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Development and Assessment of RecosDoc-MTeV to Improve the Quality of Direct Oral Anticoagulant Prescription for Venous Thromboembolic Disease

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Abstract

Potentially inappropriate prescribing of direct oral anticoagulants is frequent with the most common errors being dosage, administration, and duration of therapy. We developed RecosDoc-MTeV, a documentary-based clinical decision support system (CDSS) for the management of direct oral anticoagulant prescription to prevent and treat venous thromboembolism. Simultaneously, the network of Parisian public hospitals (AP-HP, France) developed narrative clinical practice guidelines (CPGs) and a companion smartphone application to enhance medication and patient safety related to direct oral anticoagulant prescription. To assess the effectiveness of these CDS tools, we performed a retrospective review of 274 random patients hospitalized in 2017, which were either at risk of venous thromboembolism or actually treated for the disease. Consistency between the two CDS tools was measured at 96.7%. Administered treatments were compliant in 67.2% and 72.3% of the cases, with AP-HP CPGs and RecosDoc-MTeV, respectively. These results support that implementing CDSSs for the prescription of direct oral anticoagulants may ensure safe prescribing of high-risk medications.

Keywords:

Venous Thromboembolism, Clinical Decision Support System, Guideline Adherence, Clinical Practice Guidelines, Health Care Quality Assessment

Introduction

Anticoagulants are the mainstay of therapy for the acute and long-term prevention and treatment of numerous types of thromboembolic disorders. The prevention of thromboembolic stroke among patients with chronic atrial fibrillation is one of the primary indications for anticoagulation therapy. In addition, anticoagulants are indicated in, and increasingly prescribed for, the prevention and treatment of venous thromboembolic disease including deep vein thrombosis and pulmonary embolism. Until recently, anticoagulation therapy was dominated by parenteral anticoagulants and vitamin K agonists, e.g. warfarin. Since 2009, a new therapeutic alternative has appeared with direct oral anticoagulants. They have revolutionized the management of patients undergoing anticoagulant therapy due to their rapid onset of action, fixed

dosage, and non-necessity of biological monitoring for their therapeutic effectiveness [1], becoming the first-line choice for treatment of venous thromboembolic disease and atrial fibrillation.

However, antithrombotic drugs and especially oral anticoagulants belong to the class of drugs causing the primary cause of serious adverse reactions and the primary cause of hospitalizations for adverse reactions [2]. It is estimated that more than 900,000 incidents of recurrent, fatal and non-fatal venous thromboembolic events occur in the United States annually [3]. In France, the annual incidence of venous thromboembolic disease is in the order of 50,000 to 100,000 cases responsible for 5,000 to 10,000 deaths. These situations could be avoided if clinical practice guidelines (CPGs) establishing the proper use of antithrombotic drugs were correctly implemented.

Numerous CPGs for the management of anticoagulation, like CPGs from the American College of Cardiology [4], have been published recently. However, the implementation of such narrative guidelines is complex: direct oral anticoagulants are contraindicated for patients with mechanical valve replacement, or with severe renal insufficiency. Clinical situations may sway patients and clinicians to favor one oral anticoagulant over another. Patients who prefer once-daily dosing will find both edoxaban and rivaroxaban to be more convenient than the twice-daily regimens for apixaban and dabigatran. Patients looking for single-drug treatment (especially outpatient treatment) will favor the use of apixaban or rivaroxaban, which do not require 5–10 days of pre-treatment with low molecular weight heparin as it is required for dabigatran and edoxaban. Besides, dosage, administration, and duration of therapy are quite different according to the situation (prevention vs. treatment), the patient, and the prescribed direct oral anticoagulants. As a consequence, the dissemination of narrative CPGs has had a limited effect in changing physician behavior and direct oral anticoagulant treatment remains underutilized in current clinical practice [5].

Clinical decision support systems (CDSSs) are receiving increased attention as tools to reduce costs and improve care. CDSSs embedding CPGs in their knowledge base have shown to be efficient tools to promote the adoption of CPGs by physicians [6], especially for the prescription of direct oral anticoagulants [7]. For instance, Karlsson et al. [8] demonstrated that a CDSS could increase guideline adherence with anticoagulant therapy in patients with atrial fibrillation.

This CDSS, integrated into the regular electronic health record (EHR), used medical record data to identify patients with a diagnosis of atrial fibrillation and at least one risk factor for stroke with no anticoagulant therapy and displayed a pop-up screen warning. In the same way, Borab et al. [9] evidenced that using CDSSs increased the proportion of surgical patients who were prescribed adequate prophylaxis for venous thromboembolic disease, correlated with a reduction in venous thromboembolic events. In most of the cases, when CDSSs are embedded into the EHR, decision support is implemented as the display of alerts triggered when discrepancies exist between physician prescription and guidelines. However, it has been reported that alert-based CDSSs may be counter-productive since healthcare professionals suffering from "alert fatigue" may ignore most of them [10].

