Partial economic evaluation of clinical pharmacy interventions on the prescription of direct oral anticoagulants in a teaching hospital

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ABSTRACT

Background Potential inappropriate use of direct oral anticoagulants (DOACs) increases the risk of thromboembolic and haemorrhagic events.

Purpose To determine the net cost benefit of clinical pharmacy interventions on the prescription of DOACs.

Method We constructed a decision tree model using a public payer perspective. The appropriateness of the prescription was assessed using the Medication Appropriateness Index. The theoretical risks were collected from the literature and the individual potential risks were calculated using the Nesbit risk assignment conducted by two independent clinical pharmacists. Different costs were included based on diagnosis-related group coding and data in the literature. A univariate sensitivity analysis was performed.

Results Thirty-six of 75 patients had an inappropriate prescription of DOACs. The saved difference between avoided costs (7954€) and annualised medication costs and pharmacist cost (4323€) was 3631€ for 75 patients.

Conclusions In addition to the enhancement of the quality of the prescription, our results indicate that pharmacist interventions provide a positive net cost benefit.

INTRODUCTION

In randomised controlled trials, direct oral anticoagulants (DOACs) were shown to be at least non-inferior to vitamin K antagonists (VKAs) for the prevention of stroke or systemic embolism in patients with non-valvular atrial fibrillation (NVAF). Moreover, DOACs have several advantages compared with VKAs, including a predictable therapeutic effect, no need for regular drug monitoring and fewer drug interactions. Nevertheless, the optimal use of DOACs in real life remains challenging for other reasons: appropriate patient selection, diversity of dosages, lack of a widely available biological assay, monitoring for renal function, adherence and adverse events.[1]

The haemorrhagic and thromboembolic risks of the inappropriate use of DOACs might result in 0.19–4.41 adverse drug events (ADEs) per 100 patient-years.[2] The consequences of these haemorrhagic and thromboembolic events represent a high societal and economic burden.

In a recent prospective study we evaluated the appropriateness of DOAC prescribing using the Medication Appropriateness Index and found that 49% of the prescriptions were inappropriate.[1] Collaboration with a clinical pharmacist contributed to better prescribing. Involving pharmacists in patient education, adverse event and adherence monitoring were associated with greater patient adherence to DOACs.[3]

The literature on the effect of clinical pharmacists on the quality of DOAC use is emerging but, to the best of our knowledge, no economic evaluation with comparable outcomes measures (ie, quality-adjusted life years, reductions in hospitalisations or mortality rates) has been published.[4 5] As for other healthcare services, it is necessary to evaluate the extent to which such services provide value for money for the investment made in their provision.[6]

The aim of the present study was to estimate the cost avoidance generated by interventions made by a clinical pharmacist in order to improve the appropriateness of DOAC prescriptions.

MATERIALS AND METHODS

Setting

The study was conducted at CHU UCL Namur, a 450-bed university hospital. Since 2013, a clinical pharmacist prospectively reviews DOAC prescriptions and, whenever necessary, makes interventions to optimise DOAC use. Interventions included changes in medication or dosage, discontinuation of DOAC or request to measure DOAC concentrations. We included patients presenting to the hospital from April to mid-October 2013 (period 1[1]) and from June to December 2014 (period 2) who were taking a DOAC for NVAF. In order to have a homogeneous population, we excluded surgical patients and patients who were admitted with a DOAC-related adverse event. There were no additional exclusion criteria.

Decision tree

The model took a healthcare payer's perspective over lifetime or an 11-year time horizon based on the life expectancy of the Belgian population.[7] A decision tree model was developed to evaluate the impact of pharmacist interventions on the risk of ADEs secondary to inappropriate DOAC prescriptions (see online supplement 1).

Measurement and valuation of risks and costs

The theoretical risks of haemorrhagic and thromboembolic events (major bleeding and stroke, transient ischaemic attack, pulmonary embolism, respectively) with DOACs were taken from published randomised controlled trials. We used the probabilities of apixaban, given the fact that only for this drug were all the risks published and were

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the most conservative estimates compared with the others described.[8]

Determination of the probability that an individual patient would experience harm in the absence of an intervention by a pharmacist was based on the methodology described by Nesbit *et al*.[9] An individual probability of occurrence from very low (0.01) to high (0.6) was assigned independently by two reviewers (CD and ALS). Discrepancies were adjudicated by consensus with a third pharmacist (ASL).

The probability scores for each patient were obtained by multiplying the theoretical probabilities in the literature by the individual probability (which is based on the probability that the event occurs for each clinical case) and with the cost of the consequences. In summary, the probability that an individual patient would experience harm (eg, stroke) in the absence of an intervention by a pharmacist is equal to the probability of stroke×Nesbit probability for this specific clinical case×cost of stroke.

The costs used for the calculation were determined in 2013. The principal diagnosis of the diagnosis-related group (DRG) was used to calculate the hospital costs for the different haemorrhagic and thromboembolic events over a 12-month period. Using these data, the median, minimum and maximum costs were determined. Ambulatory costs were considered only for stroke and were based on a previously published European study.[10] The ambulatory costs of other pathologies and natural mortality rates were estimated to be similar for both patient groups with and without an ADE, and were therefore not included in the calculation. Only direct and non-direct medical costs were considered. Based on a conservative assumption and on the fact that indirect costs are difficult to obtain with chart reviews, these costs were not included in the study (eg, overtime, sick leave).

