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Process Analysis of Non-Administered Drug Returns in a University Hospital: Assessment, Influencing Factors, and Management Implications–A case study from Liège, Belgium

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ABSTRACT

Objectives The return of non-administered drugs represents a significant challenge in hospital pharmacy management, contributing to increased workload, financial loss, and safety risks. This study aimed to quantify the extent of medication returns at Liège University Hospital (CHU Liège), Belgium, identify key contributing factors, and explore potential improvements within a highly digitalised hospital environment.

Methods A case study was conducted using data extracted from the hospital's robotic dispensing systems. Return rates for individually prepared doses were analysed for a period of six months. Variability was assessed according to several parameters, including care units, drug types, the time interval between dose preparation and administration, prescription stability, and patient movements (transfers or discharges).

Results During a six-month study period, a return rate of 13.4% was observed for individually prepared doses. Considerable variability emerged across care units and medication categories. Key determinants of returns included early preparation relative to administration times and medical rounds, frequent modifications to injectable prescriptions, and patient transfers or discharges. These findings enabled the identification of several operational measures within the hospital pharmacy aimed at reducing drug returns. This study highlights significant opportunities for improvement, including the discontinuation of early-day ("D0") dose preparation and the adaptation of drug distribution models to the specific characteristics and needs of each individual care unit.

Conclusion The present work underscores the value of digital tools and data-driven approaches to enhance efficiency and safety in hospital settings. It also highlights the limitations of current medication distribution systems and identifies improvement initiatives in hospital practice.

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1. Introduction

The hospital medication process is complex and multidisciplinary (Mahé, 2014). It includes both clinical (prescribing, dispensing, administration) and logistical (supply, transport, storage) aspects. Ensuring control and safety at each stage is a major challenge for hospitals. To reach this goal, implementing IT solutions throughout the medication process can significantly improve safety (Seidling & Bates, 2016). Depending on the level of digital maturity of the hospital, these solutions may include computerised prescribing (with or without decision support tools), unit dose barcoding, robotic preparation, automated medication storage in care units (CUs), digital inventory management, etc. Although robots are expensive and difficult to interface with, they can be used for Individual Nominative Dispensing (IND) of treatments. IND is now a legal requirement in countries such as Belgium or France and is increasingly adopted worldwide to reduce serious adverse drug events. Currently, treatment production planning is still largely manual, repetitive and basic, and production schedules are usually organised by CU and day of the week.

The University Hospital of Liège (CHU Liège) is one of Belgium's seven academic hospitals and the only one in Wallonia. It operates across eight sites, including four inpatient facilities. In 2024, the hospital recorded over 40,000 classic admissions. At CHU Liège, prescriptions are computerised and dispensing is individual and nominative. During a representative week in March 2025, two robots produced approximately 73.8% of prepared treatments at the central pharmacy, over 7300 individual doses per day, distributed across 3 hospital sites (32 CUs). Robots' production is organised by CU and by day of administration, maximum 3 days before administration. Manual preparation is used for medications that are incompatible with robotic systems, such as those requiring specific storage conditions or larger volumes. In addition, medication storage facilities are present in CUs, some of which are computerised.

In most hospitals in Belgium and internationally, between 10% and 30% of medications dispensed by the central pharmacy are not administered. These drugs are often returned to the pharmacy, but many are lost or become non-reusable and must be discarded. The volume of returned medications has significant negative consequences: it increases workload due to manual tasks with little added value (sorting, scanning, storing), causes financial losses, undermines the safety of the medication management process and raises ethical concerns—especially during drug shortages. The main causes of returns include patient movement (discharge, transfer) or prescription changes after the pharmacy has prepared the drugs. These causes have been investigated in several studies. According to (Renaud , Wattecamps , Blondiaux, Moens, & Zawadzki, 2014), discharge represents 47% of returns and prescription changes 15%. A paper showed that the major contributing factors for the return of medicines from CUs to the pharmacy were discharge of patients (39%) or discontinuation of medication (20%) and that 60% of returned medications were injectable formulations (Hashmi, Khaliq, & Sultana, 2017).

While numerous studies have focused on improving medication safety, few have addressed how to reduce drug returns. A study in a French hospital (Frery, Gayet, Maurer, & Collinot, 2019) showed that switching from twice-weekly to daily distribution reduced return rates from 17% to 5%. However, more frequent distribution is not always feasible. Better communication between CUs and the pharmacy—such as alerts when patients are discharged—can also help reduce returns (Renaud , Wattecamps , Blondiaux, Moens, & Zawadzki, 2014), but this alone is insufficient. The Hashmi, 2017 study concluded that medicine returns and medication errors can be controlled by upgrading CU medication stock lists and by improving the medication management system (Hashmi, Khaliq, & Sultana, 2017).

