Nature and management of duplicate medication alerts

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ABSTRACT

Objective: To investigate the nature of duplicate medication (DM) alerts, their management by community pharmacists, and potential characteristics of DM alerts that lead to interventions by pharmacists.

Methods: Observational study in 53 community pharmacies. Each pharmacist registered the nature and management of 24 DM alerts on a structured form.

Results: On average, the clinical decision support systems generated 20.4 DM alerts per 100 dispensed drugs. In half of the 1272 registered alerts, the pharmacists judged that there was no risk for concurrent use of both prescriptions. In 32% of the alerts, the DM alert was generated for an intentional combination. In 17% of the alerts, there was a risk for unintentional concurrent use. In 32% of the alerts the pharmacists decided that one or more actions were needed: the electronic patient record was updated in 15% of the alerts and in 19% of the alerts the pharmacists performed an external action—for example, informing the patient or modifying the prescription (including 5 therapeutic prescription modifications and 22 logistic prescription modifications). Alerts concerning first dispensing were more likely to be followed by an external action than alerts concerning refills (40% vs 14%, $P < .001$).

Discussion and Conclusion: In community pharmacy, prescription modifications based on DM alerts are rare, but DM alerts lead with some regularity to other actions—for example, patient instruction and update of the electronic patient record. As the current DM alerts are diverse and nonspecific in detecting situations where external action is considered relevant, other ways of alerting should therefore be considered.

Keywords: clinical decision support systems, duplicate medication, medication errors, medical order entry systems, community pharmacy services

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BACKGROUND AND SIGNIFICANCE

Clinical decision support systems (CDSS) generate a continuous flow of drug therapy alerts. In some cases these alerts lead to clinical interventions. In the majority of cases, however, the alert is judged irrelevant for a particular patient.[1–6] When too many alerts are not followed by a clinical intervention and are overridden (apart from the question whether this is appropriate), this contributes to "alert fatigue." A potential consequence is that relevant drug therapy alerts may be overridden mistakenly.[1–3,5,7] Drug–drug interaction alerts have been investigated extensively in this respect.[2,4,8–10] Little is known about most other types of drug therapy alerts.[7] Yet, duplicate medication (DM) alerts contribute substantially to the total number of alerts, so their specificity is of similar relevance as that of drug–drug interaction alerts.[11,12]

DM alerts are intended to detect inappropriate duplication of therapeutic groups or active ingredients (e.g., the unintentional combination of two different NSAIDs (non-steroidal anti-inflammatory drugs), or the concurrent use of a branded drug and a generic version containing the same active ingredient).[13,14]

Studies in several settings have estimated the proportion of relevant DM alerts from a few percent[15] to up to 70%.[12,16] In a Dutch hospital setting, 80% of DM alerts were overridden,[1] and only 4.1% of the DM alerts were rated as clinically relevant.[11] Research on DM alerts in

community pharmacy is lacking. In community pharmacies there might be even more alerts on duplicate medication than in hospitals, because there is increased likeliness that outpatients receive prescriptions from different prescribers, because community pharmacists are not always informed about changes in therapy, and because of the logistic process—for example, early refill of prescriptions because of holidays.

OBJECTIVE

Our objective was to investigate the nature of DM alerts and their management by community pharmacists. Moreover, we aimed to identify characteristics of DM alerts that lead to interventions by pharmacists.

METHODS

Data collection

DM alerts were collected by community pharmacists who were participating in a postmaster training program between March 2013 and March 2014. Each pharmacist was assigned to register a total of 24 DM alerts in daily practice. During four allocated timeslots of 2 h each, spread over the week, the pharmacists analyzed the first six DM alerts that occurred during the dispensing process.

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For each alert, details were registered on a structured, pretested form (online Supplementary Appendix 1). These included data of the patient (date of birth, sex) and of the alert itself: drugs involved, type of prescriber (general practitioner, specialist, or other), handwritten or electronic prescription, first dispensing or refill.

