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Tackling alert fatigue with a semi-automated clinical decision support system: quantitative evaluation and end-user survey

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Summary

STUDY AIMS: Clinical decision support systems (CDSS) embedded in hospital electronic health records efficiently reduce medication errors, but there is a risk of low physician adherence due to alert fatigue. At the Cantonal Hospital Aarau, a CDSS is being developed that allows the highly accurate detection and correction of medication errors. The semi-automated CDSS sends its alerts either directly to the physician or to a clinical pharmacist for review first. Our aim was to evaluate the performance of the recently implemented CDSS in terms of acceptance rate and alert burden, as well as physicians' satisfaction with the CDSS.

METHODS: All alerts generated by the clinical decision support systems between January and December 2021 were included in a retrospective quantitative evaluation. A team of clinical pharmacists performed a follow-up to determine whether the recommendation made by the CDSS was implemented by the physician. The acceptance rate was calculated including all alerts for which it was possible to determine an outcome. A web-based survey was conducted amongst physicians to assess their attitude towards the CDSS. The survey questions included overall satisfaction, helpfulness of individual algorithms, and perceived alert burden.

RESULTS: In 2021, a total of 10,556 alerts were generated, of which 619 triggered a direct notification to the physician and 2,231 notifications were send to the physician after evaluation by a clinical pharmacist. The acceptance rates were 89.8% and 68.4%, respectively, which translates as an overall acceptance rate of 72.4%. On average, clinical pharmacists received 17.2 alerts per day, while all of the hospital physicians together received 7.8 notifications per day. In the survey, 94.5% of physicians reported being satisfied or very satisfied with the CDSS. Algorithms addressing potential medication errors concerning anticoagulants received the highest usefulness ratings.

CONCLUSION: The development of this semi-automated clinical decision support system with context-based algorithms resulted in alerts with a high acceptance rate. Involving clinical pharmacists proved a promising approach to limit the alert burden of physicians and thus tackle alert fatigue. The CDSS is well accepted by our physicians.

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Introduction

A medication error is any preventable event that can cause or lead to either inappropriate medication use or harm to the patient during the process of medication [1]. Studies suggest that approximately 5% of all medication involves a medication error; the estimate varies depending on the definition of medication error and the collective of patients observed in the study [2–4]. Medication errors are not only a risk to patient safety, but they also contribute to health costs [5–7].

Clinical decision support systems (CDSSs) embedded in hospital electronic health records (EHR) can result in significant reduction of medication errors [8, 9]. However, the most frequently mentioned problem of a CDSS is the phe-nomenon of alert fatigue, which describes the ignoring or overriding of alerts [10]. Common reasons for alert fatigue are the reception of high numbers of irrelevant alerts and desensitisation from repeated exposure to the same alert, particularly in a demanding and complex working envi-ronment [11]. Especially interruptive pop-up notifications seem to trigger alert fatigue, with override rates between 50% and >90% [12, 13]. There is a trade-off between in-terruption of workflow and visibility of the alerts for inter-ruptive and non-interruptive CDSSs [14].

A CDSS can only achieve its potential if its target users ac-tually use it [15]. Therefore, the focus has changed from sensitive alerts towards the increase of CDSS alert effi-ciency and usability [16, 17]. While the number of CDSSs is increasing, information concerning physicians' percep-tion of such CDSSs is still scarce. Recent surveys reveal that some physicians seem to be completely dissatisfied, complaining of high numbers of irrelevant alerts [18], while others appear to appreciate the added value despite the system's shortcomings [19].

In our hospital, we designed and introduced a semi-automated CDSS (KPharm) into the hospital's EHR. The semi-automated approach involves role tailoring, meaning that

some alerts are automatically send to the prescribing physicians, while others are first assessed by a clinical pharmacist. With 20 different context-based algorithms currently running, we evaluated the CDSS's performance in terms of alert burden and acceptance rate. Furthermore, we captured the physicians' satisfaction with our CDSS with an end-user survey.

Methods

Setting

KPharm is a clinical decision support system that was developed and implemented in a tertiary care hospital with 669 beds in the north-western part of Switzerland. It was initiated as a collaboration between the department of internal medicine and the clinical pharmacy with the aim of increasing drug safety. The overall goal of KPharm is the early detection of medication errors or situations with an increased risk of an adverse drug event (ADE). A team of clinical pharmacists and physicians developed drug safety algorithms, each covering a variety of potential high-risk situations. The algorithms had been in use in an external system since 2018. Starting from 2020, they were continuously implemented in the hospital's EHR (KISIM™ by CISTEC).

The algorithms were designed taking the following principles into consideration:

- High specificity: To fight alert fatigue, we aim to achieve a high specificity while maintaining a tolerable sensitivity.
- Timing: Considering the daily workflow of ward rounds, we introduced a time lag of one hour. This allows physicians to complete the task of prescribing and to work autonomously from the CDSS. The CDSS acts as a safety net. Many alerts have shown to be self-limiting in the first few hours.
- Non-interruptive notifications: Each interruption in the workflow increases the probability of medication errors [20]. Unlike common CDSSs, we use non-interruptive notifications that are displayed in the patient's EHR. Here, each health care professional working with the patient can see them, which decreases the risk that they are being missed.
- Parametric: The sensitivity of the alerts can be controlled with parametric thresholds. Further, the CDSS can be easily accustomed to new drugs of hospital specific guidelines.
- Semi-automation: For each individual alert, we can define if it automatically produces a notification in the patient's EHR or if it is first evaluated by a clinical pharmacist.

The drug safety algorithms continuously check the medication of inpatients while taking into account various aspects, such as prescribed dose, already administered doses, patient characteristics, and laboratory values. Since diagnoses are not stored in a coded manner, the algorithms cannot consider them. When a potential drug-related problem is detected, an alert is triggered. The CDSS is semi-automated: alerts addressing critical errors with high specificity (e.g., duplication of anticoagulants or digoxin overdoses) are automatically displayed in the patient's EHR. For some alerts, the automatisation is only temporarily (on weekends, holidays). The remaining alerts are evaluated by the clinical pharmacist on day duty. In our hospital, clinical pharmacists' day duty mainly consists of responding to the telephone and assessing the alerts, which permits the timely evaluation of these during office hours. To assure consistency, the alerts are processed according to an internal guidebook. The guidebook takes further aspects into account that cannot be used by the algorithm, e.g., because the information is not available in a structured form. If the alert is considered relevant, a notification is generated which is displayed in the "messages" line of the EHR. In critical cases, the prescribing physician is contacted directly by telephone. The algorithms will cancel the alerts and notifications autonomously as soon as the conditions that triggered them no longer apply. The workflow is illustrated in figure 1.

