A quality improvement study of the implementation and initial results of a pragmatic clinical decision support system in the community pharmacy setting

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Abstract

Background A six year collaboration between academics, community pharmacists and informaticians, led to the development of nine guidelines for a clinical decision support system, enhancing community pharmacists' ability to address drug-related problems and improve care.

Aim The objective of this study was to assess the efficacy of clinical decision support system rules in enhancing medication management within the community pharmacy setting. This was achieved through retrospective monitoring of real-world usage and measuring the pharmacotherapeutic impact of the rules.

Method In 2019, a retrospective observational evaluation appraised the acceptance rate of the clinical decision support system components in 490 Belgian pharmacies. Among these, 51 pharmacies underwent a longitudinal analysis involving (i) co-prescription of methotrexate and folic acid, (ii) gastroprotection with non-steroidal anti-inflammatory drugs, and (iii) drug combinations causing QT prolongation. The study period spanned one year pre-launch, one year post-launch, and two years post-launch.

Results 80% of targeted pharmacies used 7 of the 9 rules. After four years, methotrexate-folic acid co-prescription increased 4%, reaching 79.8%. Gastroprotection improved by 3% among older patients and 7.47% in younger individuals (<70 year) with multiple risk factors. The QT prolongation rules faced implementation difficulties.

Conclusion Pharmacists' acceptance of the developed rules was high and coincided with a decline in drug-related problems, holding potential public health impact. This real-world data can inform the future implementation of such systems, as it demonstrated the need for more detailed data-gathering and more intensive training of pharmacists in the handling of more complex problems such as QT prolongation.

Keywords

Pharmacists, drug-related side effects and adverse reactions, clinical decision support system (CDSS), software, pharmaceutical services, Belgium

Impacts on practice

- By providing pharmacists with real-time alerts during drug dispensing, clinical decision support systems (CDSS) can help prevent drug-related problems (DRP) such as adverse drug reactions, drug interactions and medication errors, which results in better overall pharmaceutical care.
- This technology has the potential to improve pharmaceutical care and patient safety by reducing the occurrence of DRP, leading to fewer hospitalizations and adverse effects. Additionally, CDSS can help improve medication adherence and reduce medication-related costs, which positively impact patient quality of life and healthcare outcomes.
- To improve the CDSS effectiveness, more data needs to be obtained to further strengthen the link between CDSS implementation and research.
- Pharmacists must receive comprehensive training to handle mor e complex CDSS interventions.

Introduction

Drug-related problems (DRPs) are a major cause of hospitalizations, increased morbidity and mortality. In 2008, the HARM study revealed that 5.6% of unplanned hospital admissions were medication-related, with 46% being avoidable and 15% linked to non-adherence to medication [1]. In Belgium, this amounted to approximately 42 000 annual hospitalizations, costing over 200 million euros [2]. According to a follow-up study conducted in the Netherlands in 2017, the HARM recommendations however did not reduce avoidable admissions, particularly among older patients [3]. A systematic review showed that 47% of all medication errors tied to 7 drugs or drug classes, including methotrexate, non-steroidal anti-inflammatory drugs (NSAID), opioids and acetylsalicylic acid [4].

The extent of these problems necessitates comprehensive interventions, including improved pharmaceutical care in the community setting [5]. A computerized system that supports the decision-making of the community pharmacist, i.e. a clinical decision support system (CDSS), has the potential to improve this care beyond simply providing education and training about DRPs [6–8]. CDSS can also consider certain person-related factors such as age, sex, registered diseases and drug intake. Potentially inappropriate or missing medication can be detected algorithmically and, if desired, specific vulnerable groups such as patients over 70 or those with chronic conditions and polypharmacy can be targeted [9–11]. A CDSS, however, does not eliminate the need for an individualised clinical assessment [12]. Notably, these CDSS rules differ from the drug-drug interaction screening that is active in the majority of Belgian pharmacies [13]. While CDSS initiatives are reviewed in general, limited reports discuss large-scale implementation and real-world use in community pharmacies [14,15].

KOVAG, an East Flemish community pharmacists association and a major shareholder of the software company Officinall®, initiated a CDSS development. The context was to support the dispensing process based on clinical guidelines and consequently reduce DRPs. Five years after implementing the first rule, we conducted a quality improvement analysis to assess these efforts.

