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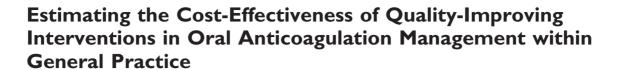
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Volume \*\* • Number \*\* • \*\* VALUE IN HEALTH



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#### ABSTRACT

Objectives: A clinical trial, "Belgian Improvement Study on Oral Anticoagulation Therapy (BISOAT)," significantly improved the quality after implementing four different quality-improving interventions in four randomly divided groups of general practitioners (GPs). The quality-improving interventions consisted of multifaceted education with or without feedback reports on their performance, international normalized ratio (INR) testing by the GP with a CoaguChek device or computer-assisted advice for adapting oral anticoagulation therapy. The quality improvement in INR control versus baseline was similar in the four groups. The aim of the current study was to calculate the cost-effectiveness and influencing factors of the four quality-improving interventions compared with usual care.

Methods: Activity-based costing techniques with questionnaires were used to determine the global costs per patient per month in the different intervention groups. Effectiveness data were obtained from the BISOAT study. Cost-effectiveness was expressed as cost per additional day within a 0.5 range from INR target.

Results: The one-time cost of multifaceted education was €49,997 for the whole study. Monthly continuous costs per intervention ranged between €37 and €54 per patient. Using the CoaguChek in combination with the multifaceted education was associated with net savings and quality improvement, hence dominated usual care. Sensitivity analyses showed improved cost-effectiveness with extended duration and with increased program size.

Conclusion: Implementation of the combination multifaceted education with the use of the CoaguChek is a costeffective new organizational model of oral anticoagulation management in general practice.

Keywords: cost-effectiveness, economics, general practitioner, oral anticoagulation management, improvement.

### Introduction

Two retrospective studies demonstrated that the quality of oral anticoagulation management is suboptimal in Belgium [1,2]. The current management of oral anticoagulation in Belgium is organized as follows: A venous blood sample is taken by the general practitioner (GP) at the patient's home or in the office. The blood analysis is performed by an external laboratory. After obtaining the international normalized ratio (INR), the patient gets information from the GP regarding the dosage for the following days or weeks. A clinical trial within 66 GP practices, "Belgian Improvement Study on Oral Anticoagulation Therapy

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(BISOAT)," significantly improved the quality compared with baseline after the randomized implementation of four quality-improving interventions [3]. Nevertheless, no statistically significant difference in quality between the different groups was found. In the BISOAT study, each group received a multifaceted education on oral anticoagulation, namely an interactive education program, a Web site with guidelines, anticoagulation files combined with patient information booklets and patient anticoagulation forms. In addition to this, GPs of group B received written feedback on their anticoagulation performance every 2 months [4]. The feedback was a comparison of the GP practice performance with the mean clinical performance of group B. In addition to the multifaceted education, group C determined the INR with a CoaguChek device in the doctor's office or at the patient's home. The CoaguChek is a portable device that instantly determines the INR using a capillary blood sample [5,6].









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Group D received, in addition to the education, Dawn AC computer-assisted advice for adapting the oral anticoagulation [7]. This computer program determines the adequate doses of the oral anticoagulant and the date for the next blood test. The GPs were free to follow the computer advice. Multifaceted education and feedback are professional interventions, whereas the CoaguChek device and computer-assisted advice are organizational interventions [8].

The latter implies a redistribution of tasks and responsibilities, leading to a new organizational model. Current reimbursement constraints have increased the need for providers to be cost conscious [9]. Therefore, implementing new professional or organizational interventions on a large scale implies the need for an economic analysis. In the current study, activity-based costing (ABC) was used to detect the global costs by including the costs associated with all related activities, for example, blood sampling, transportation of blood samples, testing... The cost of each activity includes both the cost of performing the activity (unit cost per actor multiplied with labor time) and the cost of the material required. The aim of this study was to calculate the cost-effectiveness and its influencing factors when implementing the different quality-improving interventions, in comparison with usual care. Effectiveness data were obtained from the BISOAT study.