The text of the notification itself contains, in addition to the triggering factors, a brief explanation and a specific recommendation for action (figure 2). If desired, the physician can respond to the notification for clarification, cancel it, or leave it in the EHR as a reminder.

By the end of 2021, we had integrated 19 algorithms that can trigger 194 different alerts, including error messages. The decision to automate individual alerts was taken as a group (CZ, RF, HD). We considered the frequency of alerts and how often they were correct and accepted by the physician, as well as the potential patient harm if they were not processed immediately. A list of the alerts and their automation status can be found in the appendix 1.

Data

The clinical decision support system is integrated into the hospitals' EHR. The clinical pharmacists process the alerts in an interface for checking, where the status of each alert is documented. Alerts that are technically wrong (false positive) were identified during this step. Alerts that were no longer valid before being reviewed by a clinical pharmacist were automatically flagged as "self-limiting". Alerts that were technically correct but not relevant for the individual patient were either paused or marked as "not relevant" and were not forwarded to the physician. The CDSS does not automatically capture whether the notifications are read and accepted by physicians. Thus, when the alert resulted in a notification to the physician, the clinical pharmacists performed a retrospective follow-up to assess whether the notification had been accepted or dismissed. We considered an intervention as accepted if it led to an adjustment in patient management within a reasonable period. The period considered reasonable depended on the recommendation of action in the notification and the time of day in which the notification was send. If discontinuation or dose adjustment of a drug was suggested, we expected a change in medication on the same day, or if the notification was sent late in the afternoon, the following morning. In case of uncertainty, e.g., if the notification was sent shortly before the patient was discharged from the hospital or if the medication was discontinued for a reason not related to the notification, the follow-up was deemed not assessable.

Web-based survey

The questionnaire was designed with key stakeholders of the development team in German language (appendix 2). The questionnaire is composed of three categories: demographic information, opinions specifically concerning KPharm, and opinions concerning CDSSs in general. The a priori outcome measures were overall satisfaction and the helpfulness of the individual algorithms. We collected the following demographic information: gender, age, professional title, clinic, percentage of employment, and time at workplace. Concerning KPharm, we asked about overall satisfaction, perceived frequency of alerts, and a rating of the individual algorithms. We proposed several statements covering relevant aspects of CDSSs to capture physicians' attitudes towards KPharm. Subsequently, physicians rated how important those aspects are for CDSS in general. Additional questions targeted the preferred mode of receiving notifications, further drug related problems to be solved in the future, and experience with other CDSSs. We used an even Likert scale for items that required rating. At the time of the survey, 16 algorithms were fully operating, allowing for 193 individual alerts. For the survey, the algorithms for direct oral anticoagulants (DOACs) were treated as one.

The survey was distributed to physicians working on wards in our hospital via email using electronic software (SurveyMonkey™, Momentive Inc., San Mateo, California, USA). Physicians from wards that do not work with the EHR were not contacted. The survey period was 16 days, with two reminders being sent on days 7 and 14. We promoted the survey in the hospitals intranet and raffled three vouchers for a lunch at the hospital's canteen amongst the participants as an incentive. By participating, the physicians agreed to their anonymised data being published.

Ethics approval

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the north-western and central Switzerland ethics committee (Project-ID: 2021-01379)

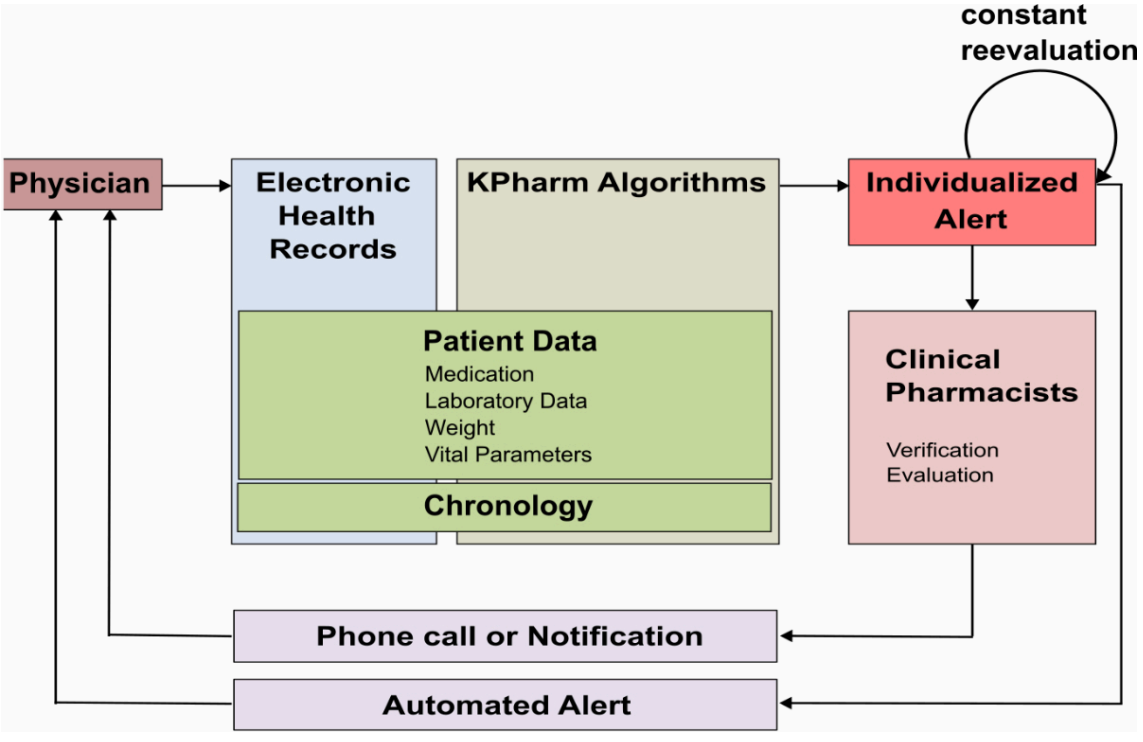
The online survey did not fall within the scope of the Swiss Human Research Act. Therefore, authorisation from the ethics committee was not required. All participants of the online survey agreed to their answers being published in an anonymised form.

