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Department of Chemistry and Applied Biosciences Institute of Pharmaceutical Sciences Master in Pharmacy

Evaluation of Clinical Decision SupportSystems to Detect Anticoagulant Duplications

Master's Thesis

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Abstract:

Purpose: Anticoagulants are among the drugs most frequently involved in causing adverse drug events in hospitalized patients, with haemorrhage being the main complication. Unrecognized duplicated and concurrent anticoagulation therapies pose risks that can be mitigated by using Clinical Decision Support System (CDSS). We investigated the impact of implementing two different CDSS designs in two different hospitals on the number of erroneously duplicated anticoagulants. The satisfaction of the physicians with the respective designs was also examined.

Methods: We conducted an observational study in two Swiss cantonal hospitals (KSA and KSB) using patient data on the administration of anticoagulants. We considered all anticoagulant applications on patients who received two or more anticoagulants per day. The observation period was one year before and after implementation of the CDSS. We estimated the adjusted odds ratio (OR_{adj}) and adjusted relative risk reduction (RRR_{adj}) of anticoagulant applications being involved in a duplication and cases containing an anticoagulant duplication using logistic regression. The duration of duplication before and after implementation was assessed. A cross-sectional survey was conducted amongst physicians at the KSB and compared to a similar, previous survey at the KSA.

Results: At the KSA the OR_{adj} of cases containing an anticoagulant duplication was 0.44 (95% CI 0.29-0.69) with a RRR_{adj} of 55%. The OR_{adj} of anticoagulant applications being involved in a duplication was 0.24 (95% CI 0.19-0.31) with an RRR_{adj} of 75%. The duration of duplication was reduced to a maximum of two days (p<.0.05). At the KSB the OR_{adj} of cases containing an anticoagulant duplication was 0.85 (95% CI 0.58-1.25) with a RRR_{adj} of 14%. The OR_{adj} of anticoagulant applications being involved in a duplication was 0.68 (95% CI 0.58-0.81) with an RRR_{adj} of 31%. The change in mean duration of duplications after implementation was insignificant (p = 0.44). The comparison of the survey showed that KSB physicians see more alerts and KSA physicians are overall more satisfied with their CDSS.

Conclusion: The implementation of a CDSS showed to have a protective effect on anticoagulant applications being involved in a duplication and the number of cases containing an anticoagulant duplication in both hospitals. However, the impact and the significance of the effect was highly dependent on the design of the CDSS.

Evaluation of CDSS to Detect Anticoagulant Duplications

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1. Introduction

Anticoagulants are essential for the prevention and treatment of thromboembolic events yet they carry a substantial risk of adverse drug events (ADE).^{1,2} The Institute for Safe Medication Practices (ISMP) considers anticoagulants in community and ambulatory care as high-alert medications. They bear a heightened risk for significant patient harm when applied innapropriately.³ Haemorrhage is the main concerning ADE with all anticoagulants.^{4,5} It is correlated with an elevated intensity of anticoagulation due to unrecognized duplicated or concurrent anticoagulation therapy.^{6,7} Anticoagulants are also among the most commonly involved drugs causing ADEs in hospitalized patients.^{8–10} In a retrospective, hospital-specific, five-year study by Piazza et al., the investigators found that 48.8% (n = 226) of all ADE involved anticoagulant-related medication errors and 70% of anticoagulants-associated ADEs were potentially preventable.¹¹

Excessive anticoagulation may occur due to errors in physicians orders, transcription of orders, pharmacy dispensing, nursing administration, and drug monitoring. 12 The stage of prescribing medications is most associated with medication errors and ADEs in general and several studies suggest that errors in the prescribing stage are the main cause of excessive anticoagulation and cause the most harm.^{2,13–17} One strategy to address prescribing errors is to implement a clinical decision support system (CDSS) in the hospital information system. 18-20 CDSSs are computer systems matched to a medical knowledge base and are designed to impact physicians decision making, in real-time, by checking electronic prescriptions entered by the physician for drug allergies, drug-drug interactions, and other risk constellations during the ordering session. 20-23 The recommended safety improvements for anticoaqulants are to employ CDSSs, automate alert notifications and use strategically placed independent double checks.7 In the case of anticoagulants it is especially important to detect relevant therapeutic duplications in overlapping prescriptions. The impact of the alerts generated by the CDSS is influenced by the balance of sensitivity and specificity. In a CDSS, sensitivity refers to the ability of the system to correctly alert in case of a risk constellation, whereas specificity is a measure of the ability to distinguish whether an actual risk exists.²⁴ Too few alerts hold the risk of overlooking possible health dangers, but if the threshold for alerting is too low, the overload can cause physicians to miss or override important alerts due to the flood of alarms of marginal value. 13,23,25–27 This tendency to ignore alerts is called alert fatigue and is associated with designs of low specificity.^{28,29} There is increasing awareness that ordercheck-alerts need to be optimally designed to achieve the appropriate level of alerting during the process of clinician order entry.30

In Switzerland various suppliers offer CDSS for hospitals and physicians' offices. Each of the 26 Cantons has legal autonomy over its own health regulation framework and there are so far no guidelines or standards for testing system design. Accordingly, little data on CDSS safety and efficiency is available. The Swiss e-Health Barometer of 2021 showed that 91% of Swiss hospital physicians work with a CDSS. A survey exploring the types and implementation of CDSSs in public hospitals and private clinics in Switzerland from 2011 showed that out of 14 institutions with a CDSS in service, 12 institutions had modules related to co-medication, of which only 4 targeted therapeutic duplications. The CDSS is either already integrated in the hospital information system or offered as an additional module by the software manufacturer. The Swiss software manufacturers Cistec, Noser Engineering, Erne Consulting and Ines offer hospital information systems and CDSSs. "KISIM" by the Zurich-based developer Cistec is particularly widely used in German-speaking Switzerland.

The cantonal hospitals of Aarau (KSA) and Baden (KSB) in Switzerland both use KISIM as their hospital information system and have comparable patient populations.³⁵ The KSA addresses the surveillance of anticoagulation duplication with a specialized algorithm in their multi-algorithm system as part of a project to individualise surveillance of pharmacotherapy called KPharm.³⁶ An interprofessional team has designed these specific algorithms and tailored them to different risk constellations. Through collaboration with Cistec, this customised CDSS has been incorporated into KISIM. The concept includes algorithms to generate a message to the hospital pharmacy if there is a medication error persistent over the period of one hour. The pharmacist on day duty will then either call the hospital ward to correct the error or write a note in the patient chart. The notes for specific risk constellations are prewritten but can still be edited by the pharmacist. The algorithm is automatically executed at the weekend, with the prewritten notes being attached directly in the patient's chart after one hour. At the KSB, a basic model of the CDSS offered by Cistec is active in the KISIM. A pop-up is displayed directly after the medication entry if there is a risk constellation. The prescribing physician is authorised to act against the recommendations of the CDSS, but active acknowledgement of the alert is required to continue with prescription processing. The pop-up is triggered upon entry of medication prescription and when

changes are made to a prescription. A small alarm icon remains in the patient's record if the risk constellation persists. The message of the pop-up is unspecific and simply differentiates in duplication, interaction, or allergic reaction to the prescribed drug. In comparison the KSA has highly specific alerts with an acceptable sensitivity, while the KSB design is very sensitive but not very specific.

The overall aim of this observational study was to investigate the impact of implementing two different CDSS designs on erroneously duplicated anticoagulant applications, the number of cases containing such duplications as well as the duration of the duplications. As a secondary objective we conducted a survey to assess the satisfaction of the physicians with the CDSS, get an indication of alert fatigue with the respective designs and to compare the results from both hospitals.

2. Methods

We conducted an observational study at the KSA and the KSB using time-series cross-section longitudinal data on administration of anticoagulants (Anatomical Therapeutic Chemical (ATC): B01A*). The outcome of interest was a relevant therapeutic anticoagulant duplication in the exposure group of patients who received two or more anticoagulants. We wanted to observe the effect the CDSS had on the number of anticoagulant applications involved in a duplication and the number of cases containing an anticoagulant duplication. The observed time periods were one year before and after implementation of the CDSS. For KSA, this included the pre-period from 21.8.2017 to 20.8.2018 and the post-period from 24.8.2020 to 23.8.2021. For the KSB the pre-period was from 1.7.2018 to 30.6.2019 and the post-period from 1.8.2019 to 31.7.2020.