The pharmacists also registered information on the situation underlying the alert generation and its management (retrieval of additional information and performed actions). They had to classify the alerts on three items (online Supplementary Appendix 1):

– Situation underlying the DM alert: in which situation had the alert been generated: no (risk for) concurrent use; intentional concurrent use; (risk for) unintentional concurrent use.
– Retrieval of additional data collection, in which way had the pharmacist retrieved the information needed to decide on whether action should be taken: by consulting the electronic patient record (EPR); contacting the prescriber; contacting the patient; or by a written clarification of the prescriber on the prescription.
– Performed action, which action had been taken by the pharmacist to manage the alert: modification of the prescription; instructing the patient; updating the EPR; or no action at all. All actions except updating the EPR were defined as external actions.

A list with all prescriptions dispensed to the patient in the previous year was printed. Information about the pharmacies and the settings of the CDSS was collected by the pharmacists on a separate form. On this form, the pharmacists also provided information on the number of DM alerts and the total number of processed prescriptions on one day of the DM alert collection.

Typology of DM alert

A DM alert is generated when two prescriptions with the same or comparable active substances are filled with an overlap in the assumed period of use. Its aim is to prevent harm caused by inappropriate DM. All Dutch community pharmacies use CDSS which generate DM alerts. We used the following DM alert categories based on the drugs involved:

– type 1: overlapping prescriptions of the same active ingredient in the same strength per dose unit and in the same dosage form.
– type 2: overlapping prescriptions of the same active ingredient, but in different strength per dose unit and/or in a different dosage form and/or in a combined preparation with another active ingredient.
– type 3: overlapping prescriptions of two different active ingredients belonging to the same pharmacological or therapeutic class.

Data analysis

All data were entered into a Microsoft Access database. The forms were checked on consistency by the primary researcher (M.H.). When there was inconsistency, a third pharmacist (M.B. or A.F.) was consulted. The data were analyzed and descriptive statistics were performed (SPSS version 20.0; SPSS Inc, Chicago, IL, USA). Logistic regression analyses were performed to analyze determinants of external action (age of the patient, sex of the patient, first dispensing, type of prescriber, handwritten, or electronic prescription). A $P < .05$ was considered statistically significant.

Ethics and confidentiality

In order to protect the patient's privacy, all medical data were anonymized by the community pharmacist. The work was conducted in compliance with the requirements of the institutional review board of the Utrecht University Pharmacy Practice Research Network.

RESULTS

Fifty-three Dutch community pharmacists participated in the study. The mean number of generated DM alerts per 100 dispensed drugs was 20.4 (range 4.4–36.7).

Each pharmacist returned 24 DM alert forms. This resulted in a total of 1272 registered alerts. Fourteen alerts were excluded, because of incomplete information on the drugs involved.

The 1258 remaining alerts were categorized based on the type of DM alert (Figure 1). Of the alerts 47% ($n = 593$) were a type 1 alert. These alerts most frequently concerned chronic medications for the cardiovascular system (ATC group C; $n = 162$), the nervous system (ATC group N; $n = 121$), or the alimentary tract (ATC group A; $n = 103$).

Twenty-two percent of the alerts ($n = 270$) were type 2 alerts. Most of these alerts resulted from combinations of medications for the nervous system (ATC group N; $n = 104$), the alimentary tract (ATC group A; $n = 39$), and systemic hormonal preparations (ATC group H; $n = 38$).

