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Doing the right things and doing things right: inpatient drug surveillance assisted by clinical decision support

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ABSTRACT

Increased budget constraints and a continuous focus on improved quality require an efficient inpatient drug surveillance process. We describe a hospital-wide drug surveillance strategy consisting of a multidisciplinary evaluation of drug surveillance activities and using clinical decision support to augment drug surveillance practices. Key characteristics of the decision support system are the integration of the Dutch national knowledge base (G-Standard), the ability to monitor the effects of drug therapy over time and prevent irrelevant alerting by adding essential patient data to the conventional medication safety checking algorithm. Integration of existing national medication safety knowledge bases into decision support systems assures the availability of up-to-date information, minimises maintenance and prevents irrelevant alerts. Developing decision algorithms based on the desired intervention decreases the burden of validation and maintenance, as duplication of multiple similar decision algorithms is prevented.

INTRODUCTION

In the Netherlands, almost €94 billion euros are spent on healthcare.[1] In 2013, >26% (€24.8 billion) was spent on hospital care. This is by far the largest healthcare expense.[1]

Since 2000, the volume of hospital care has grown substantially: hospital and day admissions have increased by an average of 3% and 10% annually, respectively.[1] Increased volume and cost of hospital-care delivery have resulted in almost a doubling of hospital-care expenditure over the past decade. Providing cost-conscious (accountable) care has been an important focus of the past decade: provide the best possible patient care and reduce unnecessary costs to the healthcare system in general[2 3] and more specifically in medication use.[4 5]

In addition to cost, there is increasing concern about quality and safety issues of inpatient medication use in terms of appropriateness and error potential. As an example, almost one-third of elderly patients admitted to the hospital receive at least one medication considered inappropriate in this population.[6 7] Furthermore, medication errors are the most common type of medical errors reported in hospitals.[8] In the Netherlands, a medical record study in 2004 showed that 5.6% of patients were unintentionally harmed during their hospital visit, of which 2.3% was potentially avoidable.[9] Medication use was associated with 21% of unintentional harm, of which a further 31% was avoidable. Based on 1.3 million hospital admissions in 2004, a total of 4740 patients would have experienced a preventable medication error resulting in harm.

Meta-analyses of medication error incidences show that prescribing errors and administration errors are the most commonly reported medication errors in hospitals worldwide.[10–12] Reports on prescribing errors vary between 7% and 60% of medication orders, 2% of patient days and 50% of hospital admissions.[12–14]

In light of these increasing budget constraints and quality of care issues, optimising inpatient medication use becomes even more important. In this case study, we introduce the concept of adding clinical decision support to standard medication safety checking. Furthermore, we describe the promising effects on alert reduction and efficiency of this approach in our institution.

Electronic prescribing and decision support: key intervention to prevent medication errors

The US Institute of Medicine reports "To Err is human: Building a Safer Health System (1999)" and "Preventing Medication Errors (2006)" resulted in a focus on preventing these errors in the USA and abroad.[8 15] Both reports conclude that errors were often the result of poorly designed systems and that healthcare facilities should rely more on information technologies to make the system less error prone. The following key interventions for the prevention of medication errors were proposed: prescribing medication orders electronically as opposed to handwritten orders (computerised provider order entry (CPOE)) and improving clinical decision-making through advice, alerts and reminders (clinical decision support systems (CDSS)). A CDSS is defined as "software that is designed to be a direct aid to clinical decision making, in which the characteristics of an individual patient are matched to a computerized clinical knowledge base resulting in patient-specific assessments or recommendations."[16] These systems can be categorised into basic and advanced CDSS.[17] Basic decision support consists of drug–drug interaction (DDI) checking, drug allergy checking, drug dosing checking and duplicate therapy checking. It does not take into account other patient-specific parameters such as age, laboratory values and concomitant medications to guide prescribers to the most appropriate drug

