



**HAL**  
open science

## A randomized simulation trial evaluating ABiMed, a clinical decision support system for medication reviews and polypharmacy management

Abdelmalek Mouazer, Sophie Dubois, Romain Léguillon, Nada Boudegzdame, Thibaud Levrard, Yoann Le Bars, Christian Simon, Brigitte Séroussi, Julien Grosjean, Romain Lelong, et al.

### ► To cite this version:

Abdelmalek Mouazer, Sophie Dubois, Romain Léguillon, Nada Boudegzdame, Thibaud Levrard, et al.. A randomized simulation trial evaluating ABiMed, a clinical decision support system for medication reviews and polypharmacy management. 2024. hal-04725448

**HAL Id: hal-04725448**

**<https://hal.science/hal-04725448v1>**

Preprint submitted on 8 Oct 2024

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial - ShareAlike 4.0 International License

# A randomized simulation trial evaluating ABiMed, a clinical decision support system for medication reviews and polypharmacy management

Abdelmalek Mouazer<sup>a</sup>, Sophie Dubois<sup>e</sup>, Romain Léguillon<sup>a,b</sup>, Nada Boudegzdame<sup>a</sup>, Thibaud Levrard<sup>c</sup>, Yoann Le Bars<sup>c</sup>, Christian Simon<sup>c</sup>, Brigitte Séroussi<sup>d</sup>, Julien Grosjean<sup>a,b</sup>, Romain Lelong<sup>a,b</sup>, Catherine Letord<sup>a,b</sup>, Stéfan Darmoni<sup>a,b</sup>, Karima Sedki<sup>a</sup>, Pierre Meneton<sup>a</sup>, Rosy Tsopra<sup>f,g</sup>, Hector Falcoff<sup>e</sup>, Jean-Baptiste Lamy<sup>a,\*</sup>

<sup>a</sup>INSERM, Université Sorbonne Paris Nord, Sorbonne Université, Laboratory of Medical Informatics and Knowledge Engineering in e-Health, LIMICS, Paris, France

<sup>b</sup>Department of Biomedical Informatics, Rouen University Hospital, France

<sup>c</sup>EIG SAS, 92400 Courbevoie, France

<sup>d</sup>Département de Médecine Générale, Université de Rouen, France

<sup>e</sup>SFTG Recherche (Société de Formation Thérapeutique du Généraliste), Paris, France

<sup>f</sup>Université Paris Cité, Sorbonne Université, Inserm, Centre de Recherche des Cordeliers, F-75006 Paris

<sup>g</sup>Department of Medical Informatics, AP-HP, Hôpital Européen Georges-Pompidou, F-75015 Paris, France

## Abstract

**Background:** Medication review is a structured interview of the patient, performed by the pharmacist and aimed at optimizing drug treatments. In practice, medication review is a long and cognitively-demanding task that requires specific knowledge. Clinical practice guidelines have been proposed, but their application is tedious.

**Methods:** We designed ABiMed, a clinical decision support system for medication reviews, based on the implementation of the STOPP/START v2 guidelines and on the visual presentation of aggregated drug knowledge using tables, graphs and flower glyphs. We evaluated ABiMed with 39 community pharmacists during a randomized simulation trial, each pharmacist performing a medication review for two fictitious patients without ABiMed, and two others with ABiMed. We recorded the problems identified by the pharmacists, the interventions proposed, the response time, the perceived usability and the comments. Pharmacists' medication reviews were compared to an expert-designed gold standard.

**Results:** With ABiMed, pharmacists found 1.6 times more relevant drug-related problems during the medication review ( $p = 1.1 \times 10^{-12}$ ) and proposed better interventions ( $p = 9.8 \times 10^{-9}$ ), without needing more time ( $p = 0.56$ ). The System Usability Scale score is 82.7, which is ranked "excellent". In their comments, pharmacists appreciated the visual aspect of ABiMed and its ability to compare the current treatment with the proposed one. A multifactor analysis showed no difference in the support offered by ABiMed according to the pharmacist's age or sex, in terms of percentage of problems identified or quality of the proposed interventions.

**Conclusions:** The use of an intelligent and visual clinical decision support system can help pharmacists when they perform medication reviews. Our main perspective is the validation of the system in clinical conditions.

**Keywords:** Clinical decision support systems, Polypharmacy management, Medication review, Visual analytics, STOPP/START, Simulation trial

## 1. Introduction

The worldwide population of people aged 65 or over is expected to double, rising from 761 million to 1.6 billion by 2050 [1]. Many of them are exposed to polypharmacy (taking 5+ long term drugs [2, 3]), which is associated with potentially inappropriate medications (PIMs) and drug-related problem (DRP) including adverse drug events (ADE) [4]. In France, inappropriate

prescriptions concern more than one in two elderly patients and their direct cost is 507 million € per year [5].

General practitioners (GPs) are open to deprescribing inappropriate drugs [6], but often lack time and pharmacological knowledge. Pharmacists could play a key role [7], by conducting Medication Review (MR), "a structured evaluation of a patient's medicines with the aim of optimizing medicines use and improving health outcomes. This entails detecting drug-related problems and recommending interventions" [8]. MR can change practices [9], reduce hospitalizations [10, 11] and saves costs [12, 13]. However, MR is a complex task, requiring efficient collaboration with the GP, but also strong skills in clinical pharmacy [14, 15].

To perform MR, pharmacists can be assisted by drug databases offering a pharmaceutical description of all marketed drugs, and clinical practice guidelines supporting MR [16, 17], e.g. STOPP/START [18, 19]. It includes STOPP rules for detecting PIMs, and START rules for detecting potential omissions. Studies demonstrated its ability to improve prescribing appropriateness [20]. However, drug databases provide one page per drug, which is tedious when the patient takes many drugs, and guidelines, in their paper format, are time-consuming

\*Corresponding author

Email addresses: malikmouazer@gmail.com (Abdelmalek Mouazer), sophie.dubois@polesante13.fr (Sophie Dubois), romain.leguillon@chu-rouen.fr (Romain Léguillon), nadaboudegzdame@gmail.com (Nada Boudegzdame), tlevrard@eig.fr (Thibaud Levrard), ylebars@eig.fr (Yoann Le Bars), csimon@eig.fr (Christian Simon), brigitte.seroussi@aphp.fr (Brigitte Séroussi), julien.grosjean@chu-rouen.fr (Julien Grosjean), romain.lelong@chu-rouen.fr (Romain Lelong), catherine.letord@chu-rouen.fr (Catherine Letord), stefan.darmoni@chu-rouen.fr (Stéfan Darmoni), sedkikarima@yahoo.fr (Karima Sedki), pierre.meneton@inserm.fr (Pierre Meneton), rosytsofra@gmail.com (Rosy Tsopra), hector.falcoff@sfr.fr (Hector Falcoff), jean-baptiste.lamy@inserm.fr (Jean-Baptiste Lamy)

and difficult to apply in clinical routine [21].

