measure any cytotoxic contamination of the immediate environment. The implementation of this audit method in a variety of settings enabled us to verify its applicability by future users.

The different tools enable a quick comparison between the practices currently used and those that are recommended, making it easy to identify areas for improvement. An action plan can then be drawn up on the basis of this thorough evaluation.

In general, the tools developed proved easy to use and were applicable in different contexts. Following our visits to the different hospitals, two additional versions of the observation checklists will be added to the toolkit in the future. The first is a specific version for chemotherapy preparation in an isolator, and the second is a version for the administration of chemotherapy by a central venous catheter for those countries with sufficient resources.

Surface-wipe sampling allowed us to highlight the levels of contamination in the different hospitals' working environments. Contamination levels differed significantly depending on the surfaces sampled. The most contaminated

TABLE 3. Results of the Cyto-SAT Evaluation: Percentage of Safe Practices Implemented in the Different Domains and Subdomains at the Three Hospitals

Domain	Subdomains	No. of Items	Hospital 1 (%)	Hospital 2 (%)	Hospital 3 (%)
Management		11	24	18	85
Personnel	Education and training	4	25	0	58
	Medical surveillance	3	78	22	67
Logistics	Receipt	5	27	NA	60
	Storage	6	50	NA	67
	Transport	5	0	0	40
Prescription		5	80	73	100
Preparation	Management and organization	4	0	8	83
	Parenteral medicine preparation areas	10	0	7	70
	Hygiene and personal protective equipment	6	11	22	72
	Preparation process setup	4	25	17	83
	Preparation technique	9	33	21	81
	Packaging and labeling	3	11	56	56
	Checking procedure	2	0	0	50
	Documentation	3	0	33	67
	Maintenance	2	NA	NA	67
	Nonsterile preparation	1	NA	NA	100
Administration	Management	2	33	83	50
	Hygiene and safety measures	5	60	73	73
	Documentation	3	11	67	100
	Work practices	4	11	11	75
Incident management	Surface contamination	6	0	11	28
	Staff contamination	3	0	0	33
	Extravasation	3	11	0	44
	Quality assurance	1	0	0	33
Waste management	Waste disposal	7	19	10	57
	Patients' excreta	3	11	22	44
Cleaning	Management and organization	2	17	33	67
	Cleaning practices	6	17	58	61
	Laundry	2	0	0	17
Patient counseling		4	42	50	25
Total		134	23	24	62

Abbreviation: NA, not applicable.

spots were found to be inside the isolators and on the equipment used for preparation. It was both interesting and valuable for each hospital to see which surfaces were the most contaminated and where occupational exposure risks were highest. Compared with the results obtained from samples from European or Swiss hospitals analyzed by Cytoxlab, the amounts of contamination we sampled were much higher (internal data). Although there are no acceptable or recommended limits, the precautionary principle implies reducing environmental contamination by chemotherapies to a minimum, notably through better working techniques, process reorganization, the use of equipment that limits the risks of contaminating personnel,

and the application of adequate cleaning or chemical decontamination procedures. Unfortunately, local analysis of the surface-wipe samples was impossible as it required specialist, high-cost equipment. Transporting samples was also challenging as no professional transport company could guarantee to get them to Cytoxlab within 24 hours to ensure their stability.

Although the literature on safe handling practices in LMICs is still scarce, several studies have reported unsafe practices and the need for improvements.^{14,18,19,33,34} Our study's findings confirmed that the level of safe practices in some institutions remained very low. Thus, implementing safety standards and continuous quality improvement