Thirty-one percent of the alerts ($n = 395$) were DM alert type 3. Most of these alerts were generated for prescriptions of medicines for the nervous system (ATC group N; $n = 138$) and the blood (ATC group B; $n = 82$).
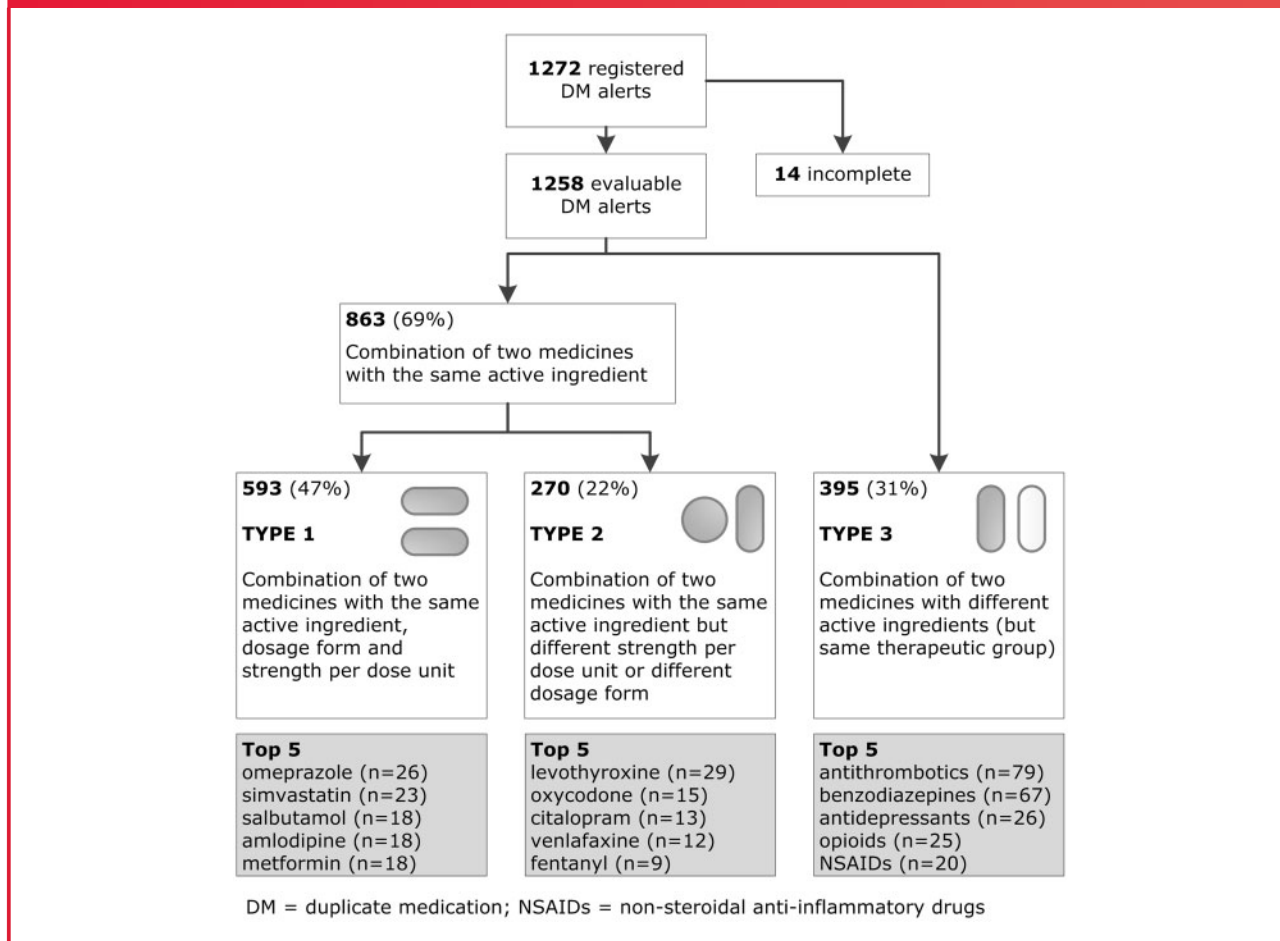
In half of the alerts (51%; $n = 631$) the pharmacists judged that there was no (risk for) concurrent use of both prescriptions (Table 1). The main reasons for these alerts were an early refill and/or a switch to a pharmaceutically identical product from another manufacturer. In 32% of the alerts ($n = 397$), the pharmacist concluded that the DM alert was generated because of an intentional combination. In 17% of the alerts ($n = 210$), the pharmacist was of the opinion that there was a risk for unintentional concurrent use. Generally these alerts related to a therapy switch between drugs from the same therapeutic group or between different strengths of the same drug ($n = 171$). In 92% of these alerts ($n = 158$) the pharmacist reported that the patient was already aware of the fact that both drugs should not be used concurrently.