Clinical Decision Support Systems (CDSSs) have been designed to overcome these limitations [22]. A recent scoping review [23] found 19 CDSSs for managing polypharmacy in the elderly. Most of them implement paper guidelines by automating their recommendations, or give access to drug knowledge. But the review highlighted limits: the targeted user is often the physician instead of the pharmacist, and the output is often displayed in a non-friendly format (*e.g.* long text).

To overcome these limitations, we designed ABiMed [24, 25], a CDSS for helping community pharmacists to perform type-3 MR (*i.e.* including patient interview and clinical data [8]). ABiMed associates two approaches: it implements STOPP/START rules but also provides aggregated drug knowledge in a visual format, based on visual analytics. The objective of this paper is to describe a randomized simulation trial [26] evaluating ABiMed in comparison to the usual practice. Our main hypothesis is that, with ABiMed, pharmacists will be able to identify more PIMs and DRP, and to propose better pharmaceutical interventions to solve these problems.

## 2. Materials and methods

### 2.1. Brief description of ABiMed

ABiMed is a CDSS for medication review and polypharmacy management [25, 24]. It helps at three levels: (1) it facilitates communication between pharmacists and GPs, and extracts patient data from the GP’s EHR; (2) it provides drug knowledge contextualized for the patient, in a visual format (Figure 1); and (3) it implements the STOPP/START v2 guidelines [18] through a rule-based system that takes into account drugs (ATC classes but also indications and doses), clinical conditions (ICD10 codes) and biology (LOINC codes and associated values). ABiMed integrates the Theriaque drug database [27]. It proposes a comparative mode, comparing the current treatment with the treatment after the interventions proposed during MR, to check that these interventions solve the problems identified without introducing new problems.

The current evaluation does not focus on the pharmacist-GP collaboration. For more details on ABiMed, system design, ergonomic assessment and qualitative evaluations, please refer to [25].

### 2.2. Recruitment

We recruited community pharmacists having a clinical practice in France. We excluded pharmacists refusing to participate or without Internet access. Pharmacists were recruited by emails, *via* lists of pharmacists from associations and territorial professional health communities. They were compensated for their participation. Pharmacists followed an online training session *via* webinar (one hour). We presented to them the project and its goal, the ABiMed software and the evaluation principles.

### 2.3. Clinical cases and gold standard

An expert comity including two pharmacists (S Dubois, R Léguillon), a GP (HF) and three researchers in health informatics with MD or PharmD (AM, RT, JBL) designed four clinical cases, A, B, C, D, based on realistic situations (Table 1). Each consisted of an elderly patient with polypharmacy, consulting his/her pharmacist for a problem leading to a MR. All clinical data was filled in the case; thus, during MRs, no data entry was needed.

Case	#drugs	#conditions	#problem	total CLEO score
A	8	8	6	10
B	7	7	5	7
C	5	6	6	7
D	5	5	5	11

Table 1: Metrics of the four clinical cases.

Intervention	without ABiMed		with ABiMed	
	#1	#2	#3	#4
Group G1	case A	case B	case C	case D
Group G2	case C	case D	case A	case B
Group G3	case B	case A	case D	case C
Group G4	case D	case C	case B	case A

Table 2: Definition of the four randomization groups.

For each case, a gold standard was devised. It consisted of a list of drug-related problems and, for each problem, a pharmaceutical intervention. Interventions consisted of deprescribing a drug, prescribing a new drug, replacing a drug, changing the dose, or prescribing lab tests. Each intervention was assigned a score using CLEO v3 clinical scale (CLinical, Economic and Organizational impacts of pharmacists’ interventions) [28], from 1 (minor) to 4 (vital).

### 2.4. Protocol

The study followed a sequential group protocol, in which each pharmacist first carried out two cases without ABiMed (*i.e.* control cases) online, and then two with ABiMed (*i.e.* test cases). Pharmacists were asked to use their usual resources when not having ABiMed. All pharmacists performed MRs both with and without ABiMed and solved the same cases, but with different order of passages. Pharmacists were randomized into 4 groups (Table 2). Control cases were carried out before test cases, to avoid any learning phenomenon when using ABiMed.

This protocol permits all pharmacists to test ABiMed, which allows collecting the qualitative opinion of all pharmacists, and increases the statistical power, each participant being its own control. Moreover, in previous studies, we found that participants in the control group lacked motivation and were more likely to give up, compromising the entire study.

The INSERM ethics evaluation committee (IRB00003888) reviewed and approved the study.

### 2.5. Data collected

For each pharmacist, we collected:

(1) demographic data (online questionnaire): age group, gender (male, female, other), number of MRs carried out the last year, previous knowledge of STOPP/START (Boolean).

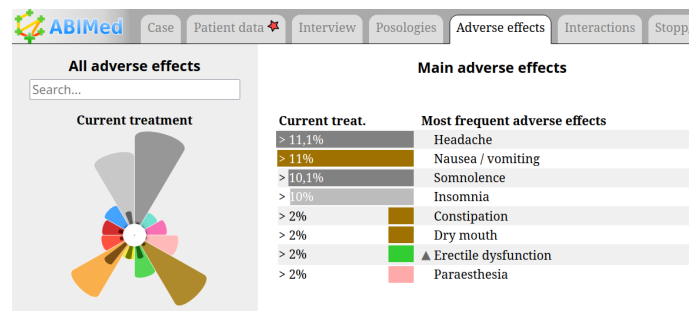
(2) for each case (automatic collection): problems identified and pharmaceutical interventions proposed by the pharmacist, response time.

(3) satisfaction questionnaire: SUS scale (System Usability Scale [29]) comprising 10 questions with 5 possible answers, and free comments.