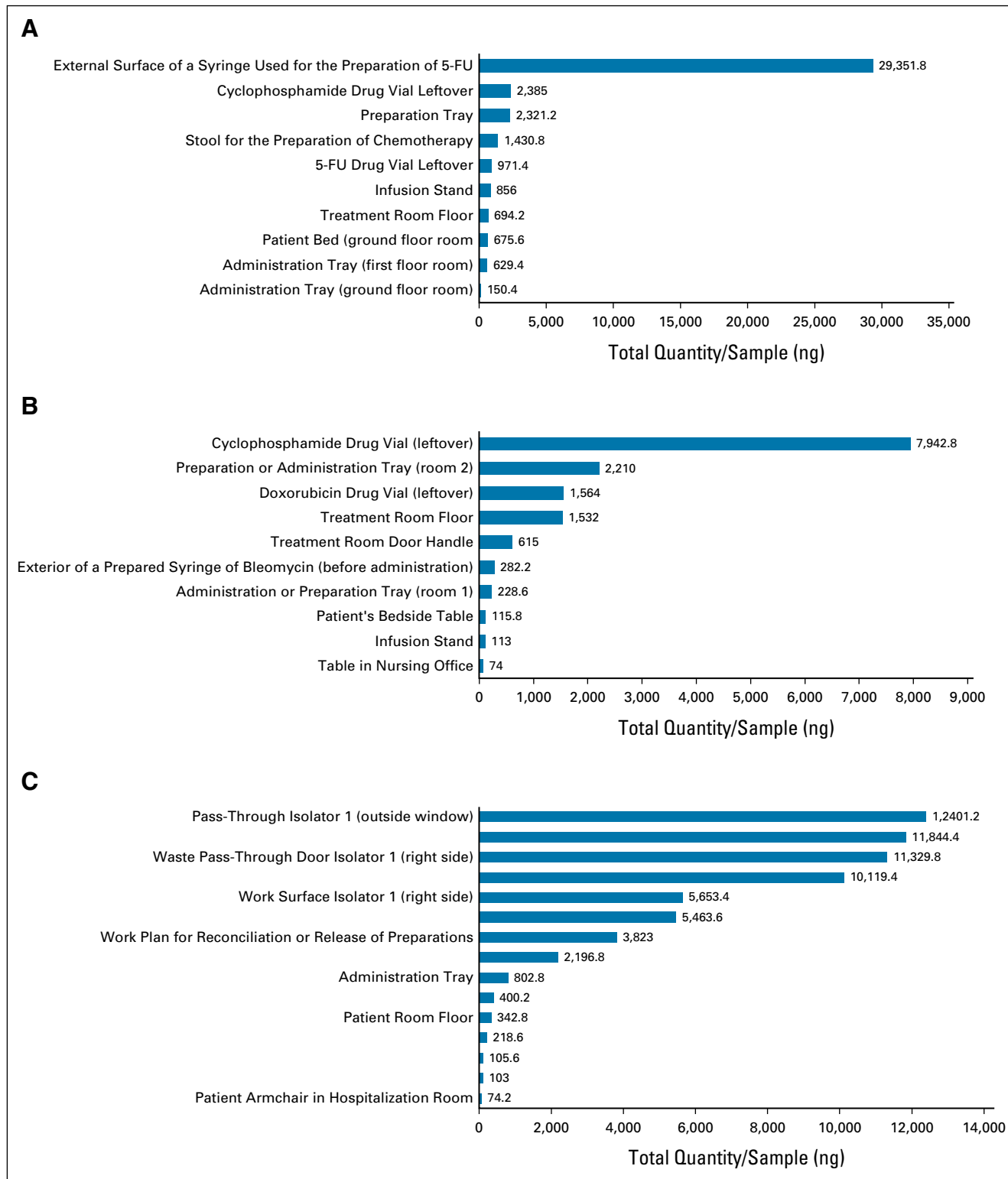


FIG 1. Surface-wipe sampling results in the three hospitals (sum of the 23 cytotoxics tested). (A) Hospital 1: total cytotoxic contamination by surface sample (ng). (B) Hospital 2: total cytotoxic contamination by surface sample (ng). (C) Hospital 3: total cytotoxic contamination by surface sample (ng). FU, fluorouracil.

approaches in this area is of utmost importance as the number of cancer treatments will continue increasing in the coming years. The audit toolkit (available in the Data

Supplement) offers LMIC health care facilities ready-to-use tools and checklists to assess their safe handling of cytotoxic medicines and ensure patient and staff safety. Our

TABLE 4. Summary of the Three Hospitals' Strengths, Areas Requiring Improvement, and Actions Required Following Their Audit

