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ORIGINAL RESEARCH ARTICLE

Reducing Inappropriate Drug Use in Older Patients by Use of Clinical Decision Support in Community Pharmacy: A Mixed-Methods Evaluation

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Abstract

Introduction Older people are prone to drug-related harm. Clinical decision support systems (CDSSs) in community pharmacies may improve appropriate prescribing in this population.

Objective This study investigated (persistent) drug therapy changes and its determinants to reduce potentially inappropriate medication (PIM) in older patients based on CDSS alerts and to investigate barriers and facilitators for implementation of drug therapy changes based on these CDSS alerts.

Methods Five clinical decision rules based on national guidelines for inappropriate drugs in older patients were incorporated in a web-based CDSS in 31 community pharmacies between February and April 2017. The CDSS generated alerts for patients aged > 70 years who had prescriptions for one of the following drugs: alprazolam, amitriptyline, barnidipine, duloxetine, fluoxetine, trazodone, quetiapine and olanzapine. The registered alert management data and medication dispensing histories were analysed to find potential determinants of persistent drug therapy changes. Ten pharmacists were interviewed about the barriers and facilitators for implementing drug therapy changes based on CDSS alerts. An inductive thematic analysis of the transcripts was performed.

Results The pharmacists recorded the management of 1810 of the 2589 generated alerts, and 158 (8.7%) alerts were associated with a persistent drug therapy change. A logistic regression analysis found that the drug triggering the alert and the type of prescription [first dispensing vs. repeat; odds ratio 2.1 (95% confidence interval 1.4–3.2)] were significantly associated with persistent drug therapy changes. No association was found between persistent changes and age, sex, number of medicines in use, or recent clinical medication review. Analysis of the interviews revealed nine barriers and facilitators associated with drug therapy change.

Conclusion When community pharmacists implemented CDSS alerts to reduce inappropriate drug use in older patients, they registered a persistent drug therapy change in 8.7% of the cases. Alerts triggered by a first prescription were two times more likely to be associated with a persistent drug therapy change than alerts triggered by repeat prescriptions. This study found that clinical rules can be used to detect inappropriate drug use in older patients and that drug therapy can change based on the alerts. This suggests that CDSS alerts are a useful tool for implementing guidelines on PIM in older patients in daily practice.

1 Introduction

Drug therapy-related problems (DTRPs) can lead to preventable drug-related hospital admissions [1–3]. Older patients are often polymedicated and are more susceptible to the harmful effects of drugs [4]. Pharmacological characteristics make certain drugs more suitable than others when treating frail older patients. Drugs known to have an unfavourable risk–benefit balance for older patients are 'potentially inappropriate medication' (PIM). Explicit prescribing criteria, such as the Beers criteria and Screening Tool of Older People's Prescriptions (STOPP), can be used to detect PIM. Although these criteria have been successfully used in this way, doubts exist about the best way to implement them in clinical practice [5]. One possibility is to take them into account when performing a clinical medication review (CMR). However, CMR is time consuming and thus only applied for select groups of patients. For structural prevention of PIM in all older patients, healthcare professionals

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Key Points

Pharmacists using clinical decision support system alerts to reduce potentially inappropriate medication registered a persistent drug therapy change in 8.7% of cases.

Alerts triggered by a first prescription were two times more likely than those triggered by repeat prescriptions to result in persistent drug therapy change.

Clear agreement between pharmacist and general practitioner on the management of drug therapy alerts is key to the successful implementation of clinical decision support.

need additional support [6, 7]. Incorporating the criteria in clinical decision support systems (CDSSs) has been successful for detecting several types of DTRPs, including PIM [8, 9]. A review of studies into the use of CDSSs to reduce prescribing of PIMs found that CDSSs seemed to be effective in reducing the prescribing of PIMs in hospitals, but results for ambulatory care settings were more variable [10].

In this study, national PIM guidelines were introduced in a CDSS in community pharmacies in the Netherlands to investigate whether this could support PIM guideline implementation. The aim was to investigate (persistent) drug therapy changes and their determinants to reduce PIM in older patients, based on CDSS alerts, and to investigate barriers and facilitators for implementation of drug therapy changes based on these CDSS alerts.

2 Methods

2.1 Design

Given the multifactorial context of drug therapy changes in primary care, we performed a retrospective database analysis of managed CDSS alerts and conducted semi-structured interviews with community pharmacists.

