

Original Research

Cost-Minimisation Analysis of Oral Anticoagulant Therapy Monitoring Methods: The Case for Prothrombin Time Self-Monitoring

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Introduction: Anticoagulant therapy is usually chronic and is indicated for the treatment of several medical conditions. The most common of these include patients with mechanical heart valves and those suffering from atrial fibrillation.

Methods: This study compares two methods of oral anticoagulant therapy (OAT) monitoring: traditional prothrombin time measurement and self-measuring or self-regulation by the patient. As numerous published studies indicate that the two methods are equally effective (while underlining significant deviations in the frequency of complications), a cost-minimisation analysis was applied. The methodology was based on the consensus of experts from different geographical regions and health service sets. All costs and benefits attributable to patient treatment were examined and analysed from the perspective of the Greek National Health System (NHS).

Results: From the analysis it was estimated that the savings from the use of self-monitoring could reach €6,132,750 at market prices for a five-year period. The potential economic benefit from the expansion of self-monitoring to all eligible patients was equal to approximately 10% of the total treatment cost of the entire patient population under OAT in Greece. In addition, the social benefits resulting from higher prevention rates of possible complications, as well as the improvement in patients' quality of life should not be underestimated. The total reduction in private expenditure deriving from the expansion of self-monitoring was estimated at €3,096,000, while savings for the NHS were estimated at €2,473,317 over a five-year period.

Conclusions: The benefit to the healthcare system from the use of self-monitoring is significant, and the further use of this technology could contribute to the rational allocation of healthcare resources.

Over recent years a constantly increasing number of patients undergo chronic anticoagulant therapy. The procedure for administering oral anticoagulants requires frequent measurement of prothrombin time (PT) using the international normalised ratio (INR). PT measurement and subsequent dose regulation are usually performed in one of two ways. The first represents the traditional method of monitoring oral anticoagulant therapy (OAT) – also called “standard manage-

ment” – and is based on patient monitoring by specialised doctors in the public or private health sector. The second method consists of self-monitoring, or even self-regulation by the patients, through the use of a specific PT measurement device (portable coagulometer).

The present study compared the incremental cost of PT measurement using the standard management and self-monitoring methods. The economic evaluation technique applied was cost-minimisation

analysis, based on the fact that data from clinical trials indicate equal clinical efficacy, while at the same time showing differences in the incidence of complications in the patient population under chronic OAT.

Methods

The incremental cost analysis was based on the assessment of the direct healthcare expenditure attributable to each of the two methods, including that due to hospitalisation for complications of moderate severity. All costs and benefits attributable to patient treatment were examined and analysed from the perspective of the Greek National Health System (NHS). Given the lack of data related to the disease management of patients under OAT in Greece, the study methodology was based on a consensus panel approach by a group of experts who agreed on the validity of the necessary data. The panel of experts consisted of 11 physicians who have significant experience in the field of OAT administration, as well as 4 health economists. The expert physicians are employed at university clinics, NHS hospitals, insurance fund health services, and the private sector, in different geographic regions.* The specific selection was made to ensure that the results can be generalised to the entire population of the country.

The consensus of expert opinions on the use of epidemiological parameters (probability of complications, patient compliance with the suggested treatment, patients' ability for self-monitoring) as well as regarding patients' resource utilisation through the course of OAT, enabled the study to be carried out.

Data on clinical effectiveness

Anticoagulant therapy is usually chronic and is indicated for the treatment of at least 10 medical conditions (Table 1). The most common of these include mechanical heart valves and atrial fibrillation.¹⁻⁵ Patients' PTs are monitored using the INR index. Clinical studies point to the optimum therapeutic result being achieved with an INR between 2 and 3, while

Table 1. Indications for oral anticoagulation.

- Pulmonary embolus
- Proximal deep vein thrombosis
- Calf vein thrombus
- Recurrence of venous thromboembolism
- Symptomatic inherited thrombophilia
- Antiphospholipid syndrome
- Non-rheumatic atrial fibrillation
- Atrial fibrillation due to rheumatic heart disease, congenital heart disease, thyrotoxicosis
- Cardioversion
- Mechanical prosthetic heart valve
- Bioprosthetic valve
- Ischaemic stroke without atrial fibrillation
- Retinal vessel occlusion
- Peripheral arterial thrombosis and grafts
- Coronary artery thrombosis
- Coronary artery graft thrombosis
- Coronary angioplasty and stents

Source: British Journal of Haematology 1998.

deviations from these values, upward or downward, have been shown to increase significantly the danger of haemorrhagic or thromboembolic episodes. Frequent INR measurements for regulating the dosage of the anticoagulant medication significantly increase the time period during which the patient's INR levels remain within the suggested therapeutic range, and therefore reduce the probability of complications.^{6,7}

Table 2 shows the probability of haemorrhagic and thromboembolic episodes according to the method of OAT monitoring used.^{2,6,8-17} The data in the table demonstrate that the frequency of complications is higher for patients monitored with the traditional method in comparison to patients under self-monitoring.