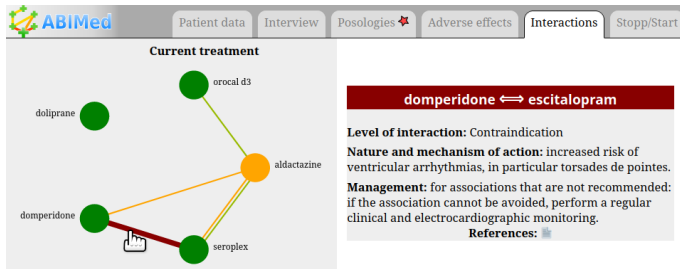
Clinical cases were corrected semi-automatically. Interventions were rated using CLEO scores, the maximum value was the value defined in the gold standard, and lower values were given for suboptimal interventions. The minimum value was -1, for harmful interventions. Interventions proposed by pharmacists were automatically matched with the gold standard. In

Drug	Current posology	Posology from SPC (considering indication, association, insufficiency)	Posology after medication review	Day dose
spironolactone altizide cpr	1 on morning	For arterial hypertension: maintenance dosage: 1/2-1 tablet/take, 1/day	1 on morning	altizide and potassium sparing agent — 15 mg spironolactone — 25 mg
allopurinol 300mg cpr	1 on evening	For gout: usual dosage: 2-10 mg/kg/day - in severe cases: max dosage: 900 mg/day  For gout (renal failure): usual dosage: adapt the dose - if renal clearance between 40-80ml/min: max dosage: 200 mg/day - in certain exceptional cases or in case of	1 on evening	allopurinol — 300 mg

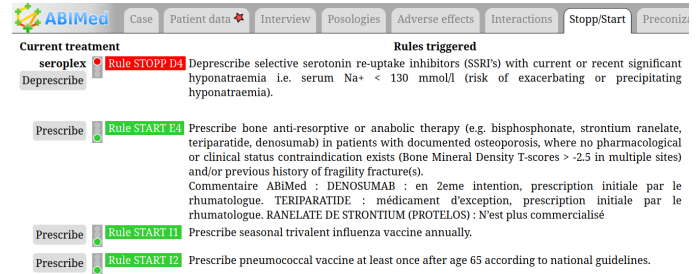
A: dosage tab



B: adverse effect tab



C: drug interaction tab



D: STOPP/START tab

Figure 1: Screenshots of ABiMed's tabs for decision support. A: table summarizing current dosages and recommended ones, taking into account age, renal and hepatic status, indications and drug associations; B: adverse effects profile expected with the entire drug order, presented as flower glyphs; C: drug interactions, presented as a radial graph; D: STOPP/START rules detected.

case of match, we considered the problem as identified and the intervention as having its maximum value. Then, cases were manually and blindly reviewed by S Dubois, HF and JBL. We verified problems and interventions, taking into account textual comments.

## 2.6. Criteria

The primary criterion was (1) the percentage of problems identified in the MR, obtained by dividing the number of problems the pharmacist identified by the number of problems in the gold standard.

Secondary criteria were:

- (2) the CLEO score ratio, obtained by dividing the sum of the pharmacist's interventions CLEO scores by the sum of the gold standard interventions CLEO scores,
- (3) the overall time spent to perform a MR,
- (4) the pharmacist perceived usability, measured by SUS.

For example, a pharmacist identified 2 problems in case #A and proposed 2 interventions, of CLEO score 1 and 2; the percentage of problems identified is 33.3% (since case #A has 6 problems) and the CLEO score ratio is 30% (since case #A has a total of 10 CLEO score and only 1 + 2 = 3 were proposed).

## 2.7. Evaluation website

The evaluation website for the pharmacists was based on ABiMed. It includes two interfaces for MRs. The "with ABiMed" interface included 8 tabs: (1) the clinical case presentation, (2) the patient data (drugs taken, clinical conditions and lab tests), (3) the patient interview, (4-7) the decision support tabs (see Figure 1), (8) the interface for the pharmacist to enter his interventions and comments. The "without ABiMed" interface was similar but without tabs #4-7.

## 2.8. Statistical analysis

Statistical analysis was performed blindly using R, with a risk  $\alpha = 5\%$  and bilateral tests. The unit of analysis is the MR, i.e. a given clinical case solved by a given pharmacist.

Criteria #1-3 were compared using Welch two-Sample t-test. Times were logged before comparison, to reduce the impact of long durations. Linear Mixed Models (LMM) were used for finer analysis. Two models were tested for each criterion #1-3: a simple model considering three fixed factors, ABiMed, Case and Group, and a complex model considering ABiMed, Case, Age class of the pharmacist, Sex, Previous knowledge of STOPP/START and Number of MRs performed the last year, as well as their interactions with ABiMed. For each, the random effect was modeled according to the pharmacist ID. Type-III ANOVA was used for computing  $p$ -values.

The carryover effect was evaluated by comparing criteria #1-3 between the first case treated by pharmacists and the second (both without ABiMed), and the third and the fourth (both with ABiMed), respectively.

Supplementary file #1 and #2 contain the datasets, and #3 contains the R sources.

## 3. Results

### 3.1. Recruited participants

We recruited 39 pharmacists in the study (Table 3).

### 3.2. Impact on problem identification

The left part of table 4 shows the percentage of problems identified by pharmacists without and with ABiMed. The overall percentage is 45.0% without ABiMed vs 71.9% with ABiMed, the difference is highly significant ( $p = 1.1 \times 10^{-12}$ ). This shows that ABiMed had a strong positive impact: using ABiMed, pharmacists identified 1.6 times more problems.

The left part of table 5 shows the LMM analysis with the simple and complex models. The simple model confirms the impact of ABiMed, and shows that there is a significant effect of clinical cases, i.e. some cases are simpler and some other more difficult. The randomization group has no significant effect.

Characteristic	Type	Modalities / Aggregation	
Sex	nominal	Male	17 (44%)
		Female	22 (56%)
		Other	0
Age	integer	20-29	6 (15%)
		30-39	13 (33%)
		40-49	10 (26%)
		50-59	7 (18%)
		60+	3 (8%)
Previous knowledge of STOPP/START	nominal	Yes	29 (74%)
		No	10 (26%)
# MR in the last year	integer	Min	0 (for 19 pharm.)
		Max	50 (for 1 pharm.)
		Mean	4.4
		Median	1
Group	nominal	G1	10
		G2	9
		G3	11
		G4	9

Table 3: Demographic characteristics of the recruited pharmacists.

The complex model tests several characteristics of pharmacists, and their interaction with ABiMed. Three factors are significant: ABiMed, cases and age. Figure 2 shows that the percentage of problems identified slightly decreases with age. This is expected because, in France, only younger pharmacists were trained in MR during their studies.

### 3.3. Impact on proposed interventions

The middle part of table 4 shows the CLEO score ratio of the interventions proposed by pharmacists, without and with ABiMed. The difference is highly significant, showing that pharmacists proposed clinically better pharmaceutical interventions with ABiMed.

The complex LLM model (Table 5, middle part) identified three significant factors: ABiMed, clinical case, age, and one interaction between ABiMed and case. Effect of age is similar to its effect on the percentage of problems identified (see above). Figure 3 analyses the case-ABiMed interaction. For case A, B and C, the use of ABiMed increased the CLEO score ratio, but not for case D.

### 3.4. Response times

The right part of table 4 shows mean and median response times, without and with ABiMed. There is no significant difference. Thus, the use of ABiMed did not require additional time for pharmacists, but did not allow gaining time either. However, as pharmacists identified more problems with ABiMed, the per-problem response time is lower.