In 62% of the alerts ($n = 779$) the EPR contained sufficient information for the pharmacist to decide whether action was needed. In 9% of the alerts ($n = 111$) the prescriber had provided a written clarification of the DM alert on the prescription itself. In one third of the DM alerts the pharmacists needed to retrieve additional information and contacted the patient or prescriber, respectively, 25% ($n = 317$) and 6% ($n = 70$). Contact with the prescriber was more frequent for type 3 alerts (11%) than for type 2 alerts (5%; $P = .017$) or type 1 alerts (2%; $P < .001$). Besides, there were situations where, according to the pharmacist, no additional information was needed at all and situations where the pharmacist contacted other related parties, e.g., homecare.

Overall, in one third of the alerts ($n = 393$) a total of 427 actions were taken by the pharmacists (Table 2). The EPR was updated in 15% of the alerts and the pharmacists performed an external action in 19% of the alerts. The most frequent external action was instructing the patient (14% of the alerts). In 2.2% of the alerts, the prescription was modified or cancelled for therapeutic reasons (0.4%) or for non-therapeutic reasons (1.8%) – the last ones being mainly logistic.

In the multiple logistic regression analysis first dispensing was the only determinant that was associated with an external action by the pharmacist: at first dispensing, 40% of the alerts led to an external action, compared to 14% for refill ($P < .001$) (Table 3). The other investigated determinants (age, sex, ATC-group-code of the prescription,

Figure 1: Nature of DM alerts.

DM = duplicate medication; NSAIDs = non-steroidal anti-inflammatory drugs

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type of prescriber, and handwritten prescription) were not associated with performing an external action.

In a stratified multiple logistic regression analysis on alert type (data not shown) none of the investigated determinants were associated with performing an external action for DM alerts type 1. For types 2 and 3 alerts, first dispensing remained the major determinant associated with an external action by the pharmacists compared to refill (type 2: 44% vs 14%, $P < .001$; type 3: 36% vs 7%, $P < .001$). Moreover, for type 3 alerts, handwritten prescriptions were more likely to be followed by external action than electronic prescriptions (35% vs 16 %, $P = .011$).

DISCUSSION

This study shows that CDSS in Dutch community pharmacies generate many DM alerts. In one fifth of these alerts the pharmacists performed an external action, for example, instructing the patient or informing other health care providers. Prescription modifications were rare (2.2%).

The majority of DM alerts were either generated because refill prescriptions were filled too early, or because patients used intended combinations such as different strengths of levothyroxine or opioids, or because patients concurrently and intentionally used drugs with comparable active substances such as two antithrombotics or psychoactive substances. For medications causing DM alerts type 2 (same active ingredient, different strength or dosage form) and type 3 (different but comparable active ingredients), both intentional combinations and therapy switches are common, so verification by the pharmacist is important. This is consistent with our finding that the DM alerts of types 2 and 3 were more likely to be followed by external action at first dispensing compared to refill, because first dispensing is the primary moment for verification.

For type 3 alerts, external action was more likely for handwritten prescriptions compared to electronic prescriptions. This could be related to the fact that electronic prescriptions mainly originate from computerized physician order entry including CDSS (with type 3 DM alerting), while for handwritten prescriptions the prescriber possibly was not aware of the potential DM.

Although the proportion of actual prescription modifications was low, our study showed that DM alerts did contribute to safe drug use in other ways. DM alerts stimulated the pharmacists to have a complete and up to date EPR, which is essential for safe drug use.[17] Moreover, DM alerts led to detection of overuse/misuse and overdose. For instance, an early refill of a benzodiazepine can be a way to detect overuse. In case of type 2 alerts, the combined doses of the active ingredient must be checked to prevent overdosing (e.g., the total daily dose of paracetamol in case of combined use of paracetamol and a preparation containing both tramadol and paracetamol).