2.2 Setting

In the Netherlands, the Dutch Expertisecentre PHarmacotherapy in Old peRsons (Ephor) publishes evidence-based guidelines about the most appropriate drug per therapeutic class for frail older patients. Five clinical decision rules based on these Ephor guidelines version 2017 [11–15] were incorporated into a web-based CDSS and implemented in 31 community pharmacies. The CDSS generated alerts for patients aged > 70 years who had a prescription for one of the following drugs: alprazolam, amitriptyline, barnidipine, duloxetine, fluoxetine, trazodone, quetiapine and olanzapine. A single alert was generated for each patient, per drug. Table 1 gives a summary of the clinical decision rules based on the Ephor guidelines, and Fig. 1 shows the algorithm. At first dispensing, a pop-up alert was generated during the process in the pharmacy (before the therapy began). The alerts for repeat prescriptions became available through a daily updated list in the CDSS. The alert text showed the management advice, including an alternative drug. The pharmacists analysed the alert, decided how to manage the alert, managed the alert and registered the way they managed the alert in the CDSS according to predefined options regarding the situation and intervention, with additional free text.

The participating pharmacies were franchisees of 'Service Apotheek', located across the Netherlands in both rural and urban areas. These pharmacists routinely used the web-based CDSS in addition to their pharmacy information systems. All pharmacists were trained in how to work with the five clinical rules in the CDSS at a web conference, which they attended before the study. The general practitioners were informed about the five clinical decision rules before the study by their own pharmacists (information materials were provided by the investigators).

2.3 Quantitative Data Collection and Analysis

Data from the CDSS were collected in a central database. Anonymised data were extracted from this database for all alerts for the period February–April 2017, including alert management (until June 2017) and medication dispensing history from 6 months before the alert until 6 months afterwards. A descriptive analysis of registered alert management was performed, and all data were checked for consistency. Free text on reasons for performing a drug therapy change were classified by LM and MH. Disagreements were discussed until consensus was reached. A logistic regression analysis was performed for determinants of persistent drug therapy changes. A drug therapy change was defined as persistent if a registered change (e.g. discontinuation of a drug or a dose reduction) was still detectable in the medication dispensing history 6 months after the alert. The determinants analysed were as follows: drug triggering the alert, age, sex, number of medicines in use, type of prescription (first time or repeat) and CMR in last 13 months. We used Microsoft Access and SPSS version 24 for this analysis.

2.4 Qualitative Data Collection and Analysis

Semi-structured interviews were conducted with 10 of the 31 participating community pharmacists in May and June 2017. The pharmacists were selected by purposive sampling based

Table 1 Summary of clinical decision rules, based on Ephor guidelines [11–15]

Therapeutic class	Potential harmful medication triggering the alert	Indication	Advice presented to pharmacist (including most appropriate drug)
Antipsychotics	Quetiapine, olanzapine	Delirium, dementia	Consult the prescriber about the indication and replace it with haloperidol or risperidone (in case of delirium) or behavioural problems (in dementia). Evidence exists for the effectiveness of haloperidol and risperidone for these indications. These drugs have fewer anticholinergic effects than olanzapine and quetiapine
Benzodiazepines	Alprazolam	Anxiety	The elimination half-life of alprazolam is increased in older patients. Benzodiazepines are not first choice for anxiety. First-time prescriptions: consult the prescriber about replacing alprazolam with lorazepam. Lorazepam has no extended elimination half-life in older patients. Repeat prescriptions: consult the prescriber about the indication and replace it with an SSRI or lorazepam
Calcium channel blockers	Barnidipine	Hypertension	Consult the prescriber about the indication and replace barnidipine with amlodipine—or nifedipine extended release when the indication is hypertension. Barnidipine is contraindicated in patients with reduced renal function (glomerular filtration rate < 50 ml/min). Evidence exists that nifedipine extended release and amlodipine reduce cardiovascular mortality in older patients, and both can be used in patients with reduced renal function
Tricyclic antidepressants	Amitriptyline	Depression	Consult the prescriber about replacing amitriptyline with nortriptyline when the indication is depression. Nortriptyline is less anticholinergic, less sedating and causes less orthostatic hypotension
Second-generation antidepressants	Fluoxetine, duloxetine, trazodone	Depression	Consult the prescriber about the indication and change to citalopram or sertraline when the indication is depression. Citalopram and sertraline have no potential for relevant cytochrome P450-mediated drug–drug interactions. Be aware of QT prolongation with citalopram