The complex LLM model (Table 5, right part) identified one significant factor and one interaction: cases and ABiMed-age interaction. Figure 4 suggests that, with ABiMed, younger pharmacists were slightly faster and older pharmacists slightly slower. Younger pharmacists might be more comfortable with computerized CDSSs. However, the difference is limited and the size of subgroups is small, so it should be interpreted cautiously.

### 3.5. Carryover effect

Figure 5 shows the impact of the order of passage of the four cases on the primary criteria. No significant differences were

found when comparing the percentage of problems identified between cases #1 and #2 ( $p = 1$ ), and between cases #3 and #4 ( $p = 0.76$ ), the CLEO score ratio ( $p = 0.37$  and  $0.37$ , respectively) and the log(time) ( $p = 0.51$  and  $0.18$ , respectively). Thus, there was no carryover effect. This was expected, the four cases covering distinct clinical problems. On the contrary, the important difference between cases #1-2 and #3-4 was caused by the intervention.

### 3.6. Perceived usability

The mean SUS score is 82.7 (55-100 depending on the pharmacists, Figure 6). This is ranked as “excellent” according to the SUS adjective rating scale [30]. The less positive answers were obtained for the last question, “I need to learn a lot of things before I can start using ABiMed”.

### 3.7. Pharmacist comments

The pharmacist comments were enthusiastic, *e.g.* “the software is really great, it is very reassuring” or “ABiMed greatly facilitates the work of the pharmacist who performs a medication review and allows him/her to quickly decide on the therapeutic decision to take.”

The pharmacists appreciated the visual aspects of ABiMed, including tables (“the summary tables are very readable and allow us to have an overview. Well done!”), the graph showing drug interactions (“I find that the interaction tab is very practical”) and the flower glyphs showing adverse effects (“the adverse effects tab is very useful and visual: it could be used on a daily basis at the counter, even outside of medication reviews! Well done”). They also appreciated the comparative mode of ABiMed (“a good way to train and learn by adding and testing several molecules together according to different patient profiles.”).

Several pharmacists mentioned that ABiMed was very useful for identifying problems, but more limited when it comes to proposing interventions and suggesting replacement drugs. They proposed the implementation of additional guidelines, targeting the main disorders for elderly patients.

## 4. Discussion

In this paper, we presented a simulation trial evaluating ABiMed, a CDSS for supporting MR. Results show that, with ABiMed, pharmacists identified more problems and proposed better interventions, without spending more time.

The participants were community pharmacists with a clinical activity, and not students, contrary to many studies. Recruiting professionals is much more difficult, as they have less time available. As being older, they may also be less open to innovation and digital tools. However, they are more representative of the target users of ABiMed.

Results suggest that the support offered by ABiMed may vary according to the patient profile: for problem identification, the mean is the same for all cases without ABiMed (about 45%) but differs with ABiMed (60-85%); for interventions (CLEO score ratio), no difference is found for case D. This was related to an alert for domperidone that was missing in ABiMed; the associated intervention (deprescription) was ranked 4 on the CLEO scale. Actually, pharmacists performed better with ABiMed for other problems of case D, but worse for the domperidone, as they were relying on ABiMed guidance. This is known as *automation bias* [31]. Thus, we should take a particular care to missing alerts.

	% problems identified		interventions CLEO score ratio		mean / median time (minutes)	
	without ABiMed	with ABiMed	without ABiMed	with ABiMed	without ABiMed	with ABiMed
Case A	46.8%	78.7%	31.0%	62.2%	30.5 / 28.3	35.0 / 21.9
Case B	43.8%	84.4%	40.8%	81.0%	22.9 / 24.7	41.4 / 25.1
Case C	43.5%	67.9%	40.5%	70.4%	25.1 / 24.1	16.0 / 15.1
Case D	45.6%	59.5%	49.2%	48.3%	31.0 / 22.5	27.4 / 23.9
<b>Overall</b>	<b>45.0%</b>	<b>71.9%</b>	<b>40.0%</b>	<b>65.0%</b>	<b>27.3 / 25.4</b>	<b>29.3 / 20.2</b>
<i>p</i> -value	$p = 1.1 \times 10^{-12} *$		$p = 9.8 \times 10^{-9} *$		$p = 0.56$	

Table 4: Mean percentages of problems that have been identified by pharmacists, mean interventions CLEO score ratios, and mean and median response time, without or with ABiMed, for each clinical case, and overall. \*: difference is statistically significant when comparing without vs with ABiMed.

Model	Factor	% problems identified		interventions CLEO score ratio		response time	
		<i>p</i> -value	inter. <i>p</i> -value	<i>p</i> -value	inter. <i>p</i> -value	<i>p</i> -value	inter. <i>p</i> -value
Simple	ABiMed	$< 2.2 \times 10^{-16} *$		$1.6 \times 10^{-12} *$		0.52	
	Case	0.0099 *		0.015 *		0.018 *	
	Group	0.14		0.16		0.16	
Complex	ABiMed	0.0028 *	-	0.0061 *	-	0.058	-
	Case	0.024 *	0.31	0.00016 *	0.0058 * (Fig 3)	0.022 *	0.11
	Age class	0.035 * (Fig 2)	0.79	0.044 *	0.92	0.34	0.0098 * (Fig 4)
	Sex	0.98	0.70	0.46	0.56	0.089	0.089
	STOPP/START known	0.76	0.14	0.89	0.45	0.75	0.81
	#MRs in the last year	0.16	0.95	0.73	0.40	0.58	0.58

Table 5: *p*-values obtained with Linear Mixed Models (LMM) for each factor, and for their interactions with ABiMed (*i.e.* inter. *p*-value) for the complex model, for each of the three variables of interest (% problems identified, CLEO score ratio, response time). \*: difference is statistically significant.

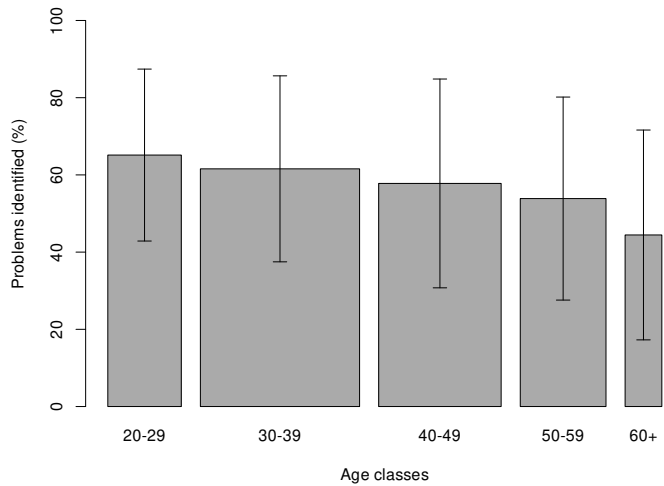


Figure 2: Bar plot showing the percentage of problems identified, for each age class. Bar width is proportional to the number of pharmacists.