#### **Methods**

#### Study Design

This study is a cost-effectiveness analysis. The effectiveness data were derived from the clinical results reported in the BISOAT study. Costs were calculated by ABC analysis of the BISOAT study using structured interviews with participating physicians. For each of the four interventions as well as for usual care (before baseline), all activities were recorded in flow charts. For each activity, the required material as well as the labor time was determined on the basis of structured interviews with involved persons. Material costs were calculated on the basis of consumption multiplied by the unit cost per item. For materials that can be used for multiple activities, a proportional cost per activity was applied.

The costs of labor time were calculated by multiplying the labor time of each person involved in a certain activity with their respective cost per unit of labor time. The structured interviews were based on the following principles: all steps in which the respondent was involved were identified and for each step the respondent was requested to list the material required, to estimate the time involved, and to estimate the frequency of performing that step. The health-care payers are the perspective of the analysis and no patient costs (e.g., travel time, missed work) are included in the calculations. The Ethics Committee of the Catholic University Leuven approved the BISOAT study. The participating GPs signed an informed consent.

#### Population

The study was performed on the health-care providers who participated in the BISOAT study [3]. In total 66 GP practices and 834 patients on oral anticoagulation were included in the latter study. All the persons who were involved in the organization of the study were interviewed: the study coordinator, biologist, laboratory assistant, and information technology (IT) specialist. Of the 66 participating GP practices, 16 GPs randomly divided over four intervention groups were selected to be interviewed by one interviewer (four GPs per group). These persons were interviewed 3 months after the end of the BISOAT study. To avoid bias on material utilized and time associated with the intervention, the interviewer asked to perform the different interventions during the interview and measured time with a chronometer. The reported frequency of performing tasks was controlled with the prospective data collection of BISOAT trial.

#### Unit Costs

Unit costs for material were obtained from the central lab, ©Roche Diagnostics, and ©4S Dawn Clinical Software. The acquisition cost for the INR device at the central laboratory was €36,300 with a depreciation period of 5 years. In addition, the annual cost for device maintenance and repair is €3500. The resulting total cost per year is €10,760. Based on the number of INR tests performed in the lab (on average 4075 per month), the cost per test equals €0.22. The unit cost of the CoaguChek device was €1053 and a depreciation period of 4 years was used. Based on the frequency of INR testing per GP practice, a proportional cost of €2.28 per test was calculated. A test strip for the device costed €4.5. The cost of a Dawn AC computer program (one user and 250 active patients) was €4310 for the first year. In the second and subsequent years the cost of major upgrades, would be €862. The resulting cost per test is €0.86 in the first year and €0.17 in subsequent years. For personnel involved in study organization, labor-time costs were based on the estimated monthly total cost to the employer. This led to the following daily costs: €159 per day for administrative personnel, €227 for medical study coordinators, €193 for IT personnel, €346 for biologists, €173 for lab technicians, and €130 for transport personnel. For study supervisors, consultancy fees of €1000 per day were applied. Unit costs for GP time were based on official consultation tariffs and labor time per consultation. Based on the reported proportion of patient visits performed at home (30%) and at the office (70%)











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with a mean duration of 24 min, respectively, 15 min and the respective tariffs of €25.3 and €17.9, the weighed average cost per minute for the GP was estimated as €1.15.

#### Overhead Costs of the Laboratory

According to the Belgian law, in addition to the cost per test, a fixed cost per laboratory request per patient per day is foreseen independent of the number of blood samples (€20.1). This cost can be considered to represent the overhead costs associated with organization of the laboratory (building, maintenance, administration, administrative personnel, handling waste . . .). A registration on three consecutive days of all samples in the laboratory revealed that only 20% of INR tests are associated with any other laboratory tests at the same day. For the entire laboratory patient population it revealed an average of two samples taken per patient per day. Hence, strictly taken, in 80% of cases the fixed honorarium can be attributed solely to the INR test. Nevertheless, given that this fixed fee can be considered as a compensation for general working costs and overhead costs, a proportional cost of €10.05 per sample was attributed, based on the average sample number per day in the entire population tested.

#### Definitions of Costs

The one-time costs of the multifaceted education are incurred only at the start of the study. These costs are presented at different levels: study, GP-practice or patient level. These costs contain the following: the preparation and organizing of the guidelines, of the educational sessions, of the GP anticoagulation files, of the patient information booklets and of the Web site.