The majority of DM alerts in our study did not lead to an external action. This indicates that the relevance of most of the alerts was judged as low by the pharmacists. This is consistent with the results

Table 1: Situations underlying the DM alerts (*n* = 1238)[a]

Situation	Details	Number of alerts (%)	Example
No (risk for) concurrent use	Early refill	336 (27.1)	Early refill of metformin because of holidays.
	EPR: assumed period of use incorrect	107 (8.6)	Assumed period of use of acenocoumarol in EPR is incorrect because of variable use.
	EPR: dose increased by prescriber	33 (2.7)	Dose of metformin was increased by the prescriber from two to three tablets daily.
	Overuse, intended	16 (1.3)	Patient used more salbutamol than prescribed because of insufficient asthma control.
	Other	139 (11.2)	Logistic reasons, mainly because of changes of trademark of the same product.
(Risk for) unintentional concurrent use	Switch, patient had already been informed	158 (12.8)	A switch from metoprolol 25 mg sustained release to metoprolol 50 mg sustained release, or a switch from nitrofurantoin to amoxicillin + clavulanic acid. Patients were aware of these therapy changes.
	Switch, patient had not been informed yet	13 (1.1)	A switch from pantoprazole to esomeprazole. Patient did not know he should not take pantoprazole any more.
	Unintentional duplicate prescription	14 (1.1)	A first prescription for morphine while codeine was in use, or two identical prescriptions on the same day (logistic error).
	Other	25 (2.0)	Dispensing two drugs for subsequent use, e.g., amoxicillin/clarithromycin/pantoprazole and pantoprazole.
Intentional concurrent use	Intentional concurrent use	397 (32.1)	Aspirin + clopidogrel (in the first year after an ischemic coronary event) or levothyroxine 100 mcg + 25 mcg

[a]Twenty alerts missing because of insufficient or inconsistent data.
DM = duplicate medication; EPR = electronic patient record.

of investigations on DM in several other settings.[7,11,15] Although the relevance of the majority of the individual DM alerts is considered low, an earlier study showed that 4.5% of prescription modifications in community pharmacies in the Netherlands were a response to DMs.[18] Moreover, Wright et al.[19] showed that in hospitals, a majority of the potential adverse drug events and a substantial part of the actually occurring adverse drug events were caused by DM. This suggests that preventing inappropriate DM may prevent patient harm.

CDSS can help to detect situations of potentially inappropriate DM. But when alerts are nonspecific in detecting situations which pharmacists assess as relevant to perform external action, this contributes to the risk of "alert fatigue." Therefore, strategies to improve the specificity of DM alerts should be considered.[20]

Based on our data, we suggest six strategies (Table 4). Currently, for DM alerts type 1, most CDSS generate a DM alert when the overlap between two prescriptions exceeds 14 days. However, the additional explanations reported by the pharmacists in our study suggest that for chronic medications, action is often limited to cases with an overlap of > 30 days. Enabling different overlap criteria per therapeutic class could reduce the number of irrelevant alerts (e.g., maintaining a short overlap criterion for drugs with a risk of misuse, such as benzodiazepines, and prolong the overlap for chronic medications without a substantial risk of overuse).

As we found that first dispensing was a major determinant of external action, enabling suppression of repeat DM alerts is a second strategy. When a pharmacist judges a certain combination as intentional at first dispensing, manual suppression of these alerts for this patient in the future could be a useful tool to reduce the total number of alerts. To do this

safely, the suppression should automatically end in case of relevant changes in the health situation of the patient—for example, change in systemic drug therapy, new contra-indications, and deviating lab values. Moreover, the pharmacist should be able to enter an end date for the alert suppression in case of combinations which are appropriate during a specific period of time, for example, the combination of two different antithrombotics in the first year after an ischemic coronary event (responsible for 6% of the DM alerts in our study). For some combinations (e.g., immunosuppressive drugs after transplantation) lifelong alert suppression may be indicated.

For type 2 alerts, it could even be considered to restrict alert generation to first dispensing instead of offering the possibility of active manual alert suppression. A precondition for this option is the availability of an advanced check on the cumulative daily dose of an active ingredient by the CDSS, rather than checking the daily dose of every prescription separately.