We have developed a guideline-based CDSS called RecosDoc-MTeV to assist decision-making for anticoagulation therapy based on state-of-the-art knowledge combined with local CPGs as elaborated by Saint-Antoine and Tenon hospitals, two hospitals of the Parisian network of public hospitals, Assistance Publique – Hôpitaux de Paris (AP-HP, France). At the same time, because there were no national guidelines to support the management of anticoagulation, the Assistance Publique – Hôpitaux de Paris published narrative CPGs to improve the quality of antithrombotic prescription within its 39 hospitals.

We conducted an analysis to assess the consistency of the propositions provided by RecosDoc-MTeV and AP-HP CPGs. Another objective was to evaluate the conformity to RecosDoc-MTeV and AP-HP CPGs of actual anticoagulation therapy prescriptions. The analysis has been performed on a sample of clinical cases randomly selected from patients hospitalized in 2017 in both Saint-Antoine and Tenon hospitals.

Materials and Methods

Description of RecosDoc-MTeV

RecosDoc-MTeV is a guideline-based CDSS applied to the management of anticoagulation therapy and the prescription of direct oral anticoagulants. The system relies on a knowledge base that models current state-of-the-art CPGs completed by the expertise of the hematologists of Tenon hospital (IE, GG) and the practice of the head of Tenon hospital pharmacy (ID).

The knowledge base of the CDSS is structured as a decision tree essentially made of two subtrees to represent the management of venous thromboembolic disease prevention and treatment (see figure 1). The prevention subtree explores various surgical situations, making the difference between orthopaedics surgery, cancer surgery, bariatric surgery, and other surgeries which have different risks of venous thromboembolic disease. In the same way, the different orthopaedics surgeries associated with different length of treatment are considered, e.g., hip replacement, knee replacement, hip fracture, and femoral neck fracture. For cancer surgery, a difference is made between the management of breast cancer, abdominopelvic cancers (either digestive, gynaecologic, or urologic cancers), and non-abdominopelvic cancers (either thoracic, otorhinolaryngologic, or brain cancers). In non-surgical situations, a pharmacological preventive treatment is recommended for hospitalized patients with high risk of venous thromboembolic disease. The treatment subtree is built in a similar way. It explores the special case of heparin-induced thrombocytopenia and some

specific clinical conditions such as the co-occurrence of venous thromboembolic disease with an active cancer, a pregnancy, or any other clinical situations with acute organ failure.

At different points of the decision tree, it happens that evidence is missing to assess the risk of venous thromboembolic disease and guide the therapeutic strategy. In these cases, the risk is computed according to specific external scores provided by the literature and accessible on the Internet by external links (scores of Caprini [11], Padua [12], and Compass in the prevention subtree; scores of Wells and 4T in the treatment subtree).

In all cases, the recommended treatment varies with the value of creatinine clearance to assess the renal function, the value of the Body Mass Index (BMI) to assess overweight and obesity, and the existence of an antecedent of heparin-induced thrombocytopenia.

RecosDoc-MTeV has been developed according to the documentary paradigm of decision support [13] which allows for contextual interpretation of patient data and guidelines knowledge. Once the knowledge base is built, it can be used as an autonomous application and browsed by the physician user. At each depth level, a question is displayed in a closed-ended form to document a clinical criterion that may either concern patient information (renal failure, obesity, pregnancy, cancer), therapeutic history (prior heparin-based treatment) or one of the scores used to assess the risk of venous thromboembolic disease.

Starting from the root of the decision tree, the physician user navigates through the knowledge base while answering questions and thus instantiates the relevant patient criteria to establish the recommended treatment. Guideline-based patient-centered therapeutic recommendations are then provided when the navigation is completed, i.e. when a leaf of the decision tree is reached.

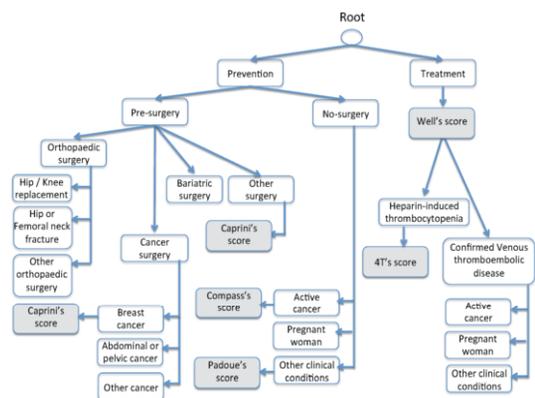


Figure 1— Excerpt of the top of the decision tree.