First, we will describe the study setting, including the organization of medication dispensing at the CHU, as well as the processes used to monitor and manage medication returns. We will then present the statistical methodology applied to identify the factors associated with these returns. Subsequently, we will report the results, including the overall return rate and the parameters influencing its variability. Finally, we will discuss these findings in light of the existing literature, highlighting their practical implications for the CHU, potential opportunities for improvement, the limitations of the study, and perspectives for future research.

2. Materials and Methods

2.1 Environmental context: CHU Liège - Dispensing organization

In Belgium, the law mandates that medications be dispensed based on a prescription issued in the patient's name, preferably using unit doses whenever feasible. The Royal Decree of September 30, 2020, authorises the use of a CU dispenser in four specific scenarios: administration of the first dose of a treatment, urgent administration following a prescription outside the hospital pharmacy's operating hours, PRN (pro re nata) medications and within acute care departments such as emergency rooms, intensive CUs and delivery rooms.

Currently, at CHU Liège, Individual and Nominative Daily Dispensing (INDD) is provided to the majority of hospitalised patients (1,002 under 1052 beds). Except for approximately fifteen drug references for which the only source of supply is the ward medication cabinet, drug dispensing comes partly from a robot that organises unit doses in bags and partly from manual preparation (large volumes, multidose formulations, etc.).

The pharmacy operates six days a week and provides two daily deliveries to CUs. The "D+1" delivery arrives at the CU at 5:30 p.m. and includes all treatments to be administered the following day, for which prescriptions have been entered by physicians into the Electronic Medical Record (EMR) between noon on the previous day and 4:00 p.m. on the current day. The "D0" delivery arrives at 2:30 p.m. and includes modifications and new patient treatments to be administered the current day for which prescriptions have been entered between 4:00 p.m. the previous day and noon on the current day. For medications requiring administration before the next scheduled delivery, nursing staff collect the medication directly from the ward medication cabinet or at the pharmacy counter, in compliance with the Royal Decree. On Saturdays and the day before public holidays, the pharmacy additionally supplies treatments for "D+2".

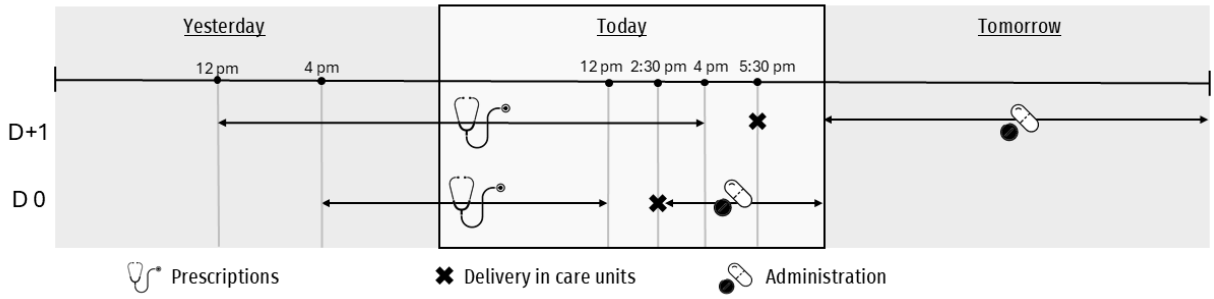


Figure 1. Delivery Schedule of Robot-Prepared Medications to CU

The INDD team comprises 11.8 Full Time Equivalent (FTE), including 1 pharmacist, 6 pharmacy assistants (3.5 dedicated to the automated system and 2.5 to manual preparation), 2 technicians, 1 operator, and 1.8 logistics assistants.

CHU Liège is undergoing expansion, having recently integrated two additional institutions accommodating 124 and 160 hospitalised patients, respectively. To standardise the medication management process, an evaluation is underway to integrate these sites into the existing INDD system. Furthermore, some units require the acquisition of automated medication cabinets, while others need to replace outdated ones. Consequently, a comprehensive review of the medication management process is in progress, aiming to optimise service quality and proactively address future challenges.

2.2 Drug Return Tracking and Measurement

The return of medications is a topic being studied worldwide, including for medications prescribed and used outside of hospitals, with the aim of reducing waste and inappropriate medication use (Kutina, Dugle, & Bawontuo, 2025). Similarly, a paper reported that numerous medicine take-back programmes have been implemented worldwide to collect unused, unwanted, or expired medications held by households. Such programmes vary considerably according to national contexts, with schemes administered by public authorities, pharmaceutical manufacturers under extended producer responsibility frameworks, or local pharmacies and municipalities (Wang, Aziz, Wang, & Chik, 2024). In its comparative analysis and policy recommendations on pharmaceutical household waste management, the Organisation for Economic Co-operation and Development (OECD) emphasised the environmental, economic, and public health risks associated with unused or expired medicines stored in patients' homes. These products, which no longer provide therapeutic value, may contribute to inappropriate drug use, accidental exposure, and environmental contamination when improperly discarded (OECD, 2022). At a global level, a substantial proportion of unused medications remain unreturned and are predominantly disposed of through inappropriate routes, including environmental release. The literature indicates that familiarity with proper medication return pathways is positively associated with return behaviours, whereas environmental awareness alone appears insufficient to significantly influence disposal practices (Wang, Leong Seng, Aziz, Wang, & Chik, 2025). The economic importance of medication management is also reflected in national pharmaceutical expenditure. In Belgium, the National Institute for Health and Disability Insurance (NIHDI) reported total pharmaceutical expenditure of 7.932 billion EUR in 2024. Since 2020, the share attributable to hospitals has exceeded that of public pharmacies, reaching 54.7% in 2024, highlighting the increasingly important role of hospital pharmacies in the management of healthcare resources and medication-related processes (National Institute for Health and Disability Insurance (NIHDI), 2026).