Suppression of repeat alerts for intentional combinations is preceded by an evaluation by the pharmacist at first dispensing. In our study, in 9% of the alerts, the pharmacist contacted the prescriber to retrieve additional information. The judgment process by the pharmacist could be facilitated by sharing the prescriber's reason for overriding an alert electronically with the pharmacist. Although the fact that two prescriptions are from the same prescriber is suggestive for an intentional combination, this single fact is too implicit to consider it sufficient to suppress DM alerts automatically.

Although our study did not specifically focus on alerts for therapeutic classes with a high risk of adverse drug reactions, restricting DM alerts to such drugs should be considered.[7]

Table 2: Performed actions by the pharmacists to manage the DM alert ($n = 1282$) based on 1248[a] DM alerts

Action		n[b] (percentage of alerts)	Example
No (external) action	No action	855 (68.5)	-
	Updating the electronic patient record	192 (15.4)	Correct dosing instructions and daily use in the electronic patient record: e.g., three tablets metformin 500 mg daily instead of two. Assumed period of use was updated accordingly.
External action	Instructing the patient	175 (14.0)	Instruct the patient not to use the new and the old prescription concurrently, e.g., diclofenac and meloxicam.
	Other action, e.g., informing other health care providers	33 (2.6)	Ask home care to check the stock at the patient's home, e.g., inhalation medication.
	Modifying the prescription/therapy	5 (0.4)	Contact the prescriber resulting in a therapy change, e.g., stopping codeine because of starting morphine.
	Modifying the prescription, not therapy-related (mainly logistic).	22 (1.8)	Dispense less than prescribed to prevent stocking at patient's houses. For example, when a patient hoards medicines because of reimbursement issues.

[a]Ten alerts missing because of insufficient or inconsistent data.
[b]More than one action per alert was possible.
DM = duplicate medication.

Table 3: Determinants of external actions based on DM alerts ($n = 1105$ alerts[a])

		Number of alerts (%)		OR external action crude (95% CI)	OR external action adjusted[b] (95% CI)
		External action n = 213	No (external) action n = 892		
Age	Per year	Mean (SD) 58.7 (21.5), years	Mean (SD) 60.1 (20.7), years	1.0 (1.0-1.0)	1.0 (1.0-1.0)
Sex	Female	128 (60.1)	502 (56.3)	1.2 (0.9-1.6)	1.1 (0.8-1.5)
First dispensing		85 (39.9)	130 (14.6)	3.9 (2.8-5.4)	3.9 (2.7-5.5)
Handwritten prescription		21 (9.9)	61 (6.8)	1.5 (0.9-2.5)	1.7 (0.9-3.3)
Prescriber	General practitioner	163 (76.5)	663 (74.3)	1 (reference)	1 (reference)
	Specialist	43 (20.2)	206 (23.1)	0.8 (0.6-1.2)	0.7 (0.4-1.1)
	Other	7 (3.3)	23 (2.6)	1.2 (0.5-2.9)	1.5 (0.6-3.6)
ATC new prescription[c]	A (alimentary)	37 (17.4)	108 (12.1)	1.2 (0.7-1.9)	1.6 (0.9-2.7)
	B (blood)	12 (5.6)	90 (10.1)	0.4 (0.2-0.9)	0.7 (0.4-1.5)
	C (cardiovascular)	48 (22.5)	170 (19.1)	0.9 (0.6-1.5)	1.4 (0.8-2.2)
	N (nervous system)	51 (23.9)	270 (30.3)	0.6 (0.4-1.0)	0.9 (0.5-1.4)
	R (respiratory)	18 (8.5)	96 (10.8)	0.6 (0.3-1.1)	0.8 (0.4-1.4)
	Other	47 (22.1)	158 (17.7)	1 (reference)	1 (reference)

[a]Analysis based on 1105 alerts (excluding all alerts with at least one missing variable).
[b]OR adjusted for all other determinants in table.
[c]Only ATC-groups with more than 100 alerts shown separately.
ATC = Anatomical Therapeutic Chemical classification; DM = duplicate medication; OR = odds ratio; SD = standard deviation; 95% CI = 95% confidence interval.