Aim

The objective of this study was to assess the efficacy of CDSS rules in enhancing medication management within the community pharmacy setting. This was achieved through retrospective monitoring of real-world usage and measuring the pharmacotherapeutic impact of the rules.

Ethics approval

Ethics approval was not required as the retrospective descriptive research was conducted using fully anonymised dispensing data [16]. Informed consent was obtained from all individual community pharmacists prior to the start of this study.

Method

Study Design

This study assessed the acceptance rate and active use of the Clinical Decision Support System (CDSS) as well as the longitudinal pharmacotherapeutic impact of three selected decision rules. In total 490 Belgian pharmacies in the customer base of Officinall® were included. The pharmacy software sequentially integrated upto nine decision rules that target DRPs. These rules examined the drug history of each patient and provide personalized recommendations through a pop-up window during dispensing. A summary of these decision rules and their design rationale can be found in Table 1. Flowcharts were developed for each decision rule to determine when an alert would appear for a particular drug delivery scenario. An example flowchart for a CDSS rule about methotrexate and folic acid is shown in Figure 1, and additional details on the development and structure of the rules can be found in the supplementary materials. All CDSS rules were activated upon implementation by default through regular software updates, with deactivation possible in the individual pharmacist software settings.

CDSS under evaluation (intervention)

Due to the complexity of the data analyses, the following three decision rules were selected and investigated.

The **CDSS rule 'methotrexate'** (Table 1; Figure 1) was triggered by the dispensing of methotrexate (ATC see supplementary information) and included 2 alerts with the aim to 1) prevent fatal

dosing errors of methotrexate due to mistakes between daily dose (cancer) and weekly dose (inflammatory diseases) and 2) reduce side effects due to the lack of concomitant use of folic acid [4,17].

Two alerts were implemented, the first one determined the indication for methotrexate (cancer or inflammatory diseases), and the second alert monitored methotrexate and folic acid dosage along with the time of intake and adherence to folic acid. Three research periods were considered: one year before the launch, one year after the launch, and two years after the launch.

The **CDSS rule 'Gastric protection with NSAID use'** (Table 1) was triggered based on the dispensing of an NSAID (ATC see supplementary information) but excluded glucosamine, chondroitin sulfate and the combination of naproxen with esomeprazole. This trigger generated three responses: 1) an inquiry about antecedents of a gastrointestinal ulcer or bleeding; 2) an inquiry about the presence of rheumatism and / or heart failure; 3) an alert to notify high-risk patients of either the absence of proton pump inhibitor (PPI) usage with the NSAID or the use of an insufficient PPI dose. The first two alerts required an additional question for the pharmacist. The answer was recorded in the patient record file. The third pop-up showed the patient's risk factors with the dispensing history of gastric protection. The action taken was not automatically recorded.

The patients risk for gastric complications enclosed patients over 70, patients with two or more risk factors or patients with a history of a gastrointestinal ulcer or bleeding. Risk factors included age between 60 and 70, rheumatism, heart failure, diabetes, or the use of any of these medications: acetylsalicylic acid, spironolactone, antithrombotics, oral glucocorticoids, selective serotonin reuptake inhibitor (SSRI) and selective serotonin and noradrenalin reuptake inhibitor (SNRI) and use of a high dose nonselective NSAID. Gastric protection is adequate if it complies with the NHG standard [18] (ATC overview of gastric protection in supplementary information). The data collection coincided with the previous research periods.

The trigger of the **CDSS rule ' Risk estimation for QT prolongation'** (Table 1) is the interaction between 2 or more drugs that appear in list 1 or list 2 of CredibleMeds and cause QT-prolongation or Torsades de Pointes [19]. The CDSS identifies these based on their ATC class and availability on the Belgian market (ATC in supplementary information). Patient specific risk factors such as age, female sex, electrolyte disturbances, congenital long QT syndrome, cardiovascular and other comorbidities were also

taken into account [20–22]. The CDSS calculates the risk score developed by Vandael [23]. For this decision rule, two research periods were investigated: period 1 at the launch, and period 2 one year after the launch of the system.

