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ORIGINAL ARTICLE

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Drug-related problems identified during medication review before and after the introduction of a clinical decision support system

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Summary

What is known and objective: To facilitate the identification of drug-related problems (DRPs) during medication review, several tools have been developed. Explicit criteria, like Beers criteria or STOPP (Screening Tool of Older Peoples' Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment) criteria, can easily be integrated into a clinical decision support system (CDSS). The aim of this study was to investigate the effect of adding a CDSS to medication review software on identifying and solving DRPs in daily pharmacy practice.

Methods: Pre- to post-analysis of clinical medication reviews (CMRs) performed by 121 pharmacies in 2012 and 2013, before and after the introduction of CDSS into medication review software. Mean number of DRPs per patient, type of DRPs and their resolution rates were compared in the pharmacies pre- and post-CDSS using paired *t* tests.

Results and discussion: In total, 9151 DRPs were identified in 3100 patients pre-CDSS and 15 268 DRPs were identified in 4303 patients post-CDSS. The mean number of identified DRPs per patient (aggregated per pharmacy) was higher after the introduction of CDSS (3.2 vs 3.6 $P < .01$). The resolution rate was lower post-CDSS (50% vs 44%; $P < .01$), which overall resulted in 1.6 resolved DRPs per patient in both groups ($P = .93$). After the introduction of CDSS, 41% of DRPs were detected by the CDSS. The resolution rate of DRPs generated by CDSS was lower than of DRPs identified without the help of CDSS (29% vs 55%; $P < .01$). The two most prevalent DRP types were "Overtreatment" and "Suboptimal therapy" in both groups. The prevalence of "Overtreatment" was equal in both groups (mean DRPs per patient: 0.84 vs 0.77; $P = .22$), and "Suboptimal therapy" was more frequently identified post-CDSS (mean DRPs per patient: 0.54 vs 1.1; $P < .01$).

What is new and conclusion: The introduction of CDSS to medication review software generated additional DRPs with a lower resolution rate. Structural assessment including a patient interview elicited the most relevant DRPs. Further development of CDSS with more specific alerts is needed to be clinical relevant.

KEYWORDS
computerised decision support, elderly, medication, pharmacist consultation, pharmacy practice

1 | WHAT IS KNOWN AND OBJECTIVE

Older patients with polypharmacy are at risk for drug-related problems (DRPs), like overtreatment and suboptimal therapy.[1] A clinical medication review (CMR), consisting of a structured assessment of the pharmacotherapy including a patient interview, is an important instrument to identify and resolve DRPs.[1–5] This is a time-consuming process.[6] Given the expected increase in older people with polypharmacy,[7,8] the amount of medication reviews will increase substantially in the near future. Therefore, standardization and facilitation of the medication review process are needed.[9]

To facilitate the identification of DRPs during medication review, several tools have been developed. These tools can be judgement based (implicit criteria) or criterion based (explicit criteria). An example of implicit criteria is the Medication Appropriateness Index (MAI).[10,11] Explicit criteria, like the Beers criteria or STOPP/START criteria, aim to identify inappropriate medication and prescribing omissions.[12–14] An advantage of explicit criteria is that they can be relatively easily integrated into clinical decision support systems (CDSS), whereas implicit criteria typically cannot. CDSS can be described as a computer program that generates alerts aimed at helping healthcare professionals to improve the quality and safety of pharmacotherapy including timely monitoring.[15,16]

Most studies describing CDSS investigate only one type of alert, for example alerts about reducing anticholinergic medication, improving antibiotic prescribing or use of medicines during pregnancy.[16–18] These alerts are usually designed to support physicians during prescribing.[19,20] Few studies have assessed CDSS in pharmacy practice to support pharmacists.[9,21–25] One study showed that the use of CDSS during medication review identified more potential DRPs than the pharmacists.[21] However, this study did not investigate the outcome of interventions aimed at resolving the identified DRPs. Another study suggested that only a minority of DRPs identified during medication review would have been found with explicit criteria. A limitation of this study was that the explicit criteria were applied retrospectively.[26]

The aim of the study was to investigate the effect of adding a CDSS to medication review software on identifying and solving DRPs in daily pharmacy practice.

