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An observational study to identify drug-related problems (DRP) in routine care and an expert panel assessment to rate clinical risk and preventability by unit-dose dispensing systems (UDDS) with computerized physician order entry (CPOE) and clinical decision-support systems (CDSS)

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Background and aim: Drug-related problems (DRP) jeopardize patient safety. Unit-dose dispensing systems (UDDS) with computerized-physician-order-entry (CPOE) and clinical-decision-support-systems (CDSS) were reported as a promising concept for preventing DRP. We aimed at identifying and categorizing DRP in peroral drug administration considering their clinical risk and preventability by UDSS/CPOE/CDSS. *Investigations:* In surgical and internal-medicine departments, we observed routine procedures in peroral drug administration for DRP. An expert panel including pharmaceutical and nursing expertise categorized the identified 18 DRP categories into three levels: DRP that have not yet resulted in medication errors (ME) (Level-I), DRP where ME have occurred but have not yet reached the patient (Level-II), and DRP where ME have occurred and have reached the patient (Level-III). Additionally, the panel categorized DRP according to their clinical risk and whether the implementation of UDSS/CPOE/CDSS can prevent them. *Results:* In 77 surgical patients, 1,849 peroral drug administration procedures, and in 149 internal-medicine patients, 1,405 procedures were observed. The 18 DRP categories were identified with a frequency of 0.6%-26.7% (Level-I), 0.1%-21.5% (Level-II), and 0.0%-1.0% (Level-III). Of those, four categories were considered of high clinical risk: "Name of the medication is not readable", "Prescribed medication is not prepared for administration", "An incorrect or non-prescribed medication is prepared", and "A medication is prepared for the wrong patient (mix-up)". Twelve DRP categories were categorized as highly preventable by UDSS/CPOE/CDSS. *Conclusions:* Under routine conditions, we identified a substantial number of DRPs. An expert panel categorized many of those DRPs as clinically highly relevant and highly preventable by UDSS/CPOE/CDSS.

1. Introduction

Drug-related problems (DRP) comprise medication errors (ME) and adverse drug reactions (ADR) (van den Bemt et al. 2000). ME are defined as unintentional but preventable events that can occur throughout the whole medication process and can result in patient harm (National Coordinating Council for Medication Error Reporting and Prevention 2020, Federal Ministry of Health 2021). In United States hospitals, 44,000 to 98,000 deaths each year are caused by ME (Kohn et al. 2000). ME are particularly frequent in prescription (Bertsche et al. 2010) and administration (Bertsche et al. 2010b).

In terms of optimizing patient safety under routine conditions, the potential of preventable DRP, ME, and ADR should therefore be exploited. In this context, it plays a special role which DRP actually arrive at the patient level and manifest themselves in ADR. It is also important to know when the combination of seemingly less relevant DRP leads to serious clinical consequences. In terms of quality optimization, it is desirable to identify and eliminate DRP at an early stage that alone have the potential but did not result in actual occurring ME or ADR. Consequently, relevant criteria for characterizing DRP and ME are their clinical risk to the patient and the frequency of their actual occurrence under routine conditions. Such differentiation of DRP and resulting clinical consequences proves to be particularly useful when it comes to initiating strategies to prevent them. Unit-dose dispensing systems (UDDS), for instance, including computerized-physician-order-entry (CPOE) with clinical decision-support-systems (CDSS), and barcode scanning within closed-loop concepts (Zheng et al. 2021) offer such an automated solution in preparing drug administration (Ahtiainen et al. 2020). The resulting structuring of processes has actually been associated with a lower probability of DRP and ME (Jessurun et al. 2021). Weighing effort and benefit against each other is particularly important from an economic point of view, as these strategies involve considerable personal and financial effort. Automation is a costly investment and the implementation process is complex and time-consuming (Hänninen et al. 2021). UDDS, especially when they include electronic prescribing consisting of CPOE and CDSS, are expensive to implement and

