Clinical rules in hospital pharmacy practice to prevent adverse drug events

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Part III

Clinical validity

4

A computerized adverse drug event alerting system using clinical rules: A retrospective and prospective comparison with conventional medication surveillance in The Netherlands

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Abstract

Background: Adverse drug events (ADEs) are an important problem in hospital practice. Computerized physician order entry (CPOE) and clinical decision support systems (CDSS) are useful tools in the prevention of ADEs. In The Netherlands there are some basic CDSS within CPOE systems, but there is not much experience with sophisticated systems. We have recently developed a more advanced CDSS, a computerized adverse drug event alerting system (ADEAS).

Objective: The aim of the study was to compare the newly developed ADEAS, which uses a set of clinical rules, with the conventional medication surveillance, a basic CDSS within a CPOE, to assess its additional value in detecting patients with a potential ADE.

Setting: Leiden University Medical Center (LUMC), a university hospital in Leiden, The Netherlands.

Design: Two studies were carried out; one retrospective and one prospective. The retrospective comparison of ADEAS with conventional medication surveillance was conducted on all patients admitted to the hospital (except intensive care unit patients) during a 1-month period (15 November – 15 December 2006). A prospective comparison of both systems was performed during a 6-month period (May – October 2007) on one general internal medicine ward.

Measurements: The endpoint was the total number of alerts and content of alerts generated by both methods. In the prospective study we also focused on the number of unique alerts and interventions by the hospital pharmacist following the alerts.

Results: In the retrospective study, ADEAS generated 2010 alerts compared with 2322 generated by the conventional method. In the prospective study, 248 and 177 alerts were generated by ADEAS and the conventional method, respectively. The number of unique alerts was 85 (of which 72 were considered true positive alerts) and 136, respectively. The hospital pharmacist made 14 (19.4%) interventions following a true positive alert with ADEAS and 5 (3.7%) with the conventional method. The contents of alerts generated by ADEAS were different to the safety alerts generated by conventional medication surveillance. The conventional medication surveillance generated safety alerts regarding drug–drug interactions and drug-overdosing. ADEAS generated alerts regarding declined renal function or other laboratory abnormalities and absence of essential concurrent medication.

Conclusions: Compared with our conventional medication surveillance, the computerized alert system ADEAS selected different patients at risk of an ADE. This makes ADEAS in our hospital of additional value to the hospital pharmacist as a suitable tool in reducing the number of preventable ADEs.

Background

A substantial number of hospitalized patients experience harm due to medication. Different studies report that adverse drug events (ADEs) occur at a wide range of rates (0.17–65%) in hospitalized patients, and that approximately 50% are considered preventable [1]. In the literature, it is suggested that computerized physician order entry (CPOE) and clinical decision support systems (CDSS) can be important tools to facilitate the prevention of ADEs [2,3]. CPOE ensures complete, legible, standardized and clear orders, and CDSS are built into almost all CPOE systems to varying degrees. They can provide computerized advice, basic alerts regarding drug–drug interaction or more sophisticated alerts regarding drug-laboratory value checks. As far back as 1991, Classen et al. [4] described the development of a computerized system using algorithms or clinical rules to detect and characterize ADEs in hospital patients. In addition, Jha et al. [5] described that computer-based monitoring is an efficient way to identify ADEs compared with traditional detection methods. Later, such computerized alert systems were also used to prevent ADEs. Raschke et al. [6] developed a computer alert system to correct errors that might lead to ADEs and detect ADEs before maximum injury occurs. Also, Silverman et al. [7] used a computer-based system to prevent ADEs with clinical rules. They modified the rules used by Jha et al. [5] to include rules that identify actionable events and exclude rules that identify an ADE after it occurs (e.g. the ordering of an antidote) [7]. Meanwhile, different studies have shown that such CDSS within CPOE are successful strategies for reducing ADEs and medication errors [8-12].

In our hospital, the CPOE system in use provides online drug–drug interaction checks and drug-overdosing checks, but is not integrated with a sophisticated CDSS [13]. This current surveillance system has some limitations: 1) there is no possibility to adapt medication surveillance to categories of patients and/or to medical specialties; [14] 2) the system does not take into account relevant laboratory values; and 3) most alerts are of low clinical relevance, with the consequence of 'alert fatigue' [15]. Moreover, a recent Dutch study showed that implementation of such a CPOE with basic CDSS does reduce certain types of medication errors but not therapeutic errors and preventable ADEs [16]. Given these limitations, we decided to develop a new pharmacy decision support system that could improve the quality of our medication surveillance. The new system should both improve the specificity of the alerts compared with the current system and cover the lacking alerts, e.g. regarding declined renal function. As a result we have developed a computerized adverse drug event alerting system (ADEAS) with which patients at risk of an ADE can be detected electronically by combining more data available from the hospital information system and CPOE, using clinical rules [17]. We have already demonstrated that both the CPOE with

basic CDSS and clinical rules are useful early strategies for preventing medication-related harm [18].