Statistical analysis

Information on all alerts in 2021 was imported from the EHR. Quantitative data were summarised using counts and proportions. We calculated the acceptance rates as the fraction of accepted notifications out of all notifications for which the outcome was known. Alert burden was defined as the mean number of alerts pharmacists and physicians must process in a day.

The results of the online survey were received via export from the SurveyMonkey™ homepage. Demographic characteristics were aggregated to conduct descriptive analysis using counts and proportions and median and range, where appropriate. Responses to the question concerning overall satisfaction and alert burden were stratified by profession. Due to the small number of participants, attending physicians and chiefs of service were analysed together. We analysed Likert scales using counts and proportions and omitted non-assessable responses. For the statements cov-

Figure 1: Workflow of the KPharm clinical decision support system: After the physician prescribes a medication, the context-based KPharm algorithms access the information in the electronic health records, as well as the chronology of events, to trigger individualised alerts. Alerts are forwarded either directly to the physician or first to a clinical pharmacist for review. An automatic constant re-evaluation assures that only relevant alerts are displayed. KPharm: semi-automated clinical decision support system.



ering relevant aspects of CDSSs, Cronbach's alpha was calculated. With a value of 0.85, it showed good validity.

All analyses were carried out using Jupyter® Notebook (version 6.1.5) with Python™ (version 3.9.2) and the additional packages numpy (version 1.23.5), pandas (version 1.5.2), and matplotlib (version 3.6.3) [21–23]. The code is available from github upon request.

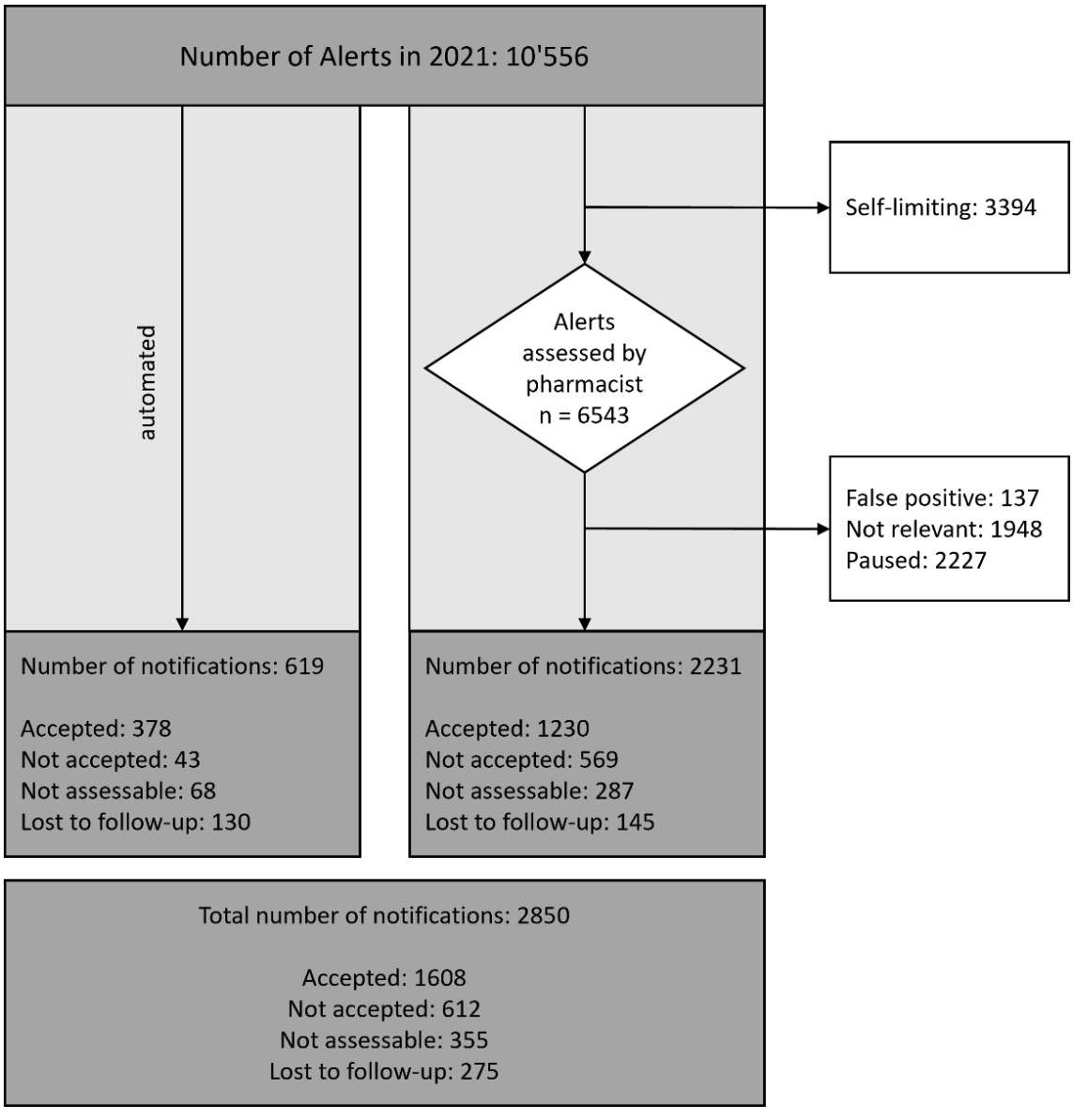
Results

Quantitative evaluation

In the year 2021, the CDSS analysed 22,195 patient charts and generated 10,556 alerts for 5,204 individual patients. The highest number of alerts received for an individual patient was 27. Only a small fraction (5.9%, n = 619) of the alerts was automated and directly generated a notification to the prescribing physician. The other alerts were directed to a clinical pharmacist for assessment. About a third of the alerts (32.2%, n = 3,394) were self-limiting, meaning that the alert had already ended itself before assessment. The remaining 6,543 alerts were assessed by the respective clinical pharmacist on duty, which corresponds to a workload of 17.2 alerts per day. In the course of 2021, clinical pharmacists performed 2,231 (34.1% of all assessed alerts) interventions by either phone call or notification. Other alerts were considered correct but not relevant for the specific clinical situation and were either ended (n = 1,948, 29.8%) or paused (n = 2,227, 34.0%). A small number of alerts (n = 135, 2.1%) were false positive. The processing of the alerts is displayed in figure 2.