Points of Evaluation (Describing the three time-periods)

To address the first aim (i) What was the acceptance rate and active use of the CDSS, we conducted an assessment on 27/01/2019 to determine the activation status of the 9 decision rules in the Belgian costumer base of Officinall®. The decision to deactivate specific pop-ups in their software was at the discretion of the pharmacist and was tracked by Officinall® support staff as part of the regular follow-up-procedure monitoring the software and data updates of the systems installed in the pharmacies.

The second aim (ii) What was the longitudinal pharmacotherapeutic impact of the 3 selected decision rules, was limited to the previously described 3 CDSS rules due to the complexity of data analysis. These were chosen due to the diversity of the pharmacotherapeutic topics involved and their spread over time during implementation.

Indicators Used to Assess Impact

a) Methotrexate: dose and folic acid supplement: The following data were collected during the three research periods: the number of patients using methotrexate with or without folic acid and the number of alerts in period 2 and period 3.

b) Gastric protection with NSAID use: The following data were collected: 1) the number of patients older than 70 with an NSAID prescription without gastric protection, 2) the number of patients older than 70 with an NSAID prescription with gastric protection 3) the number of patients under 70 with an NSAID prescription without gastric protection, 4) the number of patients under 70 with an NSAID prescription without gastric protection and having two or more risk factors and finally 5) the number of patients under 70 with an NSAID prescription with gastric protection and having two or more risk factors.

c) Risk estimation of QT prolongation: Data collected during two research periods included: 1) Number of pop-ups, 2) Actions through the QT pop-up: pharmacists response rate (x%), shown in Table 2: pop-ups ignored, medication dispensed although pop-up, medication dispensing postponed, no dispensing of medication, 3) Average number of pop-ups per pharmacy and 4) Average number of pop-ups per day. The handling of this decision rule was concisely registered in the patient file, as shown in Table 2.

Statistical Analyses

Retrospective descriptive research was conducted using complete individual, fully anonymized dispensing data from selected time periods. The handling of the 'QT interactions' decision rule was registered in the patient record. The data were analysed anonymously during the specified time periods.

Sample Description

The study sample consisted of 51 pharmacies actively working with the three selected decision rules. A call for informed consent was sent to 356 Dutch-speaking Officinall®-using pharmacies in August 2018, and 56 pharmacists provided consent for data analyses.

Ethical Considerations

A call for informed consent was sent to 356 Dutch-speaking Officinall®-using pharmacies, and 56 pharmacists provided consent for data analyses. The data pertaining to pharmacy and patient information were anonymized to ensure confidentiality.

Results

Active implementation of the CDSS rules

Figure 2 shows the use of the CDSS rules in the 490 pharmacies using the Officinall® software on 27/01/2019. Only 5 pharmacies (1%) globally disabled the CDSS. In more than 80% of the pharmacies 7 out of 9 CDSS rules were active. The low acceptance for the pneumococcal decision rule was impacted by a software glitch during the rollout of that update and was thus not analysed further.

Impact of the CDSS on the correct dosing of methotrexate and the addition of folic acid

In the second study period 536 pop-ups appeared in the 51 pharmacies. In study period 3, the number of pop-ups was approximately the same, namely 564 pop-ups. Over the 3 study periods the indication for methotrexate was registered 2102 times in the pharmaceutical file and 98.7% of these registrations was for inflammatory conditions. The number of patients receiving folic acid supplementation over the three periods showed an increase from 75.8% before the implementation (478 patients), to 78.2% in the first

year after the launch (503 patients) and 79.8% in the second year after the launch (567 patients), as shown in Figure 3.

Impact of the CDSS on gastric protection during NSAID use

Patient counts who received an NSAID with or without adequate gastric protection and regardless of age per requested period was: 51738 (period 1), 51903 (period 2) and 53312 (period 3). Patients over 70 with adequate gastric protection over the three periods increased from 35.5% in period 1 (2757 patients), to 37.2% in period 2 (2882 patients) and 38.4 % in period 3 (3075 patients). Patients under 70 who used an NSAID with adequate gastric protection and 2 or more risk factors increased over the 3 periods from 61.7% before implementation (3109 patients), to 65.7% in the first year after the launch (3303 patients) and 69.2% in the second year (3444 patients), as shown in Figure 4. The number of patients older than 70 who received an NSAID also remained stable, i.e. 5010 patients before implementation of the decision rule, to 4866 patients in the first year after launch (-1%) and 4927 patients in the second year after launch (-1%). Similar figures were observed for patients younger than 70 with 2 or more risk factors: 5039 patients in period 1, 5030 patients in period 2 (-1%) and 4979 patients in period 3 (-1%).