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choice. In the Netherlands, as of 1 January 2014, all prescribers (including prescribers in acute care hospitals) are required to use a CPOE that includes basic decision support 'based on the national standard'.[18] The G-Standard is considered the national standard for medication drug surveillance and is included in almost all CPOE and pharmacy information systems.[19 20] It includes information on dosing, duplicate therapy, contraindications and DDIs and is updated monthly. However, G-Standard does not include additional information (such as concomitant medication, laboratory values and administration times) in the decision algorithm. In addition, medication safety alerts appear when a medication order is initiated or when an existing order is modified, while the deleterious effects of many harmful drug combinations typically occur days or even weeks after first prescribing the medication. This results in frequent and often irrelevant alerts for both prescribers and pharmacists (figure 1).[5] A study performed by van Doormaal *et al* investigating the effect on medication errors after implementing CPOE with basic decision support based on the G-Standard showed a significant reduction in medication errors. However, this study did not show an effect on actual patient harm, indicating that more advanced clinical decision support is needed.[14]

Advanced clinical decision support adds additional medication data and patient-specific data to the decision logic, largely

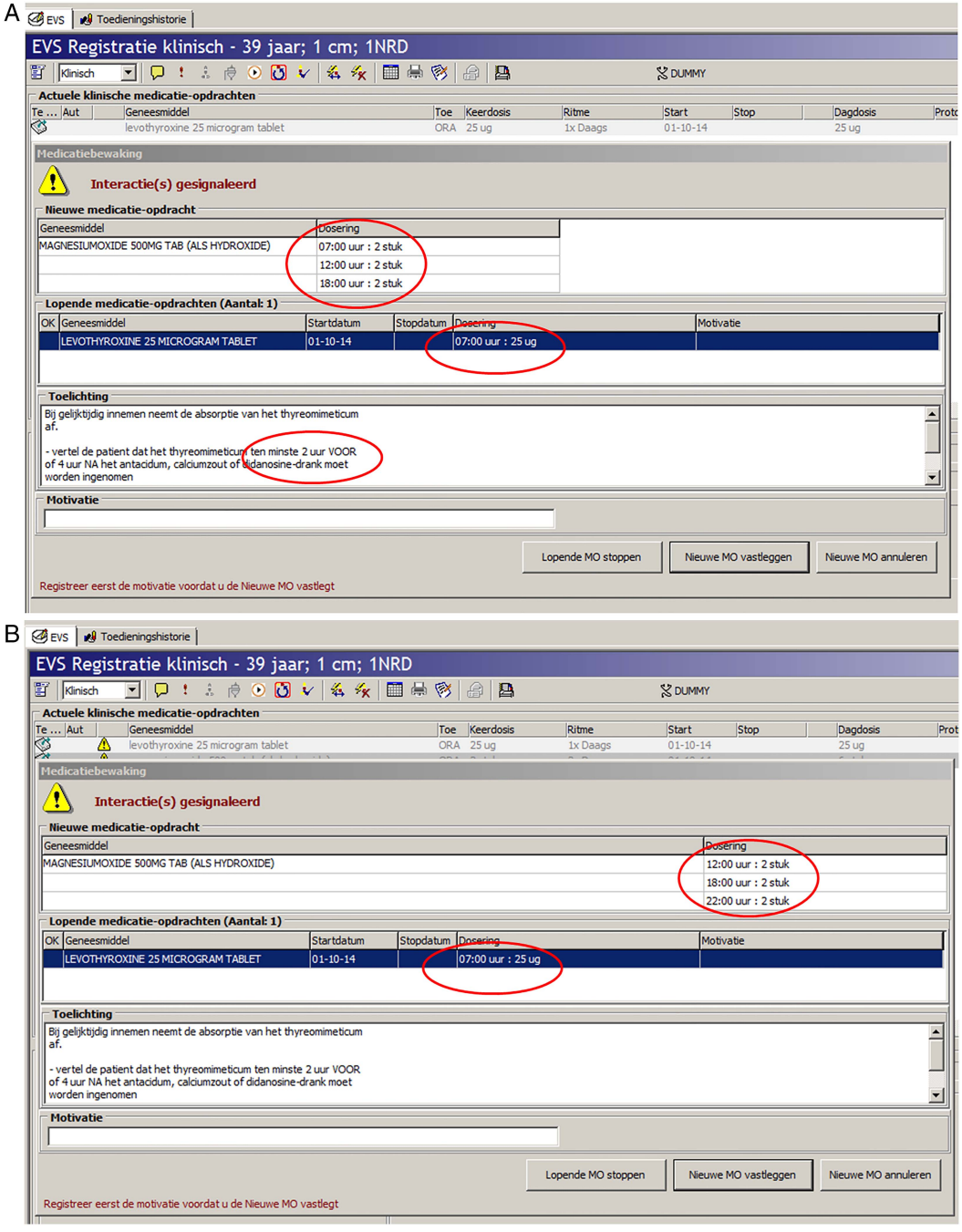

Figure 1 Conventional drug–drug interaction (DDI) alerts between levothyroxine and magnesium oxide. (A) Levothyroxine should be administered at least 2 h prior to or 4 h after magnesium oxide administration. As both drugs are administered at 07:00, this alert is appropriate. (B) After changing the administration time to 12:00, the same alert appears as administration times are not included in the DDI checking algorithm.

Box 1 Barriers to widespread adoption of clinical decision support systems (CDSS)[23]

1. Limited CDSS capabilities of existing computerised provider order entry products
2. Limited usability of systems and CDSS modules
3. Limited access to patient data needed to support a CDSS
4. Limited access to best CDSS knowledge