Ephor Dutch Expertisecentre PHarmacotherapy in Old peRsons, *SSRI* selective serotonin reuptake inhibitor

on their location (rural or urban) and the proportion of managed alerts (below or above the mean). The literature was reviewed to assess the reasons for intentional non-adherence to clinical practice guidelines. A concept interview guide was developed by the research team, and this included topics emerging from the literature search and general questions about barriers to and facilitators of the implementation of the clinical decision rules [16–25]. The interview consisted of seven general questions about the pharmacist's experience with the five clinical decision rules and 16 specific questions about ten alerts managed by the pharmacist. The interviews focused on reasons for (not) changing a drug therapy. After two pilot interviews, the interview guide was evaluated and three questions added to the general questions, as the topics were discussed in the two interviews and thought to be relevant. [See the Electronic Supplementary Material (ESM) for the interview guide.] The interviews were all conducted either in person or via phone with a research assistant (RS). The interviews were audiotaped, transcribed verbatim and anonymised for analysis. An inductive analysis was performed using NVivo 11 Pro. The interviews were coded independently by LM and RS. Disagreements in coding were discussed until consensus was reached. Another researcher (MH) was consulted if no consensus was reached. Codes were thematically clustered into barriers to and facilitators of decision making around drug therapy changes. These barriers and facilitators were repeatedly discussed by the research team until consensus was reached. The final analysis resulted in classification into three themes. Data saturation was considered to be reached when the final two interviews revealed no new barriers or facilitators.

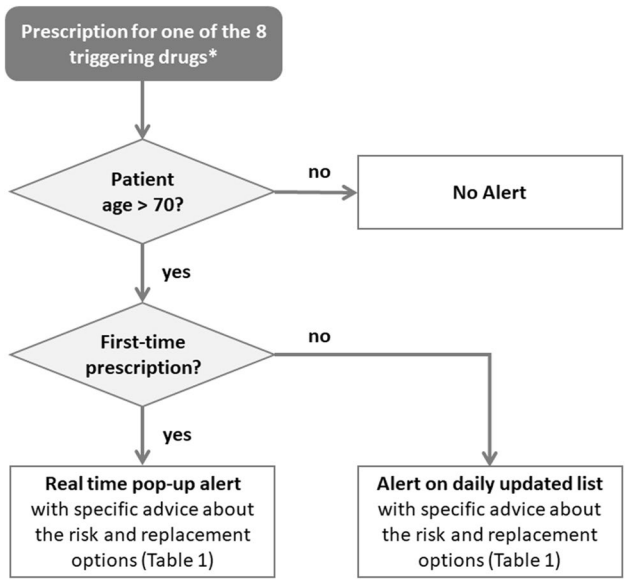

Fig. 1 The algorithm of the clinical decision rules based on the Ephor (Dutch Expertisecentre PHarmacotherapy in Old peRsons) guidelines. Asterisk: alprazolam, amitriptyline, barnidipine, duloxetine, fluoxetine, trazodone, quetiapine, olanzapine

3 Results

3.1 Quantitative Data Analysis of the Results

The CDSS in the 31 pharmacies generated 2589 unique alerts. The pharmacists registered the management of 1810 alerts (69.9%; range 8.8–100.0%). Of the registered alerts, 181 (10%) were associated with a drug therapy change; this change was persistent for 6 months in 158 cases (8.7% of the registered alerts). See Table 2 for the proportion of persistent drug therapy changes for the individual clinical decision rules. In 585 cases, pharmacists used free text to provide a reason for not changing the drug therapy. The most frequent reasons given were that the indication-specific advice in the alert was not applicable to the patient because the drug was in use for another indication (24%), that the patient had already tried the proposed alternative (23%) and that the prescriber was a specialist and not the general practitioner (14%).

A logistic regression analysis of the registered managed alerts indicated that the drug triggering the alert and the type of prescription (first time or repeat) were significantly associated with persistent drug therapy changes. No significant association was found for age, sex, number of medicines in use or recent CMR (Table 3).

3.2 Results Qualitative Data Analysis

Ten interviews were conducted with participating pharmacists, with data saturation reached after eight interviews. The characteristics of the interviewed pharmacists are detailed in the ESM. The analysis found that the decision to perform a drug therapy change based on a CDSS alert was influenced by nine barriers and facilitators, divided over three themes (see Fig. 2). Results from interviews performed by telephone were comparable to results from face-to-face interviews.