Abbreviations
ADR: adverse drug reaction(s), DRP: drug-related problem(s), ME: medication error(s), CDSS: clinical decision support system(s), CPOE: computerized physician order entries/entry, UDDS: unit-dose dispensing system(s)

maintain. In fact, there is literature on the differentiated effect of electronic prescribing and UDDS/CPOE/CDSS (Groth-Tonberge et al. 2012; Baehr et al. 2014). However, we believe that electronic prescribing, consisting of CPOE and CDSS, is the foundation for a meaningful implementation of a UDDS. While an electronic prescription without a UDDS can already be a preliminary step on the way to a closed medication process, to our opinion, UDDS implementation without CPOE and CDSS cannot be seen as a meaningful step.

Therefore, as part of this study, we aimed to perform an analysis before implementing a UDDS with CPOE and CDSS in our setting. Our comprehensive analysis included risk assessment by an expert panel of nurses and pharmacists. In addition, we conducted an assessment of whether any DRP actually observed could be prevented by a UDDS.

2. Investigations and results

2.1. Participants and setting

An observational monocentric study was performed in a 300-bed military hospital providing tertiary care for civilian (80% of beds) and military patients (20% of beds). Two departments were chosen for the analysis of routine medication procedures: the department of general, visceral and thoracic surgery, and the department of internal medicine with a focus on cardiology, gastroenterology, and pneumology. All members of the nursing staff involved in preparing peroral medication for administration were invited to participate. A paper-based patient chart was used for documentation at the time of the study. The usual preparation of peroral medications for administration by nursing staff on the ward did not include a generally defined process nor was it regulated by a standard operating procedure (SOP). Depending on the ward, the nursing staff involved, and the available staff resources, double-checking was performed.

2.2. Ethics approval statement

No patients were approached in the study. The study protocol was approved by the local Ethics Committee of the Medical Faculty of Leipzig University (#183/22-ek). All members of the nursing staff participated voluntarily and gave their consent to participate. No personal-related data were recorded. If a DRP or ME occurred during the observation, it was documented and the nursing staff was informed.

2.3. Quantitative variables

2.3.1. Observed procedures

In this study, the preparation of peroral medication administration by nurses was analyzed. This was based on the paper-based medication protocol prescribed and documented in the patient's chart. Those procedures were performed in advance (usually the day before) for all patients in the respective department. Thus, the analysis included exactly those procedures that could later be transferred to a UDDS based on CPOE/CDSS. In the routine procedures observed, physician prescriptions could be documented as both brand names and active ingredient names.

2.3.2. DRP categorization

An expert panel was established which included expertise from the fields of pharmacy and nursing. Out of 11 pharmacists in total, 7 were external members, and the others were internal members of the hospital where the study was performed. They had a median age of 34.5 (Q25; Q75: 29; 38.5) years, a professional experience of 8.75 (Q25; Q75: 4.25; 11.375) years, and all had a professional experience in medication analysis. In addition, the nursing staff from the participating departments was asked in an open interview about their experience in DRP and ME in order to include their perspective in the evaluation.

The expert panel defined DRP categories according to international literature, internal standard operating procedures (SOP) of the hospital, and the panel members' experiences in the evaluation of medication administration in the departments. Additionally, the panel categorized DRP, which had been identified in observed administration processes, according to their clinical risk and their preventability (positive or negative) by UDDS/CPOE/CDSS. For this purpose, 18 categories in 3 levels were defined in advance as shown in the first column in Tables 1, 3 and 5. The expert panel categorized the clinical risk as "high" (+3), "moderate" (+2), "low" (+1), or "nonexistent" (0) and the effect on the DRP by UDSS/CPOE/CDSS as highly (+3), moderately (+2), slightly DRP preventing (+1), no effect on DRP (0), slightly (-1), moderately (-2), or strongly DRP deteriorating (-3). The categorizations of the individual experts were included in the median shown.

2.4. Qualitative variables

Expert panel members had the opportunity to provide comments on DRP categorization regarding clinical risk and preventability by UDDS/CPOE/CDSS as free text.