Automated and non-automated alerts combined, 27.0% (n = 2,850) of all alerts in 2021 resulted in a notification to the physician. This corresponds to 7.8 alerts per day for the whole hospital. The team of clinical pharmacists performed a retrospective follow-up and was able to determine the outcome for 76.2% (n = 2,094) of the notifications. The acceptance rate was higher for the auto-

Figure 2: Processing of all alerts in 2021: The left column shows the alerts that were automatically sent to physicians. The right column shows the alerts that were first sent to clinical pharmacists. All alerts that reached physicians through both ways are summarised in the box at the bottom.



mated alerts (89.8%) than for pharmacist-reviewed alerts (68.4%). Overall, the physicians accepted 1,608 notifications, which translates to an acceptance rate of 72.4%. Alerts concerning the duplication of anticoagulants had the highest acceptance rate (93.3%, total number of alerts = 276), whereas alerts concerning the dosing of dabigatran had the lowest acceptance rate (33.3%, total number of alerts = 4).

Survey

The survey was sent to 568 physicians, of which 152 participated, representing a response rate of 26.8%. Of the participants, 113 completed the full survey, whereas 39 (24.2%) submitted only partially answered questions. The median age was 35 years (range: 25–60 years) and slightly more females participated (57.2%). Most participants were physicians at entry level, were employed full time in the internal medicine department, and had worked in our hospital for a medium of 3 years (range: 0–22 years). The characteristics of the participants are shown in table 1.

Overall satisfaction with the CDSS was high, with 66.1% being “satisfied”, 28.4% being “very satisfied”, and 5.5% being 'less satisfied'. Forty-three (28.3%) participants did not answer. Most participants (n = 75, 49.3%) indicated that they had received at least one alert in the previous year, whereas 48 (31.6%) had never received an alert and a further 29 did not respond. Five of the six doctors who were less satisfied with the system said that they had not received any alerts in the past year. Resident physicians received more notifications than attending physicians and chief of service/head of departments.

All algorithms were considered helpful, with the algorithm addressing the duplication of anticoagulants receiving the highest results and the algorithm for medication errors of proton pump inhibitors receiving the lowest rating; however, many physicians indicated not being familiar with specific algorithms (mean: 61.4% for all algorithms). The least known algorithm was “xanthine oxidase inhibitor” which was unknown to 86.6% of responding physicians (n = 119). In the course of 2021, this specific algorithm had only fired 27 alerts. An overview of all ratings is depicted in figure 3.

Physicians' attitudes towards relevant aspects of CDSSs were captured by proposing several statements and asking the physicians to rate the extent to which the statements were true in respect to our CDSS. In a second question, the physicians rated how important this statement is for CDSSs in general. All proposed statements were rated as rather important in a CDSS. For an ideal CDSS, convenient timing, relevance of medication errors, and addressing the correct health care professional received the most very important votes. KPharm received strong confirmation that the alerts were written in an understandable manner. Eight (10.1%, total respondents = 79) of the physicians did not agree to the statement that the timing of the alerts was convenient. This was the statement with the highest rate of disagreement. Overall, the agreement rates were high (figure 4).

Most physicians indicated that they preferred “pop-ups” (38.0%) as a mode of receiving notifications, followed by notifications in the EHR, emails, and phone calls (28.3%, 21.2%, and 9.2%, respectively). Physicians who responded with 'other' (3.3%) indicated that they would like the mode of notification to be adapted to the urgency of the content. With only 27 physicians making suggestions for future algorithms, we could not establish a clear hierarchy of top-

Table 1:
Characteristics of survey participants.

		Participants (n = 152)	
		n	%
Gender	Female	87	57.24
	Male	63	41.45
	Not reported	2	1.32
Age	<30 years	31	20.39
	30–34 years	35	23.03
	35–39 years	34	22.37
	40–44 years	21	13.82
	≥45 years	26	17.11
	Not reported	5	3.29
Position	Resident physician	79	51.97
	Attending physician	54	35.53
	Chief of service	14	9.21
	Head of department	5	3.29
	Not reported	0	0.00
Percentage of employment	100%	114	75.00
	80%–99%	16	10.53
	50%–79%	18	11.84
	<50%	3	1.97
	Not reported	1	0.66
Time at workplace	<1 year	23	15.13
	1–2 years	30	19.74
	2–5 years	42	27.63
	5–10 years	31	20.39
	≥10 years	25	16.45
	Not reported	1	0.66

ics. The most common answer (n = 6) was the need for an allergy alert. Out of the 114 respondents, only seven (6.1%) indicated that they already had experience with other CDSSs, obviating further questions aimed at a comparison of perceptions of different CDSSs.

Discussion

We evaluated the performance of our clinical decision support system KPharm in terms of acceptance rate and alert burden. The quantitative analysis revealed an overall acceptance rate of 72.4%, which is higher than many commercially available CDSSs [19, 24–26]. Since different methods for measuring acceptance are in use, the direct comparison of acceptance rates is difficult [27]. Recent reviews summarised the overwrite rates of CDSSs with drug-drug interaction alerts, which can be interpreted as the reciprocal of the acceptance rate, and found overwrite rates between 46.2% and 98% [12, 28]. However, those reviews included CDSSs since 2000, and advanced CDSSs with conceptualised alerts have been found to have improved performance parameters.

A promising approach to improving performance parameters is role tailoring. In a review by Hussain et al. comparing 39 CDSSs with different designs, only the four designs that involved role tailoring appeared to increase prescriber acceptance [27]. Muylle et al. implemented clinical pharmacist interventions to improve their CDSS [6].

Figure 3: Helpfulness of individual alerts. Distribution of answers on the perceived helpfulness of the individual algorithms. Helpfulness was rated using a Likert scale of 4 + 1 for each algorithm; the answer "I do not know the algorithm" was excluded in this figure. DOAC: direct oral anticoagulants (apixaban, edoxaban, rivaroxaban, and dabigatran were treated as one algorithm); NSAID: non-steroidal anti-inflammatory drugs; RAS: drugs inhibiting the renin–angiotensin system.