At the hospital level, medication returns may represent a substantial economic burden. Similar to the high-value segments identified within the pharmaceutical supply chain, such as biotechnology products and specialty medicines, high-cost medications, including injectable therapies, anticancer agents, and immunomodulators, can account for a disproportionate share of the financial value associated with medication returns. Consequently, these products warrant particular attention in the design and implementation of medication return management strategies (Sood, Mulligan , & Zhong, 2021).

One of the main challenges in comparing return rates between hospitals lies in the lack of a standardised definition of the return rate itself. Different institutions use different denominators for their calculations: some base it on the number of doses dispensed by automated systems, others on the number of doses delivered by the central pharmacy, and still others on the number of doses not administered. In addition, the unit of measurement varies—returns may be recorded per individual unit, per blister pack, or per full box—further complicating inter-hospital comparisons.

Compounding this variability is the fact that the medication management process is not a closed-loop system. Once a drug has been dispensed to a CU, its fate depends largely on local nursing practices. Medications may be administered, discarded, stored in ward medication cabinets, or returned to the central pharmacy—sometimes with no record in the hospital's information system. As a result, the actual number of unused or returned medications is often underestimated and incomplete.

Furthermore, it is essential to distinguish between drugs that are unadministered and *should* be returned, and those that *are* effectively returned and recorded. This distinction introduces additional variability that impacts the reliability of reported return rates.

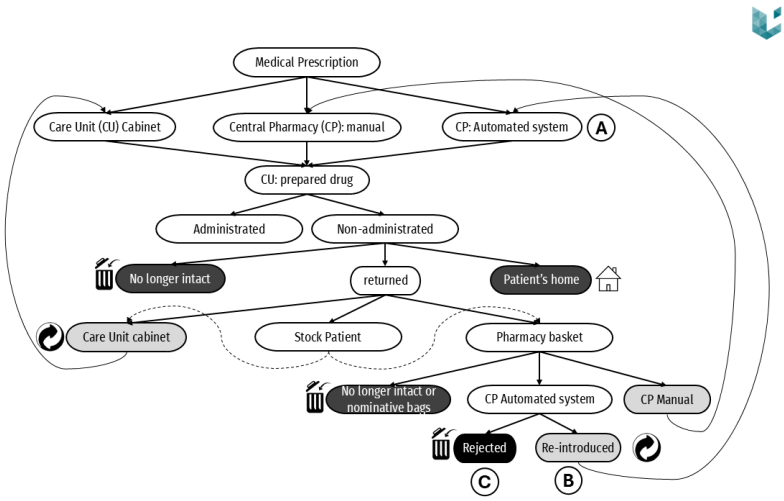


Figure 2. Drug supply chain in hospitals

To further illustrate this complexity, Figure 2 presents a schematic overview of the hospital drug supply chain, from prescription to the final physical status of a medication. It depicts both the sources of drug dispensing and the different pathways that unadministered drugs may follow.

Medications prescribed in the hospital can be dispensed via three primary channels: directly from the ward medication cabinet, from the central pharmacy through manual preparation, or via an automated dispensing system. Once prepared, the medication is either administered to the patient or remains unadministered. When a drug is not administered, its physical fate diverges into several possible routes, depending on local practices and storage conditions.

Some medications leave the hospital supply circuit entirely—these are represented in black in the diagram. This occurs when the medication is no longer intact, due to compromised sterility, damaged or incomplete packaging, or missing traceability elements such as batch number or expiration date. In other cases, drugs are given to patients at discharge and therefore leave the hospital system permanently.

Other drugs, shown in grey, may be reintegrated into the hospital supply chain and thus be reused for another patient. Certain drugs may "circulate" through the hospital multiple times before finally being administered. This reintegration can occur either at the CU level—where the drug is placed back in the ward medication cabinet—or at the central pharmacy level, where it is returned to either the manual stock or the automated system. Reintegration depends on the integrity and traceability of the returned medication and on the hospital's infrastructure and protocols.

Some hospitals use reconditioning or dispensing robots to produce patient-specific, unit-dose preparations. These individualized doses, once labelled and dispensed, typically cannot be reused if not administered, and are therefore discarded. Additionally, the timing of tracking differs across hospitals: some account for medication at the time of dispensing, others at the time of administration. This choice significantly affects how return events are captured physically and electronically.