Data collection

Both hospitals use the same electronic health care system (KISIM) to record personal information and clinical data of patients who receive medical care. We collected following data of admitted patients who received anticoagulants from the KISIM: patient number, case number, sex, date of birth, date of admission and discharge, the name and ATC code of prescribed anticoagulants, the date of application, and the clinic. The potentially retraceable case and patient numbers and personal data were pseudonymized with the use of dummy variables. All personal data was stored separately for each hospital in a coded fashion. From this data set, all patients admitted to in-patient wards who concomitantly received at least two anticoagulants were selected, and their anticoagulant applications included in the study. The following patients were excluded: patients with a written or verbally documented rejection of the general consent to use health-related personal data and patients that were underage at time of drug application. The following drug applications were excluded: anticoagulant applications of Caplacizumab/Cablivi (B01AX07), antiplatelet drugs (B01AC*), Antithrombin III/Cybernin (B01AB02) and Urokinase (B01AD04), heparin or heparin analogues based on weekly schedule typical for patients with haemodialysis and low dose alteplase (≤ 4mg) for catheter lock.

Outcome definition

All days where two or more anticoagulants were administered to a patient were manually checked for duplications, as well as one day before and after. We assessed an application sequence as a duplication if the anticoagulant was changed but switched back to the original anticoagulant again. We considered the first administration of the second anticoagulant as the beginning of the duplication. If the first anticoagulant was discontinued, we considered its last administration as the end of the duplication (I). If the second anticoagulant was discontinued, we considered the next administration of the first anticoagulant as the end of the duplication (II). If the switch to another anticoagulant was done too soon and the application schedule was not adhered to, this application was considered as the beginning and end of a duplication (III) (Figure 1). The duration of the duplication was calculated as the time between the first and last application, counted as a duplication in days. For further analysis, the anticoagulant applications were sorted by case number. If a case number contained an anticoagulant application involved in a duplication, the case was classified as containing an anticoagulant duplication. The data was reviewed independently twice. When anticoagulant applications were evaluated differently, they were discussed until consensus was reached. The Head of Haematology and Transfusion Medicine at KSA was consulted for unclear individual cases and clinical expertise.

	Monday		Tues	sday	Wednesday		Thui	sday	Fri	day	
	Anticoagulant 1	Anticoagulant 2									
7:30				Apixaban		Apixaban		Apixaban		Apixaban	(1)
17:30				Apixaban		Apixaban		Apixaban		Apixaban	
20:00	Dalteparin		Dalteparin		Dalteparin		Dalteparin				
											_
	Moi	nday	Tues	sday	Wedr	esday	Thursday		Friday		
	Anticoagulant 1	Anticoagulant 2									
7:30				Apixaban		Apixaban		Apixaban			(II)
17:30				Apixaban		Apixaban		Apixaban			
20:00	Dalteparin										
	Mor	nday	Tues	sday	Wedr	esday	Thui	rsday	Friday		
	Anticoagulant 1	Anticoagulant 2									
7:30	Apixaban		Apixaban		Apixaban						(III)
17:30	Apixaban		Apixaban		Apixaban						
20:00						Dalteparin		Dalteparin		Dalteparin	

Figure 1. Prescription scheme of two anticoagulants for visual representation of outcome definition. Anticoagulants with a yellow background are the start of a duplication. Anticoagulants with a green background are the end of a duplication. Anticoagulants with a blue background are considered involved in a duplication. Scenario (I) represents the case where the first anticoagulant is discontinued. Scenario (II) represents the case where the second anticoagulant is discontinued. Scenario (III) represents the case where a change to another anticoagulant is too early.

Data analysis

We conducted two separate logistic regression analyses per hospital. We measured the strength of association between the implementation of the CDSS and the number of anticoagulant applications involved in a duplication as well as between the implementation of the CDSS and number of cases containing an anticoagulant duplication. We performed a univariant and multivariant logistic regression to adjust the estimates for the effect of confounding variables and reported the strength of association by means of odds ratio (OR, OR_{adj}). Additionally, we calculated the unadjusted and adjusted relative risk (RR, RR_{adj}) and derived relative risk reductions (RRR, RR_{adj}). The duration of anticoagulant duplications was assessed for each case and a Welch's t-test was carried out to assess statistical significance. Statistical significance was set at p < 0.05. Python was used for data processing and all statistical analyses were performed in R Studio version 4.0.3 (R Project for Statistical Computing). The collection and analysis of the data was conducted under the guidelines approved by the Ethics Committee Northwestern and Central Switzerland (EKNZ).

Survey about alert fatigue and satisfaction of physicians with CDSS

A monocentric cross-sectional survey in German was conducted amongst voluntary sampled residents, senior residents, leading physicians, and head physicians at the Cantonal Hospital Baden from 22.4.2022 to 1.7.2022. An online self-administered close-ended survey consisting of 4 sections on 6 pages with questions regarding exposure frequency of the pop-up alert, the relevance of the displayed messages, satisfaction with the system, improvement wishes for a CDSS system and preference related to the form of the message was developed.

At the KSA, a survey on satisfaction with the algorithms of the KPharm project was previously conducted from 14.9.2021 to 1.10.2021 by PhD candidate Hendrike Dahmke. The survey design at the KSB was developed according to the KSA survey and the results between the two studies were compared. At the KSB no identifiable personal data was collected, and participants had to consent to the anonymised publication of their results to participate. To improve the response rate an incentive was offered. The inclusion criterium to participate in the study was to be a physician working in a department that uses the KISIM. The study invitation was sent out by mail by the secretariats of the department followed up by two reminders.

To ensure validity, the content and structure of the KSB survey was independently reviewed by two scientists and pharmacists from the KSA and KSB. Face validity was examined by the Deputy Head of Clinic Services and the Chief Physician and Director of the Department of Internal Medicine at the KSB. To cover the overall demographics of respondents appropriately a pilot phase was conducted with two physicians of internal medicine at the KSB. We reported the demographic characteristic of respondents, processed the answers with descriptive statistics and compared them to the KPharm Survey. The survey followed the Checklist for Reporting Of Survey Studies (CROSS) reporting guidelines, was electronically enabled by SelectSurvey.NET v5.0 and evaluated in R Studio version 4.0.3 (R Project for Statistical Computing).

3. Results

A total of 9'342 anticoagulant applications (KSA: n = 3'956, KSB: n = 5'386) were considered as involved in an anticoagulant duplication. The flowchart with the exclusion criteria and the resulting anticoagulant application for both hospitals is displayed in Figure 2.

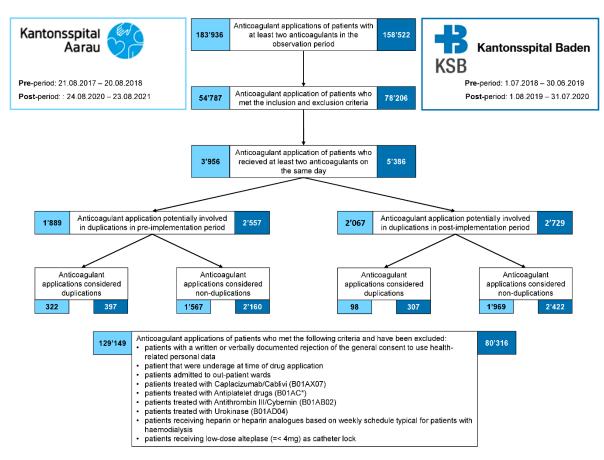


Figure 2. Flowchart of the inclusion and exclusion criteria for the anticoagulant applications for the cantonal hospital of Aarau (light blue) and the cantonal hospitals of Baden (dark blue).

Overall, there were more anticoagulant applications potentially involved in a duplication at the KSB than at the KSA (KSA: n=3956, KSB: n=5386). At both hospitals there were more anticoagulant applications in the post-period than the pre-period (KSA: n=1889 in pre-period and n=2067 in post-period, KSB: n=2557 in pre-period and n=2729 in post-period). Within each hospital, the median age of the patients was similar and between the hospitals, the median age was in the same decade (KSA: median [range] = 74 [24, 97] in pre-period and 71 [18, 97] in post-period, KSB: 78 [18, 98] in pre-period and 77 [21, 97] in post-period). More medication measures were given to men at the KSA (pre-period: 57.7%, post-period: 64.2%). At KSB, the gender distribution between pre and post period reversed (applications to males: 48.8% in pre-period and 54.1% in post-period). There was an almost identical distribution regarding the time of drug application, both within and between the hospitals (Appendix Table 1).

At the KSA the effect of the implementation of the CDSS led to a significantly reduced adjusted OR and RR for cases containing an anticoagulant duplication and for anticoagulant applications being involved in a duplication (both p < 0.05). The odds of cases containing an anticoagulant duplication were 2.3 times lower in the post-implementation period ($OR_{adj} = 0.44$, 95% CI [0.29, 0.69]) with a relative risk reduction of 55% ($RR_{adj} = 0.45 \pm 0.10$). The adjusted odds of anticoagulant applications being involved in a duplication were 4.2 times lower compared to the pre-implementation period ($OR_{adj} = 0.24$, 95% CI [0.19, 0.31]) and the relative risk of it was reduced by 75% ($RR_{adj} = 0.25 \pm 0.03$).