Impact of the CDSS on the risk estimation in QT prolongation

The QT-related CDSS rule acceptance rate was noticeably lower, namely 29% (Figure 2) possibly explained by the complexity of the algorithm and the strong recommendation to follow the preparatory e-learning before activation of this rule [23]. Analyses were performed over 2 time periods, which included 40 pharmacies in period 1 and 76 pharmacies in period 2. Results are presented in Table 3. The number of alerts handled was 60.3% for period 1 and 65.0% for period 2. As for the medication dispensing, although the pop-up appeared, the rate was 57.06% in period 1, which improved to 59.95% in period 2.

Discussion

The study aimed to evaluate the effectiveness of a CDSS initiative in reducing DRPs in the community pharmacy setting. During drug dispensing, these rules support the pharmacist's clinical decision making. Various studies have shown that CDSS implemented through computer software is superior in avoiding DRPs, as compared to non-computerized implementations [8,24].

The rule acceptance was high, although the option to ignore the alerts, as described in the literature, cannot be excluded [12]. This study showed that at least 80% of pharmacies work with 7 of the 9 CDSS components. It is always possible for pharmacists to ignore the alerts and for 8 of the 9 decision rules we have no data on how frequently this occurs. For the QT-prolongation rule, one in three pharmacists used this option (Table 3). This was similar to the 30% that was found in a CDSS study in community pharmacy in the Netherlands [10]. However, we should not conjecture that this happens with the same frequency with the less complex CDSS rules, nor should we presume that every pharmacist with an active CDSS reacts to the advice generated by the software.

The introduction of the CDSS was associated with a reduction in DRPs in each of the 3 decision rules assessed. Before implementation of the methotrexate alert, 75.8% of patients received folic acid supplementation. This is comparable to results obtained in a French retrospective cohort study, namely 73.6% [25]. Four years after launch we observed an increase of almost 4%. This could be an underestimation, as folic acid is also available without a prescription and may therefore be absent from the patient file. However, this number is considerably lower than the one recorded in the Netherlands where, likely due to the implementation of a mandatory quality indicator, only 10% of the pharmacies score below 95.5%. [26]. In the Belgian pharmacies studied, there were, on average, 13 patients taking methotrexate, and a potential DRP was thus avoided in one patient in every other pharmacy. Extrapolating this result to the total Belgian population would yield a total number of avoided DRPs of approximately 2500.

For the decision rule 'NSAID and gastric protection', 4 years after launch, there was an increase of adequate gastric protection for at-risk 70+ patients of 3%. For patients under 70 with 2 or more risk factors this increase amounted to 8.2%. In the 51 analyzed pharmacies this 3% increase amounted to 318 extra people over 70 detected with a strong risk reduction for gastrointestinal bleeding. If extrapolated to all Belgian pharmacies, this would amount to around 30 000+ patients a year. The same extrapolation for

patients younger than 70 with 2 or more risk factors, amounts to 60 000+ patients. The figures for patients at risk older than 70 clearly indicate an underuse of PPI in this age category. This trend is in line with the national figures for the combination of NSAID and PPI in the drug use of the over-65's [27].

In terms of the decision rule for QT prolongation, we observed an increased number of pop-ups in period 2 compared to period 1. Despite a slight increase in dispensing when a pop-up appeared, fewer pop-ups were ignored in period 2. Overall, all other recorded data indicates a possible positive change from period 1 to period 2 conceivably due to increased familiarity with the QT-algorithm. Several factors, alone or in combination, possibly contributed to this outcome: the complexity of this theme, the unfamiliarity of this topic for physicians and the necessity for pharmacist physician interactions [28]. The active use of each individual CDSS rule is the choice of the individual pharmacist. This makes it possible to focus selectively on a particular DRPs and/or avoid alert fatigue. Studies on CDSS for physicians have clearly shown that overwhelming physicians with many or unimportant pop-ups causes alert fatigue [11].