2.5. Data collection

A pharmacy trainee (FVW) monitored the medication preparation in both departments daily from Monday to Friday over a period of seven weeks. Data on the prescribed medication were taken from the paper-based medication documentation in the patient chart. The data acquisition was restricted to solid peroral medications for long-term use. Both, the medication schedule in the patient chart as well as the prepared medications including the packages were photographed. The photos were taken using a smartphone. The photos were numbered consecutively and assigned to the observed processes by this number. Patient-related data were neither noted nor recorded photographically. The photos were stored electronically for evaluation only and then permanently deleted. Based on the photographies of the medication schedules and the observed procedures, the identified DRP were categorized into the predefined levels and categories by the expert panel. The observations were only made during the day and not at night/evening. When something was noticeable during the observation this was also documented. This also included statements and feedback from the nursing staff. These were later considered in the evaluation by the expert panel.

2.6. Efforts to address potential sources of bias and confounders

To reduce bias and confounders all members of the nursing staff of two wards of different medical specialties were invited. Observations were performed at different time periods/weekdays as comprehensively as possible, and only one trained pharmacist observed all procedures.

2.7. Study size

We aimed at observing 1,000-1,500 procedures per department in order to include all frequently occurring procedures at least once and thus achieve a high degree of generalizability in our study. The observation period was chosen accordingly in order to achieve this number of procedures.

2.8. Statistical methods

Statistical analysis was performed by using Microsoft Excel 2019 (version 16.0, Microsoft Corporation, Redmond, WA, USA) and SPSS (version 24, IBM Corporation, Armonk, NY, USA). We used Spearman's rank-order correlation to evaluate the association between clinical risk and preventability by a UDDS/CPOE/CDSS. We used the classification according to Cohen (1992) to determine the effect size. A p-value ≤ 0.05 was considered to indicate significance.

2.9. Results – Participating nursing staff

In total, at the surgical ward 18 of 23 members of the nursing staff and at the internal ward 18 of 19 members participated. In 77 surgical patients, a total of 1,849 procedures (median 7 per patient, Q25; Q75: 4; 10, min; max: 1; 15) were observed. In 149 internal medicine patients, a total of 1,405 procedures (median 7 per patient, Q25; Q75: 5; 10, min; max: 1; 17) were documented.

2.10. Results – Categorized DRP in observed procedures

2.10.1. DRP Level-I: Problematic routine procedures that have not yet resulted in ME

The most frequently observed category was "Generic medication other than prescribed brand name is prepared" (Level-I, Category-a) with 494 (26.7%) of 1,849 observed procedures in surgical medicine and 259 (18.4%) of 1,405 observed procedures in internal medicine (Table 1).

Table 1: Observed frequencies of Level-I DRP (defined as problematic routine procedures that have not yet resulted in ME) in 77 (149) patients of the surgery department (internal medicine department) with a total of 1,849 (1,405) medication administration procedures

Categorized DRP	Observed frequency in surgical medicine (%)	Observed frequency in internal medicine n (%)	Focus group categorized clinical risk	Focus group categorized preventability by UDDS/ CPOE/CDSS
I.a. Generic medication other than prescribed brand name is prepared	494 (26.7%)	259 (18.4%)	1	0.5
I.b. Tablets are split (regardless of whether they can be split or not)	133 (7.2%)	96 (6.8%)	2	2
I.c. Multiple single doses are prepared to get the total prescribed dose	199 (10.8%)	127 (9.0%)	1	1
I.d. Combinations of active ingredients are prepared separately as mono-preparations	15 (0.8%)	8 (0.6%)	1	0
I.e. The drug is prescribed at an administration interval other than daily (e.g. once a week)	30 (1.6%)	46 (3.3%)	2.5	3
I.f. The prescription (still) contains a medication that is marked as discontinued	34 (1.8%)	119 (8.5%)	2	2

An expert panel categorized the clinical risk as "high" (+3), "moderate" (+2), "low" (+1), or "nonexistent" (0) and the effect on the DRP by UDSS/CPOE/CDSS as highly (+3), moderately (+2), slightly DRP preventing (+1), no effect on DRP (0), slightly (-1), moderately (-2), or strongly DRP deteriorating (-3). The categorizations of the individual experts were included in the median shown. Abbreviations: CDSS: clinical decision support system(s), CPOE: computerized physician order entries/entry, DRP: drug-related problem(s), ME: medication error(s), UDDS: unit-dose dispensing system(s).