In this study we report the results of a retrospective and prospective study in which the new ADEAS (a CDSS that uses a set of clinical rules) was compared with our conventional medication surveillance system (a basic CDSS within the CPOE) in order to assess its additional value in detecting patients with a potential ADE.

Methods

Setting

The two studies were performed in Leiden University Medical Center, a university hospital in Leiden, The Netherlands. Our hospital information system, Mirador® (iSOFT Nederland BV, Leiden, The Netherlands), includes integrated patient-specific data with demographics, laboratory results, discharge letters, medical diagnosis code, surgery reports, radiology reports and pharmacy orders. The existing CPOE system, Medicatie/EVS® (Medicator®; iSOFT Nederland BV), is incorporated within the hospital information system and is described in detail elsewhere [13]. Briefly, it provides online drug–drug interaction checks and drug-overdosing checks, but is not integrated with a sophisticated CDSS. The drug information on which the safety alerts are based is retrieved from a national drug information database, the 'G-standard' (Z-Index BV, The Hague, The Netherlands). The G-standard contains information about drugs available in The Netherlands, and the majority of Dutch pharmacy information systems use this database to support medication surveillance, prescribing, dispensing and logistics. Not all the features available in the G-standard are used within our CPOE with basic CDSS; only drug–drug interaction alerts and drug-overdosing alerts are generated.

Conventional medication surveillance method

The current procedure of our conventional medication surveillance is that hospital pharmacists perform daily retrospective checks of the drug–drug interaction and drug-overdosing alerts overridden by the physician. As described in the previous section, these are standard safety alerts from the national Dutch database (the G-standard) and are not fine-tuned to the local situation. In practice, most of the safety alerts are ignored by the physician while prescribing medication in the CPOE. All the ignored and overridden alerts

are collected in a Microsoft Access® database and the hospital pharmacist reviews these alerts the following day (except for the weekend, when the alerts are seen on Monday). If necessary, the hospital pharmacist checks laboratory values or co-medication, and selects potentially clinically relevant alerts to discuss with the prescribing physician.

New method: Adverse Drug Event Alerting System (ADEAS)

The new computerized alert system ADEAS uses clinical rules that describe potentially harmful drug-related situations based upon data from the hospital information system. The development of this expert system and the first set of clinical rules is described in detail elsewhere [17]. Briefly, ADEAS was composed in Gaston (Medecs BV, Eindhoven, The Netherlands), a guideline-based decision support framework consisting of both a guideline development module and a decision-support module. Selection of the potential patients at risk of an ADE occurs by combining data from the electronic patient file (EPF) [laboratory data, patient characteristics], the CPOE (prescribed medication) and the G-standard (drug data and drug–drug interaction data), using predefined algorithms, the so-called clinical rules. The guideline development module in Gaston is used to create and support the clinical rules. The decision support module is used to link Gaston with our hospital information system for the required information and to execute the clinical rules. The clinical rules were formulated in a multidisciplinary team using seven drug-related risk categories [17].

ADEAS processes the day's data throughout each night, determining potential patients at risk, and generates its output in the Pharmacy Department every morning. During both studies, approximately 121 clinical rules were used by the system [17].

Study design

Retrospective study

The retrospective study was performed during a 1-month period (15 November – 15 December 2006), in which ADEAS was compared with the conventional medication surveillance. For this study, all patients admitted to the hospital during this period, except intensive care unit (ICU) patients (because ICU uses a different EPF and CPOE), were included. During the study period the conventional medication surveillance method was performed daily as usual, as described above. ADEAS was also activated during the study period and the generated alerts were collected retrospectively at the end of the study. Consequently, no actions were taken following the alerts generated by ADEAS.