At the KSB, the implementation of the CDSS did not have a significant effect on the number of cases containing an anticoagulant duplication (p = 0.42) but did have an impact on anticoagulant applications being involved in a duplication (p < 0.05). The adjusted odds of cases containing an anticoagulant

duplication were 1.2 times lower ($OR_{adj} = 0.85$, 95% CI [0.58, 1.25]) and the relative risk reduction was 14% ($RR_{adj} = 0.86 \pm 0.17$). The adjusted odds of anticoagulant applications being involved in a duplication were 1.5 times lower post CDSS implementation ($OR_{adj} = 0.68$, 95% CI [0.58, 0.81]) and the relative risk reduced by 31% ($RR_{adj} = 0.69 \pm 0.06$). The adjusted and unadjusted logistic regression model for cases containing an anticoagulant duplication and anticoagulant applications involved in a duplication and are reported in Appendix Table 3 and Appendix Table 4 respectively.

Table 1. Results of adjusted logistic regression model with cases and anticoagulant applications as observations points for both hospitals.

	KSA	KSB
ogistic regression model with cases	3	
$ ho_{adj}{}^{\dagger}$	< 0.05	0.42
OR _{adj} †[95% CI]	0.44 [0.29, 0.69]	0.85 [0.58, 1.25]
RR _{adj} † (SD)	0.45 (0.10)	0.86(0.17)
$RRR_{adj}{}^{\dagger}$	55%	14%
ogistic regression model with antico	pagulant applications	
$ ho_{ m adj}^{\dagger}$	< 0.05	< 0.05
OR _{adj} †[95% CI]	0.24 [0.19, 0.31]	0.68 [0.58, 0.81]
$RR_{adj}^{\dagger}(SD)$	0.25 (0.03)	0.69 (0.06)
RRR _{adj} †	75%	31%

[†] adjusted for sex, age, month, weekday, time of application, anatomical therapeutic chemical (ATC) classification of applied anticoagulant, and clinic from where anticoagulant was prescribed.

Abbreviations: KSA: cantonal hospital of Aarau; KSB: cantonal hospital of Baden; OR: odds ratio; CI: confidence interval;

RR: risk reduction; SD: standard deviation; RRR: relative risk reduction.

The CDSS of both hospitals had a protective effect on the odds of anticoagulant applications being in a duplication. The CDSS of the KSA has achieved a lower odds ratio than the KSB, also with cases containing an anticoagulant duplication. The CDSS of the KSB did not show a notable effect on preventing cases of anticoagulant duplications (Figure 3).

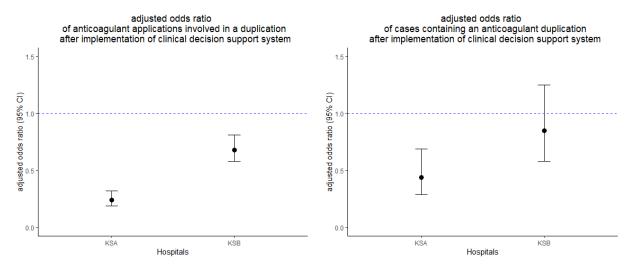


Figure 3. Forest Plot of adjusted odds ratios (OR_{adj}) with 95% confidence interval of anticoagulant applications involved in a duplication (left) and cases with an anticoagulant duplication (right) as observation points for the cantonal hospital of Aarau (KSA) and the cantonal hospitals of Baden (KSB). Y-axis represents the OR_{adj} with 95% confidence interval, and the x-axis represents the hospitals. The point estimate is the OR_{adj} while the vertical bars on the OR_{adj} point estimate indicate the 95% confidence intervals.

The number of cases with an anticoagulant duplication as well as the mean and range of duration in days, stratified by the implementation period for both hospitals, are reported in Table 2. The difference in mean duration between pre- and post-period was significant for the KSA (p < 0.05) but not for the KSB (p = 0.44). At the KSA, the maximum duration of duplication was reduced to two days from seven days, while the total amount of one- and two-day duplications also decreased from 78 to 75 cases and from 17 to 4 cases, respectively. For the KSB, the longest duration of duplication increased from seven to nine days compared to the pre-period (Figure 4).

Table 2. Characteristics of the duration of duplications stratified by hospital and implementation period.

	Number of cases with duplication	Mean duration (SD)	Range of duration [Min, Max]	
KSA				
Pre-implementation 21.8.2017 to 20.8.2018	107	1.53 (1.17)	[1, 7]	
Post-implementation 24.8.2020 to 23.8.2021	79	1.05 (0.22)	[1, 2]	
KSB				
Pre-implementation 1.7.2018 to 30.6.2019	108	1.75 (1.37)	[1, 7]	
Post-implementation 1.8.2019 to 31.7.2020	91	1.71 (1.70)	[1, 9]	

Abbreviations: SD: standard deviation; KSA: cantonal hospital of Aarau; KSB: cantonal hospital of Baden.

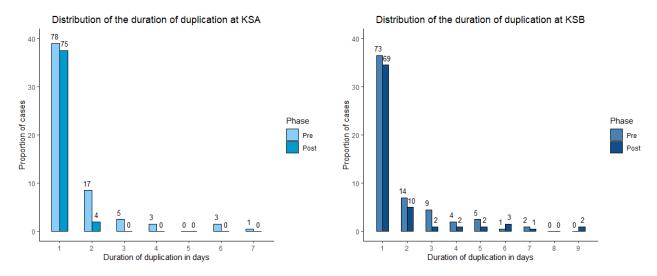


Figure 4. Distribution of duration of duplication pre- and post-implementation for the for the cantonal hospital of Aarau (KSA, left) and the cantonal hospitals of Baden (KSB, right). Y-axis represents the proportion of cases with a duplication, and the x-axis is the duration of duplication in days. The lighter shading of the bars represents the period pre-implementation of the clinical decision support system and the darker shading the post-implementation period. The number above the bars indicates the number of cases.

Survey Comparison about alert fatigue and satisfaction of physicians with CDSS

The survey at the KSB was completed by 136 physicians with a response rate of 24.4%. The KPharm Survey was completed by 152 physicians and had a response rate of 26.8%. More women completed the survey in both hospitals (KSA: 57.2%, KSB: 53.4%). The median age of participants was the same (KSA: 35 [25, 60], KSB: 35 [25, 65]). The average participant at the KSA worked with a higher employment percentage than at the KSB (KSA: 91.9 ± 16.2 , KSB: 88.1 ± 15.2), but the average participant at the KSB worked there slightly longer than at the KSA (KSA: 4.5 ± 4.56 , KSB: 4.84 ± 5.38). There was a gradient of job positions between the participants equivalent to the rank of their position in both hospitals, although it is noticeable that at the KSB almost a quarter of the participants were leading physicians. The distribution of clinics in both hospitals was similar, with the only difference being the higher number of participants from the emergency clinic at KSB. This can be explained by the fact that the emergency clinic at the KSA forms a separate unit (Appendix Table 5 and 6). The surveys can be found in Appendix Figure 1 and 2 for the KSA and the KSB, respectively.

Satisfaction with the CDSS was higher in physicians of the KSA than physicians at the KSB (Figure 5). None of the 109 KSA physician that responded to this question stated to be unsatisfied while at the KSB it was 1% (n = 1). Also 17% of KSB physicians (n = 23) stated to be less satisfied and while at the KSA it was 6% (n = 6).

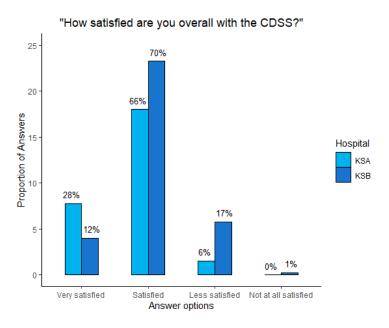


Figure 5. Survey answers of the cantonal hospital of Aarau (KSA, light blue) and the cantonal hospitals of Baden (KSB, dark blue) to the question "How satisfied are you overall with the clinical decision support system (CDSS)?". Y-axis represents the proportion of answers, and the x-axis shows the answer options. The number above the bars indicates the percentage of respondents. Number of respondents of KSA: 109. Number of respondents of KSB: 133.

Both studies asked the physicians about their perceived frequency of alerts. Physicians at the KSB tended to see more duplication reports than physicians at the KSA (Figure 6). 17% of KSB Physicians (n = 23) reported to have seen pop-up alerts several times a day. In a follow-up question to those who said they had seen a pop-up every day, we asked how many times a day they saw a pop-up. Responses varied between 2-20 times a day and some doctors stated in the comments box that an alert occurred for almost every patient. The most frequent occurrence of KSA doctors noticing alerts was several times a week however this was also the smallest proportion of responses at 6% (n = 7).