2 | METHODS

2.1 | Study design

This study was a retrospective database study including a pre- to post-design. Data of clinical medication reviews were extracted from community pharmacies' databases and compared before and after the introduction of a CDSS into medication review software.

2.2 | Setting

The study was conducted at 121 Dutch community pharmacy franchisees of "Service Apotheek" (SA). Only pharmacies that performed at least five CMRs before and after the introduction of the CDSS were included in the study. The pharmacies were located over the Netherlands in both rural and urban areas. Per pharmacy, one or more pharmacists performed the medication reviews in community-dwelling older patients. The pharmacists used medication review software to register DRPs and interventions during a medication review[3,27] In 2013, a CDSS was incorporated into this software program. The CDSS consisted of 46 explicit criteria, which generated alerts to the pharmacist at the start of a medication review.

All pharmacists previously received training in medication review as this is required by most health insurance companies to be reimbursed for medication review. A helpdesk was available in case pharmacists experienced difficulties with the CDSS.

2.3 | Ethics and patient confidentiality

Because this was a retrospective analysis of routinely collected anonymized data that could not be traced back to individual patients and pharmacies, ethical approval was not needed under the Dutch legislation.

2.4 | Explicit criteria incorporated into the CDSS

An expert team drafted a preliminary list of clinical rules, based on national prescribing guidelines, Beers, STOPP/START criteria, but also on other relevant themes in polypharmacy like inconvenience of use or economic efficiency.[12,28,29] Based on practical considerations, the developers of the CDSS incorporated 46 of these clinical rules into the CDSS in 2013 (Appendix S1).

2.5 | Clinical medication review

Patients aged ≥65 years using ≥5 chronic oral medications were eligible for a clinical medication review.[6,11] According to Dutch guidelines, a CMR should involve both pharmacist, general practitioner (GP) and patient.[6] First, the pharmacist collected both clinical and drug dispensing data from the patient. Then, the pharmacist interviewed the patient, identified DRPs and proposed recommendations (eg add or discontinue a drug) in a pharmaceutical care plan. The recommendations in this pharmaceutical care plan were discussed with the patient's GP. Agreed recommendations by the GP were discussed with the patient. After agreement of the patient, recommendations were implemented.

After the introduction of the CDSS, the pharmacists followed the same procedure for CMR, with the exception that the CDSS also automatically generated potential DRPs at the start of the medication review process. The pharmacist could discuss these potential DRPs with the patient and GP during the CMR.

2.6 | Data collection

Pharmacists were trained to document the results of the CMRs in the software program.[3,27] The following characteristics were

documented: date of the CMR, name and ATC-code (Anatomical Therapeutic Chemical classification) of the drug(s) involved, DRP type, type of recommendation (eg recommendation to add a drug) proposed by the pharmacist and type of implemented recommendation (eg the drug was added). The medication review software program was linked to the pharmacy information system. In addition, anonymized dispensing records of all included patients, including age and gender, were available for a period of 12 months prior to the CMR date.

Data before CDSS introduction were collected from January to August 2012. CDSS was introduced at January 2013. Data after introduction of CDSS were collected from January to August 2013.

2.7 | Measurements

Primary outcome measurements were the mean number of identified and resolved DRPs per patient aggregated per pharmacy before and after the implementation of CDSS. A DRP was considered resolved when the recommendation associated with the DRP was fully or partly implemented as documented by the pharmacists in the software program (eg dose reduction when complete discontinuation was proposed). Secondary outcome measurements were type of DRPs, type of implemented recommendations and prevalence of the potential DRPs generated by CDSS. The classification of DRPs was adapted from Hepler and Strand and is described in the national guidelines.[3,6,30]

2.8 | Data analysis

Duplicate DRPs, incomplete registrations and incomplete patient data were excluded from analysis. To validate the correct classification of DRPs by the pharmacists, a random sample of 100 records per DRP type was checked. The documented classification of DRPs was compared with the description in the free text box by two investigators (SV and HFK). Less than 10% of the classifications deviated from the free descriptions. This percentage was considered acceptable.