Prospective study

The prospective comparison between the two systems was performed during a 6-month period (May – October 2007). For this study, all patients admitted to one general internal medicine ward were included. Again, during the study period the conventional medication surveillance method was performed daily as usual, as described above. ADEAS was also activated during the study period, and everyday a hospital pharmacist evaluated the list of alerts generated by ADEAS to determine if the alert selected a potential clinically relevant situation that needed discussion with the prescribing physician (except for the weekend when the alerts were seen on Monday). Following alerts from both ADEAS and the conventional medications surveillance, the hospital pharmacist visited the ward or participated in the ward round to consult with the physician regarding the alert and, if necessary, gave additional advice.

Measurements

Retrospective study

The endpoints were the total number of alerts and the content of the alerts generated by the two systems.

Each day the total number of alerts, the number of patients with alerts and number of interventions by the hospital pharmacist were collected, as generated by the conventional medication surveillance method. At the end of the study period the daily total number of alerts and number of patients with alerts were collected, as generated by ADEAS.

The total number of alerts included duplicate alerts. Duplicate alerts can occur in the conventional medication surveillance; for example, when a physician prescribed then stopped and subsequently prescribed the same medication order again in a different dosage or different route, the accompanying alert is shown with each prescription. Duplicate alerts can also occur in ADEAS; for example, some clinical rules are built in a way that when the potential ADE situation continues to exist, an alert is generated every day.

Furthermore, we compared the content of the alerts (the detected potentially harmful situation regarding the patient) generated by the two systems. For ADEAS we selected the top five most frequently triggered clinical rules and determined if they were triggered by the conventional system as well.

Prospective study

The endpoints were the total number of alerts, the number of unique alerts, the content of the alerts generated by the two systems, the number of interventions by the hospital pharmacist and the number of accepted interventions.

Each day, the total number of alerts, the number of unique alerts, number of patients with alerts and number of interventions by the hospital pharmacist were collected, as generated by the two systems. Follow-up was checked for each intervention to measure the number of interventions accepted by the physician.

We determined if an alert in ADEAS was a true positive alert, i.e. a real potential ADE. Alerts in ADEAS can be false positive alerts because, for example, the rule is not specific enough (using classes of drugs instead of individual drugs). Another scenario is that drugs are prescribed by the physician as a free-text field order and not selected from the database within the CPOE. ADEAS cannot read free-text field items and can, in this way, miss prescribed drugs. Alternatively, a patient's disease, e.g. epilepsy, is identified via their specific medication for that disease, in this case antiepileptic drugs; however, in some cases the patients use the drugs for a different indication, e.g. neuropathic pain.

By reviewing the EPF of the patients, the hospital pharmacist determined if the alert was true positive or false positive. The percentage of interventions was calculated compared with the number of true positive alerts. The overall positive predictive value (PPV) for ADEAS was calculated by the quotient of the number of true positive alerts and the number of unique alerts.

Within ADEAS, for each separate clinical rule with a true positive alert we calculated the PPV for potential ADE and for intervention. The PPV per rule for potential ADE was calculated by the quotient of the number of patients with an alert considered an actual ADE and the total number of patients with an alert for that rule. The PPV per rule for intervention was calculated by the quotient of the number of interventions and the total number of patients with a true positive alert for that rule.

Results

Retrospective study

During the 31 days of the study period the mean number of patients present in the hospital was 352 per day (exclusive of ICU patients) [SD 49.1]. The conventional medication

monitoring system generated a total number of 2322 signals; on average 74.9 signals per day (SD 34.8). Results are presented in Table 4.1. Of the 2322 signals, 350 alerts resulted in an action by the pharmacist. Laboratory values of the patient were checked 255 times (mean 8.2 per day [SD 5.3]), but further intervention was not considered necessary, and 95 times (mean 3.1 per day [SD 3.6]) the pharmacist consulted the physician or nurse to propose an intervention. All the alerts generated by the conventional method were drug–drug interaction alerts and drug-overdosing alerts.

ADEAS generated a total of 2010 signals in the same period and in the same patient population; on average 64.8 signals per day (SD 22.3) [Table 4.1]. Of the 121 active rules, 53 different clinical rules were triggered at least once. The top five rules that were triggered most frequently are shown in Table 4.2. Of all these patients with potential harmful situations only some patients triggered by rule number 2 were also detected by the conventional method while the rest were not. The conventional system generated an alert in, for example, patients with the combination of an NSAID and an SSRI or corticosteroid. However, it generated this alert in all patients regardless of their age or concurrent medication, such as the use of pantoprazole. The alerts generated by ADEAS were related to laboratory value abnormalities, such as a declined renal function and concurrent use of drugs eliminated by the kidney, the absence of essential medication protecting the patient for an adverse drug reaction and other potentially harmful situations, e.g. a patient with a gastrointestinal tube. The data collection of the results with ADEAS was done retrospectively, therefore no interventions were made.