Overall, despite some limitations, we can conclude from this study that CDSS rules can have a positive impact on DRPs. The sequential CDSS implemented within the Officinall® software is a simple, feasible and inexpensive way of obtaining tangible results at the population level. Our study also informs future quality-improvement initiatives. The initial lack of registration by the computerised CDSS of the actions taken by the pharmacists limited our study. A balance will need to be found between gathering more information and increasing input complexity, as the latter may result in alert fatigue. Improved registration is undoubtedly of scientific interest, but it should also serve as valuable feedback for the pharmacy team, enabling them to monitor pharmaceutical care quality and its impact effectively. However, additional data-gathering should be compatible with the pharmacy's day-to-day functioning. While it might improve research, it's essential to consider that it could reduce participation and diminish the 'real-world' impact of the CDSS. A user survey, in-depth interviews, and usability testing should therefore be part of an improved implementation strategy. Communication and theoretical training for pharmacists can significantly enhance the implementation of the more complex CDSS, as demonstrated by the study on the QT-prolongation risk tool. Facilitating international data exchange and sharing implementation methods would be instructive for informing future developments effectively.

Conclusion

A CDSS was implemented in community pharmacy software through the sequential development of 9 decision rules. In this retrospective analysis, we showed that the acceptance rate of the CDSS was high and for the 3 studied CDSS rules a positive trend in DRPs was observed. At the population level, this inexpensive intervention could have a sizable impact. These 'real-world' data analyses provide valuable insights for the ongoing quality-driven development and implementation of the CDSS. They have highlighted the necessity for more detailed data-gathering and intensive training of pharmacists in handling issues such as QT prolongation effectively.

Declarations

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Conflicts of interest/Competing interests: 'The authors have no conflicts of interest to declare'.

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414 **Tables**

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416 **Table 1 Overview of the various CDSS rules that were implemented between 2014 and 2019.**

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Table 1: Overview of CDSS implemented decision rules in chronological order

Decision rule	Launch	Directive	Target outcome
1. Correct dosage of methotrexate and addition of folic acid	March 2015	BCFI [a] [29]	↓ fatal dosing errors for methotrexate and ↓ side effects due to a lack of folic acid intake.
2. NSAID and gastric protection	June 2015	KNMP [b] guideline [30]; NHG [c] standard stomach complaints [18]; HARM [d] study [1]	↓ gastric complications
3.Acetylsalicylic acid and gastric protection	June 2015	KNMP guideline [30]; NHG standard stomach complaints [18]	↓ gastric complications
4.Isotretinoin dispensing precautions	July 2015	BCFI [29]	↓ teratogenic and embryotoxic effects
5.Use of calcium and vitamin D in osteoporosis	August 2015	CBO [e] guidelines for osteoporosis and fracture prevention [31]; BCFI [29]; FRAX [f] tool [32]	↑ adherence to calcium and vitamin D.
6.Identification of individuals within the target groups for influenza vaccination	September 2015	Recommendations Hoge Gezondheidsraad [33]	↑ flu vaccination rate in high-risk patients
7.Use of laxatives with opioids	December 2015	Integraal kankercentrum Nederland, Pain, National Guideline 2.0; BCFI [29]	↓ opioid constipation

8.Risk estimation for QT prolongation	October 2016	CredibleMeds [19]; RISQ-PATH study	↓ risk of QT prolongation and (fatal) Torsades de Pointes.
9.Adherence to the pneumococcal vaccination schedule	January 2019	Recommendations Hoge Gezondheidsraad (2014) [33]	↑ adherence to pneumococcal vaccination schedule

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419 [a] BCFI: Belgisch Centrum voor Farmacotherapeutische Informatie

420 [b] KNMP: Koninklijke Nederlandse Maatschappij ter bevordering der Pharmacie

421 [c] NHG: Nederlands Huisartsen Genootschap

422 [d] HARM: Hospital Admissions Related to Medications

423 [e] CBO: Community-Based Organizations

424 [f] FRAX: Fracture Risk Assessment Tool

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428 **Table 2: Registration of handling QT alert in patient file**

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Table 2: Registration of handling QT alert in patient file[a]

Options for the pharmacist to manage identified interaction of the QT decision rule		
1	***2***	***3***
No dispensing of the interacting drug	Dispensing the drug despite the interaction	To follow up on the interaction in the future
➢ Stop medicine	➢ No problem for the physician	➢ Physician to be contacted
➢ Alternative medicine	➢ Physician monitors patient	➢ Physician not available
➢ Own comment	➢ Delivered with patient warning (palpitations and Torsades de Pointes)	➢ Own comment
	➢ Own comment	

430 [a] The QT decision rule in our study provided the pharmacist with several options to manage the identified
431 interaction. The pharmacist had the flexibility to choose from three possible decisions. Each decision was
432 influenced by various factors and considerations, which are explained in the following table.