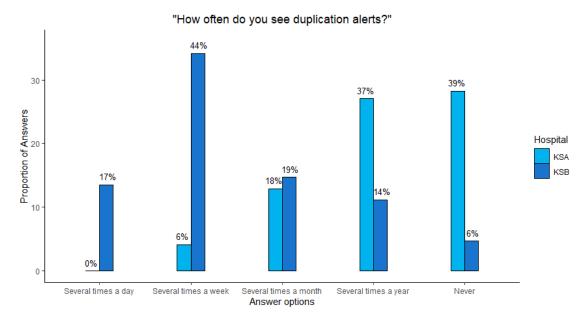


Figure 6. Survey answers of the cantonal hospital of Aarau (KSA, light blue) and the cantonal hospitals of Baden (KSB, dark blue) to the question "How often do you see duplication alerts?". Y-axis represents the proportion of answers, and the x-axis shows the answer options. The number above the bars indicates the percentage of respondents. Number of respondents of KSA: 123. Number of respondents of KSB: 133.

Regarding the method of alert delivery, the currently implemented methods of "pop-up" and "note in the patient chart" were the most popular choices in both hospitals (Figure 7). The physicians at the KSA seemed to be very sympathetic towards a "pop-up" with 46% (n = 71), even choosing it over their current system of "note in the patient chart" with 35% (n = 53). Physicians at the KSB also favoured their current pop-up system of alert delivery by far with 96% (n = 113).

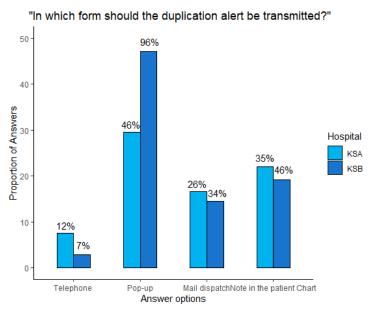


Figure 7. Survey answers of the cantonal hospital of Aarau (KSA, light blue) and the cantonal hospitals of Baden (KSB, dark blue) to the question "In which form should the duplication alert be transmitted?". Y-axis represents the proportion of answers, and the x-axis shows the answer options. The number above the bars indicates the percentage of respondents. Number of respondents of KSA: 153. Number of respondents of KSB: telephone 100, pop-up 118, mail dispatch 103, note in the patient chart 101.

4. Discussion

The aim of this study was to investigate the impact of implementing two different CDSS designs on erroneously duplicated anticoagulant applications. In the two observed Swiss cantonal hospitals, the problem of duplicated and concurrent anticoagulation therapy is being addressed by different CDSS designs. At the KSA highly specialised customized alerts generate messages to the hospital pharmacy or are directly attached as note in the patient's file. At the KSB a non-specific soft-stop pop-up indicated whether a medication duplication, interaction or allergy was present. The introduction of both CDSS Designs decreased occurrence of anticoagulant applications being involved in a duplication (KSA: ORadi = 0.24, 95% CI [0.19-0.31], KSB: ORadj = 0.68, 95% CI [0.58-0.81]). Further the odds and risk of cases containing an anticoagulant duplication were lowered with the CDSS Design of the KSA (ORadj = 0.44, 95% CI [0.29-0.69]) as well as the maximum duration reduced to two days. The CDSS Design of the KSB failed to show such an effect on cases containing an anticoagulant duplication (OR_{adj} = 0.85, 95% CI [0.58-1.25]) and the duration of duplication. As secondary objective we conducted a survey to assess the satisfaction of the physicians with the CDSS and to get an indication of alert fatigue with the respective design. The comparison of the survey responses in terms of perceived alert frequency showed that KSB physicians see more alerts. The survey question does not allow interpretation weather this is due to the CDSS Design or not. The comparison of the survey question on preferred alert delivery mode showed that physicians of both hospitals find the idea of a pop-up attractive. At the same time, we also saw that the doctors who worked with a pop-up system received more alerts. In addition, the alerts were not specific, and a high number of irrelevant alerts was shown to lead to alert fatigue. 29,37 This potential alert fatigue could be reflected in the responses on overall satisfaction. It was noticeable that the doctors at the KSA, who receive fewer alerts due to their selective CDSS, were more satisfied than the KSB doctors who received many alerts.

Similar results to those at the KSA were observed in studies of Jennings et al. and Daniel et al. Jennings et al. observed a reduction in the overall risk of bleeding (OR: 0.47, 95% CI [0.34–0.65]) by implementation of smart intravenous pump technology, pharmacist-managed anticoagulant therapy service and daily electronic report prospectively identifying potential risk-constellations with anticoagulant therapy. The lowest event rates were observed among patients managed by the collaborative physician-pharmacist model (OR 0.12, 95% CI [0.04–0.37]). In a study by Daniel et al. with a CDSS that alerted a clinical pharmacist upon risk constellations with oral anticoagulants the ADE ratio decreased significantly from 0.69% to 0.41% after implementation (p < 0.001). Both studies cannot be directly compared with ours, as different outcomes were observed, but it reinforces the assumption that a CDSS design has a positive impact on the reduction of erroneously duplicated anticoagulants and their ADE. The CDSS designs of these studies also suggest that not only the more specific alerts at the KSA had a positive impact but also the additional "safety net" with a pharmacist. The CDSS generates a message to the hospital pharmacy if a medication error persists over the period of one hour and the pharmacist on day duty can intervene. The positive contribution of a clinical pharmacist in addition to CDSS can be additionally strengthened by the prospective study of Zaal et al.⁴⁰

At the KSB it is probable that the alert fatigue due to the frequent pop-up alerts had an impact on the effectiveness of the system because alerts were no longer considered. Alert overload is a common feature of decision support systems using unmodified basic commercial models.41-43 A study by Van Der Sijs et al. described that of the 29% (n = 51) of CDSS alerts due to therapeutic duplication 80% (n = 41) were overridden. The main reasons for this were low specificity and unclear information of the alert as well as unnecessary interruption of the workflow.⁴⁴ At the KSB the alerts were not specific and not adapted to the clinical routine. A necessary double prescription of Dalteparin to achieve a therapeutic dose would generate a duplication alert, whereas an overlapping prescription of a heparin and a direct oral anticoagulant would be indicated as an interaction. Another disadvantage is that the pop-up message not clearly states which drug is involved in a risk constellation. Further, it can be concluded that KSB's pop-up design did not have a significant impact in the duration of duplication, as the pop-up alerts appears only when a drug is prescribed or changed. If a prescription extends over several days, there will only be a small alarm icon that is easily ignored. The KSA pharmacist on day duty processes all messages generated by the CDSS on a daily basis, reducing the probability of having duplications lasting longer than one day. A difference between the two designs is that at the KSA the alerts are reported to the hospital pharmacy, the notes affixed to the patient's chart, and both are documented in the patient file - this could impact physicians' performance after the implementation of the CDSS. In Addition, at the KSB there is no audit trail showing whether a pop-up alert was generated nor whether it was acted upon.

Comparing the CDSS designs in terms of clinical effectiveness and the responses from the survey leads to some conclusion regarding a few design elements. An ideal CDSS should have high specificity and presents clear information about the risk constellation in the alert and contain suggestions.³⁷ Kawamoto et al. suggested as a general principle that an effective CDSS should minimise the effort required of the physician to act on the alert. 45 Further, it was proposed that specificity could be increased with minimal loss of sensitivity and alert fatigue counteracted by customizing commercial CDSS and implementing well-tailored algorithms.^{24,43,46–48} A high sensitivity would also be desirable in order not to unnecessarily disrupt workflow.³⁷ To be able to evaluate and optimise the CDSS, it would be important to see how the doctors respond to the alerts and that requires their documentation. 49 Further measures were already taken at the KSB in January 2022 and an email dispatch to the hospital pharmacy for selected risk-medications including anticoagulants was set up in addition to the pop-up. This four-eyes principle with a pharmacist adds an additional safety measure. Murphy et al. reviewed a CDSS with a similar mailing notification mode and found that it generates a mean of 56.4 alert messages per day.⁵⁰ With sufficient resources it seems to be a reasonable measure, but at the KSB two pharmacists are responsible for the alert messages, in addition to other tasks. This puts additional pressure on resources and may not be very efficient. The alert fatigue resulting from the high frequency of pop-ups was not reduced and seems to even have extended to the pharmacist. With the new implementation of the alert email dispatch, it is now documented whether the messages to the hospital pharmacy require action and further analysis could be performed. Overall, it seems that this email dispatch is not the final solution at the KSB but represents more of an intermediate step to improve the overall process. The KPharm project at the KSA will continue to develop specialised algorithms tailored to individual drugs and will make them commercially available with CISTEC.