Description of AP-HP CPGs

AP-HP CPGs [14] have been developed in 2014 at the initiative of the Thrombosis working group of Assistance Publique – Hôpitaux de Paris to support the proper use of antithrombotics by residents and practitioners. AP-HP CPGs are described in a 55-page long document. The first part of the document is dedicated to the description of clinical conditions associated with

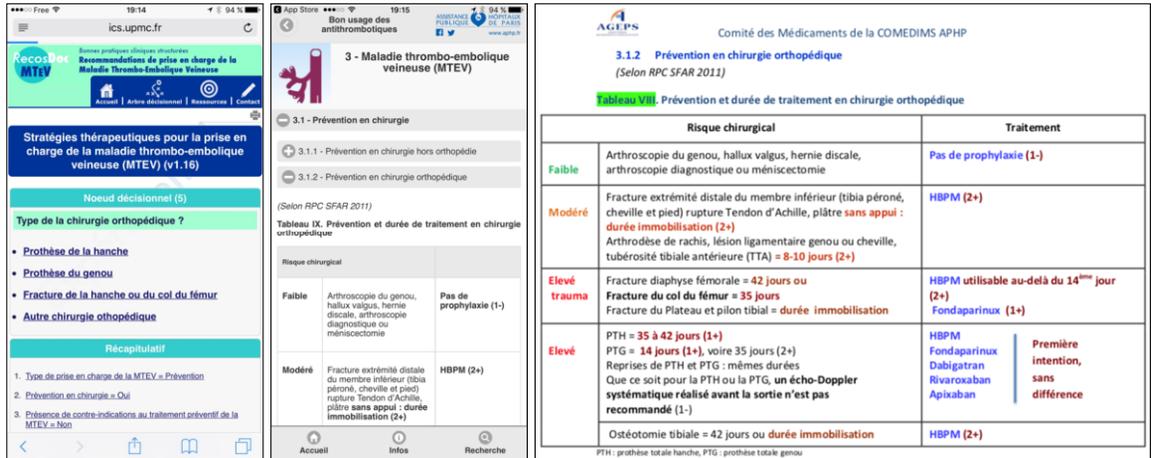


Figure 2 – Screenshots of RecosDoc-MTeV (left), and of the AP-HP app (middle) and narrative CPGs (right).

low, moderate, and high risk of thrombosis. Then, therapeutic protocols recommended for the different levels of risk are presented along with the recommended surveillance. In order to facilitate the availability of these recommendations and make healthcare professionals able to have at hand the essential information about anticoagulant drugs, AP-HP developed a smartphone application (app) named “Recos Thromboses” based on AP-HP CPGs.

Figure 2 displays the three types of interfaces: the structured patient-centered description of the patient profile as offered by RecosDoc-MTeV, the semi-structured organization of the information as provided by the AP-HP app, and tables as given by narrative AP-HP CPGs.

Selection of the population

In order to assess the consistency of the propositions provided by RecosDoc-MTeV and AP-HP CPGs, we randomly selected a sample of patients hospitalized for more than 48 hours in 2017, either in Saint-Antoine hospital or in Tenon hospital, stratified to cover the different clinical situations in the groups for prevention of, and treatment for, venous thromboembolic disease. We used ICD10 codes and CCAM codes (a French terminology to code medical acts) to identify relevant patients for the prevention group, e.g. patients undergoing orthopaedic surgery, cancer surgery, or bariatric surgery, and patients hospitalized for medical conditions at risk, such as acute renal failure, cardiac failure, respiratory failure, infection or sepsis, and pregnancy. We proceeded the same way for the treatment group to select patients diagnosed with venous thromboembolic disease according to ICD-10 codes (either deep vein thrombosis (I80, I81, or I82) or pulmonary embolism (I26)).