Table 2: Comments and preconditions for Level-I DRP (defined as problematic routine procedures that have not yet resulted in ME)

Categorized DRP	Comments and preconditions
I.a. Generic medication other than prescribed brand name is prepared	• Prescription does not necessarily have to correspond to the "brand" actually used to date. • The clinical risk depends on the active ingredient (narrow therapeutic range? dosage form?). • The potential of prevention by UDDS/CPOE/CDSS is mainly due to the fact that the prescription is checked again by the pharmacist and thus active ingredients that should not be exchanged are not exchanged. • Distinguishing whether the exchange is clinically relevant (e.g. L-thyroxine, digitoxin, etc.) or not. • In-house medication list should be considered.
I.b. Tablets are split (regardless of whether they can be split or not)	• Clinical risk should consider whether splitting is allowed or not. • Tablet splitting should consider conditions on the ward supplies since improper splitting is possible despite of UDDS/CPOE/CDSS. • Verification and approval of tablet splitting by pharmacists is useful. • Depending on the procedure, the tablet is removed from the bag, split and the half put back into the bag.
I.c. Multiple single doses are prepared to get the total prescribed dose	• Information for the patient would be helpful. • Possibility to keep several strengths in stock (more than on ward), so that number of tablets can be kept low. • It would be decisive that then, for example, 3 tablets are also put into the same sachet.
I.d. Combinations of active ingredients are prepared separately as mono-preparations	• Economically interesting, as not all potencies and combinations have to be kept in stock.
I.e. The drug is prescribed at an administration interval other than daily (e.g. once a week)	• Basis of the high clinical risk: methotrexate! For other (less critical) medications: +1 to +2. • Is the medication usually to be taken daily or not? • Benefit of UDDS/CPOE/CDSS by checking the prescription by pharmacist. • Validation of the prescription by pharmacist. • Correct implementation of the interval by machine blistering.
I.f. The prescription (still) contains a medication that is marked as discontinued	• Prerequisite: change reaches pharmacy in time. • Pause through correct electronic filing. • Correct conversion by machine blistering.

Comments were expressed by an expert panel while assessing the clinical risk and the potential effect on the respective DRP by UDDS/CPOE/CDSS. Abbreviations: CDSS: clinical decision support system(s), CPOE: computerized physician order entries/entry, DRP: drug-related problem(s), ME: medication error(s), UDDS: unit-dose dispensing system(s).

Of the 6 categories in Level-I, the expert panel assessed the clinical risk as "high" for 1 category, as "moderate" for 2 categories, and as "low" for 3 categories. The potential for prevention by UDDS/CPOE/CDSS was considered "high" in 1 of the 6 categories, "moderate" in 2, and "low" in 2, and "none" in 1 category. Comments on the clinical risk categorization and on the potential influence of UDDS/CPOE/CDSS expressed by the expert panel are presented in Table 2.

2.10.2. DRP Level-II: Problematic routine procedures where ME have occurred but have not yet reached the patient

With 398 (21.5%) of 1,849 observed procedures, "The preparation for the administration will be done later, as the medication is not available" (Level-II, Category-f) was the most frequently observed category of Level-II in surgical medicine (Table 3).