Our study has several strengths. We had data from multiple sites with evaluation periods of one year prior and post implementation of CDSSs. Our data provided real-world insights into anticoagulant applications and their occurrences in duplications in both cantonal hospitals. Since the hospitals are in the same canton, with comparable patient and physician populations, and use the same CDSS, there is a strong implication that the observed effect is indeed related to the design of the CDSS and not to external factors. Findings can be extended to facilities that care for similar patient populations and use a similar or comparable CDSS. The anticoagulant applications are routinely collected in the KISIM, so they represent the actual situation very well. By choosing them as observation points duplications that lasted over multiple days were weighted more. Since prolonged duplication increases the risk of bleeding, it is important to shorten the duplication duration - the OR reflects how this was well achieved at the KSA and that there was no significant impact at the KSB. In addition, we grouped anticoagulant applications as cases to have an understanding of how many cases were affected by anticoagulant duplications. This not only removed the weighting of the duration of the duplication, by examining and reporting both points of observation, we aimed to create a comprehensive picture of anticoagulant duplications. Other strengths are the double independent assessment of anticoagulant applications and consulting a specialist in deviating classifications.

In interpreting our results, some limitations are worth noting. The achieved reduction of the maximum duration of duplication at the KSA and the insignificant impact of the KSB design thereon is reflected in the OR. Therefore, this OR cannot be directly considered a measure of number of duplications. It does nevertheless give us an insight into how the duplication composition changed pre- and post-implementation of the CDSS. Another limitation is that we looked at different time frames for the two hospitals. This was unavoidable in part because it was dictated by the implementation timing of the CDSS into the KISIM. During the large intermediate period at the KSA there was a change in prescription patterns which we have tried to adjust for by taking the ATC code of prescribed anticoagulants as a potential confounder in the regression model. The KSB post-period overlapped with the Corona pandemic; however this did not seem to be reflected in the prescribing behaviour and quantity. When comparing the hospitals, it was noticeable that the KSA, despite being the larger hospital, had fewer patients in preand post-period. This could indicate that the hospital populations are somewhat different or that there is already a lower baseline risk of an application being involved in a duplication at the KSA represented by having fewer patients with two or more anticoagulant on the same day. There are some limitations of the data set that could not be resolved in the study design. The time of application is documented by the nurses and reflects when the medication was administered to the patient, however in the case of oral medication the documented timing does not have to reflect the exact time at which the patient ingested the medication. The time of application was used as the basis for the calculation of the duration of duplications. In addition, we classified anticoagulant applications as involved in a duplication if they were given too early, which is again strongly dependent on the documented application time. We decided to keep these "too early" cases as duplications because they represent a relevant medication error. We assessed the cases as they were documented bearing in mind the limitations of the data set: since the assessment of the measures was done in the same way for both hospitals, it does not have an impact on the data comparison between the two hospitals. One limitation of the survey is the timing of its conduct. At KSA, it was conducted in the fall of 2021, one year after the new algorithms were introduced. At KSB, on the other hand, the survey was conducted in the spring of 2022 which is two years after implementation of the CDSS. Therefore, we cannot assume that the survey participants were using the CDSS for the same amount of time. We attempted to avoid sampled and coverage error by sending the survey via the usual communication medium of physicians from the department itself. Nonresponse errors at the item level could not be omitted, even with reminders on multiple platforms and incentives.

5. Conclusion

The comparison of the CDSS provided the opportunity to evaluate the impact of two designs on efficiency and physician satisfaction, both of which impact patient safety. The implementation of a CDSS reduced the overall number of anticoagulant applications involved in a duplication and the number of cases containing a duplication as well as the duration of a duplication. Physicians were more satisfied when working with a more specific CDSS and receiving fewer messages. The magnitude of the impact and the satisfaction of the physicians with the CDSS seemed to be dependent of the CDSS design. The CDSS design elements that were found to have a positive impact were specific alerts, history of alerts, and the involvement of a clinical pharmacist.

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Appendix:

Appendix Table 1. Demographic characteristics of 3'956 anticoagulant applications at the cantonal hospital of Aarau (KSA) between august 2017 and 2021 stratified by implementation period.

	KSA					
	Pre-Impler	mentation	Post-Implementation			
	21.8.2017 to	20.8.2018	24.8.2020 to			
	N	%	N	%		
Number of patients	314	-	383	-		
Number of cases	332	-	410	-		
Number of anticoagulant	1889	-	2067	-		
applications						
To females	799	42.3	739	35.8		
To males	1090	57.7	1328	64.2		
Median age	74	-	71	-		
[Min, Max]	[24, 97]		[18, 97]			
By ATC						
Phenprocoumon	20	1.1	25	1.2		
(B01AA04)						
Acenocoumarol (B01AA07)	-	-	-	-		
Heparin (B01AB01)	562	29.8	760	36.8		
Dalteparin (B01AB04)	726	38.4	718	34.7		
Enoxaparin (B01AB05)	-	-	-	-		
Nadroparin (B01AB06)	-	-	-	-		
Danaparoid (B01AB09)	-	-	-	-		
Alteplase (B01AD02)	-	-	-	-		
Argatroban (B01AE03)	-	-	10	0.5		
Dabigatran (B01AE07)	51	2.7	4	0.2		
Rivaroxaban (B01AF01)	235	12.4	253	12.2		
Apixaban (B01AF02)	256	13.6	260	12.6		
Edoxaban (B01AF03)	21	1.1	20	1.0		
Fondaparinux (B01AX05)	18	1.0	17	0.8		
By Month						
January	207	11.0	120	5.8		
February	187	9.9	142	6.9		
March	96	5.1	174	8.4		
April	69	3.7	187	9.0		
May	108	5.7	129	6.2		
June	74	3.9	191	9.2		
July	89	4.7	197	9.5		
August	155	8.2	186	9.0		

September	215	11.4	215	10.4
October	210	11.1	200	9.7
November	209	11.1	146	7.1
December	270	14.3	180	8.7
By Weekday				
Monday	283	15.0	331	16.0
Tuesday	314	16.6	332	16.1
Wednesday	303	16.0	352	17.0
Thursday	281	14.9	345	16.7
Friday	276	14.6	282	13.6
Saturday	314	16.6	192	9.3
Sunday	303	16.0	233	11.3
Time of Drug Administration				
Night (00:00-6:00)	99	5.2	163	7.9
Morning (6:00-12:00)	772	40.9	817	39.5
Afternoon (12:00-18:00)	420	22.2	513	24.8
Evening (18:00-00:00)	598	31.7	574	27.8
By Clinic				
Surgery	778	41.2	897	43.3
Gynaecology	36	1.9	28	1.4
Internal Medicine	799	42.3	1005	48.6
Obstetrics	10	0.5	6	0.3
Orthopaedics	108	5.7	57	2.8
Paediatrics	-	-	-	-
Urology	153	8.1	74	3.6
Abbreviations: KSA: cantonal hospital of	Aarau; ATC: Anator	nical Therapeutic Che	emical classification sy	ystem.

Appendix Table 2. Demographic characteristics of 5'386 anticoagulant applications at the cantonal hospital of Baden (KSB) between july 2018 and 2020 stratified by implementation period.

			SB		
	Pre-Implementation		Post-Imple		
	1.7.2018 to 30.6.2019		1.8.2019 to		
	N	%	N	%	
Number of patients	516	-	521	-	
Number of cases	542	-	561	-	
Number of anticoagulant	2557	-	2729	-	
applications	2557		2129		
To females	1308	51.2	1253	45.9	
To males	1249	48.8	1476	54.1	
Median age	78.0		77.0		
[Min, Max]	[18, 98]	-	[21,97]	-	
By ATC					
Phenprocoumon			4.0		
(B01AA04)	29	1.1	19	0.7	
Acenocoumarol (B01AA07)	2	0.1	-	_	
Heparin (B01AB01)	574	22.4	633	23.2	
Dalteparin (B01AB04)	1104	43.2	1201	44.0	
Enoxaparin (B01AB05)	1	0.0	2	0.1	
Nadroparin (B01AB06)	5	0.2	-	_	
Danaparoid (B01AB09)	-	-	17	0.9	
Alteplase (B01AD02)	1	0.0	2	0.1	
Argatroban (B01AE03)	6	0.2	8	0.3	
Dabigatran (B01AE07)	70	2.7	31	1.1	
Rivaroxaban (B01AF01)	173	6.8	149	5.5	
Apixaban (B01AF02)	530	20.7	583	21.4	
Edoxaban (B01AF03)	48	1.9	72	2.6	
Fondaparinux (B01AX05)	14	0.5	12	0.4	
By Month					
January	200	7.8	220	8.1	
February	200	7.8	257	9.4	
March	213	8.3	284	10.4	
April	156	6.1	203	7.4	
May	290	11.4	259	9.5	
June	232	9.1	306	11.2	
July	203	7.9	11	0.4	
August	240	9.4	173	6.3	
September	220	8.6	210	7.7	

October	151	5.9	298	10.9
November	209	8.2	244	8.9
December	209	9.5	264	6.9 9.7
By Weekday	243	9.5	204	9.1
Monday	365	14.3	418	15.3
Tuesday	418	16.3	481	17.6
Wednesday	393	15.4	454	16.6
Thursday	418	16.3	428	15.7
Friday	389	15.2	365	13.4
Saturday	289	11.3	269	9.9
Sunday	285	11.1	314	11.5
Time of Drug Administration				
Night (00:00-6:00)	101	4.0	105	3.8
Morning (6:00-12:00)	1017	39.8	1132	41.5
Afternoon (12:00-18:00)	534	20.9	565	20.7
Evening (18:00-00:00)	905	35.4	927	34.0
By Clinic				
Surgery	787	30.8	761	27.9
Gynaecology	203	7.9	154	5.6
Internal Medicine	1158	45.3	1367	50.1
Obstetrics	4	0.2	12	0.4
Orthopedics	276	10.8	328	12
Pediatrics	1	0.0	-	-
Urology	128	5.0	107	3.9

Appendix Table 3. Results of unadjusted and adjusted logistic regression model with anticoagulant applications as observations points for both hospitals. The model was adjusted for adjusted for sex, age, month, weekday, time of application, ATC of applied anticoagulant, and clinic from where anticoagulant was prescribed.

