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Improving the effectiveness of drug safety alerts to increase adherence to the guideline for gastrointestinal prophylaxis

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ABSTRACT

Objective: Gastrointestinal bleedings are the most frequently occurring reason for medication-related hospital admissions, which are potentially preventable. We implemented a clinical decision support system that recommends to prescribe gastrointestinal prophylaxis in patients with an increased risk according to the Dutch guideline. Our primary objective was to determine whether the implementation resulted in improved compliance with this guideline for gastrointestinal prophylaxis. A secondary objective was to determine whether implementation resulted in a reduction of the number of drug safety alerts.

Materials and methods: This intervention study was performed at the Spaarne Gasthuis, a teaching hospital, using Epic as hospital information system. We selected prescriptions with an indication for gastrointestinal prophylaxis according to the guideline, in the three months before and after implementation of the clinical decision support in November 2014. We analyzed whether gastrointestinal prophylaxis was prescribed more frequently after implementation using the Pearson's Chi-square test and the change in the number of drug safety alerts.

Results: Before implementation in 84.0% of the included 2064 prescriptions gastrointestinal prophylaxis was co-prescribed. After implementation this percentage increased to 94.5% of the 2269 prescriptions ($p < 0.001$). The number of drug safety alerts decreased by 78.2% from 980 to 217 alerts.

Conclusion: The introduction of a clinical decision support system for gastrointestinal prophylaxis improved adherence to the Dutch guideline. This was most likely due to a reduction in the number of irrelevant drug safety alerts.

1. Introduction

A considerable part of all hospital admissions is related to adverse drug reactions, of which many are potentially avoidable [1–4]. Beijer et al. estimated that 88% of all adverse drug reaction related hospitalizations in the elderly are preventable, and for the non-elderly this proportion was 24% [2]. The most frequently occurring diagnosis for potentially preventable medication-related admissions was gastrointestinal bleeding, causing 15% of these admissions [3,4]. It is well known that certain drugs and drug combinations do increase the risk of gastrointestinal bleeding [5–9]. Other risk factors are an increasing age and several medical conditions including diabetes, severe disabling rheumatoid arthritis and a history of gastrointestinal ulcer. These and other risk factors have been included in several guidelines, that recommend to prescribe gastrointestinal prophylaxis such as a proton pump inhibitor, in patients with an increased risk of gastrointestinal bleeding to avoid potentially preventable hospital admissions [10].

In the Netherlands, a computerized physician order entry is obligatory. After order entry, medication surveillance, including the detection of clinically relevant drug-drug interactions, takes place based on the database maintained by the Royal Dutch Association for the Advancement of Pharmacy (KNMP) [11]. In this so-called G-standard, all drug-drug interactions are incorporated, including those that cause an increased risk for gastrointestinal bleeding. For these drug-drug interactions, the prescribing of gastrointestinal prophylaxis is advised.