3.2.1 Organisation

The theme of 'organisation' comprises three barriers and facilitators: the level of collaboration between pharmacist and general practitioner, a lack of time and the work process in the pharmacy.

With respect to level of collaboration, a good relationship between pharmacist and general practitioner, good

Table 2 Frequency of registered managed drug therapy alerts and (persistent) drug therapy changes

Clinical decision rule	Prescription	Registered managed drug therapy alerts (*n*)	Drug therapy changes[a]	Persistent drug therapy changes[a]
Antipsychotics	First time	59	2 (3.4)	0 (0.0)
	Repeat	188	6 (3.2)	5 (2.7)
Benzodiazepines	First time	21	4 (19.0)	3 (14.3)
	Repeat	100	9 (9.0)	8 (8.0)
Calcium channel blockers	First time	73	6 (8.2)	6 (8.2)
	Repeat	523	35 (6.7)	29 (5.5)
Tricyclic antidepressants	First time	126	33 (26.2)	30 (23.8)
	Repeat	550	80 (14.5)	71 (12.9)
Second-generation antidepressants	First time	30	0 (0.0)	0 (0.0)
	Repeat	140	6 (4.3)	6 (4.3)
Total		1810	181 (10.0)	158 (8.7)

[a]Presented as *n* (% of registered managed alerts)

accessibility of the prescriber and prior agreement on the clinical decision rules were all facilitators of drug therapy changes:

> "We have a good relationship with the general practitioners. We discussed the new guidelines with them in advance" (pharmacist [ph] 4).

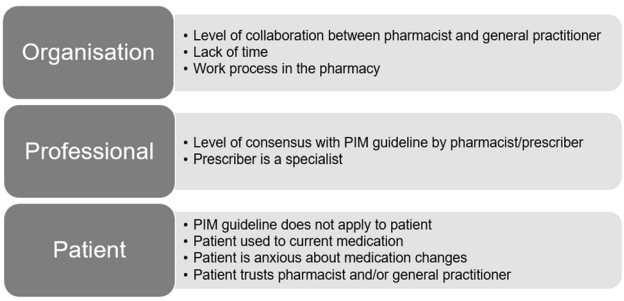

Fig. 2 Barriers and facilitators for alert-based drug therapy changes. *PIM* potentially inappropriate medication

Barriers to drug therapy changes at the level of collaboration were the presence of many prescribers and prescribers who had not previously been receptive to the pharmacist's advice. Lack of time was also a major barrier. This was described primarily as an absolute lack of time and sometimes as a matter of priority:

> "I can spend my time only once, you see. Let me put it this way: I do not detect many problems [by managing the alerts]" (ph. 6).

Regarding the work process, the pharmacists indicated that the clinical decision rules were too complicated to be managed by the pharmacy technicians at the counter. Therefore, it was important for the implementation process that the technicians were instructed to consult the pharmacist when an alert popped up:

> "The pharmacy technician did not consult me at the moment of appearance of the alert, so I have not talked to the patient at the counter. I have seen the alert only afterwards" (ph. 1).