Table 3: Observed frequencies of Level-II DRP (defined as problematic routine procedures where ME have occurred but have not yet reached the patient) in 77 (149) patients of the surgery department (internal medicine department) with a total of 1,849 (1,405) medication administration procedures

Categorized DRP	Observed frequency in surgical medicine (%)	Observed frequency in internal medicine n (%)	Focus group categorized clinical risk	Focus group categorized preventability by UDDS/CPOE/CDSS
II.a. Name of the medication is not readable	4 (0.2%)	4 (0.3%)	3	3
II.b. Dosage form is not specified	6 (0.3%)	2 (0.1%)	2	3
II.c. Dosage information is not given	115 (6.2%)	109 (7.8%)	2.5	3
II.d. Time of administration or interval are not specified	26 (1.4%)	78 (5.6%)	2	3
II.e. Instructions on how to use the medication are not given	214 (11.6%)	170 (12.1%)	1	3
II.f. The preparation for the administration will be done later, as the medication is not available	398 (21.5%)	66 (4.7%)	2	1.5

An expert panel categorized the clinical risk as "high" (+3), "moderate" (+2), "low" (+1), or "nonexistent" (0) and the effect on the DRP by UDDS/CPOE/CDSS as highly (+3), moderately (+2), slightly DRP preventing (+1), no effect on DRP (0), slightly (-1), moderately (-2), or strongly DRP deteriorating (-3). The categorizations of the individual experts were included in the median shown. Abbreviations: CDSS: clinical decision support system(s), CPOE: computerized physician order entries/entry, DRP: drug-related problem(s), ME: medication error(s), UDDS: unit-dose dispensing system(s).

Table 4: Comments and preconditions for Level-II DRP (defined as problematic routine procedures where ME have occurred but have not yet reached the patient) expressed by an expert panel while assessing the clinical risk and the potential effect on the respective DRP by UDDS/CPOE/CDSS

Categorized DRP	Comments and preconditions
II.a. Name of the medication is not readable	• Clinical risk varies depending on the medication. • Non-readability will not exist with UDDS/CPOE/CDSS. • Pharmaceutical validation of the prescription is an essential step. • Problem will be solved by electronic prescribing – then it is no longer an actual problem that UDDS/CPOE/CDSS could solve. • The pharmacist could clarify ambiguities in advance. • Problem by electronic prescribing resolved – mandatory fields for order should be defined in advance if necessary
II.b. Dosage form is not specified	• Unclear whether UDDS/CPOE/CDSS is helpful in this context. • Dosage form is clearly indicated, but the question is how deliberately the prescribing physician chooses it. • Pharmaceutical validation of the prescription is required for a high preventability by UDDS/CPOE/CDSS.
II.c. Dosage information is not given	• Non-readability will not exist with UDDS/CPOE/CDSS. • Dosage as mandatory field in electronic prescription. • Low risk, as administration usually takes place after verbal clarification. • If no indication/non-readability in the prescription, the medication cannot be prepared for administration.
II.d. Time of administration or interval are not specified	• Clinical risk dependent on active ingredient, improvement by UDDS/CPOE/CDSS if notes on sachet.
II.e. Instructions on how to use the medication are not given	• Important notes can be printed on sachet.
II.f. The preparation for the administration will be done later, as the medication is not available	• UDDS sachets are delivered to the wards at specified times. • If necessary, subsequent deliveries if the medication is not available in the pharmacy. • UDDS/CPOE/CDSS supply could lead to delay. • This is also very dependent on what medication it is in particular ... pain medications would be relevant.

Abbreviations: CDSS: clinical decision support system(s), CPOE: computerized physician order entries/entry, DRP: drug-related problem(s), ME: medication error(s), UDDS: unit-dose dispensing system(s).

With 170 (12.1%) of 1,405 observed procedures, "Instructions on how to use the medication are not given" (Level-II, Category-e) was the most frequently observed DRP category in internal medicine. Of the 6 categories in Level-II, the expert panel assessed the clinical risk as "high" for 2 categories, as "moderate" for 3, and as "low" for 1 category. The potential of prevention by UDDS/CPOE/CDSS was considered "high" in 5 of the 6 categories, and "low" in 1. Comments on the clinical risk categorization and on the prevention by UDDS/CPOE/CDSS expressed by the expert panel are presented in Table 4.

2.10.3. DRP Level-III: Problematic routine procedures where ME have occurred and have reached the patient

With each 15 (0.8%) of 1,849 observed procedures, "Prescribed medication is not prepared for administration" (Level-III, Category-a) and "Medication is prepared for a non-prescribed time of administration" (Level-III, Category-b) were the most frequently observed categories in surgical medicine (Table 5).