2.9 | Statistical analysis

Descriptive statistics were used for basic characteristics. Frequencies and percentages were reported for categorical variables. Paired *t* tests and related samples Wilcoxon signed rank tests were performed to compare differences between pre- and post-CDSS in the pharmacies, in demographics, mean number and type of identified and solved DRPs per patient and implemented recommendations between pre- and post-CDSS. All the results were aggregated per pharmacy and compared on the pharmacy level pre- and post-CDSS. The data were analysed using Microsoft Office Access, Excel Professional 2013 (Microsoft Corporation, Redmond, WA, USA) and IBM SPSS Statistics 22.0 (IBM Corporation, Armonk, NY, USA). A *P*-value <.05 was considered statistically significant.

3 | RESULTS

3.1 | Descriptive statistics

Clinical medication reviews were performed in 186 pharmacies both before and after the introduction of CDSS in medication review software (pre-CDSS and post-CDSS, respectively). We excluded 65 pharmacies because they performed <5 CMR, either pre- or post-CDSS. In the 121 included pharmacies, 3100 patients received a CMR pre-CDSS and 4303 patients post-CDSS. Pharmacies performed less CMR pre-CDSS than post-CDSS (median 16 (IQR 9-36) vs median 30 (IQR 18-49); $P < .01$). Patient characteristics aggregated per pharmacy are shown in Table 1.

3.2 | Drug-related problems

In total, 9151 DRPs were identified pre-CDSS and 15268 DRPs were identified post-CDSS. The mean number of identified DRPs per patient (aggregated per pharmacy) increased after introduction of the CDSS (3.2 (SD 1.1) vs 3.6 (SD 1.3); $P < .01$), whereas the proportion of resolved DRPs decreased (50% (SD 18%) vs 44% (SD 15%); $P < .01$). This leads to an equal number of resolved DRPs before and after the introduction of CDSS (1.6 (SD 0.82) vs 1.6 (SD 0.79); $P = .93$).

3.3 | Type of drug-related problems

The two most prevalent type of DRPs before as well as after the introduction of CDSS was "Overtreatment" and "Suboptimal therapy." The prevalence of "Overtreatment" was equal in both groups (0.84 (SD 0.66) vs 0.77 (SD 0.34); $P = .22$). Suboptimal therapy was identified more frequently after the introduction of CDSS (0.54 (SD 0.38) vs 1.1 (SD 0.44) per patient; $P < .01$). The mean number of resolved "Suboptimal therapy" issues per patient was equal among both groups (0.20 (SD 0.22) vs 0.24 (SD 0.22); $P = .15$). The other differences in type of DRPs are shown in Table 2.

3.4 | Type of implemented recommendations

The mean number of ceased drugs per patient decreased after introduction of the CDSS (0.40 (SD 0.40) vs 0.31 (SD 0.23); $P = <.01$), whereas the mean number of added drugs per patient increased (0.19 (SD 0.16) vs 0.25 (SD 0.18); $P < .01$). Post-CDSS more recommendations led to "no intervention" (1.1 (SD 0.80) vs 1.4 (SD 0.80); $P = <.01$). The other differences in types of implemented recommendations are shown in Table 3.

3.5 | Post-CDSS

Post-CDSS, 41% of all potential DRPs were detected by the CDSS and 59% were identified by structural assessment by the pharmacists during the CMR. Only 29% (SD 17%) of potential DRPs detected by CDSS were resolved compared to 55% (SD 20%) of DRPs identified by pharmacists ($P < .01$).

TABLE 1 Basic characteristics of patients aggregated per pharmacy pre- and post-CDSS

Characteristic	Pre-CDSS (N = 3100)	Post-CDSS (N = 4303)	*P*-value*
Age (year, median, IQR)	78 (75-82)	77 (75-80)	.02
Number of chronic medicines in use (median, IQR)	8 (7-9)	8 (7-8)	.01
Gender, women (%, median, IQR)	59 (50-68)	53 (46-62)	.01
10 most prescribed chronic drug classes	**Mean % of patients per pharmacy (SD)**	**Mean % of patients per pharmacy (SD)**	***P*-value****
Antithrombotic agents	74 (14)	72 (11)	.24
Drugs for peptic ulcer and GORD	68 (16)	65 (12)	.16
Lipid-modifying agents	63 (17)	68 (14)	.01
Beta-blocking agents	59 (15)	58 (12)	.64
ACE inhibitors	35 (14)	39 (12)	.02
Oral blood glucose-lowering drugs	33 (17)	34 (14)	.55
High-ceiling diuretics	30 (13)	25 (12)	<.01
Dihydropyridin calcium channel blockers	29 (16)	31 (10)	.29
Laxatives	27 (15)	25 (12)	.40
Angiotensin II antagonists	24 (11)	24 (8.5)	.67