Table 3 Determinants of persistent drug therapy changes

Determinants	No persistent drug therapy change ($n=1549$[a])	Persistent drug therapy change ($n=155$[a])	OR_{crude}	$OR_{adjusted}$[b]
Age				
70–74	463 (29.9)	35 (22.6)	Ref	Ref
75–79	433 (28.0)	49 (31.6)	1.5 (1.0–2.4)	1.5 (0.9–2.3)
80–84	350 (22.6)	37 (23.9)	1.4 (0.9–2.3)	1.3 (0.8–2.1)
85–89	207 (13.4)	25 (16.1)	1.6 (0.9–2.7)	1.6 (0.8–2.8)
≥90	96 (6.2)	9 (5.8)	1.2 (0.6–2.7)	1.2 (0.6–2.7)
Female sex	1051 (67.9)	106 (68.4)	1.0 (0.7–1.5)	0.9 (0.6–1.3)
Number of medicines in use				
0–1	180 (11.6)	14 (9.0)	Ref	Ref
2–4	377 (24.3)	31 (20.0)	1.1 (0.5–2.0)	1.1 (0.5–2.1)
5–8	581 (37.5)	64 (41.3)	1.4 (0.8–2.6)	1.5 (0.8–2.7)
≥9	411 (26.5)	46 (29.7)	1.4 (0.8–2.7)	1.5 (0.8–2.8)
Recent CMR[c]	127 (8.2)	17 (11.0)	1.4 (0.8–2.4)	1.4 (0.8–2.4)
First-time prescription	217 (14.0)	38 (24.5)	2.0 (1.3–3.0)*	2.1 (1.4–3.2)*
Clinical decision rule				
Antipsychotics	219 (14.1)	4 (2.6)	0.5 (0.1–1.7)	0.4 (0.1–1.6)
Benzodiazepines	98 (6.3)	11 (7.1)	2.9 (1.0–8.0)*	3.0 (1.1–8.6)*
Calcium channel blockers	533 (34.4)	34 (21.9)	1.6 (0.7–4.0)	1.7 (0.7–4.1)
Tricyclic antidepressants	545 (35.2)	100 (64.5)	4.7 (2.0–10.9)*	4.8 (2.1–11.2)*
Second-generation antidepressants	154 (9.9)	6 (3.9)	Ref	Ref

Data are presented as *n* (%) or OR (95% confidence interval) unless otherwise indicated

CMR clinical medication review, *OR* odds ratio

*$p \leq 0.05$

[a]106 records with missing values

[b]Adjusted for all other variables in table

[c]In 13 months preceding the alert

3.2.2 Professional

Two barriers and facilitators were identified for the theme of 'professional': level of consensus with the PIM guideline by the pharmacist and the general practitioner, and the prescriber being a specialist.

The agreement of the healthcare professional with the PIM guideline underlying the clinical decision rule was identified as a facilitator of drug therapy changes. Furthermore, the policy of an individual prescriber also influenced the pharmacist's decision to propose a drug therapy change:

> "When a doctor often prescribes barnidipine and you have contacted him many times about this issue and he keeps prescribing it, what can you do?" (ph. 6).

When medication was prescribed by a specialist, the pharmacists tended not to consider an intervention to change the therapy. They believed the drug therapy would be well-considered:

> "This medicine was prescribed by a geriatrician, so the general practitioner will not change this" (ph. 9).

3.2.3 Patient

The theme of 'patient' included four barriers and facilitators. One barrier was that the pharmacist or the prescriber decided the PIM guideline did not apply, as the patient was either using the medication for another indication or the prescriber was of the opinion that the patient was not frail:

> "The prescriber was open to change, and he knew the guidelines for prescribing in frail older patients, but he said that this patient was not frail at all" (ph. 5).

If a patient had been using the medication for some time and the risk–benefit balance seemed positive, healthcare professionals felt it was not necessary to change the therapy. In their opinion, the potentially better pharmacological properties of the suggested alternative medication did not outweigh the risk of disturbing the balance in the patient's condition:

> "When it is already started, it is hard to change the medication if there are no problems" (ph. 2).

If a patient had been anxious about medication changes in the past, this formed a significant barrier to changing the drug:

> "Because she is so anxious, every change is a reason to panic. So, we try not to stress her and that is why changing her medication is not desirable" (ph. 7).

However, patient trust in their general practitioner and/or pharmacist was a facilitator and made it easier to conduct an intervention:

> "The patient agreed, especially because I consulted the general practitioner, because the patient trusts the general practitioner" (ph. 1).

4 Discussion

The participating pharmacists managed 1810 CDSS alerts to reduce inappropriate drug use (PIM) in older patients, ultimately leading to 181 drug therapy changes (10%). This is in the range of the intervention rate commonly found in investigations of routine CDSSs [26–30]. Most of these drug therapy changes were persistent.

Alerts triggered by first prescriptions were two times more likely than those triggered by repeat prescriptions to result in a persistent drug therapy change. The pharmacists confirmed in the interviews that changing the medication in use by a patient is more difficult than changing a new medicine before the therapy has begun. In this study, alerts triggered by tricyclic antidepressants and benzodiazepines led to persistent drug therapy changes more often than those triggered by other therapeutic classes. The interviews revealed that most pharmacists and general practitioners agreed with the guidelines on which these specific clinical decision rules were based. This facilitator has been described in other studies in guideline non-adherence [17–19]. The proportion of drug therapy changes in prescriptions for antipsychotics and second-generation antidepressants was low, as the prescriber who initiated the therapy was, in many cases, a specialist and not a general practitioner. Pharmacists were less inclined to change the therapy or even consult the specialist to discuss a possible change, as they assumed that the prescription was the result of a deliberate choice.