With 14 (1.0%) of 1,405 observed procedures, "Medication is prepared for a non-prescribed time of administration" (Level-III, Category-b) was the most frequently observed category in internal medicine. Of the 6 categories in Level-III, the expert panel assessed

Table 5: Observed frequencies of Level-III DRP (defined as problematic routine procedures where ME have occurred and have reached the patient) in 77 (149) patients of the surgery department (internal medicine department) with a total of 1,849 (1,405) medication administration procedures

Categorized DRP	Observed frequency in surgical medicine (%)	Observed frequency in internal medicine n (%)	Focus group categorized clinical risk	Focus group categorized preventability by UDDS/CPOE/CDSS
III.a. Prescribed medication is not prepared for administration	15 (0.8%)	6 (0.4%)	3	3
III.b. Medication is prepared for a non-prescribed time of administration	15 (0.8%)	14 (1.0%)	2	3
III.c. An incorrect or non-prescribed medication is prepared	9 (0.5%)	1 (0.1%)	3	3
III.d. A dosage other than the prescribed is prepared for administration	12 (0.6%)	11 (0.8%)	2	3
III.e. A medication is prepared for the wrong patient (mix-up)	1 (0.1%)	0 (0.0%)	3	3
III.f. A medication that has already been discontinued is prepared for administration	3 (0.2%)	1 (0.1%)	2.5	3

An expert panel categorized the clinical risk as "high" (+3), "moderate" (+2), "low" (+1), or "nonexistent" (0) and the effect on the DRP by UDDS/CPOE/CDSS as highly (+3), moderately (+2), slightly DRP preventing (+1), no effect on DRP (0), slightly (-1), moderately (-2), or strongly DRP deteriorating (-3). The categorizations of the individual experts were included in the median shown. Abbreviations: CDSS: clinical decision support system(s), CPOE: computerized physician order entries/entry, DRP: drug-related problem(s), ME: medication error(s), UDDS: unit-dose dispensing system(s).

Table 6: Comments and preconditions for Level-III DRP (defined as problematic routine procedures where ME have occurred and have reached the patient) expressed by an expert panel while assessing the clinical risk and the potential effect on the respective DRP by UDDS/CPOE/CDSS

Categorized DRP	Comments and preconditions
III.a. Prescribed medication is not prepared for administration	• All medications submitted to UDDS/CPOE/CDSS are delivered to the wards (after pharmaceutical validation). • Control systems for blistering.
III.b. Medication is prepared for a non-prescribed time of administration	• UDDS sachets are provided with a note on the time for taking the medication. • The high rating presupposes that the sachet is forwarded to the right patient at the right time, otherwise the rating would be lower. • If the time is prescribed incorrectly, it is rather a hindrance if this time is printed on the bag.
III.c. An incorrect or non-prescribed medication is prepared	• What is electronically prescribed and pharmaceutically validated, is blister-packed for each individual patient and delivered to the wards. • Control systems for blistering.
III.d. A dosage other than the prescribed is prepared for administration	• What is electronically prescribed, pharmaceutically validated, is blistered for each individual patient and delivered to the wards.
III.e. A medication is prepared for the wrong patient (mix-up)	• What is electronically prescribed, pharmaceutically validated, is blistered for each individual patient and delivered to the wards. • Name printed on sachet, but not guaranteed that patient on ward receives correct sachet. • If combination of UDDS/CPOE/CDSS with barcode-controlled medication administration (wristband): +3.
III.f. A medication that has already been discontinued is prepared for administration	• However, a prerequisite for smooth processing via UDDS/CPOE/CDSS is that the modified prescription reaches the pharmacy in good time during the work process. • That's one of the criticisms, that you sometimes don't react fast enough with UDDS/CPOE/CDSS, and then something is filled that you don't need anymore, and on the other hand new medications are not implemented fast enough.