The one-time costs of the implementation of the different interventions are calculated separately because these are different per intervention group. These costs contain the dispensing and explaining of the information booklets and filling in the anticoagulation files for all the intervention groups at the patient level. In group B and D supplementary costs are generated at the study level. In group B, the creating of a patient file for the feedback (labor time of the IT specialist) is counted. The set-up, collecting, and introducing patient information in the Dawn AC computer program is counted in group D.

Continuous costs are costs incurred during the conduct of the study. On the level of the GPs, the costs for the blood sampling are taken into account for groups A, B, and D (Table 1). For group C costs at the GP level are related to the usage of the CoaguChek device and test strips. On the level of the laboratory the transport of the blood samples, the INR analysis, and overhead costs are counted. In addition, the costs for preparing the data files for the feedback reports every 2 months in group B are registered on this level. For group C, the only cost incurred at laboratory level is for quality control of the CoaguChek device by the laboratory personnel every 3 months. For group D a supplementary cost due to the Dawn AC computer program is taken into account on this level. These continuous costs are calculated per test. Total continuous costs per patient per month in the different intervention groups were calculated by multiplying the cost per test with the mean number of tests per month per intervention group of the BISOAT study. The mean number of tests per month during the study was 2.6 at baseline (usual care) and 2.2, 2.2, 2.6, and 1.9 for intervention groups A, B, C, and D, respectively (non significant) [1,3].

The research costs (preparing study protocol, data analysis, and manuscript) were not taken into account.

#### **Analyses**

The incremental cost-effectiveness ratio (ICER) per GP practice per 6 months versus usual care was calculated for each intervention (Table 2). The ICER represents the additional cost required to provide one unit of additional effect. The ICER was calculated using the following formula [10]:

cumulative cost per 6 months in the intervention group – cumulative cost per 6 months with usual care (number of days within 0.5 range from target)<sub>intervention</sub> - (number of days within 0.5 range from target)<sub>usual care</sub>

The cumulative cost over 6 months per GP practice is calculated by summing the one-time costs of the multifaceted education with the one-time costs of the implementation of the different interventions and the continuous costs per GP practice (Table 2). The number of days were derived from the BISOAT study [3]. Hence, the outcome of this ratio is expressed as the cost per day within range (DWR), meaning the additional cost per supplementary day within the 0.5 range from target.

#### Sensitivity Analyses

To examine the influence of uncertainties in the variables on the estimated results, one-way sensitivity analyses were performed (Table 3) [11]. Using this type of analysis the impact of each variable in the study will be examined by varying it across a plausible range of values while holding all other variables in the analysis constant at their "best estimate" or baseline value. The influences of uncertainties in the following variables will be examined: effectiveness parameter (using the 95% confidence interval [CI]); INR testing rate (2.6 instead of the mean testing rate of the intervention group); overhead costs of the laboratory (€8 and €5 instead of €10.05); duration of the study (1 year instead of 6 months); number of GP practices (150 practices instead of 66 practices) and number of patients on oral anticoagulation per GP practice (20











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Table I Continuous costs (€) per intervention group