Crucially, this diagram describes the physical handling of unadministered drugs, not their digital documentation. As such, it highlights the logistical and procedural heterogeneity across hospitals that complicates the accurate assessment and comparison of drug return rates.

At CHU Liège, return rates are monitored using data from the automated system by comparing the number of unit doses (UD) produced (A= denominator, figure 2) with those physically returned to the pharmacy and successfully reintroduced in the robot (B = numerator).

$$Return\ rate_{robot} = \frac{UD\ successfully\ reintroduced}{UD\ produced}$$

2.3 Statistical method

An in-depth analysis was conducted to identify the factors influencing medication returns, based on internal data from the CHU Liège. This data include information retrieved from three data sources: medical prescriptions that generate UD production lines, the robotic system used to produce UDs, and patient stay records. The data cover a six-month period, from 15 October 2024 to 31 March 2025, providing a detailed overview of return trends during this study period.

To identify the relevant parameters, all UDs generated by the robotic system during the analysis period were extracted (n = 1,084,210). UDs corresponding to productions that were cancelled before completion of the preparation process were excluded (n = 38,504, 3.6%), resulting in a final analytical dataset of 1,045,706 UDs. Only reliable variables, as assessed by the database experts, were included in the analysis. Missing values occurred only for variables where the database system permitted them (e.g., missing discharge dates). In these cases, the absence of a value reflected the absence of the corresponding event rather than missing information. Therefore, these variables were transformed into binary indicators (e.g., if the discharge date was missing, the patient was considered still hospitalised and a binary variable indicated whether discharge had occurred). Following the data cleaning process, medical prescriptions were linked to patient stay records via a unique identifier embedded within the data. Subsequently, the UD return data, provided by the robotic UD production system, were matched to these records using the unique UD identifier, the unique patient identifier, and ensuring that the UD production date was prior to the return date. Data quality checks were performed to verify the consistency of the extracted information. Additional derived variables describing time intervals between key events (e.g., admission, prescription, and administration dates) were generated for analysis. Physician-level characteristics, including the prescriber's medical specialty, were retrieved through linkage using the Belgian NIHDI number, a unique identifier assigned to healthcare professionals in Belgium.

The unit of analysis was the individual UD line. The outcome was binary (returned vs. not returned). Because multiple UDs could be prescribed and produced during the same hospital stay, observations were not statistically independent. Generalized Estimating Equations (GEE) were therefore used to account for clustering of observations within hospital stays while estimating population-averaged effects. Univariate GEE models were fitted using a binomial distribution with a logit link function and an independence working correlation structure, with the hospital stay identifier used as the clustering variable. For each candidate factor, the impact on the probability of UD return is expressed as odds ratios (ORs) with 95% confidence intervals (95% CIs) and p-values, using a fixed significance threshold of 0.05. All statistical analyses were performed using Python (version 3.13.1), primarily relying on the pandas, NumPy, SciPy, and statsmodels libraries.

3. Results

3.1 Return rate

During the six-month study period, 85.9% (11,164 of the 12,991) hospitalised patients were associated with at least one returned UD. The overall computed return rate was 13.4% (140,184 UDs among 1,045,706 UDs). However, this rate is likely to underestimate the true extent of medication losses. We were able to approximate other losses:

- The number of rejected bags amounted to 4,829 UDs (0.46% of the UD produced during the same period). (C, Figure 2)
- Returned medications prepared by the robot with damaged bags cannot be reintroduced into the robotic system, even when traceability and expiry information remain legible on the blister pack. These medications may nevertheless be restocked in the manual preparation area. During an 8-day study conducted in May 2025, in which all medications returned from the CUs and initially prepared by the robot were scanned and

manually counted, 1,915 UD were restocked in the manual preparation area, corresponding to 2.99% of all UDs produced during the same period.

Considering both rejected UDs (0.46%) and medications restocked in the manual preparation area (2.99%), the overall proportion of UDs returned to the central pharmacy can be estimated at 16.85%.

Return rates were further analysed according to medication type, therapeutic class, and CU.