Audit Results	Hospital 1	Hospital 2	Hospital 3
Main strengths	<p>Storage Dedicated storage area for cytotoxic drugs, separate from other medicines, in a closed cupboard</p> <p>Prescription Only by authorized prescribers Use of standard protocols Use of preformatted forms, with the minimum recommended information</p> <p>Preparation and administration Same-day laboratory results are verified before authorizing preparation of the chemotherapy The staff wear work clothes (not civilian clothes) Access to treatment room is limited to authorized staff and patients The nursing staff are kind and empathetic with patients Always one staff member present in the treatment room for patient surveillance</p> <p>Hygiene Staff respect basic hygiene (no smoking, drinking, and eating in the administration and preparation areas) The bins are emptied regularly</p>	<p>Prescribing Only by authorized prescribers Use of standard protocols Use of preformatted forms, with the minimum recommended information</p> <p>Preparation and administration The staff wear work clothes (not civilian clothes) and a lab coat during preparation and administration During the preparation and administration of chemotherapies, family and caregivers leave the room Patients are comfortably seated on individual beds Nurses report what has been done and any potential side effects that they observe on the back of the prescription</p> <p>Hygiene Staff respect basic hygiene (no smoking, drinking, and eating in the administration and preparation areas) The bins are emptied regularly</p>	<p>A continuous improvement approach to the quality and safety of the chemotherapy circuit was implemented</p> <p>Prescribing Electronic prescribing of chemotherapies Only by authorized prescribers Use of standard protocols Validation of the prescription by a pharmacist before preparation</p> <p>Preparation Centralized unit for chemotherapy preparation in the pharmacy, with separate areas for each step of the process Preparation in isolators Regular maintenance of the isolators according to a preventive maintenance plan Reconciliation of preparations with prescriptions before dispatch to the wards</p> <p>Hygiene Staff respect basic hygiene (no smoking, drinking, and eating in the administration and preparation areas) The bins are emptied regularly</p> <p>Administration Verification that the preparation and its administration plan match Patients are comfortably seated on individual chairs Final check of the patient's identity carried out at bedside</p>
Main areas requiring improvement	<p>Storage Gloves not used to handle chemotherapy drugs</p> <p>Preparation Many hygiene issues leading to potential risks of microbiologic contamination of the chemotherapy formulation and a high risk of occupational exposure Lack of appropriate personal protective equipment No BSC Lack of control, traceability, and inadequate labeling of the chemotherapy formulation Lack of specific staff training on good preparation practices</p> <p>Administration Lack of hand sanitizing Gloves not changed between patients No cross-checking between patient prescription and the chemotherapy formulation given to the patient Lack of a clear procedure in the case of extravasation</p> <p>Incident management No spill kit available and no specific procedure No clear procedure in the case of staff contamination</p> <p>Waste management Waste management process not safe</p>	<p>Preparation Many hygiene issues leading to potential risks of microbiologic contamination of the chemotherapy formulation and a high risk of occupational exposure Lack of appropriate use of personal protective equipment Preparation at patient's bedside No BSC Lack of control, traceability, and inadequate labeling of the chemotherapy formulation Lack of specific staff training on good preparation practices</p> <p>Administration Lack of hand sanitizing Gloves not changed between patients No cross-checking between patient prescription and the chemotherapy formulation given to the patient Lack of a clear procedure in the case of extravasation</p> <p>Incident management No spill kit available and no specific procedure No clear procedure in the case of staff contamination</p> <p>Waste management Use of inappropriate containers for the disposal of sharps waste</p>	<p>Storage Cytotoxic drugs stored in the same room as other drugs Gloves not always worn to handle drugs</p> <p>Preparation Labeling of the preparation done outside the isolator by another staff member when doing the reconciliation (risk of error) Lack of information on the label (eg, batch number, storage conditions etc) Lack of in-process control of drug volume and dosage Lack of regular microbiologic monitoring of equipment and the environment to ensure preparation in aseptic conditions High level of cytotoxic contamination in the isolator and on the reconciliation table (inadequate cleaning procedure)</p> <p>Administration Insufficient use of PPE during administration and handling of excreta Lack of clear written procedure in the case of extravasation and no extravasation kit available</p> <p>Incident management No spill kit available and no specific procedure No clear procedure in the case of staff contamination</p>

(Continued on following page)

TABLE 4. Summary of the Three Hospitals' Strengths, Areas Requiring Improvement, and Actions Required Following Their Audit (Continued)