5. Local management and maintenance of the CDSS knowledge base
6. Lack of standards for data, medication dictionaries, cost calculations, etc.
7. High cost and difficulty of implementation
8. High cost of use and maintenance
9. Difficulty in recognising and objectifying value
10. Perception of increased liability if CDSS recommendations are rejected

decreasing the number of irrelevant alerts. Advanced decision support is currently only implemented in 14% of US[21] and Dutch hospitals.[22]

Barriers to implementation

Already in 2005, Teich *et al*[23] reported on the major barriers to widespread adoption of CDSS (box 1). They can be summarised into three major hurdles: performance issues (barriers 1–3), content issues (barriers 4–6) and return-on-investment issues (barriers 7–9). Performance issues are becoming more and more manageable as most patient data needed for effective drug surveillance are now readily available in most hospitals.[18] Furthermore, commercially available CDSS modules are becoming more user-friendly, allowing clinicians to build decision algorithms without requiring extensive programming experience. However, CDSS modules are typically installed without any validated decision algorithms, which have to be developed and/or validated in each individual institution (also called 'having to reinvent the wheel'). It is not yet possible to import relevant and validated decision algorithms in CDSS, although the current infrastructure in the Netherlands is promising. Already, a single drug surveillance knowledge base (G-Standard) is in place, which is updated monthly. If this knowledge base can be expanded with computer-interpretable decision algorithms (so-called 'clinical rules'), this would greatly decrease the validation and maintenance issues that current users of CDSS experience.

Lastly, early adopters of advanced decision support developed these systems over many years based on site-specific infrastructures (so-called 'home-grown' systems). As a result, most studies showing beneficial effects of advanced CDSS were performed in only four institutions in the USA after years of fine-tuning and testing, limiting the external validity of the results.[24] This makes it difficult for new adopters of commercially available CDSS to create a positive business case.