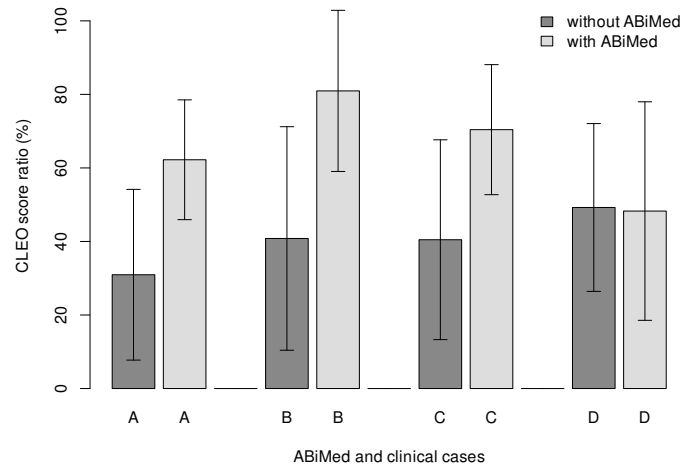


Figure 3: Bar plot showing the CLEO score ratio, without or with ABiMed (left and right), for each clinical case (A-D).

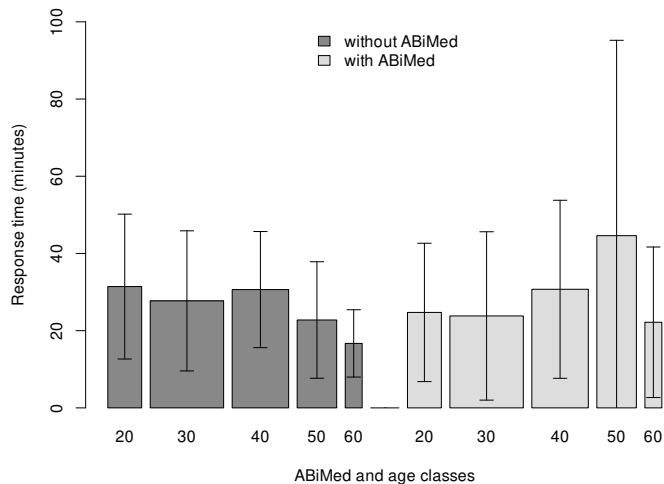


Figure 4: Bar plot showing the response time, without or with ABiMed, for each age class. Bar width is proportional to the number of pharmacists.

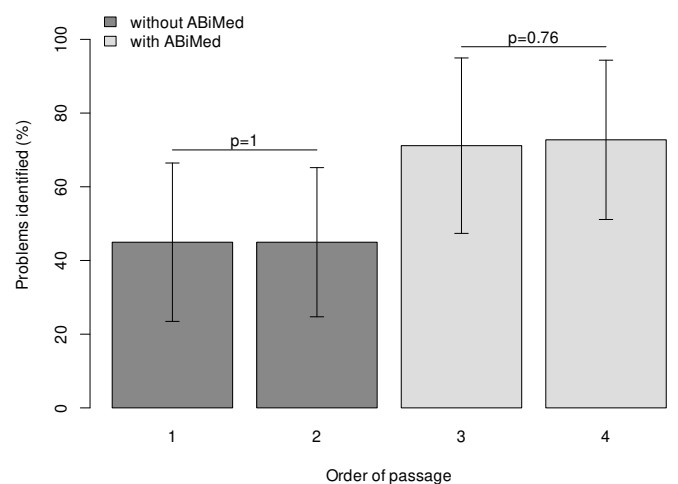


Figure 5: Bar plot showing the mean percentage of problems identified according to the order of passage of the four clinical cases.

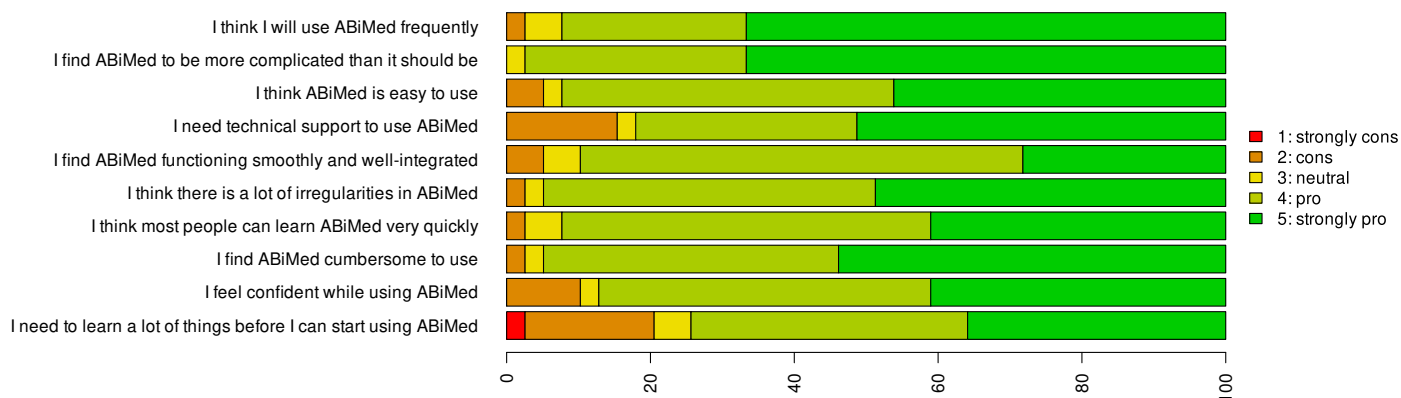


Figure 6: Distribution of answers to each question of the SUS usability test, in percent (colors were reversed for even questions, for which an approbation corresponds to a negative opinion about ABiMed: here, “pro” and “cons” mean “pro-ABiMed” and “cons-ABiMed”).

Sex had no significant impact, as well as the sex-ABiMed interaction. It means that the support provided by ABiMed is the same for males and females, despite cognitive capacities sometimes differ, *e.g.* color perception [32].

Surprisingly, the previous knowledge of STOPP/START and the number of MRs performed in the last year had no significant impact. Possibly, the knowledge of STOPP/START is not enough to execute the numerous and complex rules manually, and many pharmacists did zero or one MR, thus the impact of this factor may be difficult to analyze.

The main limit of the study is that it is a simulation trial [26]: pharmacists may not have acted as they would on real patients. However, simulation trials are often used for CDSSs because of their simplicity to set up, *e.g.* [33]. They also permit a better comparison, since the same fictitious patients can be treated both with and without the CDSS.