IQR, interquartile range, CDSS, clinical decision support system; ATC, Anatomical Therapeutical Chemical classification; GORD, gastro-oesophageal reflux disease; N = 121 pharmacies.
*Related samples Wilcoxon signed rank test.
**Paired *t* test.

TABLE 2 Prevalence and implementation rate of various DRP types pre- and post-CDSS

	Pre-CDSS (N = 3100 patients)		Post-CDSS (N = 4303 patients)		*P*-value*	
DRP type per patient aggregated per pharmacy	**DRPs identified (mean, SD)**	**Percentage resolved (%)**	**DRPs identified (mean, SD)**	**Percentage resolved(%)**	**DRPs identified**	**Percentage resolved**
Overtreatment	0.84 (0.68)	43	0.77 (0.34)	45	.22	.53
Suboptimal therapy	0.54 (0.38)	38	1.1 (0.44)	23	<.01	.15
Contra-indication	0.28 (0.40)	43	0.28 (0.40)	45	.97	.85
Drug not effective	0.27 (0.28)	51	0.22 (0.20)	46	.027	.033
Adverse effect	0.27 (0.24)	58	0.27 (0.21)	57	.85	.96
Drug interaction	0.22 (0.32)	63	0.06 (0.09)	44	<.01	<.01
Inconvenience of use	0.18 (0.18)	70	0.32 (0.23)	54	<.01	<.01
Non-compliance	0.16 (0.19)	71	0.12 (0.13)	76	.017	.10
Dose too low	0.16 (0.17)	47	0.13 (0.09)	35	.071	.012
Dose too high	0.16 (0.18)	60	0.06 (0.06)	53	<.01	<.01
Miscellaneous	0.13 (0.27)	44	0.28 (0.33)	35	<.01	<.01
Inappropriate dosage form	0.03 (0.06)	53	0.07 (0.07)	64	<.01	<.01

N = 121 pharmacies, Numbers are aggregated per pharmacy; DRP, drug-related problem; CDSS, clinical decision support system.
*Paired *t* test.

Table 4 shows the 10 most prevalent alerts based on explicit criteria generated by the CDSS. The most prevalent alert was "Cardiovascular disease without a statin," which is related to the DRP type: "Suboptimal therapy." The implementation rate of the associated recommendation to add a statin was 23%. The alert in the CDSS with the lowest implementation rate was "Absence of antiplatelet therapy in cardiovascular disease" (14%), and the alert with the highest implementation rate was "Lack of vitamin D in osteoporosis" (71%).

4 | DISCUSSION

This study demonstrated the mean number of identified DRPs increased after the addition of clinical decision support system (CDSS) to medication review software. On the contrary, the implementation rate of the recommendations associated with the DRPs decreased resulting in an equal number of resolved DRPs before and after the introduction of the CDSS.

TABLE 3 Differences in type of implemented recommendations pre- vs post-CDSS

Type of implemented recommendation per patient	Pre-CDSS (N = 3100 patients)	Post-CDSS (N = 4303 patients)	*P*-value*
Drug changes			
Drug added	0.19	0.25	<.01
Drug ceased	0.40	0.31	<.01
Drug replaced	0.18	0.15	.23
Dosage (regimen) changed	0.26	0.22	.18
Dosage form changed	0.03	0.04	.083
Other changes			
Performed monitoring	0.39	0.54	<.01
Information/advice provided	0.48	0.50	.71
Synchronization of all prescriptions	0.06	0.10	.019
Other	0.15	0.09	.033
No intervention	1.1	1.4	<.01

N = 121 pharmacies. Numbers are aggregated per pharmacy; CDSS, clinical decision support system.
*Paired *t* test.