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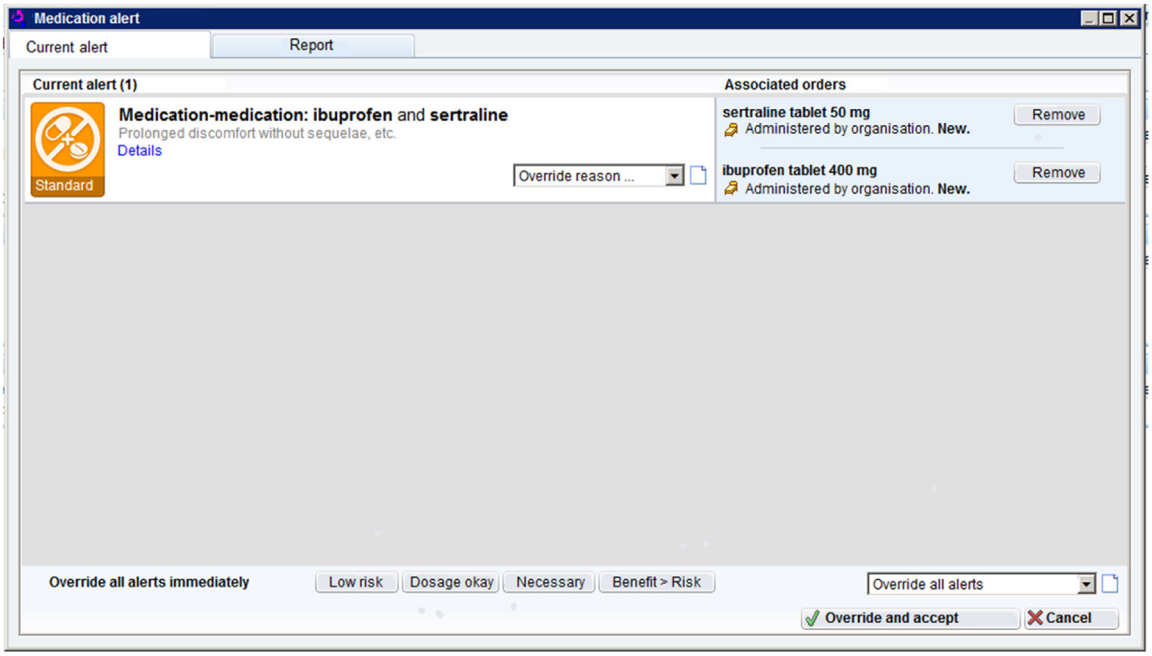

Fig. 1. Drug safety alerts for adding gastrointestinal prophylaxis shown to prescribers before implementation of the clinical decision support system (translated into English).

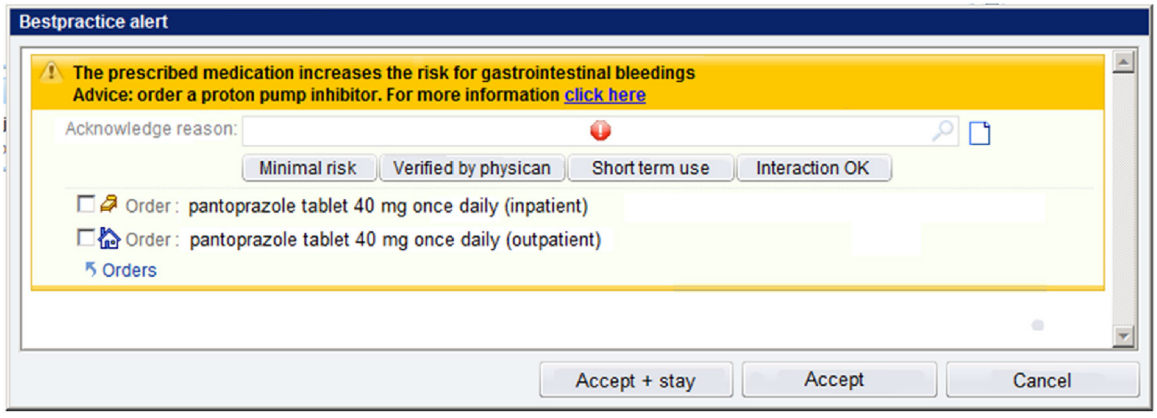

Fig. 2. Drug safety alerts for adding gastrointestinal prophylaxis shown to prescribers after implementation of the clinical decision support system (translated into English).