Audit Results	Hospital 1	Hospital 2	Hospital 3
Summary of actions required	<p>Storage</p> <ul style="list-style-type: none"> Wearing of gloves when receiving, storing, and dispensing anticancer drugs <p>Preparation</p> <ul style="list-style-type: none"> Establishment of a procedure for double-checking the doses of the anticancer drugs prescribed Staff training on good preparation practices with regular supervision Wearing of appropriate PPE during preparation Centralization of preparation in a separate area from other activities and limitation of access to it Preparation of chemotherapy in a type IIb BSC or isolator Improvement of hygiene measures during preparation Implementation of an in-process control procedure for the dose of anticancer drugs Introduction of a traceability system for chemotherapy formulations <p>Improvement of chemotherapy formulation labeling</p> <p>Administration</p> <ul style="list-style-type: none"> Improvement of hygiene measures during administration Implementation of a process for a final verification that the patient, their prescription, and their drugs (identities and dosage) match at the patient's bedside <p>Establishment of a procedure for managing extravasations</p> <p>Incident management</p> <ul style="list-style-type: none"> Availability of spill kits wherever chemotherapies are handled <p>Staff training on spill management procedures</p> <p>Establishment of a procedure in the case of staff contamination</p> <p>Waste management</p> <ul style="list-style-type: none"> Making the waste management process safe Use of lidded bins to maintain contamination (pedal system recommended) Training for cleaning and waste management staff Making the transport of waste to its destruction site safe by using closed containers 	<p>Preparation</p> <ul style="list-style-type: none"> Establishment of a procedure for double-checking the doses of the anticancer drugs prescribed Staff training on good preparation practices with regular supervision <p>Wearing of appropriate PPE during preparation</p> <ul style="list-style-type: none"> Centralization of preparation in a separate area from other activities and limitation of access to it <p>Preparation of chemotherapy in a type IIb BSC or isolator</p> <ul style="list-style-type: none"> Improvement of hygiene measures during preparation Implementation of an in-process control procedure for the dose of anticancer drugs Introduction of a traceability system for chemotherapy formulations Improvement of chemotherapy formulation labeling preparations <p>Administration</p> <ul style="list-style-type: none"> Improvement of hygiene measures during administration Implementation of a process for a final verification that the patient, their prescription, and their drugs (identities and dosage) match at the patient's bedside Establishment of a procedure for managing extravasations <p>Incident management</p> <ul style="list-style-type: none"> Availability of spill kits wherever chemotherapies are handled Staff training on spill management procedures Establishment of a procedure in the case of staff contamination <p>Waste management</p> <ul style="list-style-type: none"> Making the waste management process safe Procurement of appropriate sharp waste containers Use of lidded bins to maintain contamination (pedal system recommended) Training for cleaning and waste management staff Making the transport of waste to its destruction site safe by using closed containers 	<p>Storage</p> <ul style="list-style-type: none"> Storage of anticancer drugs in a separate room from other drugs <p>Preparation</p> <ul style="list-style-type: none"> Strengthening of operator training and supervision Strengthening proper use of PPE Limiting access to the preparation room to authorized staff only Improvement of the traceability of chemotherapy formulation (batch number, volume, expiry date etc) Improvement of chemotherapy formulation labeling procedures (directly in the isolators) Implementation of an in-process control procedure for the dose of anticancer drugs Introduction of regular microbiologic monitoring of equipment and the environment Implementation of annual checks of the preparation room according to the room's classification Adapting the cleaning procedures for isolators and the preparation room to reduce chemical contamination <p>Administration</p> <ul style="list-style-type: none"> Establishment of a written procedure for dealing with extravasations Provision of an extravasation kit Strengthening proper wearing of PPE during chemotherapy administration and excreta handling <p>Incident management</p> <ul style="list-style-type: none"> Availability of spill kit wherever chemotherapies are handled Staff training on spill management procedures Establishment of a procedure in the case of staff contamination

Abbreviations: BSC, biosafety cabinet; PPE, personal protective equipment.

goal would be for any health facility using our toolkit to conduct regular audits and measurements of their environmental contamination to monitor their progress as they implement their action plan.