- Return rates varied considerably from one drug to another. For example, Calcium Carbonate 1g tablets, which are among the drugs with the highest production volume by the robots, have a return rate of 12.9%. In contrast, Rosuvastatin10 mg tablets had the highest return volume overall, with a return rate of 20.4%. Another notable case is Tradonal (tramadol) 50 mg capsules, which showed a return rate of 49.5%. This variation in return rates is likely related to patient profiles. For example, calcium carbonate is typically prescribed to geriatric patients with longer hospital stays, whereas patients receiving rosuvastatin usually have cardiovascular risk factors and are more likely to undergo surgical procedures.
- Return rates varied across the first level of the Anatomical Therapeutic Chemical (ATC) classification system, ranging from 10.0% to 23.2%. In our hospital, medications belonging to ATC-level L (Antineoplastic and Immunomodulating Agents) showed the highest return rate (23.2%), followed by ATC-level S (Sensory Organs) with a return rate of 22.7%.
- To complement the model-based findings, we present the return rate of robot-prepared drugs, which show significant variations across CUs (Figure 3). Figure 3 presents the medication return rate and the corresponding volume of unit doses (UDs) produced across CUs. Bars represent the return rate (%) for each CU, whereas the dashed line indicates the volume of UDs produced. Considerable variability was observed between CUs. Notably, the rehabilitation unit combined a high production volume with a low return rate, whereas the maternity, paediatric, and neonatology units exhibited the highest return rates (> 40%) despite relatively low production volumes. CUs characterised by frequent admissions, transfers, and discharges may face a structurally higher risk of medication returns. In contrast, long-stay units, such as the rehabilitation unit, benefit from greater continuity of care and more stable medication regimens, which may contribute to lower return rates.

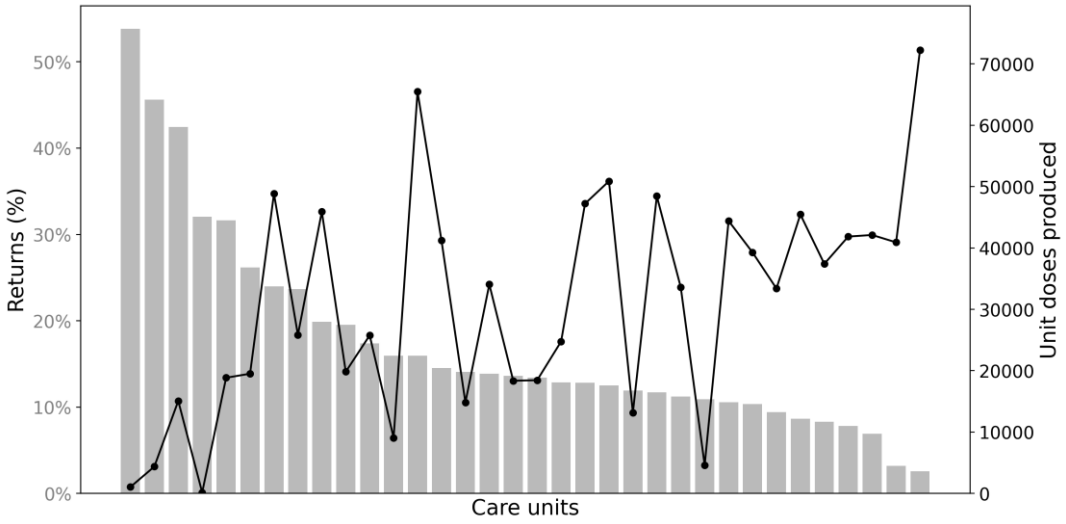


Figure 3. Robot-produced unit dose volume and return rates by CU.

3.2 Parameters influencing the returns

Several parameters were found to significantly influence the likelihood of a drug being returned (Table 1).

Table 1. Univariate analysis of parameters influencing the risk of return (GEE)

Parameters	OR (95% CI)	p-value
Administration PM (14h31 to 23h59)	2.04 (2.00 - 2.09)	<0.0001
Age/10	0.954 (0.933 - 0.975)	<0.0001
Urgency admission	0.798 (0.744 - 0.855)	<0.0001
IV Administration mode	2.32 (2.17 - 2.48)	<0.0001
In formation prescriber	1.14 (1.06 - 1.22)	0.0001
Production during weekend (Saturday)	0.650 (0.623 - 0.678)	<0.0001
Days between production and administration	0.539 (0.510 - 0.570)	<0.0001
Days between admission and administration	0.984 (0.980 - 0.987)	<0.0001
Days between admission and prescription	0.988 (0.985 - 0.990)	<0.0001
Days between prescription and administration	0.973 (0.968 - 0.978)	<0.0001
Days between prescription and production	0.973 (0.968 - 0.979)	<0.0001
Patient transferred the day of the administration	3.65 (3.07 - 4.33)	<0.0001
Patient discharged the day of the administration	5.97 (5.72 - 6.23)	<0.0001
Patient transferred before administration	7.26 (6.06 - 8.70)	<0.0001
Patient discharged before administration	20.1 (19.0 - 21.2)	<0.0001

- ***Time of administration***. At the time of the analysis, the average interval between production and scheduled administration was 1.2 days. The robots prepared doses each morning for same-day ("D0") administration scheduled after 2:30 PM. The study revealed that the risk of return was twice as high for drugs scheduled for same-day ("D0") administration compared with those scheduled for "D+1" administration.
- ***Emergency admission***. The probability of a drug being returned was 20% lower for patients admitted through the emergency department compared to those admitted for scheduled hospitalizations.
- ***Weekend production***. The risk of return was 40% lower for drugs scheduled for administration on Sundays, compared to those scheduled for Mondays and Tuesdays. This results from a decrease in prescription modifications, no patient discharges, and the absence of medical rounds in CUs on Sundays.
- ***Time since admission or prescription.*** The study of the impact of the number of days since admission or prescription showed that the risk of drug return decreases as the time since admission or prescription increases.
- ***Transfer and discharge***. The risk of drug return increases significantly when a patient transfer to another CU or discharge is planned, rising by a factor of 4 to 20 depending on the time interval between the scheduled administration and the transfer or discharge.