			Usual				
	Person	Cost type	care	Α	В	С	D
Cost per test-GP level							
Blood sampling/INR testing	GP	Material	0.32	0.32	0.32	7.30	0.32
INR testing	GP	Labor	0.00	0.00	0.00	2.57	0.00
Handling samples	GP	Labor	2.30	2.30	2.30	0.00	2.30
Handling INR results	GP	Labor	3.16	3.16	3.16	0.80	3.16
Patients questions	GP	Labor	0.89	0.89	0.89	0.89	0.89
Handling stock	GP	Labor	1.32	1.32	1.32	0.10	1.32
Control/calibration	GP	Labor	0.00	0.00	0.00	0.10	0.00
Discuss information booklets*	GP	Labor	0.00	0.06	0.06	0.06	0.06
Filling in AC file	GP	Labor	0.00	2.26	2.26	2.26	2.20
Review quality reports*	GP	Labor	0.00	0.00	0.07	0.00	0.00
Computer-generated advice	GP	Labor	0.00	0.00	0.00	0.00	1.15
Cost per test-laboratory level							
Transportation of samples	Transport	Labor + transport	0.99	0.99	0.99	0.00	0.99
Sample receipt + preparation	LabTec	Labor	0.56	0.56	0.56	0.00	0.56
Material for blood testing		Material	0.56	0.56	0.56	0.00	0.56
Performing the test	LabTec	Labor	0.06	0.06	0.06	0.00	0.0
Handling test results	Clin Biol	Labor	0.09	0.09	0.09	0.00	0.09
Handling test results	LabTec	Labor	0.24	0.24	0.24	0.00	0.24
Repeated testing	LabTec	Labor	0.15	0.15	0.15	0.00	0.15
Overhead costs		Overhead	10.05	10.05	10.05	0.00	10.0
Transport (control + calibration)	Transport	Labor + transport	0.00	0.00	0.00	0.02	0.00
Device control and calibration	LabTec	Labor	0.00	0.00	0.00	0.03	0.00
Dawn AC software use <sup>†</sup>		Cost	0.00	0.00	0.00	0.00	0.86
Data entry INRs in Dawn	Clin Biol	Labor	0.00	0.00	0.00	0.00	1.08
Print out advices	Clin Biol	Labor	0.00	0.00	0.00	0.00	0.18
Fax advices	Clin Biol	Labor	0.00	0.00	0.00	0.00	0.18
Material		Material	0.00	0.00	0.00	0.00	0.25
Advice communications	Clin Biol	Labor	0.00	0.00	0.00	0.00	1.08
Weekly queries from database	IT	Labor	0.00	0.00	0.00	0.00	0.17
Monthly maintenance software	IT	Labor	0.00	0.00	0.00	0.00	0.04
Extract data for report	IT	Labor	0.00	0.00	0.02	0.00	0.00
Analysis for reports	StCo	Labor	0.00	0.00	0.19	0.00	0.00
Produce reports (material)		Material	0.00	0.00	0.04	0.00	0.00
Administrative cost	Se	Labor	0.00	0.00	0.13	0.00	0.00
Total cost per test			20.69	23.01	23.46	14.13	28.00
Total cost per patient per month <sup>‡</sup>			53.79	50.62	51.61	36.74	53.20

<sup>\*</sup>Costs per test are calculated based on the labor cost per month, and the frequency of INR testing.

BISOAT, Belgian Improvement Study on Oral Anticoagulation Therapy; GP, general practitioner; INR, international normalized ratio

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patients instead of 12.6 patients). All analyses were processed with Excel XP Professional.

#### Results

#### One-TimeCostsoftheMultifacetedEducation( Table 2)

The total cost of organizing the multifaceted education was €49,997. Costs at study level (setting up guidelines, setting up a Web site, preparing the content of documents for GPs and patients) accounted for a total amount of €33,695. These costs are not dependent on the size or duration of the program. Sixty-six GP practices were included in the study so this represented a cost of €511 per GP practice. Costs at the GP-practice level (holding educational sessions and producing GP anticoagulation files) amounted to €13,325. An additional fee for the presence at the educational sessions of €208 per GP practice was foreseen. This led to a

total cost of €410 per GP practice. Per patient, a cost of €3.6 was incurred for producing and handling patient documentation booklets. With a mean number of 12.6 patients on oral anticoagulation per GP practice, this counted for €45 per GP practice.

### One-Time Costs of the Implementation of the Different Interventions (Table 2)

The average labor time of the GP for dispensing and explaining of the information booklets and filling in the anticoagulation files at the start of the study was reported as 16.5 min, hence accounting for €19 per patient or €241 per GP practice. Supplementary to the latter costs, in group D €4.78 per patient was calculated for introducing patient information in the Dawn AC program by the biologist. As a result the total cost per GP practice amounts to €301. In group B a one-time









<sup>†</sup>Fixed cost of €4310 per 250 patients per year Costs per test are based on the mean number of tests per day and the number of days per year. Note that in subsequent years this cost goes down to 862 per year, hence 0.17 per test. Hence, the total cost per test decreases to €31.12 after I year.