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436 **Table 3: Comparison of pharmacists handling QT alerts – results from 2 time periods**

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Table 3: Comparison of pharmacists handling QT alerts – results from 2 time periods

	Period 1 15/12/ 2016 - 7/03/2017 *49 pharmacies*	**Period 2** 15/12/2017 - 7/03/2018 *76 pharmacies*
Number of participating pharmacies		
Number of total QT-pop ups	1006	2869
Actions through the QT- pop up:		
• **Pop-ups ignored**	**399** (39.66%)	**1003** (34.96%)
• **Pop-ups handled**	**607** (60.34%)	**1866** (65.04%)
o *Medication dispensing although the pop-up appeared (2: Table 2)*	***574*** *(57.06%)*	***1720*** *(59.95%)*
o *Medication dispensing postponed, more information required. (3: Table 2)*	***30*** *(2.98%)*	***125*** *(4.36%)*
o *No dispension of medication (1:Table 2)*	***3*** *(0.30%)*	***21*** *(0.73%)*
Average # of QT-pop-ups per pharmacy	25.15	37.75
Average # QT-pop-ups per pharmacy per day (83 days)	0.3	0.45

438

439 **Figures**

440

441 **Figure 1**

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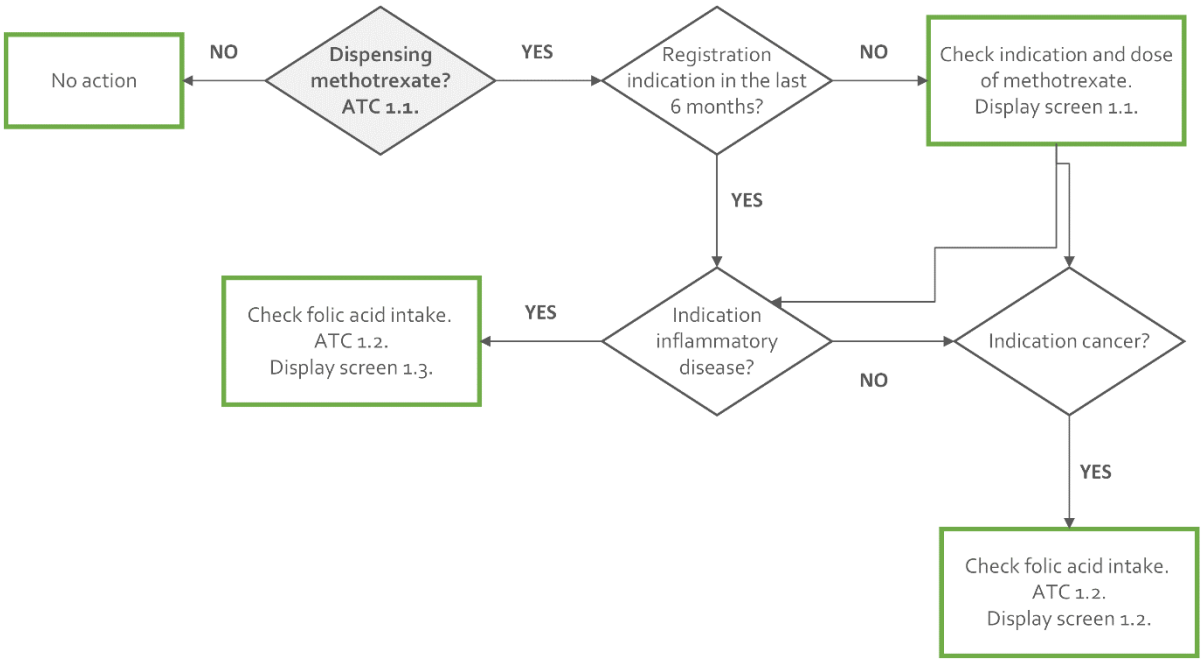