Prospective study

During the 6-month study period, measurements were performed on 139 consecutive days. The mean number of patients present at the general internal medicine ward was 5.6 per day (SD 3.1). Results are presented in Table 4.3.

Table 4.1 Results of the retrospective comparison of the Adverse Drug Event Alerting System (ADEAS) and conventional medication surveillance (CMS), hospital wide, during a 1-month period

Parameter	CMS	ADEAS
Total numbers of alerts	2322	2010
Average number of alerts per day (SD)	74.9 (34.8)	64.8 (22.3)
Average number of patients with an alert per day (SD)	41.4 (16.7)	54.6 (13.7)
Number of interventions	95	NA

NA, not applicable; SD, standard deviation.

Table 4.2 Retrospective study result of the Adverse Drug Event Alerting System (ADEAS); 'top five' most frequently triggered clinical rules during a 1-month study period

	Clinical rule	Total no. alerts	Total no. patients
1	Opioid receptor agonist prescribed more than 2 days ago, and no laxative added to the therapy to alleviate constipation	250	220
2	Patient > 70 years of age prescribed a NSAID (not COX-2 selective) and has no ulcer protection, or patient > 60 years of age prescribed NSAID (not COX-2 selective) with an additional risk factor for ulcer and has no PPI.	244	53
3	Patient with oral iron medication and addition prescription of a laxative for possible treatment of the adverse event constipation	198	26
4	Patient with a prescription for an oral drug given via the gastrointestinal tube	170	19
5	Patient with a creatinine clearance of less than 50 mL/min or a serum creatinine value > 150 µmol/L	137	56

COX, cyclooxygenase; PPI, proton pump inhibitor.

Table 4.3 Results of the prospective comparison of the Adverse Drug Event Alerting System (ADEAS) and conventional medication surveillance (CMS) on one general internal medicine ward during a 6-month period

Alerts and interventions	CMS	ADEAS
Total number of alerts	177	248
Number of unique alerts	136	85
Number of true positive alerts	136	72
Total number of patients with alert	57	48
Average number of alerts per day (SD)	1.3 (1.8)	1.8 (2.2)
Average number of patients with an alert per day (SD)	0.8 (0.9)	1.0 (1.1)
Number of interventions (%)	5 (3.7)	14 (19.4)
Number of interventions accepted by physician (%)	3 (60)	10 (71)

The total number of alerts with the conventional method was 177 and the number of unique alerts was 136. All 136 were true positive alerts. In five situations (3.7%) the pharmacist consulted the physician to propose an intervention, twice regarding a drug–drug interaction (lithium + diuretic and methadone + erythromycin) and three times concerning the dosages of a drug (possible incorrect dose of nitrofurantoin, cefuroxime and nadroparin regardless of renal function). Three times the proposed intervention was accepted by the physician.

Table 4.4 Prospective study result of the Adverse Drug Event Alerting System (ADEAS): the 20 different clinical rules responsible for the 72 true positive alerts

Clinical rule	No. patients with alert (A)	No. patients with real potential ADE [true positive] (B)	No. interventions (C)	PPV for real potential ADE [true positive] (B/A)	PPV for intervention (C/B)
Patient with CL_{CR} < 50 mL/min or plasma creatinine > 150 µmol/L	12	12	0[a]	1.00	0.00
Patient with therapeutic drug monitoring result of aminoglycoside or vancomycine therapy	8	8	2	1.00	0.25
Opioid receptor agonist prescribed more than 2 days ago, and no laxative added to the therapy to alleviate constipation	8	8	0[b]	1.00	0.00
Patient with plasma creatinine rise > 50% or > 50 µmol/L	10	7	1	0.70	0.14
Patient with low molecular weight heparin and CL_{CR} < 25 mL/min	4	3	1	0.75	0.33
Patient > 70 years of age prescribed a NSAID (not COX-2 selective) and has no ulcer protection, or patient > 60 years of age prescribed NSAID (not COX-2 selective) with an additional risk factor for ulcer and has no PPI	3	3	2	1.00	0.67
Patient (> 70 years) with digoxin (> 0.125 mg/day) or patient (> 70 years) with digoxin and CL_{CR} < 50 mL/min or creatinine rise > 50% or > 50 µmol/L	3	2	2	0.67	1.00
Patient with ciprofloxacin or norfloxacin and antiepileptic agents	2	2	0	1.00	0.00
Patient with biphosphonate and drug affecting absorption (iron, calcium, antacid)	3	2	0	0.67	0.00
Patient with iron (oral) and penicillamine, methyldopa, antacid or levodopa	1	1	0	1.00	0.00