DOING THE RIGHT THING: ALIGN MEDICATION SAFETY ACTIVITIES WITH PRESCRIBERS

The majority of irrelevant alerts at the time of prescribing are DDI alerts.[25 26] Our approach to optimise inpatient DDI checking at St Jansdal Hospital is described in more detail elsewhere[27] but is summarised here. First, we identified the most frequently occurring DDIs. Although the G-Standard contains hundreds of interacting drug pairs, at St Jansdal Hospital only 29 DDIs accounted for 86% of total DDI alerts. We discussed these DDIs in a multidisciplinary expert panel consisting of a haematologist,

Table 1 Performance of clinical decision support systems (CDSS)-assisted drug–drug interaction checking at St Jansdal Hospital

Decision algorithm based on required intervention	Conventional G-Standard interactions (#)	Additional variables added by the CDSS	Conventional alerts generated*	CDSS-assisted alerts generated*	Alert reduction (%)
Gastric protection addition	6	Concomitant medication (PPI, H2 antagonists) Laboratory values (magnesium)	35	4	89
Hyperkalaemia monitoring	3	Patient demographics (admission date) Laboratory values (potassium)	19	2	89
Hypokalaemia monitoring	3	Patient demographics (admission date) Laboratory values (potassium)	1	0	100
Hyponatraemia monitoring	3	Patient demographics (admission date) Laboratory values (sodium)	2	0	100
Administration time modification	25	Medication characteristic (administration time) Laboratory values (haemoglobin)†	10	4	60
Anticoagulation monitoring, increased INR	13	Medication characteristic (start time) Laboratory values (INR)	30	5	83
Anticoagulation monitoring, decreased INR	7	Medication characteristic (start time) Laboratory values (INR)	11	2	82
		Total	108	17	86

*Number of patients triggering an alert during their hospital stay from 3 October to 10 October 2014.
†Time-dependent interactions with iron products only.
INR, international normalised ratio; PPI, proton pump inhibitors.