 $<sup>\</sup>ensuremath{^\dagger} Applying the monthly testing rates observed in the BISOAT study.$ 

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Table 2 Cost-effectiveness over 6 months per GP practice

	Usual care	Α	В	С	D
Unique costs (€) of multifaceted education per level and counted per GP practice					
Study level	0	511	511	511	511
GP level	0	410	410	410	410
Patient level	0	45	45	45	45
Costs (€) due to different interventions					
Study level	0	0	1	0	22
Patient level	0	241	241	241	301
Continuous	4080	3839	3914	2786	4035
(6 months)*					
Cumulative costs	4080	5046	5122	3993	5323
Incremental cost vs. usual care <sup>†</sup>		966	1042	-87	1243
% improvement <sup>‡</sup>					
Mean (%)		8	9	11	- 11
95% CI		2.0	4.0	6.0	5.5
95% CI		13.5	13.5	16.5	16.5
Absolute improvement (6 months)§					
Mean (N days/GP)		185	208	254	254
95% CI		46	92	138	127
95% CI		311	311	381	381
Incremental cost-effectiveness vs. usual care	5.23	5.02	Dominant <sup>  </sup>	4.90	

<sup>\*</sup>Continuous cost per patient per month multiplied by 12.64 (mean number of patients per GP practice) and multiplied by 6 (6 months).

cost of €65 at study level was generated and accounting for a supplementary cost of €1 per GP practice. In group D €1423 were generated as a result of labor time of the IT specialist and the study team for setting up, collecting, and introducing patient information in the Dawn AC computer program. This represented an additional cost of €22 per GP practice in this study group.

### Continuous Costs of Usual Anticoagulation Management(Table 1)

The total cost of usual care results from adding up the costs at the GP level and at the laboratory level. Taking into account labor time, material, and overhead, the total cost of INR testing was calculated as €20.69 per

Table 3 One-way sensitivity analysis on the ICERs as expressed in € per supplementary day within range compared with usual care

Variables		Usual care	Α	В	С	D
Absolute improvement (days within range)						
Minimum value 95% CI	ICER vs. UC		20.93	11.29	Dominant*	9.80
Maximum value 95% CI	ICER vs. UC		3.10	3.35	Dominant*	3.27
Testing rate/patient/month (base case = study data)						
2.6 tests/patient/month	Cost	4080	5744	5833	3993	6809
·	ICER vs. UC		9.02	8.45	Dominant*	10.76
Overhead costs central lab (base case = 10.05)						
€8.0 per sample	Total cost	3587	4628	4704	3993	4963
	ICER vs. UC		5.64	5.38	1.60	5.42
€5.0 per sample	Total cost	2995	4128	4204	3993	4530
·	ICER vs. UC		6.14	5.82	3.93	6.05
Extend duration to I year <sup>†</sup>						
•	Total cost	8159	8885	9036	6779	9358
	Total effectiveness		369	415	507	507
	ICER vs. UC		1.96	2.11	Dominant*	2.36
Extend target to 150 GPs						
•	Total cost	4080	4760	4835	3707	5025
	Total effectiveness		185	208	254	254
	ICER vs. UC		3.68	3.64	Dominant*	3.73
Average of 20 patients per GP						
	Total cost	6455	7447	7567	5781	7874
	Total effectiveness		292	329	402	402
	ICER vs. UC		3.40	3.38	Dominant*	3.53

<sup>\*</sup>Strategy C is less costly and more effective than usual care. Therefore, it is dominant over usual care.





<sup>†</sup>Incremental cost: total cost usual care—total cost per intervention group.

<sup>†%</sup> improvement of days within 0.5 range from target per intervention group compared with usual care.

§182.5 days (days in 6 months) \* 0.08 (percentage improvement) multiplied with 12.64 (mean number of patients per GP practice) = absolute improvement.

Strategy C is less costly and more effective than usual care. Therefore, it is dominant over usual care.

Cl, confidence interval; GP, general practitioner.

<sup>&</sup>lt;sup>†</sup>With the assumption that effectiveness remains throughout the year.

CI, confidence interval; GP, general practitioner; ICER, incremental cost-effectiveness ratio; UC, usual care.