TABLE 4 Top 10 most prevalent potential DRPs generated by the CDSS

Top	Description alert of the CDSS (Potential DRP type)	Prevalence in total number of DRPs (N = 15268 DRPs)		Percentage resolved (%)
		N	%	
1	Cardiovascular disease without a statin (Suboptimal therapy)	669	4.4	23
2	Concomitant use of three or more antihypertensives (Overtreatment)	647	4.2	24
3	Absence of antiplatelet therapy in cardiovascular disease (Suboptimal therapy)	594	3.9	14
4	Inconvenience of use of ACE inhibitor: once-daily alternative or combination available (Inconvenience of use)	490	3.2	32
5	Inappropriate use of inhaled corticosteroids in COPD (Overtreatment)	457	3.0	26
6	Concomitant use of two or more antithrombotics (Overtreatment)	397	2.6	52
7	Use of aerosol without a spacer (Inappropriate dosage form)	390	2.6	53
8	Loop-diuretics as first-line treatment of hypertension (Suboptimal therapy)	324	2.1	31
9	Lack of vitamin D in osteoporosis (Suboptimal therapy)	298	2.0	71
10	Heart failure without an ACE inhibitor (Suboptimal therapy)	289	1.9	17

Our finding that a CDSS leads to the identification of more potential but less relevant DRPs is comparable to other studies. A study of Curtain et al[21] also showed that a CDSS detected more DRPs than a structural assessment by the pharmacist. A previous study found that only a minority of the DRPs were associated with explicit criteria and a lower resolution rate of these DRPs.[26] A limitation of that study was that the investigators applied explicit criteria retrospectively. Our current study investigated the applicability of explicit criteria incorporated into software, by pharmacists during CMR in daily pharmacy practice.

Several reasons for the low implementation rate and limited effectiveness of CDSS alerts have been described in the literature. Some studies have suggested low specificity and alert fatigue as the main reasons for the limited effectiveness of CDSS alerts.[16,22] There are several comparable explanations for the low-resolution rate of DRPs generated by the CDSS in this study. One reason could be that the alerts were not specific enough, like, for example, the clinical rule that aims to detect heart failure not yet treated with an ACE inhibitor. This clinical rule is triggered by the presence of a diuretic without concomitant use of an ACE inhibitor in the drug dispensing records. Probably many patients identified by this clinical rule will use diuretics for other indications. In this case, the diagnosis heart failure is derived from the use of a drug (diuretic) and this often leads to false assumptions. It would be better to incorporate a heart failure diagnosis in the system that generates the clinical rule. Another reason that clinical rules often do not lead to medications changes may be that patients are intolerant for the suggested medication. The percentage of implemented recommendations for the alert of the explicit criterion: "Cardiovascular disease without a statin," was very low, namely 23%. Many patients have already discontinued using statins because of myopathy. In general, alerts are based on algorithms derived from guidelines developed for use

on population level, whereas CMRs are focused on the needs of individual patients.[31]

Other studies have shown that pharmacists encounter barriers like resistance to change, low consumer contact and lack of time.[16,22] In our study, low consumer contact and lack of time were no problem, because the CDSS was used during a CMR, where there is a multidisciplinary collaboration between pharmacist, GP and patient. Robertsen et al[22] also described that a professional relationship between pharmacist and physician is essential for the benefit of CDSS. In this setting, patient and GP are more inclined to cooperate with recommendations for drug changes.

Considering the DRPs that were identified by the pharmacists themselves during the CMR, the resolution rate of the DRPs was much higher. Fifty per cent or more of these DRPs were resolved, both before and after the introduction of the CDSS. These DRPs were mainly derived by an implicit method of medication review, by a structural assessment and interview between the pharmacist and the patient. Overtreatment, suboptimal therapy, non-compliance and adverse effects are examples of DRPs that mostly derive from information from the patient interview.[26] The higher implementation rate of the recommendations associated with these DRPs could be explained by a higher relevance for the patient. Kwint et al[32] also showed that DRPs identified during patient interviews were more frequently assigned a higher clinical relevance. Also Roane et al showed that consultation with a patient can lead to more appropriate recommendations.[33]

This study has several strengths. A major strength is the analysis of the large number of CMRs both before and after the introduction of CDSS. These CMRs represent the daily clinical practice of an average pharmacy in the Netherlands, which make the results likely to be more generalizable. A second strength is that this study is a direct comparison of medication review data before and after the implementation of a CDSS. Another strength is that we used a variety of clinical rules in the CDSS, which focused both on inappropriate prescribing and suboptimal therapy, but also on other relevant practical aspects for older people with polypharmacy.