4. Discussion

4.1 Principal findings

Results confirm literature regarding the high impact of patient movement (discharge and transfer) on the risk of drug return (Renaud , Wattecamps , Blondiaux, Moens, & Zawadzki, 2014) (Hashmi, Khaliq, & Sultana, 2017) rising by a factor of 4 to 20 depending on the time interval between the scheduled administration and the transfer or discharge. The current hospital organization involves preparing all drugs for "D+1" administration without considering the provisional status of patient transfers or departures. Consequently, if a patient is expected to be discharged at 10 AM the next day, all their drugs, including those intended for later in the day, are still prepared. Because the patient will no longer be present, this frequently results in a substantial number of returned drugs.

We also observed that the risk of drug return is highest during the early days of hospitalisation and progressively decreases as the time since admission increased. Our findings are consistent with literature identifying hospital admission as the most vulnerable stage of the medication process. 45.9% of all unintentional medication discrepancies occurred at admission. These frequent treatment modifications during the early phase of hospitalization may contribute to the higher rate of medication returns observed shortly after admission (Hermann, et al., 2026). This perspective is consistent with the growing emphasis on integrating prescribing, dispensing, and clinical information systems to reduce medication errors during transitions of care. Similarly, a fully traceable return process integrated with both the patient health record and inventory management systems may help limit medication errors, improve continuity of care and enhance the safety and reliability of the medication-use process.

The study revealed that the risk of return was twice as high for drugs scheduled for same-day ("D0") administration compared to "D+1" administration. This can be explained by the fact that nurses collect drugs from automated dispensing cabinets for the morning rounds, and some of them anticipate the collection of the subsequent doses, even though these doses are prepared by the robot and delivered to the CUs. The mismatch between medical rounds scheduling and pharmacy medication preparation negatively impacts the return rate. For example, anaesthesiologists typically conduct their rounds in the surgical CU early in the morning, before beginning their operating room schedule. Consequently, a significant number of prescriptions are issued between 7:00 and 8:00 AM. Although the pharmacy prepares drugs for "D+1", these treatments are often adjusted during the next morning's rounds, leading to increased returns.

Results confirm literature regarding the higher proportion of returns among injectable forms, with the likelihood of return for injectable drugs being 2.3 times higher than that for oral drugs (Hashmi, Khaliq, & Sultana, 2017). Whenever clinically appropriate, a switch from intravenous to oral administration is implemented as early as possible to minimise the risk of nosocomial infections associated with prolonged intravenous therapy. Moreover, oral medications are generally less costly than their intravenous counterparts (Chen, et al., 2025) and contribute to faster patient recovery and earlier hospital discharge.

In our hospital, ATC-level L showed the highest return rate (23.2%), whereas return rates for ATC-levels A and C were 11.2% and 14.1%, respectively. In contrast, a previous study conducted in hospital departments identified ATC-level A (21.2%) as the predominant class of unused medications, followed by ATC-level C (20.6%) (Chen, et al., 2025). ATC-level L represented only 2.6% of unused medications in that study. Therefore, the ranking of therapeutic classes differs substantially between the two studies. Direct comparisons are limited because the definitions of unused and returned drugs differ and the data collection periods are not the same.

The lower probability of a drug being returned for patients admitted through the emergency department compared to those admitted for scheduled hospitalisations may be explained by the fact that patients scheduled for surgery are typically sent to surgical CUs, which may be more prone to variations in drug prescriptions.

4.2 Implication for practice

From the pharmacy perspective, data analysis has identified several quick win actions to reduce drug returns, which could facilitate the integration of the two upcoming sites into the automated dispensing system.

- "D0" preparations account for a significant portion of returns. Work practices vary across CUs and may contribute to this phenomenon. For example, in some units, night-shift nurses prepare treatments for the following day before the morning medical rounds by retrieving medications directly from ward stock rather than waiting for deliveries from the pharmacy. In addition, the timing of "D0" preparation in the pharmacy does not always coincide with the completion of medical rounds and therefore may not reflect treatment discontinuations or modifications. These findings support the decision to discontinue the production of "D0" medications and should be considered when redefining the composition and stock levels of ward medication cabinets.

- As recommended in many healthcare institutions, the duration of intravenous (IV) therapy is limited, leading to more frequent prescription modifications. Additionally, technical limitations of the robot—particularly regarding the handling of glass ampoules—result in a cumbersome and time-consuming management process. These factors, combined with the high return rates observed for these products, suggest considering their removal from the automated dispensing system and direct picking from the ward medication cabinet.