We applied the daily reimbursement tariff of the DOACs which is applied in Belgium (INAMI/RIZIV). In a sensitivity analysis we assessed the impact of cost reduction if the generic price was applied.

The hourly rate of employing a pharmacist was calculated based on an average seniority and the manual for cost-based pricing of hospital interventions.[11] For a hospital pharmacist with 15 years of experience, the hourly cost is 54.4€. The average time of an intervention was based on our previous study, which showed that the evaluation of the appropriateness of each DOAC prescription took on average 45 min.[1]

The discount rate for costs was 3%. Where the ambulatory non-direct medical costs after stroke were only considered for the first year, we discounted ambulatory direct medical costs after stroke and the drug costs over the time horizon.

Sensitivity analysis

The robustness needs to be evaluated by changing the parameters up to the limit of cost efficiency. As shown in table 1, all known variables underwent a one-way sensitivity analysis based on known ranges or through a scenario analysis based on inappropriate rates and ADE cost estimates. Summary statistics were calculated using Microsoft Excel 2010 (Microsoft Corp, Washington, USA).

RESULTS

The appropriateness of DOAC prescriptions was analysed in 75 medical patients with the following characteristics: median age 77 years (range 52–93), $CHAD_2S_2$-VASC and HAS-BLED scores of 4.3 (range 2–7) and 2.5 (range 1–4) respectively, and glomerular filtration rate calculated by Cockroft and Gault of 64 mL/min (range 23–145).[1]

Table 1 Univariate sensitivity analysis

Parameter involved in the sensitivity analysis	Avoided costs	Cost for service	Net cost benefit for the whole population (75 patients)
Prevalence of inappropriate prescriptions (%)			
28	4597€	4323€	−274€
25	3063€	4323€	461€
Minimal costs for each pathology	363€	4323€	3959€
Reduction of the median cost for each pathology (%)			
20	6363€	4323€	−2040€
30	5567€	4323€	−1244€
40	4772€	4323€	−449€
45	4373€	4323€	−50€
20% increase of the median cost for each pathology	8440€	4323€	−4117€
Nesbit probability at 0.1 for all patients	4391€	4323€	−68€
30% reduction of drug costs (generics cost)	7954€	4070€	−3884€

Cost for service includes pharmacist wages and drug cost. The costs used for the calculation were determined in 2013. The median ADE cost estimates and the appropriateness of the prescriptions were gradually reduced until the cut-off of the net benefit for the clinical pharmacist intervention was reached.
ADE, adverse drug events.

The prescription was inappropriate in 48% of the patients. The most prevalent type of intervention was a modification of the dose or of the medication.

These interventions generated a median cost avoidance of 7954€ (363€–27 984€). The cost of providing these interventions (drug costs and pharmacist salary) was 4323€. The net cost benefit for 75 patients was therefore 3631€.

The robustness of the model was investigated during the course of sensitivity analyses. As shown in table 1, the median ADE cost estimates and the appropriateness of the prescriptions were gradually reduced until the cut-off of the net benefit for the clinical pharmacist intervention was reached.

No cost benefit was obtained if we reduced the ADE cost estimates by 45% and when 28% of the prescriptions were inappropriate.

A net cost benefit is still achievable with a Nesbit probability of 0.1 for all patients or a reduction of the cost of DOACs of 30%, corresponding to the adoption of generics. Only if the minimal ADE cost estimates for all pathologies were used were savings not realised.

DISCUSSION

A median cost avoidance of 48.4€ per intervention was generated. The net cost benefit remained positive under all conditions examined, except when the minimal ADE cost estimates were taken into account. Even with a small number of patients, we could demonstrate a significant societal net benefit.

Calculation of cost avoidance will have interstudy variations in the cost assigned to an ADE, methodologies, healthcare settings, duration of study and number of pharmacists employed. However, other studies have indicated that pharmacist interventions in the follow-up of patients with VKAs generate significant cost avoidance.[12] Moreover, a recent study showed similar figures on the inappropriateness of the prescription.[13] Both

inappropriateness ratios were above 28%, which is the net cost benefit breakpoint in our sensitivity analysis.

One limitation of our study is that the net cost benefit calculation was based on estimates of time and avoidance of cost rather than hard economic data. Furthermore, evaluation of a clinical pharmacy service is strengthened when it also includes an assessment of the clinical outcomes involved. Therefore, a complete economic analysis should be considered in the future.

Second, theoretical risks of ADEs were based on randomised controlled trials. However, recently published observational studies provide similar risk results.[14–16] Moreover, assigning probabilities to ADEs was subjective. We reduced this variation through assignment of independent consensus scores with three pharmacists. A significant level of agreement was found.

Finally, the generalisability of pharmacoeconomic analysis remains uncertain. For the reasons mentioned above, calculation of cost avoidance will have interstudy variations in the cost assigned to an ADE, methodologies and healthcare setting. The cost calculation was conducted over a 14-month period in a single hospital. The ratio could potentially be an overestimate. Sensitivity analysis undertaken in this study showed that the benefit breakpoint occurred only at a 45% reduction of the ADE cost estimates.

This study has confirmed previous opinions and supplemented the body of evidence that the provision of clinical pharmacy services provides value for money to the healthcare payer.

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