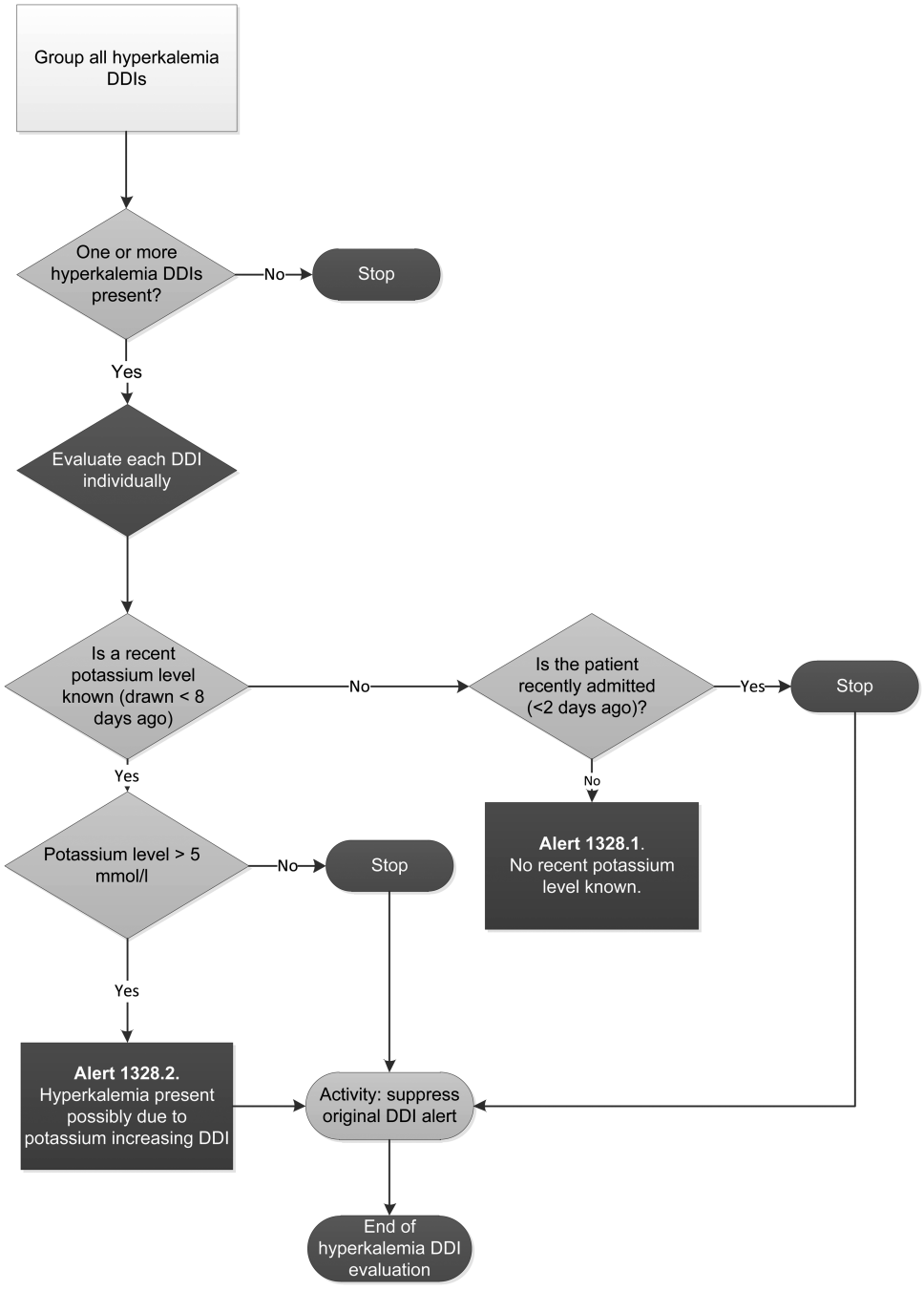

Figure 2 Screenshot of a clinical decision support system (CDSS)-assisted drug–drug interaction (DDI) algorithm. Top rectangle: grouping step, groups DDIs with similar effects. As a result, multiple DDIs can be refined with one clinical rule. Light grey diamond: decision step, only yes and no decisions are allowed. Dark grey diamond and bottom square: start and end of a 'loop': each patient's active medication is evaluated multiple times for each DDI in the group. For example: if two DDIs are present resulting in potential hyperkalaemia, the clinical rule does not stop after evaluating the first DDI, but continues with the second DDI. Dark grey square: refined alert, which is presented to the pharmacist for evaluation. Dark grey 'stop' oval: guideline remark to highlight the end of a decision step. Light grey oval: 'activity step': suppresses the original alert generated by basic DDI checking. CDSS-assisted DDI checking evaluates all active medication orders three times daily. Consequently, many more alerts will initially be generated compared with conventional DDI checking where only alerts are generated when an order is initiated or revised. Therefore, CDSS-assisted DDI checking is configured to (1) suppress conventional DDI alerts that were evaluated as not relevant during the previous DDI checking episode and (2) to suppress conventional DDI alerts of those DDIs that were refined using the CDSS (the final step of each CDSS-assisted DDI algorithm). As a result, only relevant (refined) alerts (grey squares in the algorithm) are presented to the pharmacist.

nephrologist, geriatrician, cardiologist, rheumatologist, neurologist, paediatrician and a hospital pharmacist. Expert panels are frequently used to address the relevance of computerised prescribing alerts and clinical decision rules.[28 29] We identified the members of our expert panel based on the high prevalence of DDIs in their patient populations and/or increased susceptibility to the deleterious effects of DDIs.

DDIs were categorised into three groups: (1) YES–YES interactions: pop-up alerts were shown to both the prescriber at the moment of prescribing and the pharmacist. This strategy applied

when an interaction should be prevented at the time of prescribing. (2) NO–YES interactions: no alert was presented to the prescriber, but only a yellow exclamation mark indicating a DDI is present was shown on the medication profile. However, pharmacists reviewed and corrected the order if needed. This strategy applied when an interaction should be addressed, but a lag time of a maximum of 24 h was acceptable. (3) NO–NO interactions: only a yellow exclamation mark was shown in the medication profile at the moment of prescribing, but the pharmacist did not review the interaction. These interactions were considered not clinically relevant for the inpatient population. Agreement was reached based on consensus. The result of the expert panel evaluation of the most frequently occurring DDIs is shown in online supplementary table S1.