The medication surveillance alert that used to be shown in our hospital to both the physician and the pharmacy technician, is presented in Fig. 1. These alerts were shown for drug-drug and drug-disease interactions, dosing, duplicate therapy, pregnancy, lactation and allergies without taking additional risk factors into account. We use the term classical alert for these alerts in this article. In this classical alert, a (list of) drug safety alert(s) appeared which is applicable to the prescribed drug(s) at the moment the prescriber signs the order. After clicking on the 'details' icon, the user can obtain information about the reason for the alert. For inpatient orders, all alerts were reviewed on a daily basis by a pharmacy technician and pharmacist, and the prescriber was contacted by telephone if necessary. The disadvantage of this type of medication surveillance is that prescribers and pharmacists receive a redundant number of drug safety alerts if the patient has already been prescribed gastrointestinal prophylaxis. Presenting redundant warnings too frequently increases the risk of '*alert fatigue*', overriding of all generated drug safety alerts, including those that are relevant [12–14]. Moreover, risk factors were not taken into account, and therefore for some patients with an increased risk of gastrointestinal bleeding, no drug safety alert was generated.

In our hospital we implemented a clinical decision support system for gastrointestinal prophylaxis, based on the Dutch guideline for gastrointestinal prophylaxis. [10]. A summary of this guideline is given in Supplemental Table 1. In the clinical decision support system alert, a single pop-up is shown with a short description and the possibility to order pantoprazole 40 mg once daily by clicking once (Fig. 2). Pantoprazole 40 mg once daily is mentioned in the Dutch guideline as a suitable drug and dose for gastrointestinal prophylaxis [10]. In case of children, a similar alert is shown which advise to start with gastrointestinal prophylaxis, without recommending an order. If the prescriber does not order gastrointestinal prophylaxis, a reason should be selected from the menu in the alert. The way physicians can override this alert without ordering gastrointestinal prophylaxis is similar to overriding the classical medication surveillance alert. Prescribers were informed about the introduction of this clinical decision support system in the newsletter that accompanies each update of the hospital information system. For inpatient orders, a list with patients with an indication for gastrointestinal prophylaxis but without a prescription, is reviewed on a daily basis by a pharmacist, and prescribers are contacted by telephone if needed.

The alert in the clinical decision support system is based on an algorithm, in which patient characteristics are taken into account for the generation of patient specific drug safety alerts. The clinical decision support for gastrointestinal prophylaxis includes use of risk medication(s), the use of gastrointestinal prophylaxis and age as a risk factor. Other risk factors, such as a diagnosis of diabetes, were not incorporated, because this information is not unequivocally documented in the hospital information system. The algorithm does not generate an alert if the patient has already been prescribed gastrointestinal prophylaxis, thereby further limiting the pop-up of irrelevant alerts.

In the pharmacy, we intended to evaluate whether the implementation of the clinical decision support system resulted in better patient care. The main objective of this study was to determine whether implementation of a clinical decision support system for gastrointestinal prophylaxis resulted in improved compliance with the Dutch guideline for gastrointestinal prophylaxis. We analyzed the proportion of patients for whom treatment with gastrointestinal prophylaxis was ordered within one hour after ordering the risk medication, before and after implementation of the clinical decision support system. Secondary objectives were whether implementation resulted in a change in the number and quality of drug safety alerts and whether a drug safety alert resulted in a prescription for gastrointestinal prophylaxis.

2. Material and methods

2.1. Organizational setting

The study was initiated by the Pharmacy Foundation of Haarlem Hospitals (Haarlem, the Netherlands), a hospital pharmacy providing pharmaceutical care for the teaching hospital Spaarne Gasthuis. This study was performed in the Hoofddorp site of the Spaarne Gasthuis, a site with 455 beds. Both inpatient and outpatient visits were analyzed.

2.2. System details and system in use

The study was performed using the hospital information system Epic which contains integrated computerized physician order entry and includes functionalities for the implementation of a clinical decision support system. The implementation of the clinical decision support system started in August 2014, and on 24 November 2014 the whole system was implemented. After implementation of the clinical decision support system, only the alerts of the decision support system were shown to the physicians. The alerts of the classical medication surveillance system regarding gastrointestinal prophylaxis were suppressed.