Table 4: Improvement strategies for DM alerting

Strategy	Most applicable for
Adaption of overlap criteria for alert generation (per therapeutic class)	DM alert type 1
Manual suppression of repeat DM alerts	DM alert type 3
Automatic suppression of repeat DM alerts	DM alert type 2
Sharing override reasons between prescriber and pharmacist	DM alert types 1, 2, and 3
Restriction of alerts to high risk drugs	DM alert types 1, 2, and 3
Advanced clinical decision support, generating alerts based on all patient characteristics in the EPR	DM alert type 3

DM = duplicate medication; EPR = electronic patient record.

In addition, for therapeutic groups where combinations are commonly intentional but also carry a high clinical risk, the use of advanced clinical decision support should be considered.[11,21,22] When indications, risk factors, lab monitoring results, age, etc. can be incorporated in the decision algorithm for alert generation, increased specificity can be expected. In case of an intentional combination of antithrombotics, more specific alerting is possible when the decision algorithm is using data like indication, start date, exact combination of drugs, and the advised period of concurrent use. To realize this kind of clinical decision rules, DM alerts of drugs that are frequently intentionally combined should be investigated in more detail to elucidate specific factors (such as lab values, indications, and duration of use) determining their relevance. Such factors, which were not included in our study (although they were reported in the additional explanations), will probably differ highly among the different therapeutic groups.

Changing CDSS criteria for alert generation should be done with caution, as experiences with refining drug-drug interaction alerting has shown that improved specificity without loss of sensitivity is difficult to realize and may even have unexpected results, for example, more alert overriding instead of less.[22–24] The use of advanced CDSS tends to be promising, but both theoretical estimations and practical experiences are mainly limited to refining alert generation by integrating lab values in the decision algorithms in hospitals.[11,25–27] About the impact of other suggested strategies for refinement of DM alerts, little is known. Historically there is a tendency of alerting every possible risk and this tendency has been reinforced by the legitimate focus on patient safety and drug related problems.[28–30] However, reducing patient harm by clinical risk management does not only include identifying potential risks, but also assessing and prioritizing them. Risk reducing strategies, like the implementation of changes in (advanced) clinical decision support systems, should result from such an assessment rather than from the fear of missing alerts.

Our study has several limitations. It reflects how pharmacists perceived and managed DM alerts in daily practice. Their judgment (e.g., not to perform any action) was not checked independently by a second pharmacist and it is possible that it was incorrect in a few cases. For a few combinations of medicines, the judgment of the pharmacist that it was an intentional and appropriate combination raised a question, because it was not clearly supported by the explanation provided. In one of these rare cases, the combination of chlorthalidone and hydrochlorothiazide was judged as intentional by the managing pharmacist, without proper explanation.

The fact that the pharmacists had to document the alerts may sometimes have influenced their management. If this was the case, it would probably have led to an overestimation of the number of external actions.

Nevertheless, the overall number of therapy changes and external actions we found still was quite low.

CONCLUSION

In community pharmacy DM alerts are generated frequently (20 alerts per 100 dispensed drugs). One-fifth of the alerts trigger pharmacists to perform an external action. Most frequently the patient is instructed and seldom prescriptions are modified for drug therapy related reasons. The current DM alerts are nonspecific in detecting situations where external action is considered relevant. Because of the diversity of the DM alerts, different CDSS improvement strategies should be considered for different types of DM alerts.

COMPETING INTERESTS

The authors have no conflicts of interest that are directly relevant to the content of this study.

CONTRIBUTORS

All authors contributed to the study design, the study protocol and the manuscript. M.H. collected the data and performed the data analysis. A.F. and M.B. contributed to the data consistency check and M.B. contributed to the data analysis. All authors approved the final manuscript.

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SUPPLEMENTARY MATERIAL

Supplementary material is available online at http://jamia.oxfordjournals.org/.

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