Self-monitoring or self-regulation is performed by the patients themselves using a specific device for measuring PT (portable coagulometer). According to the literature, the functionality, reliability and accuracy of these devices are their basic advantages.¹⁸⁻²⁰ The portable coagulometers are small, lightweight, portable devices that provide rapid laboratory results in the form of INR within two or three minutes. The analysis requires merely one drop of capillary blood from the patient's finger.

Direct cost estimations

The direct cost estimations of the two PT measurement methods under comparison were based on the

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Table 2. Complications associated with different methods of monitoring oral anticoagulant therapy.

	Reference	Patient years	Haemorrhagic episodes (%)	Thromboembolic episodes (%)
Traditional	Ansell and Hughes 1996, Ansell et al 2001	941	10.9	16.2
	Horstkotte et al 1996		2.1	0.7-4.6
	Horstkotte et al 1998		10.9	4.5
	Saour et al 1990		6.2	4.0
	Cortelazzo et al 1993	669	4.7	6.6
	Ibrahim et al 2000	4,936	2.2	4.2
Anticoagulation clinics	Ansell 1999	993	2.8	2.4
	Cortelazzo et al 1993	669	1.0	0.6
	Cannegieter et al 1995	6,475	2.7	0.7
Self-monitoring	Bernardo 1997	834	1.2	0.5
	Heidinger et al 2000	1,424	1.6	1.1
	Horstkotte et al 1998		4.5	0.9
	Kortke et al 2001		1.7	1.2

costs of diagnostic procedures, doctor visits, and the costs of hospitalisation due to complications. In order to estimate the average cost per patient under OAT, private market prices and 2006 Greek NHS “shadow prices” were used. The former refer to the average prices for laboratory tests, doctor visits and *per diem* hospitalisation in the private healthcare sector. The latter refer to the estimated actual average prices of the aforementioned medical procedures in the Greek public healthcare sector. The choice of “shadow prices” as opposed to the official (nominal) NHS prices is due to the significant discrepancies between nominal and actual prices that are observed in the Greek public healthcare sector.²¹

The estimation of the costs attributable to hospitalisation for complications was based on calculations of the probabilities of occurrence of a moderate haemorrhagic or thromboembolic episode in patients undergoing chronic OAT in Greece. The specific probabilities were the result of the expert panel’s consensus, based on the management of patients under OAT in Greece and the review and discussion of international literature.

Patients under self-monitoring used the CoaguChek S device (Roche Diagnostics) for PT measurement. A five-year period was used as a timeframe for the analysis. This timeframe was chosen based on the technical specifications of the device and matches the guaranteed proper functioning period as set by the manufacturer. Unit costs, including the costs of medical procedures in the public and private healthcare sector, as well as the

cost of the device and the necessary consumables, were calculated based on 2006 prices.

Results

Consensus of the expert panel

After a detailed discussion of the experts’ views and experience of the disease management of patients undergoing OAT in Greece, their opinions converged at the following points:

a) Health service utilisation by patients monitored with the traditional method usually includes one visit to the doctor’s practice plus one set of diagnostic tests per month, whereas for those under self-monitoring it consists of one visit to the doctor per month. In the case of a moderately severe episode, hospitalisation is required for approximately five days in a standard (not intensive) care bed in a general hospital.

b) With regard to the healthcare services provider, there was a consensus that approximately 60% of patients are monitored by the private healthcare sector and 40% by the public healthcare sector (30% by insurance funds’ healthcare facilities and 10% through specialised OAT hospital clinics). Less than 0.1% of patients are self-monitored using the device.

c) Based on their experience of the clinical management of patients under OAT in Greece, the panel estimated the probability of complications for patients monitored with the traditional method as 2.8% for haemorrhagic and 5.3% for thromboembolic episodes;

the respective rates were 2.5% and 0.9% for patients monitored at specialised OAT clinics, and 1.5% and 0.9% for self-monitored patients. As a result, the cumulative incidence of episodes was estimated as 8.1% for the traditional method, 3.4% for specialised OAT clinics, and 2.4% in the self-monitoring group.

d) The total number of patients undergoing chronic anticoagulant therapy in Greece is estimated at 20,000. The percentage of patients monitored with the traditional method who fail to comply with the suggested treatment is between 20% and 30%. In addition, the experts agreed that 60-70% of the patients who undergo chronic anticoagulant therapy are eligible for self-monitoring using the coagulometer. Eligibility criteria include patients' willingness to be self-monitored, functional ability to perform the test (i.e. absence of severe vision impairment or other permanent functional impairment, for example, Parkinson's disease or previous severe stroke), compliance with the treatment, ability to receive adequate training regarding the use of the device and an acceptable level of collaboration with the consulting physician.