Safe chemotherapy handling practices are an essential element in cancer management and ensuring staff and patient safety. Besides this audit toolkit, which is available free of charge through our Pharm-Ed platform,³⁵ we also provide e-learning courses on various aspects of safe chemotherapy handling practices. Many practical tools (eg, procedures, checklists, etc) and video tutorials are also available to facilitate the

implementation of good practices. The overall impact of such a training program on practice improvements within a health care institution or a group of health care institutions is yet to be studied.

In conclusion, the toolkit described in the present work was successfully applied in a variety of LMIC settings and provided comprehensive evaluations of the quality and safety of the chemotherapy drug handling practices in three health care facilities in Africa. The toolkit can help facilities in LMICs to implement a continuous quality improvement approach, implement better practices, and, ultimately, ensure patient and staff safety.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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REFERENCES

- Falck K, Gröhn P, Sorsa M, et al: Mutagenicity in urine of nurses handling cytostatic drugs. *Lancet* 1:1250-1251, 1979
- Connor TH, Burroughs G, McDiarmid M, et al: NIOSH Alert: Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. Atlanta, GA, DHHS NIOSH, 2004, pp 1-50
- Occupational Safety and Health Administration: Controlling Occupational Exposure to Hazardous Drugs. United States Department of Labor. https://www.osha.gov/SLTC/hazardousdrugs/controlling_occex_hazardousdrugs.html
- International Society of Oncology Pharmacy Practitioners Standards Committee: ISOPP standards of practice. Safe handling of cytotoxics. *J Oncol Pharm Pract* 13:1-81, 2007 (suppl)
- ASHP Council on Professional Affairs: ASHP guidelines on preventing medication errors with antineoplastic agents. *Am J Health Syst Pharm* 59:1648-1668, 2002
- Pan American Health Organization: Safe Handling of Hazardous Chemotherapy Drugs in Limited-Resource Settings. Washington, DC, PAHO, 2013. <https://iris.paho.org/handle/10665.2/28554>
- Neuss MN, Gilmore TR, Belderson KM, et al: 2016 Updated American Society of Clinical Oncology/Oncology Nursing Society Chemotherapy Administration Safety Standards, Including Standards for Pediatric Oncology. *Oncol Nurs Forum* 44:31-43:2017
- Wild C, Weiderpass E, Stewart BW: World Cancer Report: Cancer Research for Cancer Prevention. Lyon, France, International Agency for Research on Cancer, 2020. <http://publications.iarc.fr/586>
- Bray F, Soerjomataram I: The changing global burden of cancer: Transitions in human development and implications for cancer prevention and control, in Gelband H, Jha P, Sankaranarayanan R, et al (eds): *Cancer: Disease Control Priorities, Volume 3* (ed 3). Washington, DC, The International Bank for Reconstruction and Development/The World Bank, 2015. <http://www.ncbi.nlm.nih.gov/books/NBK343643/>
- World Health Organization: Cancer Fact Sheets, 2021. <https://www.who.int/news-room/fact-sheets/detail/cancer>
- Sung H, Ferlay J, Siegel RL, et al: Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 71:209-249, 2021
- International Agency for Research on Cancer (IARC): Cancer Today, 2020. <http://gco.iarc.fr/today/home>
- International Atomic Energy Agency: London Forum Pledges Support for Africa Cancer Plan, 2007. <https://www.iaea.org/newscenter/news/london-forum-pledges-support-africa-cancer-plan>
- von Grünigen S, Geissbühler A, Bonnabry P: The safe handling of chemotherapy drugs in low- and middle-income countries: An overview of practices. *J Oncol Pharm Pract* 10.1177/1078155221995539 [epub ahead of print on February 23 2021]
- Taylor MJ, McNicholas C, Nicolay C, et al: Systematic review of the application of the plan–do–study–act method to improve quality in healthcare. *BMJ Qual Saf* 23:290-298, 2014
- Institute for Healthcare Improvement. How to Improve | Institute for Healthcare Improvement, <http://www.ihc.org:80/resources/Pages/HowtoImprove/default.aspx>
- Boiano JM, Steege AL, Sweeney MH: Adherence to safe handling guidelines by health care workers who administer antineoplastic drugs. *J Occup Environ Hyg* 11:728-740, 2014
- Chaudhary R, Karn BK: Chemotherapy-knowledge and handling practice of nurses working in a medical university of Nepal. *J Cancer Ther* 3:110, 2012