Abbreviations: CDSS: clinical decision support system(s), CPOE: computerized physician order entries/entry, DRP: drug-related problem(s), ME: medication error(s), UDDS: unit-dose dispensing system(s).

the clinical risk as "high" for 4 categories and as "moderate" for 2 categories. The potential of DRP prevention by UDDS/CPOE/CDSS was considered "high" in all 6 categories. Comments on the clinical risk categorization and on the prevention by UDDS/CPOE/CDSS expressed by the expert panel are presented in Table 6.

2.11. Results – Correlation of clinical risk and preventability

In a correlation analysis, we compared the clinical risk and the preventability independently assessed by the expert panel. We found a strong correlation (r_s=0.653, p=0.003, n=18). This means that the higher the clinical risk of the DRP categories was, the higher was the preventability through a UDDS/CPOE/CDSS.

3. Discussion

3.1. Principle findings

In this study, the preparation for medication administration in routine care was observed and evaluated in a detailed analysis by an expert panel that includes internal and external expertise of nurses and pharmacists. We identified a considerable number of DRP some of which could only potentially lead to ME, some of which actually did lead to ME, and some of which even resulted in ME at the patient level. While the number of DRP that actually reached the patient level was expectedly small, a substantial number of DRP potentially leading to ME were identified. The expert panel estimated the clinical risk on many of the DRP as high or moderate, particularly for those resulting in actual occurring ME. The preventability by UDDS/CPOE/CDSS was judged to be high for most of the categories. The clinical risk strongly correlated with the preventability by a UDDS/CPOE/CDSS, meaning that in particular high-risk DRP were categorized as preventable by UDDS/CPOE/CDSS.

3.2. UDDS/CPOE/CDSS

A recent Cochrane review also showed that evidence supports the use of UDDS/CPOE/CDSS to reduce ME (Ciapponi et al. 2021). However, the evidence was categorized as low to moderate indicating that there is a need for additional research. We complied with this request with the present study, even though it was not our intention to investigate the effect of UDDS/CPOE/CDSS per se. Rather, with this study we intended to use a real-world data analysis to first find out how often certain DRP actually occur in routine practice. Experts with pharmaceutical and nursing expertise were then involved to assess what risk those DRP posed and whether the introduction of UDDS/CPOE/CDSS would be an appropriate method in principle to solve a quite fraction of the identified DRP. It was therefore a matter for us to investigate and adjust the UDDS/CPOE/CDSS to actual DRP as required, before a high level of personnel and financial effort had to be made for its introduction and permanent operation. By doing so, we believe that we have developed a general concept that may be of interest to other hospitals and fills a gap in the literature.

3.3. Level-I DRP

All categories at Level-I defined as "Problematic routine procedures that have not yet resulted in ME" in our study dealt with quite common medication procedures in everyday clinical care. Additionally, other authors (Magalhães et al. 2015) describe common aspects such as the organization of work shifts and the use of new technologies as the main strategies to solve DRP (Magalhães et al. 2015). In our study, "Generic medication other than prescribed brand name is prepared" was the most frequently observed category in both departments. However, the clinical risk was considered to be low by our expert panel as also the preventability by UDDS/CPOE/CDSS was considered to be low. In this context, the question arises as to what extent an active substance-related prescription without naming brand names would make more sense in principle. This could also better reflect the current problem of variable delivery capabilities. In the prescription, the physician would clearly state by specifying the active ingredient that he/she only wants to define the active ingredient and not the brand name. In special cases, the need to choose a specific brand name could then be specifically and explicitly pointed out (provided that this is justified at all in the case of special galenic requirements).

With 1.6% of all procedures in our surgery department and 3.3% in our internal medicine, the category "The drug is prescribed at an administration interval other than daily (e.g. once a week)" was less common than other categories. However, the corresponding risk was categorized high. As reported by experts, this categorization was related to the risk associated with methotrexate if administered at myelotoxic doses daily rather than weekly as reported in (Schicchi et al. 2021). However, the expert panel determined a high preventability by UDDS/CPOE/CDSS for this category. This can be related to the fact that – by implementing those prescribing and dispensing systems – medication preparation for administration can be automated and shifted to the pharmacy. In this context, it is noteworthy that pharmaceutical validation in UDDS was highlighted as particularly important in quality assurance by our panel. Additionally, also a recent study by others (Jessurun et al. 2022) showed that UDDS prevented potentially harmful ME very cost-effectively despite certain costs incurring during their implementation.