	Predictor Variable	Estimate	Std. Error	Z value	р	OR [95% CI]	RR (SD)	RRR
KSA								
unadjusted	Post	-1.42	0.12	-11.80	<.05	0.24 [0.19, 0.31]	0.28 (0.03)	72%
adjusted	Post	-1.42	0.12	-11.35	<.05	0.24 [0.19, 0.31]	0.25 (0.03)	75%
	Sex (M)	0.41	0.11	3.45	<.05	1.50 [1.19, 1.89]		
	Age	0.02	0.00	3.96	<.05	1.02 [1.01, 1.03]		
	Month	-0.03	0.02	-2.11	<.05	0.97 [0.94, 1.00]		
	Weekday	0.08	0.03	2.95	<.05	1.09 [1.02, 1.15]		
	Time	0.26	0.06	4.21	<.05	1.30 [1.15, 1.47]		
	ATC	0.35	0.03	12.92	<.05	1.41 [1.34, 1.49]		
	Clinic	-0.01	0.06	-0.21	0.84	0.99 [0.87, 1.12]		
KSB								
unadjusted	Post	-0.37	0.08	-4.56	<.05	0.69 [0.58, 0.81]	0.72 (0.05)	28%
adjusted	Post	-0.38	0.08	-4.48	<.05	0.68 [0.58, 0.81]	0.69 (0.06)	31%
	Sex (M)	-0.13	0.08	-1.53	0.13	0.88 [0.74, 1.04]		
	Age	0.01	0.00	3.96	<.05	1.01 [1.01, 1.02]		
	Month	-0.01	0.01	-1.24	0.21	0.99 [0.96, 1.01]		
	Weekday	0.05	0.02	2.13	<.05	1.05 [1.00, 1.09]		
	Time	0.56	0.05	10.88	<.05	1.75 [1.58, 1.93]		
	ATC	0.17	0.01	14.67	<.05	1.18 [1.16, 1.21]		
	Clinic	0.00	0.03	0.06	0.95	1.00 [0.95, 1.06]		

Abbreviations: OR: odds ratio; CI: confidence interval; RR: risk reduction; SD: standard deviation; RRR: relative risk reduction; KSA: cantonal hospital of Aarau; KSB: cantonal hospital of Baden; ATC: Anatomical Therapeutic Chemical classification system.

Appendix Table 4. Results of unadjusted and adjusted logistic regression model with cases as observations points for both hospitals. The model was adjusted for adjusted for sex, age, month, weekday, time of application, ATC of applied anticoagulant, and clinic from where anticoagulant was prescribed.

	Predictor Variable	Estimate	Std. Error	Z value	р	OR [95% CI]	RR (SD)	RRR
KSA								
unadjusted	Post	-0.74	0.18	-4.25	<.05	0.47 [0.34, 0.67]	0.57 (0.08)	43%
adjusted	Post	-0.81	0.22	-3.65	<.05	0.44 [0.29, 0.69]	0.45 (0.10)	55%
	Sex (M)	0.32	0.23	1.37	0.17	1.37 [0.88, 2.17]		
	Age	0.01	0.01	1.06	0.29	1.01 [0.99, 1.03]		
	Month	-0.00	0.03	-0.12	0.91	1.00 [0.94, 1.06]		
	Weekday	0.07	0.06	1.26	0.21	1.07 [0.96, 1.20]		
	Time	1.21	0.14	8.97	<.05	3.36 [2.60, 4.31]		
	ATC	0.69	0.06	11.52	<.05	2.00 [1.79, 2.26]		
	Clinic	-0.29	0.14	-2.14	<.05	0.75 [0.57, 0.97]		
KSB								
unadjusted	Post	-0.31	0.16	-1.90	0.06	0.74 [0.54, 1.01]	0.79 (0.10)	21%
adjusted	Post	-0.16	0.19	-0.81	0.42	0.85 [0.58, 1.25]	0.86 (0.17)	14%
	Sex (M)	-0.20	0.20	-1.02	0.31	0.82 [0.56, 1.20]		
	Age	0.01	0.01	0.94	0.35	1.01 [0.99, 1.02]		
	Month	-0.01	0.03	-0.19	0.85	0.99 [0.94, 1.05]		
	Weekday	-0.01	0.05	-0.13	0.89	0.99 [0.90, 1.10]		
	Time	1.27	0.12	10.19	<.05	3.57 [2.82, 4.60]		
	ATC	0.31	0.03	11.23	<.05	1.37 [1.30, 1.45]		
	Clinic	-0.14	0.06	-2.20	<.05	0.87 [0.77, 0.98]		

Abbreviations: OR: odds ratio; CI: confidence interval; RR: risk reduction; SD: standard deviation; RRR: relative risk reduction; KSA: cantonal hospital of Aarau; KSB: cantonal hospital of Baden; ATC: Anatomical Therapeutic Chemical classification system.

Appendix Figure 1. Survey conducted at the cantonal hospital of Aarau (KSA) between 14.9.2021 to 1.10.2021 by Hendrike Dahmke. The responses were analysed and used for comparison purposes.



Multiagentensystem KPHARM

Umfrage KPHARM

Liebe KollegInnen

Vielleicht haben Sie ja auch schon mal eine solche Meldung in der Kurve gesehen oder einen Anruf aus der Spitalpharmazie erhalten, der Sie daran erinnert, eine Medikamentengabe anzupassen.



Wenn das der Fall ist, war ein Agent des KPHARM am Werk. Der Fachbereich KPHARM des Kantonsspitals Aarau ist eine interdisziplinäre Kooperation zwischen der Klinischen Pharmazie und der Allgemeinen Inneren und Notfallmedizin. Gemeinsam haben wir ein Multiagentensystem entwickelt, um Situationen, welche zu einem unerwünschten Arzneimittelereignis führen könnten, rechtzeitig zu entdecken. Die hierfür entwickelten Algorithmen, sogenannte Agenten, nutzen die vorhandenen Daten in der elektronischen Patientenakte (KISIM) und erstellen Warnmeldungen, wenn Risikokonstellationen auftreten.

Um das Projekt weiter zu verbessern und optimal auf die Bedürfnisse von ÄrztInnen anzupassen, führen wir eine Umfrage zur Zufriedenheit mit unseren KPHARM-Meldungen durch. Die Umfrage dauert max. 10 Minuten. Ihre Angaben werden vertraulich behandelt. Mit der Teilnahme an der Umfrage erklären Sie sich einverstanden, dass die Ergebnisse in anonymisierter Form veröffentlicht werden können.



Multiagentensystem KPHARM

Personendaten

1. In welcher Funktion arbeiten Sie?
Assistenzarzt/ärztin
Oberarzt/ärztin
Leitender Arzt/ Leitende Ärztin
Chefarzt/ärztin
Gleialzivalzuri
2. In welcher Abteilung arbeiten Sie?
•
Sonstiges (bitte angeben):
3. Wie viel Stellenprozent arbeiten Sie?
4. Wie lange arbeiten Sie bereits am KSA? (In Jahren)
5. Wie alt sind Sie? (In Jahren)
6. Geschlecht
Männlich
Weiblich
Divers
Keine Angabe
Neille Alligabe
Kantonsspital Aarau

Multiagentensystem KPHARM

Bekanntheit und Akzeptanz des KPHARM-Projekts

Die Agenten des KPHARM-Projektes bestehen jeweils aus mehreren Algorithmen, die verschiedene Arzneimittelrisiken eines Wirkstoffes bzw. einer Wirkstoffklasse abdecken.

So prüft der Agent 'Parenterale Antikoagulantien' beispielsweise die Dosis von Fragmin in Abhängigkeit von der Nierenfunktion und des Körpergewichts.