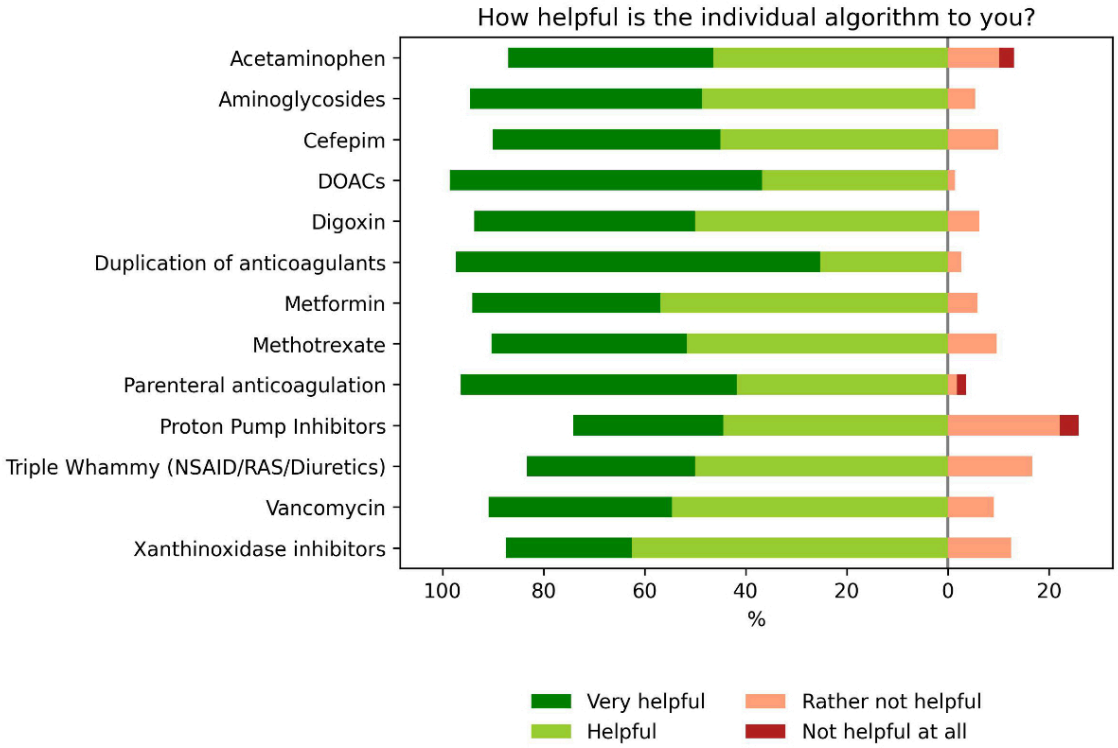
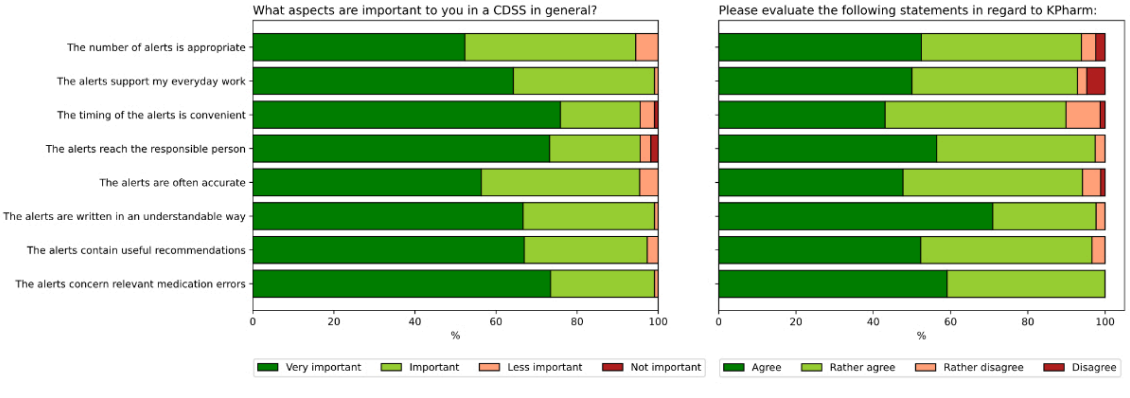


Figure 4: Agreement to satisfaction parameters for clinical decision support systems in general and for KPharm. Distribution of answers regarding satisfaction parameters. Physicians were asked how important each parameter is for a clinical decision support system in general (left) and if those statements were true in regards to KPharm (right). KPharm: semi-automated clinical decision support system.



Out of a total of 2,630 alerts within 8 months, 61 (2.3%) led to an intervention through clinical pharmacy. These interventions were accepted 53 times (86.9%). Likewise, Skalafouris et al. presented a CDSS that involves clinical pharmacists [29]. Of the 447 alerts within 132 days, 20.1% were forwarded to the physician by the clinical pharmacist. The physicians accepted 71.0% of the suggested interventions. The acceptance of CDSS alerts preselected by clinical pharmacists may be compared with the acceptance of pharmacist interventions without a CDSS, which have been studied more thoroughly [30–32]. According to the setting and medication errors addressed, the acceptance rates vary greatly and can range between 41% and 95% [30, 33]. While the acceptance rates of CDSSs with clinical pharmacists are not lower than those of pharmacists' interventions, they are more time efficient [29].

With KPharm, we combine two strategies by having high priority and specificity alerts that go directly to the physician and semi-automated alerts that are first evaluated by a clinical pharmacist. In our analysis, the acceptance rate was higher for direct alerts than for pharmacist interventions. This may be due to an underlying selection bias, since we only automated alerts that have shown a high specificity and acceptance rate in the past.

A major factor contributing to alert fatigue is alert burden. The more alerts a physician receives, the less likely he will accept the intervention due to desensitisation [11]. The comparison of alert burden between different CDSSs is often not meaningful, since it depends largely on the number of medication errors covered by the algorithms. Nonetheless, in a cross-sectional survey with more than 1000 participants from 8 countries, around half of the respondents regarded possible alert overload as a major problem [34]. We found the alert burden of KPharm to be acceptable for both clinical pharmacists and physicians. In our experience, up to 20 alerts a day are very well manageable for one pharmacist, especially since the text for the notifications is already pre-written and rarely needs adjustment. Positive feedback from pharmacists indicates little alert fatigue on their side. Also, the physicians' alert burden was perceived as low, with only 4.6% of physicians receiving several alerts per week. Moreover, 93.9% of physicians participating in the survey agreed with the statement that the number of alerts was appropriate.