Quantitative analysis

We considered that the recommendations provided by AP-HP CPGs were the gold standard. We evaluated RecosDoc-MTeV by comparing the set of propositions issued by RecosDoc-MTeV, denoted $\{\text{RecosDoc-MTeV}\}_i$ to those generated by AP-HP CPGs, denoted $\{\text{CPG}_{\text{AP-HP}}\}_i$ on each patient P_i of the randomized sample of clinical cases. We defined that AP-HP- and RecosDoc-MTeV-generated proposition sets were:

- *Identical* when $\{\text{RecosDoc-MTeV}\}_i = \{\text{CPG}_{\text{AP-HP}}\}_i$

- *Consistent* when $\{\text{RecosDoc-MTeV}\}_i \neq \{\text{CPG}_{\text{AP-HP}}\}_i$ and $\{\text{RecosDoc-MTeV}\}_i \cap \{\text{CPG}_{\text{AP-HP}}\}_i \neq \emptyset$
- *Different* when $\{\text{RecosDoc-MTeV}\}_i \cap \{\text{CPG}_{\text{AP-HP}}\}_i = \emptyset$

We assessed the quality of RecosDoc-MTeV by computing the frequency of identical and consistent propositions of both systems on the population sample. We also evaluated the clinical practices at Saint-Antoine and Tenon hospitals by computing the frequency the treatment actually received by a patient P_i was compliant with RecosDoc-MTeV (when included into $\{\text{RecosDoc-MTeV}\}_i$) and compliant with AP-HP CPGs (when included into $\{\text{CPG}_{\text{AP-HP}}\}_i$). Computations have been made in the prevention and treatment groups.

Although hospitalized patients gave their consent for the re-use of their clinical data for research purposes at the time of admission, we asked for the authorization of the heads of the departments concerned with the patient cases we used in this study before proceeding with the collection and use of data.

Results

Study population

The target population for ICD-10 queries on Saint-Antoine and Tenon hospitals for the year 2017 was made of 6,881 patients. 355 were randomly selected, from which 81 were excluded (42 clinical cases were out of the scope, 10 medical records were unavailable, and 29 clinical cases had too many missing data) leading to a study population of 274 cases, 182 and 92 dispatched in the prevention and treatment groups, respectively. Patient characteristics are reported for the two groups in Table 1.

Comparison of RecosDoc-MTeV and AP-HP CPGs

For each clinical situation corresponding to each patient, the propositions of RecosDoc-MTeV were compared to the recommendations of AP-HP CPGs. The numbers for each configuration, either identical, consistent, or different are reported in Table 2.

Table 1– Main characteristics of the study population

	Prevention (n=182)		Treatment (n=92)	
	n	%	n	%
Sex				
Female	118	64.8	46	50.0
Male	64	35.2	46	50.0
Age group				
< 40	30	16.5	7	7.5
[40–75]	92	50.6	44	47.8
> 75	60	33.0	41	44.6
Prevention group				
Cancer surgery	59	32.4	—	—
Bariatric surgery	7	3.8	—	—
Orthopedic surgery	96	52.7	—	—
Other surgeries	12	6.6	—	—
Non-surgical management	8	4.4	—	—
Treatment group				
Current cancer	—	—	35	38.0
Other	—	—	57	62.0

Table 2– Consistency of RecosDoc-MTeV with respect to AP-HP CPGs

	Prevention	Treatment	Total
Identical	120 (65.9%)	50 (54.3%)	170 (62.0%)
Consistent	55 (30.2%)	40 (43.5%)	95 (34.7%)
Different	7 (3.8%)	2 (2.2%)	9 (3.3%)

On the whole, CDSS propositions differed from AP-HP recommendations in 3.3% of the cases (CI 95%: [1.5%–6.1%]). The nine clinical situations where the propositions of RecoDoc-MTeV were different of those provided by AP-HP CPGs are displayed in Table 3.

Table 3– Inconsistencies between RecosDoc-MTeV and AP-HP CPGs

Clinical situations	N	RecosDoc-MTeV	AP-HP CPGs
Hallux Valgus in obese patients	2	Pharmacological prevention	No prophylaxis
Hospitalized patients with a low risk of venous thromboembolic disease	4	Non-pharmacological prevention	No prophylaxis
Venous thromboembolic disease with cancer	2	Unfractionated Heparin	Unfractionated Heparin relayed by Vitamin K Agonists

Compliance of clinical practices with state of the art recommendations

For each patient, the administered treatment, both in the prevention and treatment groups, was compared to each of the propositions provided by RecosDoc-MTeV and AP-HP CPGs. Table 4 reports for each group the compliance level with each decision support resource.

The global compliance of administered treatments with AP-HP CPGs was measured at 67.2% (CI 95% : [61.2%-72.7%]). This compliance was significantly higher in the prevention

group than in the treatment group (72.0% vs 57.6%, $p = 0.024$).

When administered treatments were compared to RecosDoc-MTeV propositions, the compliance level was 72.3% (CI 95%: [66.6%-77.5%]). No significant difference was observed between the prevention and treatment groups (73.6% vs 69.6%).