Lack of time, a common barrier for guideline adherence and deprescribing in other studies [19–21, 31, 32], was a major barrier identified in this study. To overcome this, it is important to efficiently organise the overall process. Mutual accessibility of the prescriber and pharmacist is key, as are discussion of the clinical decision rules before implementation and agreement on the preferred management option. Good collaboration between the pharmacist and general practitioner facilitated the alert management. For a fruitful collaboration between pharmacist and prescriber, acknowledging and respecting each other's profession and expertise is essential. This has also been found in other studies [21, 22, 31, 32].

The prescribing situation and patient-specific considerations and values, which are also known from investigations into guideline adherence and deprescribing, are too complex to be replaced by an algorithm. However, better exchange of patient information between the prescriber and pharmacist about the indication of the prescribed medication and vulnerability of the patient, with integration of this

information into the clinical decision rule, would increase alert specificity and thus the efficiency of the alert management. Low alert specificity and limited usability of the CDSS are known reasons for limited therapy changes [33, 34]. Other indications of the prescribed medication, as well as former negative experiences with the advised drug, were the primary reasons for not changing therapy. Therefore, it would be useful to integrate more patient characteristics (e.g. frailty, drug indication, former experience with specific drugs) into the clinical decision rule. A precondition is that these characteristics are coded in the pharmacy information system and can be easily shared with the computerised physician order entry system. This approach, also referred to as 'advanced clinical decision support', can substantially increase alert specificity [28, 35].

Anxiety has previously been identified as a barrier to medication change; conversely, trust in healthcare providers is a facilitator [18, 21, 22]. A patient being accustomed to their current medication is not recognised as a barrier in the literature on guideline non-adherence, which is probably because most previous studies have focused on the start of therapy, but it is a well-known issue from the perspective of deprescribing [31, 32]. Furthermore, the literature on the management of CDSS alerts indicates that alerts on first-time prescriptions are more likely than those regarding repeat prescriptions to lead to intervention [29, 36].

This mixed-methods study has strengths and limitations. One major strength is its combination of quantitative and qualitative data. Furthermore, the study was performed in daily clinical practice, revealing the reality of the broad implementation of the investigated clinical decision rules. However, one consequence of using routine care data is that the available patient data are limited to general characteristics and drug use. Furthermore, our data source meant it was not possible to include a control group, so the causality of the found associations needs further investigation. The pharmacists participated voluntarily in this project, which may have led to selection bias towards pharmaceutical care-focused pharmacies. The differences between pharmacies in terms of the proportion of alerts for which the management of alerts was recorded reflect the variability of pharmacists' attitudes and pharmacy daily practice (e.g. local priorities and local prescribing policy, proportion of elderly patients, consensus with guideline).

Another factor to consider is that alert management and registration of the alert management in the CDSS can be incomplete despite pharmacists being trained in registration of the alert management. However, the availability of drug dispensing history data enabled us to assess all the data for consistency.

Another limitation is that only pharmacists' viewpoints were evaluated in the qualitative part of our investigation. For a more comprehensive view and further research, the experiences of the general practitioner and the patients should be also taken into account.

5 Conclusion

This study revealed that clinical decision rules can be used to detect inappropriate drug use in older patients. Pharmacists registered a persistent drug therapy change in 8.7% of the managed drug therapy alerts, suggesting that CDSS alerts are a useful tool for implementing PIM guidelines for older patients in community pharmacy practice.

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Compliance with Ethical Standards

Conflict of interest LM, MH, AF, PAFJ and MLB have no conflicts of interest that are directly relevant to the content of this study.

Author contributions All authors contributed to the study design, the data interpretation and the manuscript. LM and MH performed the data analysis and drafted the manuscript. All authors approved the final manuscript.

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Ethics and confidentiality Formal consent is not required for this type of study. This study was not subject to the Dutch Medical Research Involving Human Subjects Act. The UPPER institutional review board reviewed the study, and the research was conducted in compliance with its requirements. To protect patients' privacy, only anonymous data were extracted from the clinical decision support system. These data could not be used to identify individual patients or pharmacies. Informed consent was obtained from all pharmacists who participated in the interview study.

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