Another limit is that all patient data was available in the system, thus pharmacists did not have to enter any additional data and just focused on the analysis. This does not correspond to reality: pharmacists often have limited access to patient data [34] (usually stored in electronic health records owned by GPs or hospitals), and some data is of questionable quality, or still in textual format, that machines cannot interpret [35]. Data entry has been a huge barrier when testing the PRIMA-eDS CDSS for managing polypharmacy [36]. To overcome this problem, we proposed in another work an adaptive questionnaire for facilitating the entry of patient clinical conditions for the automatic execution of STOPP/START rules [37]. Nevertheless, the integration of ABiMed into the medical workflow remains a matter of future research.

Finally, pharmacists were paid volunteers, which might bias the results.

In the literature, several CDSSs were clinically evaluated for the support of MR, and were reviewed in [38]. However, most were less sophisticated than ABiMed, being limited to triggering guideline-based alerts or detecting adverse reactions, or focused on hospital rather than primary care. Hospital CDSSs for polypharmacy obtain better results [39], possibly due to the use of EHR. Outside hospital, examples include: the detection of outlier prescriptions *via* machine-learning for outpatients [40], the use of PHARAO, a system evaluating risk for common side-effects in hospital and primary care [41], the execution of STOPP rules in nursing homes [13], and the triggering of alerts from an electronic expert support system in geriatric clinics and primary care [42].

Contrary to ABiMed, few visual approaches were proposed,

*e.g.* the use of colored tables to present interactions [43], and most systems targeted physicians rather than pharmacists. Exceptions include: a limited 5-rule alert system [44], and a more substantial alert system but associated with a low sensitivity [45]. In that context, the visual presentation of drug knowledge can be a complementary approach, as it is less intrusive than alerts, and not limited to a few situations but can include all drug interactions.

## 5. Conclusion

In conclusion, a simulation trial showed that ABiMed, a CDSS for helping pharmacists perform MR, allowed them to identify 1.6 times more problems than with their usual tools, and proposing better interventions, without taking more time. Pharmacists appreciated ABiMed and gave it a high perceived usability, ranked “excellent”. Our main perspectives are the improvement of ABiMed *e.g.* integrating STOPP/START v3 and clinical practice guidelines for common disorders to better support the proposition of pharmaceutical interventions, the use of formal argumentation to structure the discussion between pharmacists and GPs, and the evaluation of ABiMed in clinical situations with real patients, including the pharmacist-GP collaboration aspect.

## 6. Summary table

### 6.1. What was already known on the topic

- Medication review reduces hospitalizations and saves costs, but is a long and tedious task for pharmacists.
- Clinical practice guidelines for managing polypharmacy, such as STOPP/START, are complex.
- Most clinical decision support systems for polypharmacy focus on hospital, physicians, and alert triggering.
- On the contrary, ABiMed focuses on pharmacists, and combines the STOPP/START v2 guidelines with visual drug knowledge using tables, graphs and glyphs.

### 6.2. What this study added to our knowledge

- We conducted a randomized simulated trial comparing ABiMed to usual resources used by pharmacists, on clinical cases.



- Results show that, with ABiMed, pharmacists identify 1.6 times more problems and proposed better intervention, without requiring more time.
- The perceived usability was ranked as “excellent”.

### CRedit authorship contribution statement

Abdelmalek Mouazer: Conceptualization, Methodology, Software, Visualization

Sophie Dubois: Conceptualization, Methodology, Validation, Investigation, Resources

Romain Léguillon: Methodology, Validation, Resources

Nada Boudegz dame: Methodology

Thibaud Levrard: Software

Yoann Le Bars: Methodology, Software

Christian Simon: Software, Supervision

Brigitte Séroussi: Methodology

Julien Grosjean: Methodology

Romain Lelong: Methodology

Catherine Letord: Methodology

Stéfan Darmoni: Supervision

Karima Sedki: Methodology

Pierre Meneton: Formal analysis, Writing - Review & Editing

Rosy Tsopra: Methodology, Validation, Writing - Original Draft

Hector Falcoff: Conceptualization, Methodology, Validation, Investigation, Resources

Jean-Baptiste Lamy: Conceptualization, Methodology, Software, Validation, Formal analysis, Writing - Original Draft, Visualization, Supervision, Project administration, Funding acquisition

### Acknowledgments

This work was funded by the French Research Agency (ANR) through the ABiMed project [Grant No. ANR-20-CE19-0017].