19. Patil VM, Chakraborty S, Bhattacharjee A, et al: Survey of the state of implementation of the American Society of Clinical Oncology/Oncology Nursing Society safety standards for chemotherapy administration in India. *JCO Oncol Pract* 11:365-369, 2015
20. European Society of Oncology Pharmacy: Quapos 4. Quality Standard for the Oncology Pharmacy Service With Commentary. https://www.esop.li/downloads/library/quapos4_english.pdf
21. Power LA, Coyne JW: ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm* 75:1996-2031, 2018
22. USP Expert Committee: USP General Chapter <800> Hazardous Drugs—Handling in Healthcare Settings, 2017. <http://www.usp.org/sites/default/files/usp/document/our-work/healthcare-quality-safety/general-chapter-800.pdf>
23. Agence Française de Sécurité Sanitaire des Produits de Santé: Bonnes pratiques de préparation. Saint-Denis cedex: AFSSAPS, 2007. [https://www.ansm.sante.fr/Activites/Elaboration-de-bonnes-pratiques/Bonnes-pratiques-de-preparation/\(offset\)/7](https://www.ansm.sante.fr/Activites/Elaboration-de-bonnes-pratiques/Bonnes-pratiques-de-preparation/(offset)/7)
24. Sécurité dans l'emploi des cytostatiques (Safe handling of cytostatics), 2018, <https://www.suva.ch/fr-CH/materiel/documentation/mesures-de-protection-relatives-e-la-manipulation-des-medicaments>
25. World Health Organization: Annex 3: WHO Good Manufacturing Practices for Pharmaceutical Products Containing Hazardous Substances, 2010. WHO Technical Report Series 957 https://www.who.int/medicines/areas/quality_safety/quality_assurance/GMPPharmaceuticalProductsContainingHazardousSubstances/TRS957Annex3.pdf
26. von Grünigen S, Geissbühler A, Bonnabry P: Cyto-SAT: A self-assessment tool for the safe handling of cytotoxic drugs adapted for use in low- and middle-income countries. *J Oncol Pharm Pract* 27:1422-1431, 2020
27. Connor TH, Zock MD, Snow AH: Surface wipe sampling for antineoplastic (chemotherapy) and other hazardous drug residue in healthcare settings: Methodology and recommendations. *J Occup Environ Hyg* 13:658-667, 2016
28. Guichard N, Boccard J, Rudaz S, et al: Wipe-sampling procedure optimisation for the determination of 23 antineoplastic drugs used in the hospital pharmacy. *Eur J Hosp Pharm* 28:94-99, 2021
29. Guichard N, Fekete S, Guillarme D, et al: Computer-assisted UHPLC-MS method development and optimization for the determination of 24 antineoplastic drugs used in hospital pharmacy. *J Pharm Biomed Anal* 164:395-401, 2019
30. Guichard N, Rudaz S, Bonnabry P, et al: Validation and uncertainty estimation for trace amounts determination of 25 drugs used in hospital chemotherapy compounding units. *J Pharm Biomed Anal* 172:139-148, 2019
31. Cytoxlab - Laboratory specialized in the analysis of anticancer drugs. Cytoxlab. September 28, 2021. <https://cytoxlab.ch/?lang=en>
32. Cyto-SAT: A self-assessment tool for safe handling of cytotoxic medicines. September 28, 2021. https://pharmed.datapharma.ch/cyto-sat_en/
33. Simegn W, Dagne B, Dagne H: Knowledge and associated factors towards cytotoxic drug handling among University of Gondar Comprehensive Specialized Hospital health professionals, institutional-based cross-sectional study. *Environ Health Prev Med* 25:11, 2020
34. Khan N, Khowaja KZA, Ali TS: Assessment of knowledge, skill and attitude of oncology nurses in chemotherapy administration in tertiary hospital Pakistan. *Open J Nurs* 2:97, 2012
35. Pharm-Ed: Educational and collaborative platform for efficient, safe and rational management of medicines in hospitals. September 28, 2021. www.Pharm-Ed.net