Wenn	n der Agent	eine k	ritische	Situation	entdeckt,	wird (eine	Meldung	generiert,	welche als
Statio	onsmitteilu	ng in c	ler Kurve	e dargeste	ellt wird.					

7. W	ie häufig wurden Ihnen im vergangenen Jahr Meldungen des KPHARM Projektes im KISIM angezeigt?
\bigcirc	Mehrmals pro Tag
$\cdot \bigcirc$	Mehrmals pro Woche
\bigcirc	Mehrmals pro Monat
\bigcirc	Mehrmals pro Jahr
0	Noch nie

8. Derzeit sind 16 Agenten aktiv im KISIM. Sie generieren Meldungen sowohl zu häufigen, als auch zu selteneren, dafür aber potentiell schwerwiegenden Medikationsfehlern.

Empfinden Sie die folgenden Algorithmen als hilfreich? Sollten Sie einen Algorithmus nicht kennen, klicken Sie bitte auf Algorithmus unbekannt.

	Sehr hilfreich	Hilfreich	Eher nicht hilfreich	Nicht hilfreich	Algorithmus unbekannt		
DOAKs (Apixaban, Dabigatran, Edoxaban, Rivaroxaban)							
Duplikationen Antikoagulantien	\circ			\circ	\circ		
Paracetamol	0						
Metformin	\circ	\circ	0	0	\circ		
Triple Whammy							
Methotrexat	\bigcirc	\bigcirc	\circ	\circ	\circ		
Xanthinoxidasehemmer							
Digoxin	\circ			0	\circ		
Vancomycin							
Cefepim	\bigcirc	\bigcirc	\bigcirc	\bigcirc	\bigcirc		
Aminoglykoside							
Parenterale Antikoagulantien	\circ		\circ	\circ	\circ		
Protonenpumpeninhibitoren							
Haben Sie Kommentare zu den	einzelnen Algorithn	nen?					
9. Wie zufrieden sind sie insgesamt mit dem Multiagentensystem? Sehr zufrieden							
Zufrieden							
Weniger zufrieden							
Überhaupt nicht zufri	eden						

10. Bitte beurteilen Sie folgende Aussagen in Bezug auf das Multiagentensystem

	Trifft zu	Trifft eher zu	Trifft eher nicht zu	Trifft nicht zu	Nicht beurteilbar
Die Meldungen betreffen relevante Arzneimittelprobleme	0	0	0	0	0
Die Meldungen enthalten sinnvolle Empfehlungen	0	\circ	0	\circ	\circ
Die Meldungen sind verständlich formuliert	0	0	0	0	\circ
Die Meldungen sind häufig zutreffend	0	0	0	\bigcirc	0
Die Meldungen erreichen die verantwortliche Person	0	0	0	0	0
Die Meldungen kommen zum richtigen Zeitpunkt	0	0	0	0	0
Die Meldungen unterstützen mich Arbeitsalltag	0	0	0	0	0
Die Anzahl der Meldungen ist angemessen	0	\circ	0	0	C



Multiagentensystem KPHARM

Wünsche und Anforderungen an ein Clinical Decision Support System

Clinical Decision Support Systems haben das Ziel, ÄrztInnen relevante Informationen zum richtigen Zeitpunkt zur Verfügung zu stellen und so die Patientenversorgung zu verbessern. In der Schweiz sind mehrere Systeme in Betrieb, die sich in der Art der Informationen (z.B. Interaktionscheck, Allergie Alert), der Anzeige der Meldungen und der Sensitivität der Algorithmen unterscheiden.

Im Folgenden möchten wir erfahren, wie wir unser System verbessern können.

 Welche Aspekte sind Ihnen bei einem CDSS im Allgemeinen besonders wid

	Sehr wichtig	Wichtig	Weniger wichtig	Gar nicht wichtig				
Die Meldungen betreffen relevante Arzneimittelprobleme	0							
Die Meldungen enthalten sinnvolle Empfehlungen	0	\circ	0	\circ				
Die Meldungen sind verständlich formuliert	0	0	0	0				
Die Meldungen sind häufig zutreffend	\circ	\circ	0	\circ				
Die Meldungen erreichen die verantwortliche Person								
Die Meldungen kommen zum richtigen Zeitpunkt	\circ	\circ	0	\circ				
Die Meldungen unterstützen mich Arbeitsalltag								
Die Anzahl der Meldungen ist angemessen	\circ	\circ	\circ	\circ				
12. In welcher Form sollen die Meldungen vorzugsweise übermittelt werden? Telefon Pop-up Fenster Mailversand im KISIM Notiz in der Kurve (Stationsmitteilung) Sonstiges (bitte angeben) 13. Welche Medikamentenbezogenen Probleme müssten Ihrer Meinung nach in der Zukunft noch gelöst werden?								
14. Haben Sie bereits Erfahrungen mit anderen Systemen für Clinical Decision Support? Ja Nein								

15. Wenn Sie bereits r	nit anderen Clinical Decision Support Systemen Erfahrungen gemac	ht haben
Welches Klinikinformationssystem (z.B.: KISIM, Phoenix)?		
Was wurde gemeldet (z.B.:		
Allergie, Interaktion)?		
Wie werden Ärzte in diesem System informiert (z.B.: Pop-Up, Stationsmitteilung)?		
Wo sehen Sie Vorteile im		
Vergleich zum KSA?		
Wo sehen Sie Nachteile im Vergleich zum KSA?		

Appendix Table 5. Demographic characteristics of the respondents to the conducted survey at the cantonal hospital of Aarau (KSA) from 14.9.2021 to the 1.10.2021.

KSA Survey from 14.9.2021 to 1.10.2021					
Survey IIOIII 14.9.2021 to 1.10.2	N	%			
Number of respondents to demographic question	152	100			
Sex					
Female	87	57.2			
Male	63	41.4			
Median age [Min, Max]	35 [25, 60]	-			
Average length of employment in years (SD)	4.50 (4.56)	-			
Average job percentage worked (SD)	91.9 (16.2)	-			
Job position					
Resident	79	52.0			
Senior resident	54	35.5			
Leading physicians	14	9.2			
Head physicians	5	3.3			
Clinic					
Surgery	31	20.4			
Obstetrics & Gynaecology	20	13.2			
Internal Medicine	85	55.9			
Orthopedics	3	2.0			
Emergency	4	2.6			
Urology	7	4.6			
Medical Services	-	-			
No answer	2	1.3			

Appendix Figure 2. Survey at the cantonal hospital of Baden (KSB) about the clinical decision support in the hospital information system KISIM from 22.4.2022 to the 26.6.2022.



Umfrage CDSS KISIM

Seite 1 von 6

Umfrage zum Clinical Decision Support System im KISIM

1. Liebe Ärztinnen und Ärzte des KSB

Vielleicht haben Sie auch schon mal eine solche Meldung im KISIM gesehen oder einen Anruf aus der Spitalapotheke erhalten, der Sie daran erinnert, eine Medikationsverordnung im KISIM anzupassen.

Speichern Sp	eichern + Neu Be	arbeiten Löschen	Visieren	Etiketten	Drucken	Extras Schliessen		
STAEMPFL/24.02.202	2 14:57:28					3		
Patienten-Info	Medi-Allergien	Allergie-Angaben	fehlen					
Medi-Check	Allerg (1)	▲ Dupl	(1)	✓ Inte	er (0)			
Medikament	Achtung!							
		Es wurden l	Doppelverordnu	ngen gefunden	!			
Verabreichung		Woller	Sie trotzdem s	peichern? lein				
○ 1x	1 - 24.02.2022	11:45 🗸 🔐 bis	Einheit Stk	Dauer:				
Abrechenbarkeit Erweiterungen Bemerkung	☐ Von Patient mit	gebrachtes Medikamen	t 🗌 Studienm	nedikament	▽	Hinzufügen		

Wenn das der Fall ist, war das Clinical Decision Support System (CDSS) am Werk. Basierend auf den vorhandenen Daten in der elektronischen Patientenakte (KISIM) werden Warnmeldungen erstellt, wenn Risikokonstellationen im Bereich Duplikation und Interaktion auftreten. Diese werden Ihnen in Form eines Pop-Ups angezeigt und brauchen eine Quittierung.

Im Rahmen meiner Forschungsarbeit für den Master Pharmazie an der ETH Zürich im Bereich der Pharmakoepidemiologie untersuche ich die Zufriedenheit der medizinischen Fachpersonen mit dem CDSS und den Pop-Up Meldungen und evaluiere das Verbesserungspotential diesbezüglich.

Bei Fragen und Anmerkungen dürfen Sie sich jederzeit bei Sophie Stoop <u>sstoop@ethz.ch</u> oder alternativ bei Dr. Dominik Stämpfli <u>Dominik.Staempfli@ksb.ch</u> melden.

Die Umfrage dauert max. 10 Minuten. Ihre Angaben werden vertraulich behandelt.