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test. With a mean of 2.6 tests per patients per month, this represents a cost of €53.79 per patient per month, hence an average of €4080 per 6 months per GP practice.

#### Continuous Costs due to the Different Interventions (Table 1)

The monthly cost per patient was €50.62 in group A. This is lower than for usual care as a result of a lower testing frequency in this group. In group B, the feedback reports every 2 months incurred an extra cost, leading to a total of €23.46 per test or €51.61 per patient per month. In group C, the average duration of the patient visit was slightly increased because of the testing of the INR on the spot. On the other hand, no blood sample handling was required in this group and results were immediately available for interpretation and treatment adaptation. Additional activities required for this group consisted of stock management for test strips and performing calibration of the CoaguChek device every 3 months. As a result of the important savings in this group at the laboratory level, the cost per test was reduced to €14.13. This accounts for €36.74 per patient per month. In group D multifaceted education and computer-assisted anticoagulation monitoring were foreseen. The costs associated with this intervention include the cost of computer software, entering daily the required patient information in the computer and generating and communicating the advice. At the GP level, costs are incurred by the labor time involved in reviewing the recommendations, as well as by potential actions in response to the computer advice. The total cost estimate is €28.00 per test and €53.20 per patient per month.

#### Cost-Effectiveness ( Table 2)

In the base case ICER calculations, intervention C was shown dominant over usual care because of cost savings combined with quality improvement. The ICER for intervention A was €5.2 per DWR, for intervention B €5 per DWR, and for intervention D €4.9 per DWR. Interventions A and B are less effective but also slightly less costly compared with D resulting in comparable cost-effectiveness ratios.

## One-Way Sensitivity Analysis ( Table 3)

The impact of effectiveness was tested by applying confidence intervals for the mean improvement. The cost-effectiveness ratio for intervention A is shown to be unstable because of the large confidence interval for improvement. Among the other strategies, the costeffectiveness variations are similar and less wide. In one-way sensitivity analysis the same testing frequency was applied for all intervention groups for the calculation of the continuous costs. These results show that this parameter significantly influences the relative position of the different strategies in terms of costeffectiveness. Indeed, in the study, group D showed lower testing frequency than the other groups that favorably influenced cost-effectiveness results for this intervention. The impact of the overhead cost per INR measurement for the central laboratory was thirdly tested. If the amount for overhead costs is varied, the relative position of intervention C within the group changes. This intervention is highly sensitive to the overhead cost, which is an important source of savings from eliminating central lab testing. At an overhead cost of €8 instead of €10.05, the dominance of intervention C versus usual care is lost. Nevertheless, within the interventions, it remains the most favorable option in terms of ICER versus usual care beyond a 50% decrease in overhead costs, up to the level of €2. Prolonging program duration, assuming sustained effectiveness, up to 1 year improves the cost-effectiveness ratio. Cost-effectiveness results were also shown to improve with assuming larger scale implementation of each strategy up to 150 GP practices or assuming a mean number of 20 patients per practice on oral anticoagulation instead of 12.6. The latter improvements in ICERs are the result of reduced one-time costs.

#### **Discussion**

The present study evaluates costs and cost-effectiveness of implementing four quality-improving interventions versus usual care in general practice. The subject of the study is the oral anticoagulation management within the GP practice. ABC techniques with questionnaires were used to detect the global costs per patient per month in the different intervention groups. Being part of the BISOAT study, the effectiveness data expressed as the number of days within 0.5 target range were obtained from this clustered randomized clinical trial [3]. The interventions significantly improved the quality without, however, a significant difference between the randomized GP practices. Costs could be distinguished as one-time costs and continuous costs. Continuous costs differed among the different interventions in favor for group C. In this group multifaceted education and the use of a CoaguChek device by the GPs were implemented. In the latter new organizational model the GP analyses the INR on capillary blood in usual care the INR analysis is performed on a venous blood sample in the clinical laboratory. This implies a reduced continuous cost for intervention C due to the elimination of venous blood sampling and overhead costs for the laboratory. These results are in accordance with literature finding a significant cost saving per test comparing standard (\$15.64) versus capillary (\$7.55) prothrombine time method [12]. In addition to its cost savings, this new model showed to significantly increase the quality of care. A new healthcare intervention is referred to as the dominant strat-







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egy if it is more effective and less expensive then the alternative strategy considered in the evaluation (usual care) [13]. The non significant difference in effectiveness between interventions may suggest that the multifaceted education is the driving factor in quality improvement.