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446 ***Figure 1: flowchart of the CDSS-decision rule - methotrexate and folic acid***

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448 **Figure 2**

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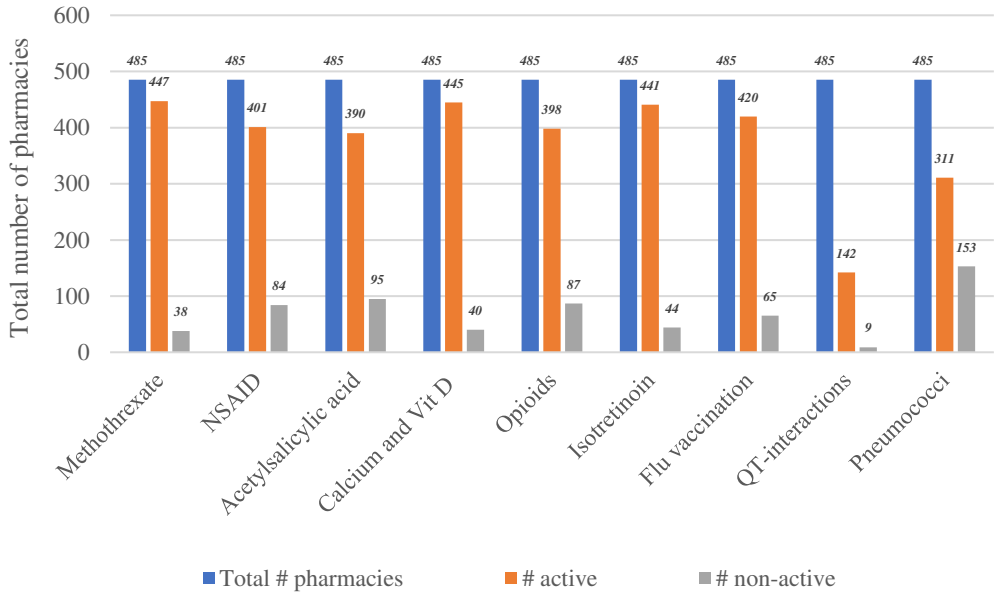

Figure 2 : Active use of the CDSS rules in the 490 pharmacies

Active = the pop-up alert of this topic is activated and being used.
Non-active = the pharmacist has manually deactivated this CDSS rule.

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452 **Figure 3: Impact of the CDSS on the number of patients using folic acid supplementation**

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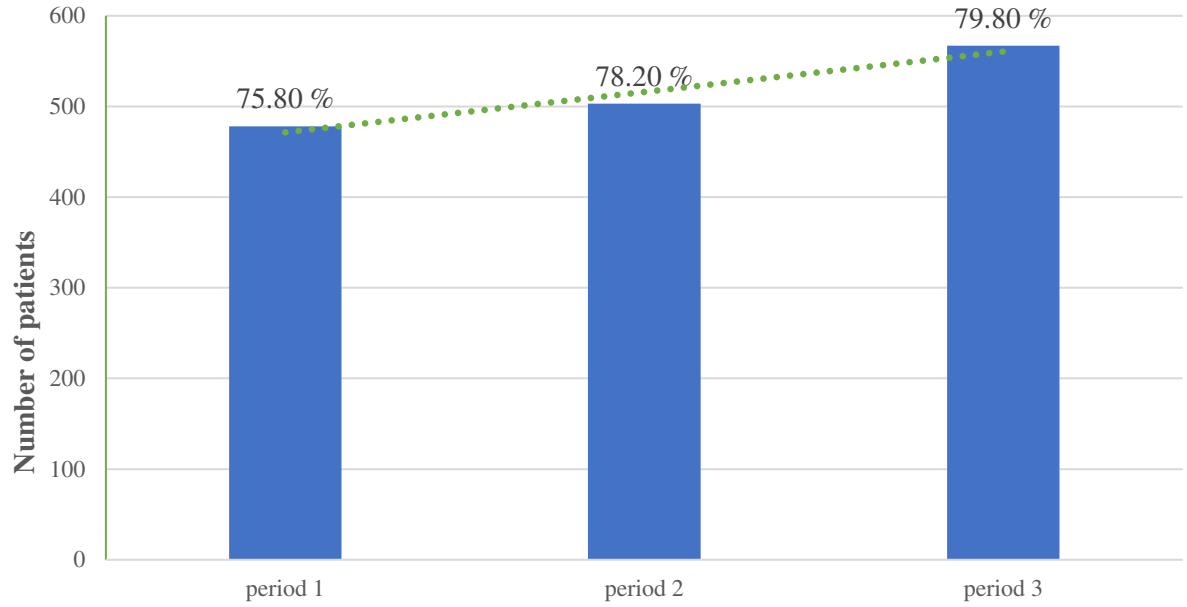