2.3. Study design

We performed an intervention study, in which we compared the occurrence and characteristics of generated drug safety alerts and their handling in the period before and after implementation of the clinical decision support system for gastrointestinal prophylaxis. Because implementation of the clinical decision support system was part of improving regular care, no approval of an ethical committee was needed.

2.4. Participants

We included patients who were at risk for developing a gastrointestinal bleeding and should be prescribed gastrointestinal prophylaxis according to the Dutch guideline, regardless whether gastrointestinal prophylaxis was already prescribed or not [10]. All inpatients and outpatients in the Hoofddorp site of the Spaarne Gasthuis who had an indication for gastrointestinal prophylaxis were included. We excluded orders that were prescribed during or directly after surgery, because these orders were part of short-term supportive care.

2.5. Study flow

We analyzed three months before (May 1st 2014–August 1st 2014) and three months after implementation (December 1st 2014–March 1st 2015). The four months' period between August and December 2014 functioned as an implementation period and was therefore excluded from the analysis.

2.6. Outcome measures and evaluation criteria

Our primary endpoint was the proportion of patients who were prescribed an order for gastrointestinal prophylaxis at the same time or within one hour after the order for the risk medication in the two time periods. Secondary endpoints were the number of drug safety alerts before and after the implementation, and whether the alert or absence of alert was correct. We defined a correct alert as an alert in case no gastrointestinal prophylaxis was prescribed, while there was an indication for according to the guideline. In case a drug safety alert was shown, we analyzed whether this alert resulted in a prescription for gastrointestinal prophylaxis. We also analyzed risk factors that could influence whether correct drug safety alerts were ignored by the prescriber in the post implementation period. These risk factors included patient age, patient gender, specialty of prescriber (surgical versus non-surgical) and frequency (once or as needed versus other frequencies).

2.7. Methods for data acquisition and measurement

Data acquisition was performed using Crystal Reports to extract all relevant medication orders and alert data from Epic. A summary of the guideline is given in Supplementary Table 1, and the drug-drug and drug-(drug-)age combinations included in this study in Supplementary Table 2. We included all orders that resulted in increased risk of gastrointestinal bleeding both before and after implementation of the clinical decision support system in a database.

2.8. Methods for data analysis

We analyzed differences in categorical variables in the period before and after the implementation period, using the Pearson's Chi-square test. For analyzing risk factors associated with ignoring drug safety alerts, we used logistic regression. We first analyzed all variables in an univariate analysis. Variables with a p-value < 0.20 in the univariate analysis, were analyzed in a multivariate model. Analyses were performed using SPSS version 20.0 software (SPSS Inc., Chicago, IL). A p-value < 0.05 was considered to be statistically significant. We used the Statement on Reporting of Evaluation Studies in Health Informatics (STARE-HI) guideline for writing this article [15].

3. Results

3.1. Demographic and other study coverage data

Before implementation, a total number of 2064 prescriptions with an indication for gastrointestinal prophylaxis were ordered. In the post-implementation period, a total of 2269 prescriptions with an indication were prescribed (Table 1). In Supplemental Table 2, an overview of all drug-drug interactions, drug-age interactions

Table 1
Baseline characteristics.

	Before implementation	After Implementation
Number of prescriptions	2064	2269
Number of patients	932	966
Inpatient prescriptions (%)	1736 (84.1)	1977 (87.1)
Female patients (%)	575 (61.7)	537 (55.6)
Age (median, IQR)	76.10 (20.20)	75.99 (17.43)
Medical specialty (number, %)		
- Surgical	789 (38.2)	818 (36.1)
- Non-surgical	1275 (61.8)	1451 (63.9)

and drug-drug-age interactions, that caused the increased risk for gastrointestinal bleeding, is given.

3.2. Study findings and outcome data

Before implementation of the clinical decision support system in 1733 of the 2064 (84.0%) prescriptions gastrointestinal prophylaxis was co-prescribed during or within one hour after the order. After implementation this number increased to 2145 of the 2269 prescriptions (94.5%). This difference was statistically significant ($p < 0.001$). The observed increase was similar for inpatients (85.0–95.3%, $p < 0.001$) and outpatients (78.7–89.4%, $p < 0.001$).