DOING THINGS RIGHT: MAKE MEDICATION SAFETY PRACTICES BETTER AND MORE EFFICIENT

Causes of irrelevant alerting

Irrelevant medication safety alerts have three main causes. First, the alert is not relevant for the clinical setting. As an example, adding an ACE inhibitor to a patient using a diuretic can cause a sudden drop in blood pressure. The advice is to initiate this therapy carefully and take the first dose at bedtime to prevent dizziness. When therapy with an ACE inhibitor is initiated in a hospital, patients are typically in a bed and under careful monitoring. Second, the alert is irrelevant as a result of flawed or incomplete logic. Figure 1 illustrates this issue as doing the right thing (changing the administration time) still results in an alert as administration time is not included in the logic. Lastly, alerts are generated at the time of prescribing, while potentially harmful effects often occur several days or weeks later. This is predominantly the case for DDIs, drug dosing in renal failure and some duplicate therapy alerts. An example of the latter is a duplicate therapy alert when a vitamin K antagonist is intentionally combined with a low-molecular-weight heparin until an adequate international normalised ratio (INR) is achieved. This typically occurs after several days, resulting in an irrelevant alert at the time of initiating therapy. However, it would be relevant to receive an alert to stop the low-molecular-weight heparin after 5 days when a therapeutic INR is achieved.

CDSS-assisted drug surveillance

The Departments of Pharmacy of St Jansdal Hospital in Harderwijk and the University Medical Center Groningen in the Netherlands use the CDSS Gaston (Medecs BV, Eindhoven, the Netherlands) for drug surveillance efforts. Out of the box, the CDSS includes the conventional G-Standard DDI and the G-Standard drug use in renal failure knowledge bases, which are updated automatically every month. However, the CDSS also includes patient-specific data such as laboratory data, concomitant medication, medication order details (such as administration times) and patient demographics. All clinically admitted patients are monitored by the CDSS, except patients admitted to the intensive care unit (ICU) as the ICU uses a separate electronic medical record. The CDSS consists of three modules: (1) a guideline editor that allows clinicians to create decision algorithms and displays them as flowcharts; (2) a rules engine that matches all active medication orders of all non-ICU inpatients three times daily to the