### References

- [1] United Nations department of economic and social affairs., World Social Report 2023: Leaving no one behind in an ageing world, 2023.
- [2] D. Gnjidic, S. N. Hilmer, F. M. Blyth, V. Naganathan, L. Waite, M. J. Seibel, A. J. McLachlan, R. G. Cumming, D. J. Handelsman, D. G. Le Couteur, Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes, *J Clin Epidemiol* 65 (9) (2012) 989–95. doi: 10.1016/j.jclinepi.2012.02.018.
- [3] M. Monégat, C. Sermet, M. Perronnin, E. Rococo, Polypharmacy: Definitions, Measurement and Stakes Involved, *IRDES Questions d'économie de la santé* 204 (2014) 1–8.
- [4] A. H. Lavan, P. F. Gallagher, D. O'Mahony, Methods to reduce prescribing errors in elderly patients with multimorbidity, *Clinical interventions in aging* 11 (2016) 857–66. doi:10.2147/CIA.S80280.
- [5] B. Roux, J. Bezin, C. Morival, P. Noize, M. L. Laroche, Prevalence and direct costs of potentially inappropriate prescriptions in France: a population-based study, Expert review of pharmacoeconomics & outcomes research 22 (4) (2022) 627–636. doi:10.1080/14737167.2021.1981863.
- [6] K. T. Jungo, S. Mantelli, Z. Rozsnyai, A. Missiou, B. G. Kitanovska, B. Weltermann, C. Mallen, C. Collins, D. Bonfim, D. Kurpas, F. Petrazzuoli, G. Dumitra, H. Thulesius, H. Lingner, K. L. Johansen, K. Wallis, K. Hoffmann, L. Peremans, L. Pilv, M. P. Šter, M. Bleckwenn, M. Sattler, M. van der Ploeg, P. Torzsa, P. B. Kánská, S. Vinker, R. Assenova, R. G. Bravo, R. P. A. Viegas, R. Tsopra, S. K. Pestic, S. Gintere, T. H. Koskela, V. Lazic, V. Tkachenko, E. Reeve, C. Luymes, R. K. E. Poortvliet, N. Rodondi, J. Gussekloo, S. Streit, General practitioners' deprescribing decisions in older adults with polypharmacy: a case vignette study in 31 countries, *BMC geriatrics* 21 (1) (2021) 19. doi:10.1186/s12877-020-01953-6.
- [7] A. Croke, K. Cardwell, B. Clyne, F. Moriarty, L. McCullagh, S. M. Smith, The effectiveness and cost of integrating pharmacists within general practice to optimize prescribing and health outcomes in primary care patients with polypharmacy: a systematic review, *BMC primary care* 24 (1) (2023) 41. doi:10.1186/s12875-022-01952-z.
- [8] N. Griese-Mammen, K. E. Hersberger, M. Messerli, S. Leikola, N. Horvat, J. W. F. van Mil, M. Kos, PCNE definition of medication review: reaching agreement, *International journal of clinical pharmacy* 40 (5) (2018) 1199–1208. doi:10.1007/s11096-018-0696-7.
- [9] G. Zermansky A, R. Petty D, K. Raynor D, N. Freemantle, A. Vail, J. Lowe C, Randomised controlled trial of clinical medication review by a pharmacist of elderly patients receiving repeat prescriptions in general practice, *BMJ (Clinical research ed.)* 323 (7325) (2001) 1340–3.
- [10] A. Payen, C. Godard-Sebillotte, N. Sourial, J. Soula, D. Verloop, M. M. Defebvre, C. Dupont, D. Dambre, A. Lamer, J. B. Beuscart, The impact of including a medication review in an integrated care pathway: a pilot study, *Br J Clin Pharmacol* (2022). doi:10.1111/bcp.15543.
- [11] S. Tsai, N. Kumpat, P. Dilokthornsakul, N. Chaikunapruk, B. Saini, T. Dhippayom, Impact of Medication Reviews Delivered by Community Pharmacist to Elderly Patients on Polypharmacy: A Meta-analysis of Randomized Controlled Trials, *Journal of patient safety* 17 (4) (2021) 290–298. doi:10.1097/PTS.0000000000000599.
- [12] A. Malet-Larrea, E. Goyenechea, M. A. Gastelurrutia, B. Calvo, V. García-Cárdenas, J. M. Cabases, A. Noain, F. Martínez-Martínez, D. Sabater-Hernández, S. I. Benrimoj, Cost analysis and cost-benefit analysis of a medication review with follow-up service in aged polypharmacy patients, *The European journal of health economics : HEPAC : health economics in prevention and care* 18 (9) (2017) 1069–1078. doi:10.1007/s10198-016-0853-7.
- [13] T. M. García-Caballero, J. Lojo, C. Menéndez, R. Fernández-Álvarez, R. Mateos, A. Garcia-Caballero, Polimedication: applicability of a computer tool to reduce polypharmacy in nursing homes, *Int Psychogeriatr* 30 (7) (2018) 1001–1008. doi:10.1017/S1041610217002411.
- [14] A. Robberechts, M. Brumer, V. Garcia-Cardenas, N. M. Dupotey, S. Steurbaut, G. R. Y. De Meyer, H. De Loof, Medication Review: What's in a Name and What Is It about?, *Pharmacy (Basel, Switzerland)* 12 (1) (2024). doi:10.3390/pharmacy12010039.
- [15] J. B. Beuscart, S. Pelayo, L. Robert, S. Thevelin, S. Marien, O. Dalleur, Medication review and reconciliation in older adults, *European geriatric medicine* 12 (3) (2021) 499–507. doi:10.1007/s41999-021-00449-9.
- [16] M. Michiels-Corsten, N. Gerlach, T. Schleeff, U. Junius-Walker, N. Donner-Banzhoff, A. Viniol, Generic instruments for drug discontinuation in primary care: A systematic review, *Br J Clin Pharmacol* 86 (7) (2020) 1251–1266. doi:10.1111/bcp.14287.
- [17] A. Mouazer, K. Sedki, R. Tsopra, J. B. Lamy, Visual comparison of guidelines: Method and application to potentially inappropriate medication lists, in: *Studies in health technology and informatics (MIE)*, Vol. 281, 2021, pp. 248–252. doi:https://doi.org/10.3233/shti210158.
- [18] D. O'Mahony, D. O'Sullivan, S. Byrne, M. N. O'Connor, C. Ryan, P. Gallagher, STOPP/START criteria for potentially inappropriate prescribing in older people: version 2, *Age Ageing* 44 (2) (2015) 213–8. doi:10.1093/ageing/afu145.
- [19] D. O'Mahony, A. Cherubini, A. R. Guiteras, M. Denkinge, J. B. Beuscart, G. Onder, A. Gudmundsson, A. J. Cruz-Jentoft, W. Knol, G. Bahat, N. van der Velde, M. Petrovic, D. Curtin, STOPP/START criteria for potentially inappropriate prescribing in older people: version 3, *European geriatric medicine* 14 (4) (2023) 625–632. doi:10.1007/s41999-023-00777-y.
- [20] F. Gallagher P, N. O'Connor M, D. O'Mahony, Prevention of potentially inappropriate prescribing for elderly patients: a randomized controlled trial using STOPP/START criteria, *Clin Pharmacol Ther* 89 (6) (2011) 845–54. doi:10.1038/clpt.2011.44.
- [21] M. Kurczewska-Michalak, P. Lewek, B. Jankowska-Polańska, A. Giardini, N. Granata, M. Maffoni, E. Costa, L. Midão, P. Kardas, Polypharmacy Management in the Older Adults: A Scoping Review of Available Interventions, *Frontiers in pharmacology* 12 (2021) 734045. doi:10.3389/fphar.2021.734045.
- [22] E. K. Crowley, B. T. G. M. Sallevelt, C. J. A. Huibers, K. D. Murphy, M. Spruit, Z. Shen, B. Boland, A. Spinewine, O. Dalleur, E. Moutzouri, A. Löwe, M. Feller, N. Schwab, L. Adam, I. Wilting, W. Knol, N. Rodondi, S. Byrne, D. O'Mahony, Intervention protocol: Optimising theRapy to prevent avoidable hospital Admission in the Multi-morbid elderly (OPERAM): a structured medication review with support of a computerised decision support system, *BMC health services research* 20 (1) (2020) 220. doi:10.1186/s12913-020-5056-3.
- [23] A. Mouazer, R. Tsopra, K. Sedki, C. Letord, J. B. Lamy, Decision-support systems for managing polypharmacy in the elderly: A scoping review, *J Biomed Inform* 130 (2022) 104074.