Table 4– Compliance of administered treatments with RecosDoc-MTeV and AP-HP CPGs

	N	Compliance / AP-HP CPGs		Compliance / RecosDoc-MTeV	
		n	%	n	%
Prevention	182	131	72.0	134	73.6
Treatment	92	53	57.6	64	69.6
Total	274	184	67.2	198	72.3

When compared, the two compliance measures are not significantly different. The contingency tables of the two compliance variables were built for each subgroup, prevention and treatment, to measure the agreement between the two decision support resources, RecosDoc-MTeV and AP-HP CPGs (Table 5).

Table 5– Contingency tables for the compliance variables with respect to RecosDoc-MTeV (RM) and to AP-HP CPGs (AP) in both prevention and treatment groups

	Prevention			Treatment		
	AP+	AP-	Total	AP+	AP-	Total
RM+	129	5	134	52	12	64
RM-	2	46	48	1	27	28
Total	131	51	182	53	39	92

For the prevention and treatment groups, the unweighted Kappa measures were 0.903 and 0.700, respectively, considered as “almost perfect agreement” and “substantial agreement”. However, in 26% of the study population, the administered treatment was neither compliant with RecosDoc-MTeV nor compliant with AP-HP CPGs. These non-compliant treatments represented 33% of the decisions in the treatment group with the use of drugs not mentioned in the resources. In the prevention group, the combined non-compliance reached 25% (46 cases), distributed in 15% of decisions where the therapeutic scheme was different than the one recommended, 7% of non-pharmacological prophylaxis, and 3% of decisions based on drugs not mentioned in the resources.

Discussion and conclusion

RecosDoc-MTeV is a guideline-based patient-centered decision support system applied to the prescription of direct oral anticoagulants for the management of venous thromboembolic disease. The system is developed according to the documentary paradigm of decision support [13] which allows the user to interactively navigate through the knowledge base to describe a given patient case and get the patient-specific recommendations. Compared to AP-HP CPGs considered as the gold standard in this study, we found on a randomized sample of 274 patient cases that 62.0% of the propositions were identical, 34.7% were similar and 3.3% were different. It should be noticed that most discrepancies were observed in the prevention group. The nine situations

where inconsistencies were observed concerned the management of the venous thromboembolic disease risk with propositions of pharmacological and non-pharmacological prevention by RecosDoc-MTeV in medium and low risk clinical situations respectively, whereas AP-HP CPGs recommended no prophylaxis at all. When comparing the treatments actually received by the patients to the propositions provided by both resources, we observed that clinical practices were compliant with AP-HP CPGs in 67.2% of the cases, and compliant with RecosDoc-MTeV propositions in 72.3% of the cases (no significant difference). It is interesting to notice that 46 therapeutic decisions in the prevention group and 27 therapeutic decisions of the treatment group were neither compliant with AP-HP CPGs nor compliant with RecosDoc-MTeV propositions. For these 73 decisions, RecosDoc-MTeV propositions and AP-HP CPGs were identical in 100% of the cases. This tends to evidence that in these specific situations, clinical practices are suboptimal and would be improved by the use of a CDSS such as RecosDoc-MTeV.

This study has various limitations. We have chosen AP-HP CPGs as the gold standard which could be questioned since AP-HP CPGs, published in 2014, are older than RecoDoc-MTeV, elaborated in 2016. In addition, the randomized sample incompletely covered the set of possible clinical cases since, for instance, we didn't find any medical record with a history of heparin-induced thrombocytopenia. Indeed there is no ICD-10 code for this disease, and all the ICD-10 codes that we used to target the disease didn't retrieve appropriate clinical cases. The study was also conducted on a small sample of clinical cases and on only two hospitals. Finally, compliance rates are probably overstated since we only took into account the class of anticoagulant drugs for the comparison of medical decisions with RecosDoc-MTeV and AP-HP CPG propositions, while dosage and duration of prescriptions were not considered (data were often missing).

We performed a retrospective review of 274 patients hospitalized in 2017 at Tenon and Saint-Antoine hospitals (Paris, France) who were candidates for direct oral anticoagulant treatment either to prevent or treat venous thromboembolic disease. We assessed the prescription of direct oral anticoagulants according to both RecosDoc-MTeV and AP-HP CPGs. Compliance with the CDSS was 72.3% when only taking into account the drugs used. These results support that implementing CDSS for venous thromboembolic disease prevention and treatment in routine practice should improve the quality of care ensuring safe prescribing of high-risk medications. Further work needs to be carried on to assess in a prospective study whether the use of RecosDoc-MTeV upon order entry would increase the compliance rate of therapeutic decisions and thus improve the quality of care.

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