The cost of oral anticoagulant therapy monitoring

The economic evaluation of the two PT monitoring methods under discussion was performed based on the disease management of patients under OAT in Greece and the subsequent healthcare resource utilisation, as agreed by the expert panel. Results are presented in

Table 3, which shows the total average cost per patient for each method, according to the type, frequency and volume of care provided, with or without the incidence of complications, over a five-year period.

From the data in the table it is clear that the incidence of complications significantly increases the average cost per patient in both methods of PT monitoring, irrespectively of whether prices for the public or the private healthcare sector are used. Hospitalisation required to treat complications is the major cost driver, significantly increasing the cost per patient.

Table 4 shows the results of the comparative economic evaluation of both PT monitoring methods over a five-year period, using market prices. Results indicate total savings of €6,132,750 through the use of the self-monitoring method in patients who would be eligible to use either method for PT monitoring. Based on the experts' consensus that approximately 35% of patients (approximately 7,000) are ineligible to use the device, it is estimated that a residual cost of €23,126,250 would be unavoidable. Consequently, based on average costs, the economic benefit arising from the use of self-monitoring is estimated at €471.75 per patient over five years.

The outcomes of the economic evaluation are similar when shadow prices are used instead of market prices. Results of the analysis, presented in Table 5, indicate total savings of €5,011,500 through the use of self-monitoring for patients eligible to use either PT monitoring method, and a fixed expenditure of

Table 3. Average cost per patient according to monitoring method used to measure prothrombin time.

Type of health service		Unit cost (€)	Traditional method - patient cost		Self-monitoring - patient cost					
			No complications	Complications	No complications		Complications			
Medical visits	Market price	30	1,800	1,800	1,800		1,800			
	Shadow price	20	1,200	1,200	1,200		1,200	1,200		
Hospitalisation	Market price	150		3,750			3,750			
	Shadow price	300		7,500			7,500			
Diagnostic tests	Market price	20	1,200	1,200						
	Shadow price	15	900	900						
Self-monitoring	Coagulometer cost / 60 months	10.7			642	642	642	642		
	Consumables cost per measurement	5			300	300	300	300		
Average cost			3,000	2,100	6,750	9,600	2,742	2,142	6,492	9,642

Table 4. Comparative financial evaluation, in market prices, of the two methods of measuring prothrombin time according to cumulative incidence of complications and eligibility to use self-monitoring.

Traditional Method		Self-monitoring	
Total cost according to incidence of complications in the 13,000 patients eligible of using the coagulometer			
No complications	Complications	No complications	Complications
€3,000 x 11,947 patients = €35,841,000	€6,750 x 1,053 patients = €7,107,750	€2,742 x 12,688 patients = €34,790,496	€6,492 x 312 patients = €2,025,504
Total cost: €42,948,750	Incremental cost: - €6,132,750	Total cost: €36,816,000	
Economic burden attributable to the 7,000 patients unable to use the coagulometer			
No complications		Complications	
€3,000 x 6,433 patients = €19,299,000	€6,750 x 567 patients = €3,827,250	Total cost: €36,816,000	
Total cost: €23,126,250		Average cost per patient: €2,832	
Average cost per patient: €3,303.75	Incremental average cost per patient: -€471.75		

Table 5. Comparative financial evaluation, in shadow prices, of the two methods of measuring prothrombin time according to cumulative incidence of complications and eligibility to use self-monitoring.

Traditional Method		Self-monitoring	
Total cost according to incidence of complications in the 13,000 patients eligible of using the coagulometer			
No complications	Complications	No complications	Complications
€2,100 x 11,947 patients = €25,088,700	€9,600 x 1,053 patients = €10,108,800	€2,142 x 12,688 patients = €27,177,696	€9,642 x 312 patients = €3,008,304
Total cost: €35,197,500	Incremental cost: -€5,011,500	Total cost: €30,186,000	
Economic burden attributable to the 7,000 patients unable to use the coagulometer			
No complications		Complications	
€2,100 x 6,433 patients = €13,509,300	€9,600 x 567 patients = €5,443,200	Total cost: €30,186,000	
Total cost: €18,952,500		Average cost per patient: €2,322	
Average cost per patient: €2,707.5	Incremental average cost per patient: -€385.50		

€18,952,500 for the 35% of patients ineligible to use the device. Based on the above, the economic benefit that arises from the use of self-monitoring is estimated at €385.50 per patient over the five-year period.

Sensitivity analysis

In order to test the reliability of the outcomes, an analysis was performed of the sensitivity of the results to fluctuations in the variables.