The methodology of cost calculations based on interviews rather than actual time and motion methodology could be regarded as a weakness because it relies on estimates rather than actual measurements. Strength of this study on the other hand is that both costs and efficacy data were obtained from the same population. In both cases the same individual provided information of usual care and of care during the interventions.

Doing cost-effectiveness analysis in implementation studies to change behavior of health professionals is still new and little literature is published [8,13,14]. It is expected that, in the era of increasing costs in health care partly resulting from new costly techniques and an aging population in the western countries, this sort of research will become more important in the future. This sort of studies is important for policy-makers who are responsible for the health-care budget. Therefore, to estimate incremental cost-effectiveness from the health-care payers perspective, Mason principles were used [10].

The driving factor in the conclusions with regard to the dominance of intervention C is the overhead cost assigned to the INR test at the laboratory level. In sensitivity analysis it was shown that decreasing the cost quickly eliminates the dominance of intervention C. Its position toward interventions A, B, and D, however, is quite robust. To assess the robustness of conclusions in this case, it is important to consider the scale at which the intervention is supposed to be implemented. If only a small proportion of practices were to convert to point of care testing with the CoaguChek device, no change in overhead or organizational structure at the lab would be possible. In this situation it might be argued that the overhead costs would not be eliminated by eliminating the small proportion of INR tests. Considering, however, as in the current analysis, a comparison between strategies on a large scale, the overhead cost can be attributed to the test because eliminating all INR tests would likely lead to organizational changes in the lab. It must be noted here that this discussion would be quite different taking a health-care payers perspective in cost calculations because in such case the entire fixed honorarium of €20 can be attributed to approximately 80% of INR tests. Hence, from the payer's perspective, the cost savings of this intervention seem more straightforward. On the other hand, large scale implementation is then likely to lead to other changes in budgeting, for example, budget transfer from current lab tests to reimbursement of CoaguChek device and material and technical acts at the GP level. For policy decisionmaking it is important to assess the cost-effectiveness of interventions at larger scale and/or duration. In our sensitivity analysis the ICERs of all the different interventions improved with longer duration, with implementation on a lager scale of GP practices and patients. These latter improvements in ICERs are the result of reduced one-time costs, especially the cost of multifaceted education. The one-time costs for multifaceted education were quite high, namely €965 per GP practice per 6 months. Verstappen et al. performed a cost minimization analyses in an implementation study comparing two quality strategies (feedback, education on guidelines, and quality improvement sessions vs. feedback alone) on the number of test ordering in general practice [15]. The cost for the full intervention group was €702 per GP practice per 6 months. The intervention led to reduced laboratory test ordering by the GPs. No effectiveness data on the quality of health care were available in this study. In our study a decrease in the number of test was found from 2.6 tests per patient per month to 2.2 tests per patient per month. This decrease was due to the education where GPs were educated to test the stable patients only once a month. In our sensitivity analysis, testing frequency was found to have an important impact on costs and cost-effectiveness results.

This study pointed out the importance of multifaceted education in general practice. Our elaborated multifaceted education program could be easily implemented in real world, only interactive education sessions have to be arranged. This will generate an extra cost of €200 per GP per education session, €208 per GP-practice attendance fee and €45 for the patient education material. Supplementary, implementing this program in real world needs a good follow-up: namely follow-up education sessions in the event of guidelines change and update of the Web site, anticoagulation booklets and files. This follow-up cost will be counted in the one-time costs for the next 6 months. One of the pitfalls for implementation in real world is the lack of reimbursement for postgraduate education in Belgium. In conclusion, our study suggests that the combination of multifaceted education and INR testing by the GP using the CoaguChek device is a cost saving alternative for usual care. Proving the cost-effectiveness of this new model of care, the Belgian health-care payers have to consider reimbursement for this new model of care.

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