The lack of readability of the medication name as reported by Zheng et al. (2021) was a rare event in our study. It can, however, have clinically serious consequences as categorized by our expert panel. Handwritten prescriptions have been reported to facilitate complications from sound-alikes (Sendlhofer et al. 2019, Heck et al. 2020). However, this risk for DRP and ME can be easily reduced if CPOE/CDSS is introduced together with implemented UDDS.

3.4. Level-II DRP

Other categories at Level-II defined as "Problematic routine procedures where ME have occurred but have not yet reached the patient" relate to missing information on dosage form, dosage, and administration interval. Those DRP should become obsolete with electronic prescribing systems, as physicians have to provide clear dosage information, which at best will be verified by a pharmacist. With more than 10% on each ward, the category "Instructions on how to use the medication are not given" was a frequently identified problem. For example, incorrect concomitant use of food can lead to pharmacokinetic interactions (Koziolek et al. 2019). The risk should be lower after electronic prescribing implementation offering the respective information to the prescriber, as also assessed for this category by the expert panel. Even here, however, it cannot be ruled out that important instructions for use do not reach the patient (Guo et al. 2020).

The unavailability of medication was identified to be a particular problem in surgery. Supply bottlenecks are in principle not a problem that can be solved by UDDS/CPOE/CDSS. However, storage on the ward that is not optimally matched to demand can clearly be prevented by those systems. This also applies to overstocking, especially of cost-intensive products. Another problem is that certain medicines prescribed by the physician are not ordered in the pharmacy (in good time) by the nursing staff and are then not available on the ward in time for taking. Such bottlenecks could be better avoided by using automated ordering processes.

3.5. Level-III DRP

Remarkably, the frequency of actually committed ME as in our Level-III category, was comparatively low. All categories at this level were categorized as highly clinically relevant and highly preventable by UDDS/CPOE/CDSS. The committed ME extended to missing medication as well as wrong time of administration or wrong dosage. As reported by Benoit et al. (2012), the safety of the medication process affected by those ME can be improved by simple and inexpensive interventions. This raises the question if other strategies would be appropriate outside of the UDDS/CPOE/CDSS in order to quickly and effectively solve precisely these highly relevant DRP.

3.6. Limitations

This study has the following limitations: Firstly, the study was carried out only in one hospital. Therefore, generalizability might be limited. However, two very different departments were included, but the similar results for those two argue for low influence of bias. Secondly, the occurrence of ADR at the patient level was not a subject of this study. However, ME are a predictor of risks that increase the likelihood of harm for the patients. Thirdly, this study focused on solid peroral dosage forms. However, these tend to be most common in routine care and are usually the main dosage forms, for which UDSS are used. Fourthly, this study did not examine the actual effect of a UDDS/CPOE/CDSS on the occurrence of DRP, but made an estimate in advance based on the actual number of such DRP actually observed in routine care and categorized by a non-validated expert panel. Last but not least, for the purposes of this study, we have not done any root cause research to find out what was causing the DRP. Of course, implementing electronic prescribing and/or a UDDS will not solve all DRP. The number of staff members, their workload, and inexperienced staff all contribute to DRP and ME. However, focusing on pharmacy by UDDS/CPOE/CDSS might help reduce workload for the nursing staff outside your core tasks and better leverage pharmacy expertise in this area.

3.7. Conclusions

We performed a comprehensive observational study in a surgical and an internal medicine department and let an expert panel categorize the DRPs identified. We found that a wide range of DRPs occurred, with some of those DRPs leading to patient-level consequences. DRPs with high clinical risk were particularly preventable by UDDS/CPOE/CDSS.

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