The number of drug safety alerts before implementation was 812, and 91 (11.2%) were correct according to the guideline (Fig. 3). We reviewed the 2064 prescriptions and identified 244 orders (11.8%) for which an indication for gastrointestinal prophylaxis was present, but no drug safety alert was shown. The sensitivity of these alerts was 27% and the specificity 58%. After implementation of the clinical decision support, 217 drug safety alerts were shown. All alerts (100%) were correct according to the guideline, and we identified four prescriptions (0.2%) with an indication for gastrointestinal prophylaxis where no drug safety alert was shown. The sensitivity was 100% and specificity 99.8%.

After implementation of the clinical decision support system, we suppressed all classical medication surveillance alerts, but these alerts were available for evaluation. A total of 980 classical drug safety alerts were suppressed, and instead the clinical decision support system generated a total of 217 alerts. This resulted in a reduction of 78.2% in generated drug safety alerts for gastrointestinal prophylaxis.

Before implementation, 4 of the 91 correct drug safety alerts (4.4%) resulted in the addition of gastrointestinal prophylaxis within one hour after ordering the medication, while in the post-implementation period 97 of the 217 clinical rule pop-ups (44.7%) resulted in the addition of gastrointestinal prophylaxis. This difference was statistically significant ($P < 0.001$).

In the period after implementation, we assessed whether certain risk factors were associated with the prescribing of gastrointestinal prophylaxis after the alert. A lower age and surgical compared to non surgical specialty of the prescriber were significantly associated with an increased risk of ignoring the alert in the univariate model (Table 2). In the multivariate model, these variables lost statistical significance.

4. Discussion

The implementation of a clinical decision support system for gastrointestinal prophylaxis resulted in a 78.2% reduction in the number of drug safety alerts and a significant improvement in compliance with the guideline from 84.0 to 94.5%. As a result of the implementation, the absolute number and proportion of irrelevant signals decreased and the number of relevant signals increased. Gastrointestinal prophylaxis was prescribed more frequently (44.7 versus 4.4%) in response to a drug safety alert. In the univariate analysis, the risk of ignoring the drug safety alert was higher for a surgical prescriber versus a non-surgical prescriber and for younger patients, but no significant associations were found in the multivariate analysis.

The results suggest that the generation of more specific 'personalized' alerts leads to a situation in which prescribers are less likely to ignore the generated alert. In other words by implementation of a clinical decision support system for gastrointestinal prophylaxis, 'alert fatigue' was less likely to occur. In addition, the number of prescriptions that did not trigger a drug safety alert while there was an indication for gastrointestinal prophylaxis decreased. These results show that a clinical decision support system is capable of improving patient safety. A clinical decision support system with more specific drug safety alerts should be used instead of the classical medication surveillance to improve the compliance with this guideline. The algorithm of our clinical decision support system can be easily implemented in other hospital information systems that support pop-up alerts. Possibly a clinical decision support system may also improve the compliance with other guidelines, although further research is needed.

Other studies have also shown that clinical decision support systems are capable of supporting adherence to various guidelines [16–18]. To our knowledge, our study is the first to evaluate a clinical decision support system by comparing it with classical medication surveillance with the aim of determining whether this results in increased compliance. Because clinical decision support systems of different complexity are evaluated in various ways, it is difficult to compare our results with other evaluation studies.