Another factor that largely contributes to the low alert burden is the timing of the alerts. Taking clinical reality in hospitals into account, we introduced the time lag of one hour, in which the physicians had the possibility to detect and correct potential medication errors by themselves. Further, the implementation of the CDSS in the EHR allows for an hourly re-evaluation of the alerts, and the alert is cancelled automatically when the conditions that trigger it no longer apply. Interestingly, even with the time lag of an hour, a large proportion of alerts were self-limiting within the first four hours. Overall, the involvement of pharmacists and the hourly re-evaluation of alerts effectively reduced the alert burden of physicians by 73.4% from 10,705 alerts to 2850 alerts in 2021, eliminating one major risk factor for alert fatigue: irrelevant alerts.

When designing alerts with high specificity, we encountered several difficulties. In our EHR, diagnoses are not coded until after the patient leaves the hospital. Thus, they could not be integrated in the algorithms but would have been tremendously helpful in some situations. For example, the algorithm detecting unnecessary proton pump inhibitors would be better if patients with gastrointestinal bleeding were excluded automatically. In some cases, we found workarounds: the prescription of Entresto® (sacubitril/valsartan) or Verquvo® (vericiguat) can be used as a proxy for the diagnosis of heart insufficiency since this is the only indication for those drugs. Alerts that consider the chronology of events are dependent on a timely documentation.

We measured the physicians' satisfaction with our CDSS with an end-user survey. The results of the online survey showed a vast support amongst physicians for our CDSS. This is also supported by the response rate, which is higher than in similar surveys [18, 19, 35]. Some participants indicated that they were not receiving alerts in their daily work but participated in the survey because they welcomed the project and considered it relevant for drug safety.

While all algorithms were generally well accepted, those addressing haematological medication errors received the highest support. We assume that physicians' perceptions of usefulness are determined by the gravity of the medication error: a duplicated anticoagulant is worse than receiving a proton pump inhibitor without indication. Interestingly, many physicians indicated not being familiar with

Table 2:
Frequency of alerts and satisfaction stratified by professional position.

Questions and possible responses		Overall		Resident physician		Attending physician		Chief of service or head of department	
		n = 152	[%]	n = 79	[%]	n = 54	[%]	n = 19	[%]
How often did you receive alerts over the past year?	Several times per week	7	4.61	4	5.06	2	3.7	1	5.26
	Several times per month	22	14.47	15	18.99	6	11.11	1	5.26
	Several times per year	46	30.26	24	30.38	17	31.48	5	26.32
	Never	48	31.58	18	22.78	19	35.19	11	57.89
	Not reported	29	19.08	18	22.78	10	18.52	1	5.26
How satisfied are you overall?	Very satisfied	31	20.39	17	21.52	11	20.37	3	15.79
	Satisfied	72	47.37	35	44.3	26	48.15	11	57.89
	Less satisfied	6	3.95	4	5.06	1	1.85	1	5.26
	Not satisfied at all	0	0	0	0	0	0	0	0
	Not reported	43	28.29	23	29.11	16	29.63	4	21.05

certain algorithms. For this, we provide the following hypotheses. Firstly, high specificity reduces the number of alerts, and the quantity of alerts produced by the individual algorithms differs greatly. Therefore, some physicians may never have encountered such an alert. Secondly, not every algorithm is equally relevant to certain clinics. For example, a physician from the clinic of ophthalmology may rarely encounter an alert for methotrexate.

Limitations

The quantitative evaluation comes with several limitations. The CDSS does not automatically register if a notification is read by the physician. Therefore, it was necessary to perform a follow-up by revisiting the patient's chart. The follow-up was performed retrospectively by a team of clinical pharmacists. Due to the large number of different recommendations, we had no universal standard as to what "accepted" means. When in doubt, the alert was discussed with a colleague. However, in cases where such consent was not sought, personal interpretations of the clinical situation may differ. There is a possibility that measures such as dose adjustments were done independently from the notification. We tried to account for this by paying close attention to the chronology of events after the notification was posted in the patient's chart. When in doubt, the alert was deemed 'not assessable' and excluded from the calculation of the acceptance rate. Since 9.6% (275 of 2850) of notifications were lost to follow-up and could not be evaluated, the data may be skewed. Moreover, if a patient received several relevant alerts on the same day, they were combined in one notification in order to reduce the "message burden", while the others were paused. This analysis does not account for this, so the number of interventions is underestimated.

A limitation to the online survey may be an underlying selection bias. Since participation was voluntary, physicians with a positive attitude towards our CDSS may have been more inclined to participate. However, the response rate was high in comparison to other surveys [18, 19]. The raffling of a free lunch voucher, valued at approx. 15 CHF, may have been a strong incentive. Although we showed a picture of an alert and asked if physicians had already seen such an alert, other physicians may have been motivated to participate. The high number of physicians who claim to never have received an alert may influence the generality of the responses. Those physicians might be either senior physicians and/or physicians working in a ward predominantly using another EHR. Due to the raffle incentive, the email addresses of the participants were known to the authors, and fear of being identified as a poor prescriber might have influenced the responses, especially regarding the number of received alerts. Somewhat surprisingly, most of the physicians who indicated to be less satisfied with the system also stated that they had never received any alerts. Since we did not include a free text option to this question, the reasoning behind the dissatisfaction remains speculative.

For the evaluation of clinical decision support, PPV (positive predictive value) and NPV (negative predictive value) are relevant parameters. Previous studies have shown that the PPV of CDSSs is commonly low [36]. CDSSs that include a greater number of patients' individual parameters tend to have a higher PPV than automated CDSSs. We are not able to provide those metrics at this point but are currently performing such analysis for individual alerts and intend to publish the results in the future.

Outlook

As of May 2022, we have 20 context-based algorithms embedded in the EHR, which allow us to find 202 individual potential drug-related problems. We plan to develop further algorithms in the future in close collaboration with our hospitals' physicians. We also seek cooperation with other developers of CDSSs, as the improvement and spreading of effective and specific contextualised algorithms will ultimately benefit all patients. The KPharm algorithms and their implementation into our EHR (KISIM™) will be commercially available in the future.