There were also some limitations to this study. The first limitation is the potential variability in classifications of the type of DRPs and interventions by the different pharmacists. However, we did check the encodings and we found that <10% deviated, which we found acceptable in such a large database. A second limitation is that the resolution of DRPs was based on the partly or full implementation of the associated recommendation registered by the pharmacists in the database. Implementations of medication changes were not checked by either analysis of drug dispensing records or by asking patients if the DRPs were solved. A third limitation is that the increase in number of identified DRPs may be associated with other factors than the addition of the CDSS, such as increased experience of pharmacists in performing CMR. However, given the number of participating pharmacies (N = 121), we are of the opinion that the only factor that has changed in every pharmacy has been the introduction of the CDSS. Another limitation is that we only measured process outcomes, like DRPs. Until now the association between DRPs and clinical outcomes has not been confirmed.[4,5] The increase in number of identified DRPs per patients is relatively small (approximately 12,5%). On a population level, however, this adds thousands of DRPs. Although not every DRP will have clinical consequences for the patient, we are of the opinion that a proportion certainly will.

Finally, the last limitation is more linked to the CDSS itself. There was a lack of clinical information in the generation of specific alerts by the CDDS. The alerts in the CDSS were mainly based on drug dispensing records, because laboratory values and medical information are often unavailable in the pharmacy information system. This lack of clinical information influenced the implementation rate of the different alerts. This influence was reflected by a broad range in implementation rates between the different alerts in the top 10 potential DRPs identified by the CDSS. The implementation rates ranged from 14% (Absence of antiplatelet therapy in cardiovascular disease) to 71% ("lack of vitamin D in osteoporosis)." For the first alert, more clinical information about the patient's history is needed to give a recommendation about whether an antithrombotic agent should be started. The second alert is based on the use of a bisphosphonate, which is used for osteoporosis and always requires additional supplementation with calcium and vitamin D.[34] Another explaining factor for the high implementation rate for this alert could be that there is little resistance to initiate vitamin D.

Our results have several implications for future use and studies of CDSS during CMR. First, we saw that the current CDSS led to the detection of additional potential DRPs, but subsequently a low proportion of these DRPs were resolved. We suggest that the CDSS alerts should be more specific to have added value in detecting clinically relevant DRPs. More specific alerts could be generated by linking dispensing data with clinical diagnoses or laboratory values. Secondly, the aim of a CDSS is to perform a CMR more efficiently by facilitating the identification of potential DRPs. Future studies should include an analysis of the time spent on medication review with and without CDSS is needed to evaluate the added value of the CDSS. Besides that, future studies should not only measure DRPs, but also more clinical and patient-related outcomes to investigate the real benefits for the patients. Finally, we are of the opinion that a patient interview will always remain essential, because that interview identifies the health issues that are most relevant for the patient.

5 | WHAT IS NEW AND CONCLUSION

This study shows that the introduction of CDSS into medication review software identified more potential DRPs. However, DRPs identified by CDSS were less frequently resolved compared to DRPs identified by a clinical medication review. Probably, a structural assessment including a patient interview, facilitated by a CDSS, would identify the most relevant DRPs. Further development of CDSS with more specific alerts, linking dispensing and clinical information, could make the medication review process more efficient.

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AUTHOR CONTRIBUTIONS

All authors contributed to the study design, the study protocol and the manuscript. SV performed the data analysis. All authors approved the final manuscript.

CONFLICTS OF INTEREST

SV was funded by an unconditional grant for her PhD project to conduct this research, and PH worked for Service Apotheek and delivered the data to the other researchers, but did not have any influence on the analysis or interpretation of the data. HFK, MB and JG have no conflict of interests relevant to the content of this study.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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