The adherence to the guideline would ideally be 100%. However, the prescriber may have a deliberate reason to ignore the alert and not adhere to the guideline. Examples include prescriptions for a single order or short term use of medication that increases the risk of gastrointestinal bleeding. The proportion of overridden drug safety alerts in our study is consistent with other studies [13,14,16]. It is well known in the literature that drug safety alerts concerning drug-drug interactions were most frequently overridden [13,14]. In the pre-implementation period 87 of the 91 alerts (95.6%) were overridden. There are two explanations for the large number of overridden alerts. First, gastrointestinal prophylaxis is

Table 2
Univariate and multivariate logistic model for the chance of prescribing gastrointestinal prophylaxis following the clinical decision support alert in the period after the implementation.

Univariate logistic regression			Multivariate logistic regression		
Variable	OR (95% CI)	P-value	Variable	OR (95% CI)	P-value
Gender	1.05 (0.61–1.79)	0.87	Gender	–	–
Patient age	1.02 (1.01–1.03)	0.008	Patient age	1.01 (0.99 – 1.03)	0.11
Specialty[a]	2.27 (1.24–4.14)	0.007	Specialty[a]	1.72 (0.86 – 3.41)	0.12
Frequency[b]	1.34 (0.74–2.44)	0.33	Frequency[b]	–	–

[a] Non-surgical specialty versus surgical specialty.
[b] Continuous frequencies (once daily, etc.) versus once or as needed frequencies for gastrointestinal prophylaxis.

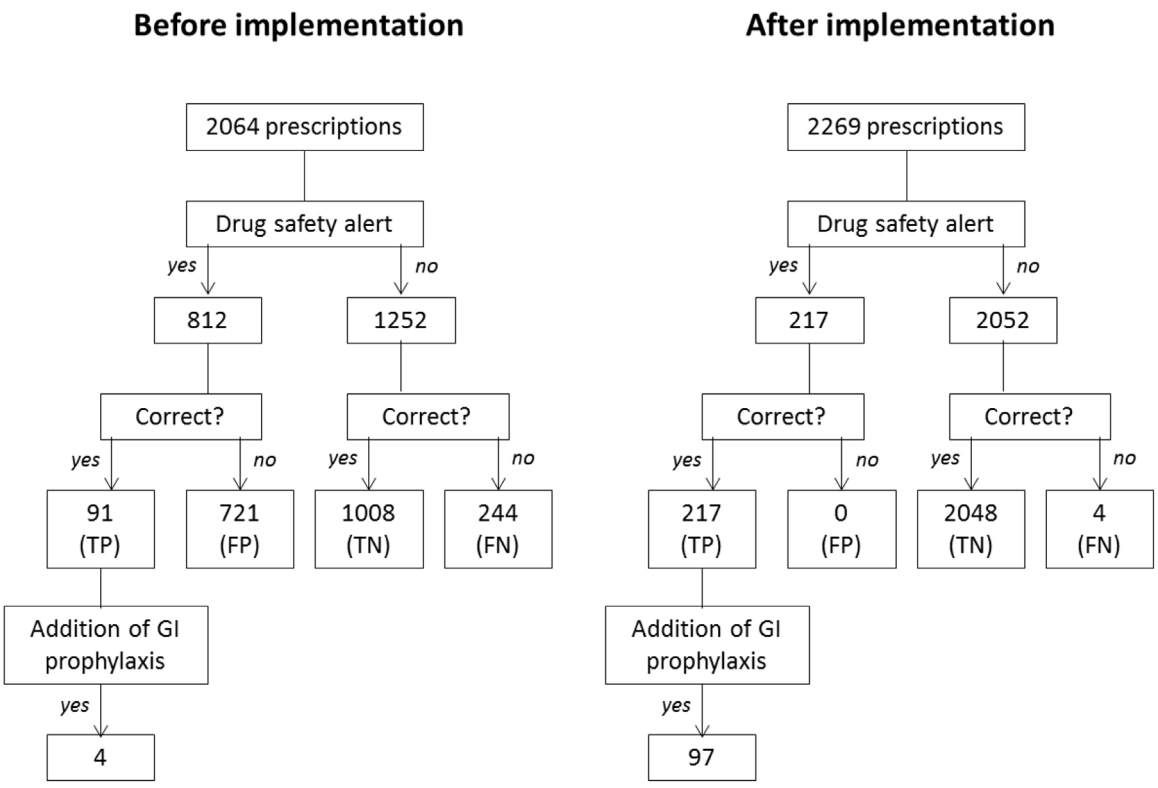

Fig. 3. Flow diagram of prescriptions included in this study.