We carefully considered the feedback from the survey to find ways to further tailor KPharm according to physicians' needs. When comparing the physicians' agreement in relation to the statements regarding important aspects of a CDSS, we noticed that while timing is regarded as very important in a CDSS in general, KPharm's rating in relation to this was comparably low. Moreover, physicians indicated that their preferred way of receiving notifications was a pop-up alert. Both aspects, timing and mode of notification, were discussed within the development team. While we will maintain our paradigm of non-interruptive alerts, we plan to automate further alerts with high specificity and acceptance rates. This will reduce the alert delay resulting from pharmacists assessing alerts.

Conclusion

The development of context-based algorithms with specific algorithms resulted in alerts with a comparably high acceptance rate. The involvement of clinical pharmacists in a semi-automated CDSS is a promising approach to limit the alert burden of physicians and tackle alert fatigue. The alert burden for the physicians was low, and a vast majority indicated that the number of alerts was appropriate. The CDSS is well accepted amongst our physicians.

Data sharing

The datasets are available from the authors upon reasonable request.

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HD, RF, PS and CZ hold positions at the Cantonal Hospital of Aarau, Switzerland. RDI is employed by CISTEC AG.

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Appendix 1

Table S1: Algorithms included in the online survey and their corresponding alerts.

Appendix 2

The **appendix 2** is available for download as a separate file at https://doi.org/10.57187/smw.2023.40082.

Table S1:
Algorithms included in the online survey and their corresponding alerts.

Algorithm	Alert No.	Alert	Automated
Duplication of anticoagulants	1	Duplication of anticoagulants	Only on weekends
	2	Heparin/fondaparinux prescription for therapeutic INR during/after vitamin K antagonist therapy	Only on weekends
	3	The heparin (or fondaparinux) may be started at an INR >2	No
	4	DOAC is started too early when switching from VKA	Yes
	5	DOAC is started too early when switching from fondaparinux	No
	6	DOAC is started too early when switching from low molecular weight heparins	No
	7	Error in the calculation of one of the dosages of the affected preparations	No
Aminoglycoside	1.1	High aminoglycoside dosage	No
	1.2	High aminoglycoside dosage based on corrected weight	No
	1.3	Aminoglycoside therapy for high body weight; the corrected body weight cannot be calculated	No
	1.4	No current weight available with aminoglycoside therapy	No
	2	Aminoglycoside and eGFR <30ml/min	No
	3	Aminoglycoside and dialysis	No
	4	Drop in eGFR during aminoglycoside therapy	No
	5.1	No adequate renal monitoring during aminoglycoside therapy	No
	5.2	No adequate renal monitoring during aminogylcoside therapy in combination with a drug that elevates the serum creatinine	No
	5.3	No adequate renal monitoring during aminogylcoside therapy in pediatric patients	No
	5.4	No adequate therapeutic drug monitoring during aminogylcoside therapy in pediatric patients	No
	6	Multiple aminoglycoside therapies in the last 3 months	No
	7	Probably not a trough level. The blood sample was taken at the wrong time	No
	8	Aminoglycoside in combination with a drug that elevates the serum creatinine	No
	9	Long duration of aminoglycoside therapy	No
	10	Error during one of the tests	No
Apixaban	1	Apixaban with a strong inductor of CYP3A4 and P-gp	No
	2	Apixaban dosage may be too high	No
	3	Apixaban with dual inhibitor of CYP3A4 / P-gp	No
	4.1	Apixaban dosage is possibly too low in the absence of criteria for dose reduction	No
	4.2	Apixaban dosage is possibly too low in the presence of only one criterion for dose reduction	No
	5	Apixaban and eGFR <15 ml/min	No
	6	Apixaban dosage is possibly too high in triple anticoagulation	No
	7	Apixaban during dual antiplatelet therapy	No
	8	Off-label apixaban treatment regimen	No
	9	Multiple apixaban prescriptions	No
	10	Apixaban and body weight >150 kg	No
Cefepime	1	Drop in eGFR during cefepime therapy	No
	2	Cefepime and eGFR <10 ml/min or dialysis	No
	3	Cefepime and GFR 10–30 ml/min/1.73 m^2	No
	4	Cefepime and GFR 30–50 ml/min/1.73 m^2	No
	5.1	No adequate renal monitoring during cefepime therapy	No
	5.2	No adequate renal monitoring during cefepime therapy in combination with a drug that elevates the serum creatinine	No
	6	Cefepime in combination with a drug that elevates the serum creatinine	No
	7	Cefepime and epilepsy	No
	8	Error during one of the tests	No
Dabigatran	1	Dabigatran with strong inductor of P-gp	No
	2	Dabigatran dosage may be too high	No
	3	Dabigatran with inhibitor of P-gp	No
	4	Dabigatran dosage may be too low	No
	5	Dabigatran and eGFR <30 ml/min	No
	6	Dabigatran dosage may be too high during triple anticoagulation	No
	7	Dabigatran dosage may be too high during dual antiplatelet therapy	No
	8	Wrong dabigatran therapy regimen	No
	9	Multiple dabigatran prescriptions	No
	10	Dabigatran via feeding tube	No
	11	Dabigatran and body weight >150 kg	No
Digoxin	1	Digoxin saturation is reached/exceeded or daily dose is given in two doses	Yes
	2	Digoxin dosage may be too high	No
	3	Digoxin dosage may be too high in geriatric patients (>65 years)	No