- The study reveals variability in practices according to unit-specific characteristics. CUs with more stable prescriptions, typically those managing medium- to long-term stays, may benefit from distribution models covering longer administration periods. Conversely, CUs with less stable prescriptions might require distribution strategies tailored to the specific medical discipline. Accordingly, the pharmacy will develop distinct distribution models tailored to the activities of different CU types, including surgical, geriatric, recovery, and medical units.

- Particular attention should be given to CUs exhibiting return rates above the overall average and generating substantial volumes of robot-produced unit doses, as shown in Figure 3. These units represent the greatest opportunity for impactful interventions, as even modest reductions in return rates could translate into a significant decrease in the absolute number of returned medications. Further investigation of local workflows, prescribing practices, and organizational factors, in close collaboration with healthcare professionals working in these units, may help identify targeted and operationally feasible measures to reduce returns and optimise the medication-use process.

4.3 Limitations & perspectives

This study focuses on a specific segment of the medication management process and does not address the prescribing phase, which constitutes the true starting point of the process. The quality and appropriateness of prescribing are critical, as they directly affect the efficiency and safety of subsequent steps. Similarly, other important stages—such as drug administration by nursing staff and accurate electronic documentation necessary for proper billing by administrative personnel—are also outside the scope of this analysis.

The dataset used to identify the factors associated with the return rate covers a period of 6 months from October 2024 to March 2025. This limited period does not us allow to evaluate the seasonal effects. Using a larger period (more than one year) would have reduced the potential influence of the seasonal variations and provide a more comprehensive assessment of the determinants of UD returns. However, we were limited due to technical constraints related to data extraction.

The factors identified in this study provide actionable targets for reducing medication returns. Future work should focus first on implementing and evaluating the most promising improvement actions within the hospital. Any intervention should be developed in collaboration with the pharmacy department and the CUs concerned. The impact of these actions could be assessed using appropriate indicators. In order to support the implementation of the quick win actions identified to reduce drug returns, a structured evaluation plan should be defined. Their effectiveness could be assessed using an Interrupted Time Series (ITS) design, monitoring changes in medication cabinet activity, return rates, and the number of calls to a dedicated support hotline. Alternatively, a stepped-wedge design could be adopted, with the gradual introduction of interventions in selected pilot units, enabling both intra-unit and inter-unit comparisons. Protective measures such as pilot phases, close monitoring, and continuous adjustments could be incorporated to ensure the safety and reversibility of actions. An analysis of the return rate could be carried out after each action, taking into account the fact that simultaneous changes in the drug management process or hospital operations may influence these results.

In addition, further research should evaluate the economic consequences of medication returns. Such analyses should consider medication costs, robot consumables, repackaging costs for the relevant drugs, and the human resources required to manage returned medications.

The present work was conducted in a single institution. Future studies should assess the external validity of the identified factors in other hospital settings. Comparing workflows, dispensing practices, and return rates across institutions would help determine the generalisability of the findings and identify context-specific factors influencing medication returns. However, such comparisons present several methodological challenges. First, access to patient-level and medication-use data may be restricted by data protection and privacy regulations, limiting the availability of comparable datasets across institutions. Second, even when hospitals use the same pharmacy information systems or automated dispensing technologies, local customizations and differences in organizational workflows may substantially affect data structure, collection methods, and operational processes. Finally, variables that appear similar across institutions may not necessarily share the same definition, clinical meaning, or coding practices, potentially introducing biases in cross-institutional comparisons.

Analysing each factor separately using univariate models represents a limitation of this study. Consequently, the reported associations do not represent independent effects and may be influenced by confounding factors or interactions between variables. Future work should therefore include multivariable analyses to assess the independent contribution of the identified factors within a unified modelling framework. Furthermore, these factors could be used to develop a predictive model estimating the probability of medication returns based on patient-, prescription-, and organisation-related characteristics.

4.4 Future development of DACS project

As a pilot site, CHU Liège is participating in the DACS (Drugs Dispensing Automation and Communication System) project, a 36-month research initiative launched in February 2024 and supported by Logistics in Wallonia. Conducted by a public-private consortium, the project aims to develop a decision-support platform designed to reduce medication waste. By integrating clinical, logistical, and pharmaceutical data and interfacing with robotic dispensing systems, the platform seeks to optimise medication preparation schedules, anticipate prescription changes, and reduce the volume of returned medications to pharmacy. DACS targets a return rate below 5% . Within this framework, the present study represents the first phase of the project. The DACS project offers several structural opportunities to further reduce medication returns. First, enhanced interoperability between hospital information systems, robotic dispensing equipment, and pharmacy software will enable automated access to essential clinical and logistical data, including real-time patient movements and discharge information. Indeed, a major barrier to digital transformation in hospitals—especially within hospital pharmacies—is the lack of interoperability between systems (Sensmeier, 2022). Building on the factors identified in the present study, a prescription return coefficient will be developed to estimate the likelihood

of medication returns for each prescription line. This coefficient will be integrated into an existing combinatorial optimization tool (Fayolle, Meurisse, De Landtsheer, Germeau, & Michelini, 2025). It will also take into account logistical and production constraints to generate an optimized production schedule. The project will also explore the creation of standardised anonymised datasets compliant with FAIR principles, which could facilitate multicentric collaborations.