Patient with cefuroxim and CL_{CR} < 50 mL/min.	3	1	1	0.33	1.00
Patient with ceftazidim and CL_{CR} < 100 mL/min.	4	1	1	0.25	1.00
Patient with ciprofloxacin and CL_{CR} < 25 mL/min	2	1	0	0.50	0.00
Patient with cotrimoxazole or dapson and no folic acid	2	1	1	0.50	1.00
Patient with ranitidine and CL_{CR} < 50 mL/min	1	1	0	1.00	0.00
Patient with acrivastine, levocetirizine or cetirizine and CL_{CR} < 10 mL/min	1	1	1	1.00	1.00
Patient with sulfonylurea agent and CL_{CR} < 10 mL/min or ALAT > 135 U/L or ASAT > 135 U/L	1	1	1	1.00	1.00
Patient with antipsychotic drug or antidepressant drug and ALAT > 135 U/L and ASAT > 135 U/L or bilirubine > 40 µmol/L	2	1	0	0.50	0.00
Patient receiving azathioprine[c]	1	1	0	1.00	0.00
Patient with gabapentin or pregabalin and CL_{CR} < 50 mL/min	1	1	1	1.00	1.00

a) Screening risk medication; if present and wrong dosages, then intervention
b) Mostly postsurgical "methadone if necessary"
c) Dosage check recommended by Dutch inspectorate authority; maximum daily dose 5 mg/kg.
ADE, adverse drug event; CL_{CR}, creatinine clearance; COX, cyclooxygenase; PPI, proton pump inhibitor; PPV, positive predictive value.

In the same period and in the same patient population, the total number of alerts generated by ADEAS was 248. The number of unique alerts was 85, of which 72 were considered true positive alerts, i.e. alerts regarding a real potential ADE. In 14 situations (19.4%) the pharmacist consulted the physician and gave additional advice. Ten times the intervention was accepted by the physician. The overall PPV for ADEAS was 0.85 (72/85).

Twenty different clinical rules were responsible for the 72 true positive alerts (Table 4.4). 'Creatinine clearance < 50 mL/min or plasma creatinine > 150 mmol/L' was the rule with the highest number of alerts (12 patients). For the 20 different clinical rules, the PPV for actual potential ADE varied between 0.25 and 1.00 (Table 4.4). The PPV for intervention varied between 0.00 and 1.00 (Table 4.4). For example, the rule regarding a declined renal function with the highest number of alerts never led to an intervention by the pharmacist. The pharmacist did screen the medication for dosage errors but none were found. Still, this rule detects a potential harmful situation, and was therefore considered a true positive alert with a high PPV for an actual potential ADE, but consequently a low PPV for intervention.

Discussion

With ADEAS, different kinds of patients at risk for an ADE were detected compared with the conventional medication surveillance. The number of alerts with ADEAS was lower than with the conventional surveillance method (both total number of alerts in the retrospective study and unique number of alerts in the prospective study), but the percentage of interventions by the hospital pharmacist with ADEAS was higher.

Safety alerts generated by the conventional medication surveillance in our CPOE consist of drug–drug interaction signals and drug-overdosing signals. As mentioned, these safety alerts are retrieved from the G-standard, a national database. They are not fine-tuned to the local situation or specialized to individual patients or medical specialties. ADEAS was developed to overcome these limitations so we could detect more, and in a more sensitive way, patients at risk of an ADE. The strength of ADEAS is that it uses more sources of information from the integrated databases available in the EPF, such as laboratory data, patient age and concurrent medication, to search for potentially harmful situations. Consequently, the alerts generated by ADEAS were related to laboratory value abnormalities, such as declined renal function, the absence of essential medication to protect the patient for an ADE, and the use of a gastrointestinal tube. In this way, ADEAS has, in our hospital, an additional value in detecting patients at risk of a potential ADE compared with conventional medication surveillance.