	4	Digoxin dosage may be too high due to reduced kidney function	No
	5	Digoxin and GFR <20 ml/min	No
	6	Risk of digoxin toxicity in the presence of hypokalemia or hypomagnesemia	No
	7	Digoxin and risk of hypokalemia	No
	8	Therapeutic drug monitoring of digoxin: the blood sample was not taken at the right time	No
	9	Digoxin level is too high without previous documented measure	No
	10	Digoxin and inhibitors of P-gp	No
	11	Digoxin and inductors of P-gp	No
	12	Potentially inadequate monitoring of renal function during digoxin therapy	No
	13	An error occured	No
Edoxaban	1	Edoxaban and strong inductors of P-gp	No
	2	Edoxaban dosage may be too high	No
	3	Edoxaban and strong inhibitors of P-gp	No
	4	Edoxaban dosage may be too low	No
	5	Edoxaban and eGFR <15 ml/min	No
	6	Edoxaban and eGFR >95 ml/min	No
	7	The edoxaban dosage may be too high in triple anticoagulation with ASA and clopidogrel	No
	8	Edoxaban dosage of 60 mg/d with two antiplatelet agents	No
	9	Wrong therapy regimen	No
	10	Multiple edoxaban prescriptions	No
	11	Edoxaban and body weight >150 kg	No
Metformin	1	Metformin and eGFR <30 ml/min	No
	2	Metformin and eGFR 30–45 ml/min	No
	3	Metformin and eGFR 45–60 ml/min	No
	4	No adequate renal monitoring during metformin therapy in patients with eGFR <60 ml/min	No
	5	Renal function unknown and metformin therapy	No
	6	Errors in calculating the metformin dose	No
Methotrexate	1	Weekly dose of methotrexate potentially too high or two active prescriptions	No
	2	Inappropriate frequency of methotrexate administration	No
	3	Methotrexate dosage may be too high due to reduced kidney function	No
	4	Methotrexate and eGFR <20 ml/min	no
	5	Lack of folic acid supplementation	No
	6	Inappropriate folic acid supplementation	No
	7	Increased ALAT levels during methotrexate therapy	No
	8	Potential interaction with high dose methotrexate therapy	No
	9	Potential interaction with low dose methotrexate therapy	No
	10	Methotrexate in women of childbearing age without contraception	No
	11	Methotrexate prescription in case of suspected infection	No
	12	Potentially erroneous prescription	No
	13	Methotrexate prescribed periodically	No
	14	Error: one of the calculations could not be performed	No
Paracetamol (acetaminophen)	1	Potential overdose of paracetamol	Yes
	2	The prescribed paracetamol dosage is higher than the maximum daily dose	Yes
	3	Paracetamol overdose when reserve medication is exhausted	Yes
	4	High paracetamol dosage and low body weight (50–60 kg)	No
	5	Paracetamol dosage too high for body weight <50 kg	Yes
	6	Paracetamol is dosed too high in combination with inductor	No
	7	Error: one of the calculations could not be performed	No
Parenterale AK	1	Fondaparinux and eGFR < 16 ml/min	No
	2	Fondaparinux and eGFR 16-30 ml/min	No
	3	Fondaparinux thromboprophylaxis and body weight <50 kg: use with caution	No
	4	Fondaparinux and body weight <50 kg: consider dose adjustments	No
	5	Fondaparinux and body weight 51–100 kg: consider dose adjustments	No
	6	Fondaparinux and body weight >100 kg: consider dose adjustments	No
	7	Therapeutic dalteparin and eGFR <20 ml/min	No
	8.1	No monitoring of kidney function during dalteparin prophylaxis and eGFR <15 ml/min	No
	8.2	Monitoring of kidney function during dalteparin prophylaxis and eGFR <15 ml/min	No
	9	Therapy with low molecular weight heparins and eGFR <30 ml/min	No
	10	Thrombosis prophylaxis with low molecular weight heparins and body weight <50 kg: dose adjustment recommended	Yes
	11	Thrombosis prophylaxis with low molecular weight heparins and body weight >100 kg: consider dose adjustment	No
	12	Check dose of low molecular weight heparins	No
	13	Exceeded maximum daily dose of low molecular weight heparins	No
	14	An error has occurred	No

Proton pump inhibitors (PPI)	1	Absence of PPI: NSAID and antiplatelet therapy	No
	2	Absence of PPI: NSAID and therapeutic anticoagulation	No
	3	Absence of PPI: NSAID and glucocorticoid therapy	No
	4	Absence of PPI: NSAID therapy and other drug with GI bleeding risk	No
	5	Absence of PPI: NSAID and age ≥65 years	No
	6	Absence of PPI: NSAID and thrombocytes <30 G/l	No
	7	Absence of PPI: triple anticoagulation	No
	8	Absence of PPI: therapeutic anticoagulation, low-dose ASA and additional risk factor	No
	9	Absence of PPI: dual antiplatelet therapy and additional risk factor	No
	10	Absence of PPI: ASS, glucocorticoids and age ≥65 years	No
	11	Absence of PPI in the presence of at least 4 risk factors	No
	12	Prescription of PPI without risk factors	No
Rivaroxaban	1	Rivaroxaban with strong CYP3A4 inductor	No
	2	Rivaroxaban and eGFR <15 ml/min	No
	3	Rivaroxaban and eGFR 15–29 ml/min	No
	4	Rivaroxaban and eGFR 30–49 ml/min	No
	5	Rivaroxaban dose of 20 mg/day may be too high during triple anticoagulation	No
	6	Rivaroxaban dosage may be too high during triple anticoagulation	No
	7	Rivaroxaban dosage may be too high during triple anticoagulation and eGFR >50 ml/min	No
	8	Multiple rivaroxaban prescriptions	No
	9	Rivaroxaban with dual CYP3A4 / P-gp inhibitor	No
	10	Rivaroxaban dosage 20 mg/d and two platelet aggregation inhibitors	No
	11	Rivaroxaban and a body weight >150 kg	No
Triple Whammy	1	Triple Whammy and GFR <30 ml/min	No
	2	Triple Whammy and GFR 30–60 ml/min: increased risk of kidney failure	No
	3	Triple Whammy and age ≥75 : increased risk of kidney failure	No
	4	No adequate renal monitoring during triple whammy	No
	5	Error in the calculation of one of the dosages	No
Vancomycin	1	Drop of kidney function during vancomycin therapy	No
	2.1	No adequate renal monitoring during vancomycin therapy	No
	2.2	No adequate renal monitoring during vancomycin therapy in combination with creatinine falsifier	No
	3	Vancomycin levels too low	No
	4	Vancomycin levels too high	No
	5	Probably not a trough level. The blood sample was taken at the wrong time	No
	6	Vancomycin in combination with substances that can alter creatinine levels	No
	7	Continuous infusion of vancomycin	No
	8	An error has occurred	No
Xanthine oxidase inhibitors	1	Xanthine oxidase inhibitors with azathioprine or mercaptopurine	No
	2	The dosage of the xanthine oxidase inhibitor may be too high due to reduced kidney function	No
	3	The dosage of the xanthine oxidase inhibitor when combined with capecitabine	No
	4	An error has occurred	No