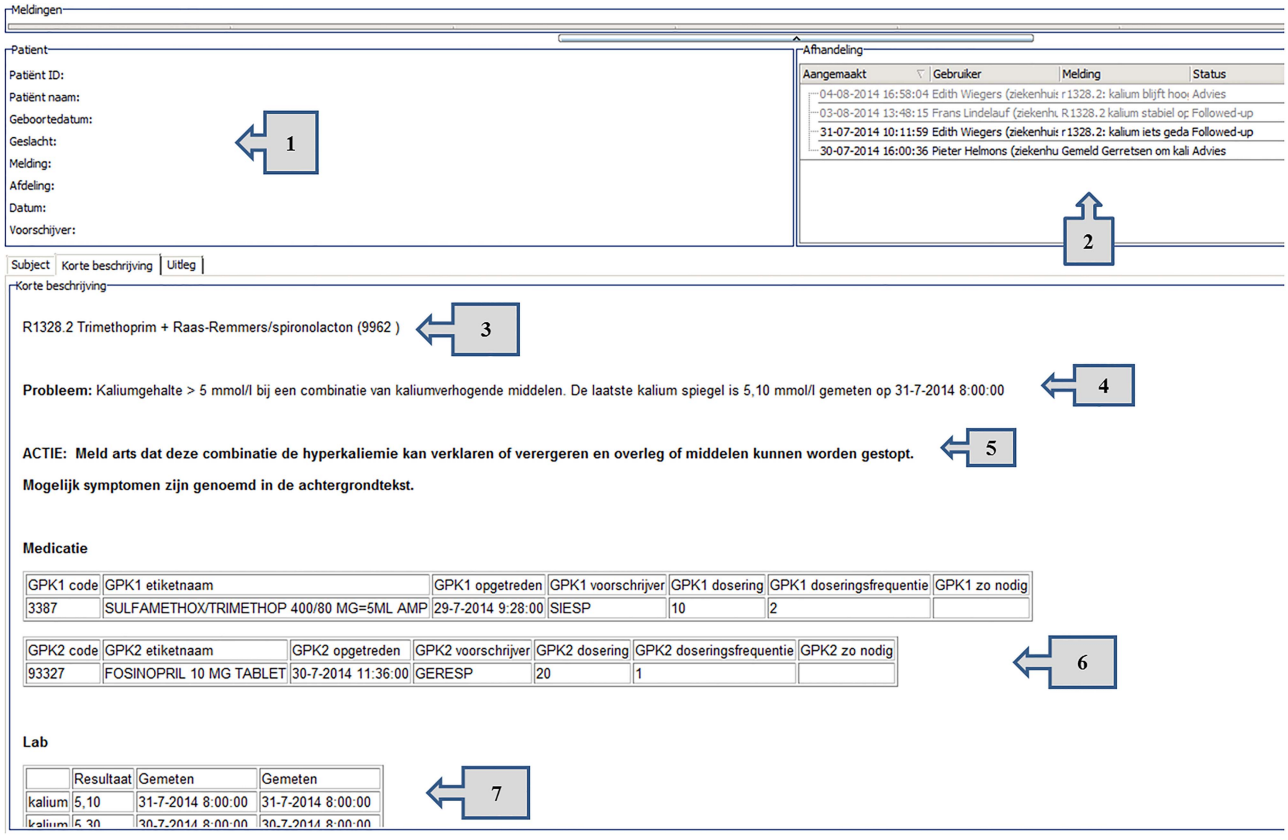

Figure 3 Alert resulting from clinical decision support systems-assisted drug–drug interaction (DDI) checking (Dutch). (1) Patient characteristics (not shown for privacy reasons). (2) Audit trail of prior interventions by other clinical pharmacists. (3) Conventional DDI triggering the alert. (4) Description of the issue at hand, including the most recent laboratory value. (5) Desired action by the clinical pharmacist. (6) Relevant medication data triggering the alert. (7) Relevant historical laboratory values.

additional variables in the hospital database for potentially harmful combinations and (3) an alert management module that allows the end user to manage the alert and record potential interventions or remarks. The CDSS therefore monitors the patient over time and alerts clinicians proactively.

Development of decision algorithms (so-called 'clinical rules')

We developed decision algorithms based on the following characteristics: they should be based on the G-Standard where possible to prevent 'reinventing the wheel'; to facilitate maintenance, they should be thoroughly validated, and most importantly, decision algorithms should be based on the required intervention to prevent duplication of similar algorithms. Table 1 shows some of the decision algorithms currently in production and illustrates the importance of the latter characteristic. Irrelevant alerts of 60 frequently occurring DDIs can be prevented by only 9 clinical rules: 1 gastric protection rule (6 DDIs), 1 hyperkalaemia rule (3 DDIs), 1 hypokalaemia rule (3 DDIs), 1 hyponatraemia rule (3 DDIs), 3 absorption rules (25 DDIs) and 2 anticoagulation rules (20 DDIs). Examples of an advanced DDI checking algorithm and resulting alert are shown in figures 2 and 3.