TP: true-positive, FP: false-positive, TN: true-negative, FN: false-negative

Summary points

What was already known on this topic

- Gastrointestinal bleeding is the most frequently occurring reason for medication-related hospital admissions, which are potentially preventable. Prescription of gastrointestinal prophylaxis is recommended to avoid gastrointestinal bleedings.
- Presenting redundant medication surveillance warnings, for example with the advice to prescribe gastrointestinal prophylaxis if it has already been prescribed, increases the risk of overriding relevant drug safety alerts. This is called '*alert fatigue*'.

What this study added to our knowledge

- Implementation of a clinical decision support system that generates an alert according to the Dutch guideline for gastrointestinal prophylaxis, instead of the classical medication surveillance alerts, results in a reduction in the number of alerts with 78% and reduces the risk of '*alert fatigue*'.
- Due to the reduction in '*alert fatigue*', the compliance with the guideline increased significantly from 84.0 to 94.5%.
- Clinical decision support systems are a more intelligent way of medication surveillance and support the adherence to guidelines. This may result in improved patient safety.

often already co-prescribed making the alert irrelevant. Second, for various drug-drug interactions, the risk is only present above a certain age threshold. In patients below this age threshold, the alert is redundant. After implementation of the clinical decision support system, 120 of the 217 (55.3%) alerts were overridden. This is in line with other studies, that determined proportions ranging from 40% to nearly 50% for clinical decision support systems or systems in which action-orientated alerts were generated [14,19].

Our study has some potential strengths and limitations. By analyzing the prescriptions that involved an increased risk of gastrointestinal bleeding in exactly identical ways before and after the implementation, we excluded information bias. We compared the adherence to the guideline before and after the implementation, and with this information we could analyze what the clinical decision support system really adds to the initial situation. By including patients based on the Dutch guideline for gastrointestinal prophylaxis, we believe that we may have prevented patient harm. Ideally, a study should be done to determine whether the introduction of a clinical decision support system decreases the incidence of gastrointestinal complications. However, a larger number of patients should be included in such a study to have enough power to find a significant difference. Prescribing gastrointestinal prophylaxis may also have unintentional consequences, for example reducing the absorption of other drugs. Since there is a wide variation in unintentional effects, we could not study these effects. In case of unintended drug-drug interactions with gastrointestinal prophylaxis, drug safety alerts were shown to the prescriber. Another limitation is that we did not include other risk factors than medication use and increased age, that were mentioned in the guideline. These risk factors, such as a diagnosis of peptic ulcer in the past, are not documented in the hospital information system in such a way that we could use them in the clinical decision support system or in the analyses of this study. We analyzed differences in categorical variables using the Pearson's Chi-square test. This test assumes independence between cases. However, since prescribers will have received multiple drug safety alerts in the study periods and may have taken similar clinical decisions in similar cases, the cases may not be completely independent, overestimating the statistical significance. For outpatient visits, it is possible that not all

home medications were registered as such in Epic and medication surveillance was incomplete.

To conclude, the implementation of our clinical decision support system for gastrointestinal prophylaxis resulted in an improved adherence to the guideline. This was most likely due to a reduction in the total number of drug safety alerts and an increase in the quality of these alerts.

Author contributions

All authors contributed substantially to the study design, data gathering, data analyses and writing of the manuscript. All authors agreed on the final manuscript.

Competing interests

None of the authors has any conflict of interests. No sources of funding were received for performing this study.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ijmedinf.2016.10.002.

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