Figure 3: Impact of the CDSS on the number of patients using folic acid supplementation

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457 **Figure 4: Impact of the CDSS on gastric protection during NSAID use**

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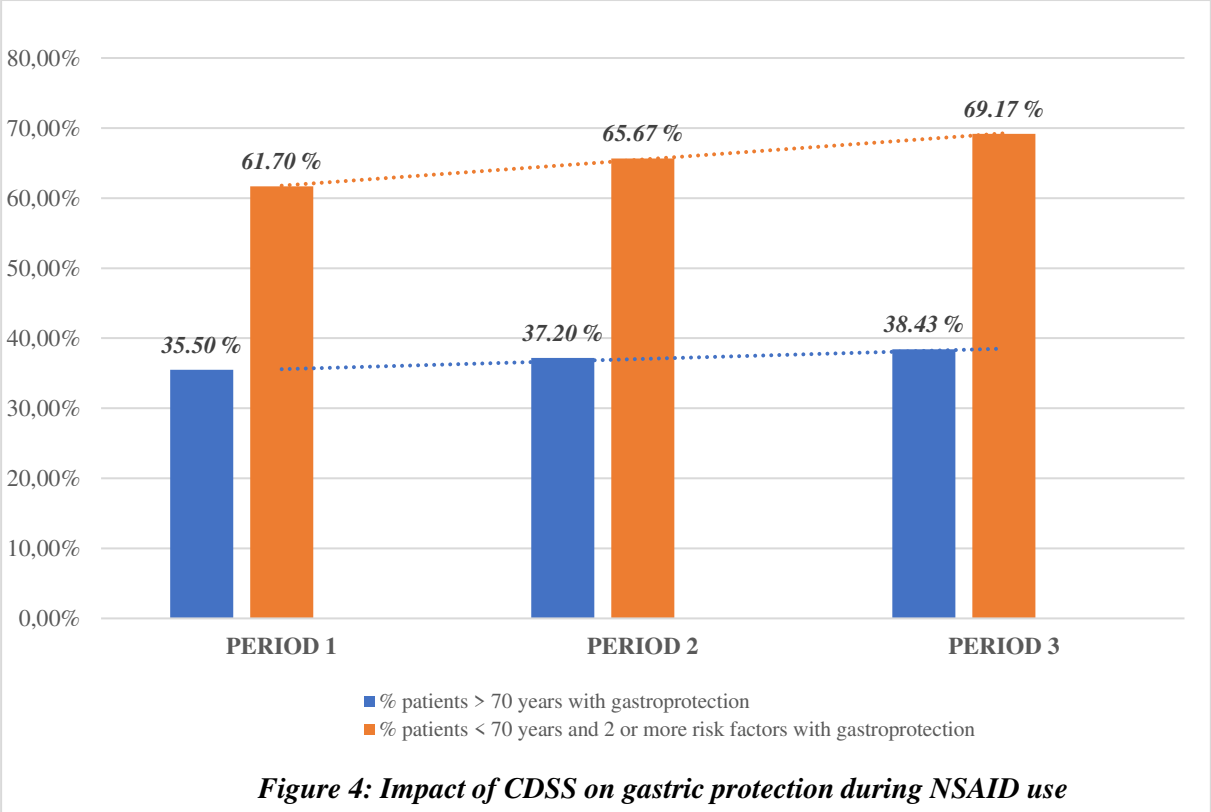

Figure 4: Impact of CDSS on gastric protection during NSAID use

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