DISCUSSION AND FUTURE DIRECTIONS

CDSS-assisted drug surveillance based on the G-Standard knowledge base optimises current medication checking practices. We have applied a similar approach as the DDI checking example described here to other modules in the G-Standard such as renal dosing and general drug-dose checking. For example, the G-Standard contains hundreds of drugs with renal failure as a contraindication. However, in our institution only 29 drugs account for almost 92% of conventional renal failure alerts. The G-Standard contains specific dosing recommendations for only 15 of these drugs. Recommendations of other drugs include cautions for side effects and slowly increasing dose, which are frequently not relevant for the clinical setting. Suppressing these 14 drugs without actionable recommendations would decrease the number of conventional renal dose checking alerts by 72%. Irrelevant alerting of the remaining 28% can be minimised if dose and dosing frequency are added to the decision algorithm.

CDSS-assisted drug surveillance also allows for new efficient monitoring possibilities. Electronic medical records store vast amounts of patient data. A CDSS can help in extracting relevant data and transforming them into relevant information for the clinician. As an example, since 1 January 2014 every hospital in the Netherlands is required to have a mandatory antibiotic stewardship programme in place. In our institutions, the CDSS is used to review patients receiving restricted antibiotics, to detect intravenous antibiotics that can be switched to oral administration and to review the efficacy of antibiotic therapy by monitoring duration and C-reactive protein levels.

Lastly, efficiency can be further improved by identifying the appropriate route of alerting. Conventionally, all alerts are shown to the prescriber at the time of order entry and to the pharmacist for review. By identifying those alerts that require immediate action at the time of prescribing, less acute alerts can be restricted to pharmacists. And within pharmacy, further efficiency can be gained if less severe DDI alerts with relatively standard and well-defined actions are handled by pharmacy technicians. At St Jansdal Hospital, technicians log into the CDSS and review the alerts assigned to them. Examples are changing administration times and adding gastric protection only when indicated per approved hospital-wide protocols. This maximises efficiency and greatly adds to the job satisfaction of the pharmacy technician.

Since its inception, many barriers hamper adoption of clinical decision support. The major barrier was the need to rebuild and revalidate the content of decision support systems. This barrier is greatly reduced by including G-Standard content in the CDSS out of the box and assuring automatic updates of new content. Currently, refining the standard medication safety checking algorithms with local clinical content is still required.

The G-Standard already includes advanced decision support logic to refine medication safety checking (so-called 'medical–pharmaceutical decision rules') but implementation is limited. Furthermore, decision algorithms resulting in the same intervention are not grouped into one algorithm. As a result, many (similar) algorithms need to be developed, resulting in high development and maintenance efforts. We are collaborating with the G-Standard to develop a national standard for refined algorithms based on our approach. The goal is to create a general format for advanced medication safety checking algorithms so they can be used by electronic medical record and pharmacy information systems. New adopters of decision support can then rapidly benefit from increased medication safety checking functionality and efficiency.

CONCLUSION

Integration of existing national medication safety knowledge bases into decision support systems assures the availability of up-to-date information, minimises maintenance and prevents irrelevant alerts. In our setting, irrelevant alerts decreased on average by 86% on adding only limited additional data to the standard medication safety checking algorithm. Furthermore, developing decision algorithms based on the desired intervention prevents duplication of similar decision algorithms and decreases the burden of validation and maintenance.

What this paper adds

What is already known on this subject

- Medication safety checking in electronic prescribing systems typically takes place when medication orders are initiated or modified, while the deleterious effects of harmful drug combinations often occur days or weeks later.
- Medication safety checking software in electronic prescribing systems currently does not take into account patient-specific characteristics.
- As a result, current (basic) medication safety checking software results in many irrelevant alerts and questionable effectiveness.

What this study adds

- More than 85% of almost all drug–drug interaction (DDI) alerts and drug use in renal failure alerts are the results of <30 DDIs and renally excreted drugs.
- Irrelevant alerts and increased efficiency can be achieved by adding only a limited patient-specific variables (such as a limited set of laboratory values, administration times and concomitant medications to basic medication safety checking algorithms).
- Maintaining a national knowledge base as the core of augmented medication safety checking software greatly decreased the need for locally building and validating decision algorithms.

Competing interests None declared.

Provenance and peer review Commissioned; externally peer reviewed.

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