Mit der Teilnahme an der Umfrage erklären Sie sich damit einverstanden, dass die Ergebnisse in anonymisierter Form ausgewertet werden können.

Weiter





Umfrage CDSS KISIM

Seite 2 von 6

Bekanntheit und Zufriedenheit mit dem CDSS

Das Clinical Decision Support System (CDSS) im KISIM generiert Meldungen in Form eines Pop-Ups wenn Risikokonstellationen im Bereich Duplikation und Interaktion auftreten.

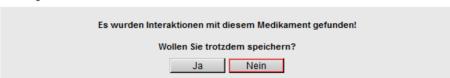
 Wenn das CDSS eine doppelte Medikationsverordnung entdeckt, wird eine Meldung generiert, welche als Pop-Up in der Kurve dargestellt wird.



Wie häufig wurden Ihnen im vergangenen Jahr Duplikationsmeldungen des CDSS im KISIM angezeigt?

- O Mehrmals pro Tag
- Mehrmals pro Woche
- Mehrmals pro Monat
- O Mehrmals pro Jahr
- O Noch nie
- Wenn das CDSS eine potentielle Medikationsinteraktion entdeckt, wird eine Meldung generiert, welche als Pop-Up in der Kurve dargestellt wird.

Achtung!



Wie häufig wurden Ihnen im vergangenen Jahr Interaktionsmeldungen des CDSS im KISIM angezeigt? *

- O Mehrmals pro Tag
- O Mehrmals pro Woche
- Mehrmals pro Monat
- O Mehrmals pro Jahr
- O Noch nie
- Wenn das CDSS eine Allergie entdeckt, wird eine Meldung generiert, welche als Pop-Up in der Kurve dargestellt wird.

Achtung!

Meldungen ist

angemessen

	E	s wurden Allergier	gefunden!		
	w	/ollen Sie trotzdem	speichern?		
		Ja	Nein		
Wie häufig wurden Ihnen in Mehrmals pro Tag Mehrmals pro Woche Mehrmals pro Monat Mehrmals pro Jahr Noch nie	m vergangenen J	Jahr Allergiemeldu	ingen des CDSS	im KISIM angeze	igt? *
Wie zufrieden sind Sie inso Sehr zufrieden Zufrieden Weniger zufrieden Überhaupt nicht zufried		CDSS?*			
Wenn Sie Ihre Zufriedenhe Kommentarbox tun.	eit mit dem CDSS	kommentieren n	nöchten, dürfen Si	ie dies gerne in fo	olgender
Bitte beurteilen Sie folgend	de Aussagen in B Trifft zu	Trifft	SS: * Trifft eher	Trifft picht zu	Nicht beurteilba
			Trifft	Trifft nicht zu	Nicht beurteilba
Bitte beurteilen Sie folgend Die Meldungen betreffen relevante Arzneimittelprobleme		Trifft	Trifft eher		
Die Meldungen betreffen relevante Arzneimittelprobleme Die Meldungen enthalten sinnvolle		Trifft eher zu	Trifft eher		beurteilba
Die Meldungen betreffen relevante Arzneimittelprobleme Die Meldungen		Trifft eher zu	Trifft eher		beurteilba
Die Meldungen betreffen relevante Arzneimittelprobleme Die Meldungen enthalten sinnvolle Empfehlungen Die Meldungen sind verständlich formuliert Die Meldungen sind häufig zutreffend		Trifft eher zu	Trifft eher		beurteilba
Die Meldungen betreffen relevante Arzneimittelprobleme Die Meldungen enthalten sinnvolle Empfehlungen Die Meldungen sind verständlich formuliert Die Meldungen sind	Trifft zu	Trifft eher zu	Trifft eher		beurteilba
Die Meldungen betreffen relevante Arzneimittelprobleme Die Meldungen enthalten sinnvolle Empfehlungen Die Meldungen sind verständlich formuliert Die Meldungen sind häufig zutreffend Die Meldungen erreichen die verantwortliche	Trifft zu	Trifft eher zu	Trifft eher nicht zu	nicht zu	beurteilba

0

0

0

0

0





Umfrage CDSS KISIM

Seite	3	von	6
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Wünsche und A	Anforderungen	an ein	CDSS
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Clinical Decision Support Systems haben das Ziel, Ärztinnen und Ärzten relevante Informationen zum richtigen Zeitpunkt zur Verfügung zu stellen und so die Patientensicherheit zu verbessern. In der Schweiz sind mehrere Systeme in Betrieb, die sich in der Art der Informationen (z.B. Interaktionscheck, Allergie Alert), der Anzeige der Meldungen und der Sensitivität der Algorithmen unterscheiden.

Im Folgenden möchten wir in Erfahrung bringen, was man am aktuellen CDSS noch verbessern könnte.

1. Welche Aspekte sind Ihnen bei einem CDSS im Allgemeinen besonders wichtig?

	Sehr wichtig	Wichtig	weniger wichtig	Nicht wichtig
Die Meldungen betreffen relevante Arzneimittelprobleme	0	0	0	0
Die Meldungen enthalten sinnvolle Empfehlungen	0	0	0	0
Die Meldungen sind verständlich formuliert	0	0	0	0
Die Meldungen sind häufig zutreffend	0	0	0	0
Die Meldungen erreichen die verantwortliche Person	0	0	0	0
Die Meldungen kommen zum richtigen Zeitpunkt	0	0	0	0
Die Meldungen unterstützen mich im Arbeitsalltag	0	0	0	0
Die Anzahl der Meldungen ist angemessen	0	0	0	0

2.	Medikationsfehler umfassen relevante Interaktionen, Duplikationen, Dosierungsanpassungen an Nierenfunktion,
	fehlende Laborparameter und Weiteres.

Zu welchen Arzneimitteln würden Sie einen Algorithmus als hilfreich empfinden?

	Sehr hilfreich	Hilfreich	Eher nicht hilfreich	Nicht hilfreich	Keine Angabe
Aminoglykoside	0	0	0	0	0
Antiinfektiva Oral Switch	0	0	0	0	0
Apixaban	0	0	0	0	0
Cefepim	0	0	0	0	0

Evaluation of CDSS to Detect Anticoagulant Duplications

	Dabigatran	0	0	0	0	0
	Digoxin	0	0	0	0	0
	Edoxaban	0	0	0	0	0
	Metformin	0	0	0	0	0
	Methotrexat	0	0	0	0	0
	Nichtsteroidales Antirheumatikum (NSAR)	0	0	0	0	0
	Orale Antikoagulantien	0	0	0	0	0
	Paracetamol	0	0	0	0	0
	Parenterale Antikoagulantien	0	0	0	0	0
	Protonenpumpenhemmer	0	0	0	0	0
	Rivaroxaban	0	0	0	0	0
	Triple Whammy (ACE inhibitor/ARB + Diuretika+ NSAR)	0	0	0	0	0
	Valproat	0	0	0	0	0
	Vancomycin	0	0	0	0	0
	Xanthinoxidasehemmer (Allopurinol)	0	0	0	0	0
3.	In welcher Form sollen die	e Meldungen vorzugs	weise übermittelt	werden?		
			Ja		Nein	
	Telefon		0		0	
	Pop-up Fenster		0		0	
	Mailversand im KISIM		0		0	
	Notiz in der Kurve (Stationsmitteilung)		0		0	
4.	Haben Sie bereits Erfahru	ngen mit anderen Sy			ort?*	
	○ Ja		○ Ne	in		
		z	Zurück Weit	er		
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1.	Wenn Sie uns sonst noch etwas zum CDSS oder zur Umfrage sagen möchten, dürfen Sie dies gerne in folgende Kommentarbox tun.
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Ende der Umfrage

Vielen Dank für Ihre Teilnahme!

Bei Fragen und Anmerkungen dürfen Sie sich jederzeit bei Sophie Stoop $\underline{sstoop@ethz.ch}$ oder alternativ bei Dr. Dominik Stämpfli $\underline{Dominik.Staempfli@ksb.ch}$ melden.

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Appendix Table 6. Demographic characteristics of the respondents to the survey at the cantonal hospital of Baden (KSB) from 22.4.2022 to the 26.6.2022.

KSB Survey from 22.4.2022 to 26.6.2022				
Number of respondents to demographic question	118	100		
Sex				
Female	63	53.4		
Male	51	43.2		
Median age [Min, Max]	35 [25, 65]	-		
Average length of employment in years (SD)	4.84 (5.38)	-		
Average job percentage worked (SD)	88.1 (15.2)	-		
Job position				
Resident	47	39.8		
Senior resident	44	37.3		
Leading physicians	24	20.3		
Head physicians	3	2.5		
Clinic				
Surgery	16	13.6		
Obstetrics & Gynaecology	13	11.0		
Internal Medicine	66	55.9		
Orthopedics	3	2.5		
Emergency	15	12.7		
Urology	2	1.7		
Medical Services	3	2.5		