Our study shows that, in particular, clinical rules related to unadjusted drug dosages in patients with declined renal function are important triggers for potential ADEs, which is in line with the findings of other investigators [19-23]. The additional value of the new ADEAS system is also illustrated by the rule 'opioid receptor agonist and no prescription for laxative'. This rule gave a high number of alerts, both in the retrospective and prospective studies, whereas it did not generate alerts when using the conventional medication surveillance method.

Moreover, the added value of the new ADEAS system is also illustrated by a clinical rule regarding the prescription of an NSAID in a patient with a risk factor for ulcer-related bleeding and without a prescription for a proton pump inhibitor. The conventional system does generate an alert in, for example, a patient with the combination of an NSAID and an SSRI or corticosteroid. However, it gives an alert in all patients regardless of their age or concurrent medication, such as the use of pantoprazole. In the latter situation, the conventional system generates a false positive alert, which may lead to alert fatigue by the physician [15,24]. The system cannot 'read' the age of the patient or the concurrent medication, like ADEAS can. ADEAS only generates an alert when a proton pump inhibitor was absent and the patient was older than 70 years of age or older than 60 years of age with an additional risk factor.

Beside the content of the alerts, the number of alerts was also an endpoint in both studies. The total number of alerts included duplicate alerts. In an ideal system, duplicate signals are switched off or hidden when seen by the physician or pharmacist. Unfortunately, both our conventional system and the new ADEAS still show duplicate alerts. That is why we choose to compare the total number of alerts in the retrospective study. Although it gives less information, it is a reflection of our current practice. A limitation of ADEAS was that it generated more duplicate alerts than the conventional method. ADEAS has to become smarter in the future. In the prospective study we also focused on the number of unique alerts, which give more information about the capability of the system. Comparing the number of alerts between the prospective and retrospective studies is not desirable because the two studies are conducted on a different patient population. An official comparison of the two systems by means of PPV is not possible because the conventional system is a system designed to detect drug–drug interactions and drug-overdosing. It is not designed to be an ADE prediction system, as the new ADEAS is. This means we cannot calculate a PPV for the conventional method.

A limitation of the prospective study is that it was conducted on a small internal medicine ward. This also has consequences for the number of interventions and the proportion of accepted pharmacist interventions by the physician. They were higher with ADEAS than

with the conventional medication surveillance, but the absolute numbers were small (14 interventions, of which 10 were accepted, vs. 5 interventions, of which 3 were accepted).

Another limitation of our study is that we compared only two particular systems, and the systems are only used by a few hospitals in The Netherlands. This makes the generalizability of our results poor; however, as with most CPOE and CDSS, different commercial and locally designed applications are used worldwide. Comparability and generalizability of these investigations is usually poor, but the methods used in the different studies can be of help for other investigators.

Only a relatively small number of the clinical rules active in the system ADEAS resulted in alerts and the PPV for some rules was low. For example, the rule regarding a declined renal function with the highest number of alerts never led to an intervention by the pharmacist. The pharmacist did screen the medication for dosages errors but none were found. More specific rules, with a combination of a specific drug prescription and a declined renal function, had higher PPVs for intervention. Our set of clinical rules needs adaptation and modification in order to enlarge the amount of positive alerts. Adapting the content of the rules during use is an acceptable way to enlarge the PPV for the clinical rules [7]. In this way, with smarter clinical rules, the added value of ADEAS in detecting patients at risk can be greater. The overall PPV for ADEAS was good (0.85), but can be better. In the future we should investigate the possibility of combining the features of ADEAS with the G-standard and the conventional surveillance method to create a more sophisticated alerting system. Overall, ADEAS can be seen as a first step towards more advanced clinical decision support. The importance of preventing ADEs by using these types of alerts and computerized systems, such as ADEAS, is also stressed by others [6,25-28].

We believe that interaction between pharmacists and physicians will be increasingly appreciated when pharmacist interventions focus on specific patients at risk of developing ADEs. Studies have shown that participation of clinical pharmacists with the healthcare team on patient rounds indeed results in improved care [29]. ADEAS may be useful to create a more individualized patient-oriented pharmacy service on the hospital ward. By selecting at risk patients, and making goal-oriented visits to the ward, the pharmacist can be more time-efficient than by participating on ward rounds.

Conclusions

Compared with our conventional medication surveillance, the computerized alert system ADEAS selected different patients at risk of an ADE. This makes ADEAS in our hospital of added value to the hospital pharmacist as a suitable tool in reducing the number of preventable ADEs.

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