5. Conclusion

In a context of increasing pressure on healthcare resources and the need to improve the efficiency and sustainability of healthcare systems, understanding and reducing medication returns has become an important objective for hospital pharmacies. Beyond their direct financial impact, returned non-administered medications reflect inefficiencies within the medication-use process and offer valuable opportunities to optimise pharmaceutical practices, resource utilisation, and patient safety.

This study conducted at the University Hospital of Liège highlights the magnitude and complexity of returned non-administered medications within a highly digitalised hospital environment. With a robotic return rate of 13.4% from 15 October 2024 to 31 March 2025, the associated material, financial, and operational burdens remain substantial. These findings demonstrate that even technologically advanced medication management process still offer significant opportunities for improvement. The detailed analysis of influencing factors confirmed the major impact of patient discharges, transfers, intravenous therapies, preparation timing, and the early phase of hospitalisation on medication return rates, while also revealing substantial variability across CUs and medication classes. These findings emphasise the need to tailor distribution models and medication supply strategies to the specific clinical and organisational characteristics of individual CUs. Close collaboration between hospital pharmacy teams and healthcare professionals working within CUs is essential to better understand local practices, identify root causes of returns, and implement sustainable corrective actions.

The findings further demonstrate that meaningful reductions in returns can be achieved through operational adjustments, such as discontinuing “D0” preparations, removing injectable medications from the automated management process, adapting distribution strategies to CU profiles, or reviewing the management of specific medication classes. However, the effectiveness and sustainability of such interventions depend on the availability of accurate and continuously updated data. Consequently, the automated capture and analysis of medication return information through integrated digital systems appears essential for reliable monitoring, performance assessment, and decision-making. Manual data collection remains labor-intensive and limits the ability to identify trends, benchmark practices, and evaluate the impact of corrective actions over time.

Beyond these quick wins, this study constitutes the first step of the DACS project. The identified determinants of medication returns provide a valuable foundation for the development of predictive tools and decision-support algorithms aimed at optimising production planning, reducing medication waste, and supporting a safer, more efficient, and more sustainable hospital medication-use process.

Ultimately, this study demonstrates that reducing medication returns is not merely an operational objective but a key driver of improvements in the efficiency, safety, and sustainability of the hospital medication-use process. Combining organisational improvements with advanced digital technologies offers a promising pathway for hospitals seeking to optimise pharmaceutical practices and address emerging logistical, clinical and economic challenges facing modern healthcare systems.

Author Contributions

Conceptualization, 2, 4, 5, 6, 7 and 8; methodology, 1, 2, 3, 4, 5, 6, 7 and 8; software, 1, 3, 5 and 8; validation, 1, 2, 3 and 8; formal analysis, 1, 2 and 8; investigation, 2, 3 and 5; resources, 4, 5 and 7; data curation, 1, 3 and 8; writing—original draft preparation, 1, 2 and 8; writing—review and editing, 3, 4, 5, 6 and 7; visualization, 1, 2, 3 and 8; supervision, 6 and 7; project administration, 2, 3 and 8; funding acquisition, 6, 7 and 8;

All authors contributed equally to the conceptualization of the article and writing of the original and subsequent drafts.

Data Availability Statement

Data available on request due to privacy/ethical restrictions.

The supporting data for this study contains sensitive clinical information and operational hospital data. Due to ethical and legal restrictions associated with patient confidentiality, and because participants did not provide legal consent for public data sharing, the dataset cannot be made publicly available. Metadata supporting the findings of this study are available from the authors upon request.

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Ethical considerations

The authors avoided data fabrication, falsification, and plagiarism, and any form of misconduct.

Conflict of interest

The authors declare no conflict of interest.

Appendix A: Abbreviations

Acronym	*Definition*
ATC	*Anatomical Therapeutic Chemical*
CHU	*University Hospital Centre*
CU	*Care Unit*
D+1	*Day +1, the following day*
D0	*Day 0, the current day*
DACS	*Drugs Dispensing Automation and Communication Software*
EHDS	*European Health Data Space*
EMR	*Electronic Medical Record*
FAIR	*Findable, Accessible, Interoperable, Reusable*
FTE	*Full Time Equivalent*
IND	*Individual Nominative Dispensing*
INDD	*Individual Nominative Daily Dispensing*
IT	*Information Technology*
ITS	*Interrupted Time Series*
IV	*Intravenous*
NIHDI	*National Institute for Health and Disability Insurance identifier*
PRN	*Pre Re Nata*
SPW	*Public Service of Wallonia*
UD	*Unit Dose*

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