- [24] A. Mouazer, R. Leguillon, B. Leroy, K. Sedki, C. Simon, H. Falcoff, M. Schuers, S. Dubois, C. Bousquet, L. Soualmia, C. Letord, S. Darmoni, J. Bouaud, B. Séroussi, R. Tsopra, J. B. Lamy, ABiMed: Towards an innovative clinical decision support system for medication reviews and polypharmacy management, in: *Studies in health technology and informatics (ICIMTH)*, Vol. 289, 2021, pp. 61–64.
- [25] A. Mouazer, R. Léguillon, N. Boudegzdame, T. Levrard, Y. Le Bars, C. Simon, B. Séroussi, J. Grosjean, R. Lelong, C. Letord, S. Darmoni, M. Schuers, K. Sedki, S. Dubois, H. Falcoff, R. Tsopra, J. B. Lamy, ABiMed: An intelligent and visual clinical decision support system for medication reviews and polypharmacy management, *Arxiv preprint arXiv:2312.11526* (2023).
- [26] A. Cheng, D. Kessler, R. Mackinnon, T. P. Chang, V. M. Nadkarni, E. A. Hunt, J. Duval-Arnould, Y. Lin, D. A. Cook, M. Pusic, J. Hui, D. Moher, M. Egger, M. Auerbach, Reporting guidelines for health care simulation research: extensions to the CONSORT and STROBE statements, *Advances in simulation* (London, England) 1 (2016) 25. doi: 10.1186/s41077-016-0025-y.
- [27] Husson MC, Theriaque: independent-drug database for good use of drugs by health practitioners (2008).
- [28] H. T. Vo, B. Charpiat, S. Chanoine, M. Juste, R. Roubille, F. X. Rose, O. Conort, B. Allenet, P. Bedouch, CLEO: a multidimensional tool to assess clinical, economic and organisational impacts of pharmacists' interventions, *European journal of hospital pharmacy : science and practice* 28 (4) (2021) 193–200. doi:10.1136/ejhpharm-2020-002642.
- [29] Brooke J, Usability evaluation in industry, Taylor and Francis, London, 1996, Ch. SUS: a "quick and dirty" usability scale.
- [30] A. Bangor, P. Kortum, J. Miller, Determining what individual SUS score mean: adding an adjective rating scale, *J Usability Stud* 4 (2009) 114–123.
- [31] K. Goddard, A. Roudsari, J. C. Wyatt, Automation bias: empirical results assessing influencing factors, *Int J Med Inf* 83 (5) (2014) 368–75. doi: 10.1016/j.ijmedinf.2014.01.001.
- [32] A. Jameson K, M. Highnote S, M. Wasserman L, Richer color experience in observers with multiple photopigment opsin genes, *Psychonomic bulletin & review* 8 (2) (2001) 244–61.
- [33] L. Higi, R. Schmitt, K. Käser, M. Wälti, M. Grotzer, P. Vonbach, Impact of a clinical decision support system on paediatric drug dose prescribing: a randomised within-subject simulation trial, *BMJ paediatrics open* 7 (1) (2023). doi:10.1136/bmjpo-2022-001726.
- [34] S. D. Nelson, J. Poikonen, T. Reese, D. El Halta, C. Weir, The pharmacist and the EHR, *J Am Med Inform Assoc* 24 (1) (2017) 193–197. doi: 10.1093/jamia/ocw044.
- [35] I. S. Kohane, B. J. Aronow, P. Avillach, B. K. Beaulieu-Jones, R. Bellazzi, R. L. Bradford, G. A. Brat, M. Cannataro, J. J. Cimino, N. García-Barrio, N. Gehlenborg, M. Ghassemi, A. Gutiérrez-Sacristán, D. A. Hanauer, J. H. Holmes, C. Hong, J. G. Klann, N. H. W. Loh, Y. Luo, K. D. Mandl, M. Daniar, J. H. Moore, S. N. Murphy, A. Neuraz, K. Y. Ngiam, G. S. Omenn, N. Palmer, L. P. Patel, M. Pedrera-Jiménez, P. Sliz, A. M. South, A. L. M. Tan, D. M. Taylor, B. W. Taylor, C. Torti, A. K. Vallejos, K. B. Wagholikar, G. M. Weber, T. Cai, What Every Reader Should Know About Studies Using Electronic Health Record Data but May Be Afraid to Ask, *J Med Internet Res* 23 (3) (2021) e22219. doi:10.2196/22219.
- [36] A. Rieckert, C. Sommerauer, A. Krumeich, A. Sönnichsen, Reduction of inappropriate medication in older populations by electronic decision support (the PRIMA-eDS study): a qualitative study of practical implementation in primary care, *BMC family practice* 19 (1) (2018) 110. doi:10.1186/s12875-018-0789-3.
- [37] J. B. Lamy, A. Mouazer, K. Sedki, S. Dubois, H. Falcoff, Adaptive questionnaires for facilitating patient data entry in clinical decision support systems: Methods and application to STOPP/START v2 (2023).
- [38] B. A. Damoiseaux-Volman, S. Medlock, D. M. van der Meulen, J. de Boer, J. A. Romijn, N. van der Velde, A. Abu-Hanna, Clinical validation of clinical decision support systems for medication review: A scoping review, *Br J Clin Pharmacol* 88 (5) (2022) 2035–2051. doi:10.1111/bcp.15160.
- [39] I. A. Scott, P. I. Pillans, M. Barras, C. Morris, Using EMR-enabled computerized decision support systems to reduce prescribing of potentially inappropriate medications: a narrative review, *Therapeutic advances in drug safety* 9 (9) (2018) 559–573. doi:10.1177/2042098618784809.
- [40] G. D. Schiff, L. A. Volk, M. Volodarskaya, D. H. Williams, L. Walsh, S. G. Myers, D. W. Bates, R. Rozenblum, Screening for medication errors using an outlier detection system, *J Am Med Inform Assoc* 24 (2) (2017) 281–287. doi:10.1093/jamia/ocw171.
- [41] K. Hedna, M. L. Andersson, H. Gyllensten, S. Hägg, Y. Böttiger, Clinical relevance of alerts from a decision support system, PHARAO, for drug safety assessment in the older adults, *BMC geriatrics* 19 (1) (2019) 164. doi:10.1186/s12877-019-1179-y.
- [42] T. Hammar, B. Lidström, G. Petersson, Y. Gustafson, B. Eiermann, Potential drug-related problems detected by electronic expert support system: physicians' views on clinical relevance, *International journal of clinical pharmacy* 37 (5) (2015) 941–8. doi:10.1007/s11096-015-0146-8.
- [43] L. Schmidtchen, M. Willis, J. Christoph, W. Rödle, Usability Analysis of a Medication Visualization Tool for Decision Support, *Stud Health Technol Inform* 307 (2023) 110–116. doi:10.3233/SHTI230701.
- [44] L. G. M. Mulder-Wildemors, M. Heringa, A. Floor-Schreudering, P. A. F. Jansen, M. L. Bouvy, Reducing Inappropriate Drug Use in Older Patients by Use of Clinical Decision Support in Community Pharmacy: A Mixed-Methods Evaluation, *Drugs & aging* 37 (2) (2020) 115–123. doi:10.1007/s40266-019-00728-y.
- [45] S. Verdoorn, F. Kwint H, P. Hoogland, J. Gussekloo, L. Bouvy M, Drug-related problems identified during medication review before and after the introduction of a clinical decision support system, *J Clin Pharm Ther* 43 (2) (2018) 224–231. doi:10.1111/jcpt.12637.