Given that: a) the cost variable for doctor visits contributes equally to the average cost of both methods; b) the cost variable for laboratory tests contributes to a relatively limited degree to the calculation of the average cost for the traditional method and, as a result, a variation (increase or decrease) of 20% would not result in a significant change in the outcomes; and c) the cost variable of the device and consumables prices is fixed, a sensitivity analysis of the results was performed for the following hypotheses (scenarios):

1. 20% increase in hospitalisation costs (shadow and market prices);
2. 20% decrease in hospitalisation costs (shadow and market prices);
3. 20% decrease in the cumulative incidence of episodes in patients under standard management;
4. 20% increase in the cumulative incidence of episodes in self-monitored patients.

The results of the analysis are presented in Table 6. According to the sensitivity analysis, fluctuations in the previously mentioned variables do not change the direction of the outcomes, namely the advantage of self-monitoring over the traditional method with re-

gard to the reduction in the average cost per patient, even in the extreme case where scenarios (3) and (4) occur simultaneously. In essence, should the cumulative incidence of complications decrease by 20% in the traditional method at the same time that it increases by 20% in the self-monitored patient group, study outcomes would still be robust.

Discussion

The purpose of this study was to assess the traditional PT measurement method against the self-monitoring system (CoaguChek S device) in patients undergoing oral anticoagulant therapy. A cost-minimisation analysis was applied, since clinical trial data of the two methods under investigation indicate equal effectiveness but reveal significant variations in the incidence of complications. The research methodology was based on the formation of a panel of experts from different geographical regions in the country and analysed their consensus regarding disease management and resource utilisation for patients under OAT in Greece. The scope of the analysis was focused on the financial consequences for the healthcare system and for society in general, taking into consideration not only the macro-economic dimensions, but also consequences affecting the income and quality of life of the affected patients.

The results of the analysis are in accordance with the respective findings in studies formerly published in the international literature^{8,16,22-27} and indicate the superiority of the self-monitoring method for PT measurement, as it fulfills to a greater degree the criteria of clinical effectiveness and economic efficiency. However, as shown in a recent meta-analysis by Henegan et

Table 6. Sensitivity analysis

	Base case scenario	Scenario 1	Scenario 2	Scenario 3	Scenario 4
Average cost per patient under self-monitoring in shadow prices	€2,322	€2,358	€2,286	€2,322	€2,357.70
Average cost per patient under the traditional method in shadow prices	€2,707.50	€2,829	€2,586	€2,585.70	€2,707.50
Average cost per patient under self-monitoring in market prices	€2,832	€2,850	€2,814	€2,832	€2,863
Average cost per patient under the traditional method in market prices	€3,303.75	€3,364.50	€3,243	€3,242.80	€3,303.75

Scenarios: 1 – 20% increase in hospitalisation costs; 2 – 20% decrease in hospitalisation costs; 3 – 20% decrease in the cumulative incidence of complications in the traditional method; 4 – 20% increase in the cumulative incidence of episodes in the self-monitoring method.

al,²⁸ although self-management improves the quality of oral anticoagulation and reduces thromboembolic events and mortality, the identification and education of eligible patients is of great importance. The expected benefits from the use of this particular technology are not limited to cost containment, but further extend to aspects regarding the patients' quality of life. The high rate of noncompliance observed in patients monitored through the traditional method is accompanied by negative effects on health, as well as by unfavourable socioeconomic consequences. The negative effects on health due to patient noncompliance reflect the decrease in the time period during which the INR index remains within the acceptable range of 2-3. Clinical studies have shown that the increased frequency of PT measurements noted in patients using the self-monitoring method leads to a significant increase in the time for which the INR values remain within the therapeutic range, a factor related to a significant decrease in the frequency of episodes and complications.^{9,10,12,18-20,22,29}

As far as socioeconomic consequences are concerned, these are principally related to time costs and difficulties in accessing health services for OAT monitoring, in addition to absenteeism. These are factors that inhibit patients' compliance with scheduled doctor appointments and are directly related to patient dissatisfaction and quality-of-life issues.^{9,16,25,26} Clearly, problems are magnified in the case of residents of rural and isolated areas, elderly, and lower-income patients.¹³

A significant finding of this study is the saving in resources resulting from the use of self-monitoring at the macroeconomic level and at the patient level. In 2006 the cost of administering anticoagulant therapy to the total patient population in Greece, allowing for the full expansion of self-monitoring to all eligible patients, could amount to €60,082,650 at market prices. As a result, the economic benefit that would have derived from expanding the use of self-monitoring to the 13,000 potentially eligible patients would be equal to approximately 10% of the total cost of treating the entire patient population under OAT in Greece. In addition, the social benefit resulting from a higher rate of episode prevention and improvement in the patients' quality of life should not be underestimated.

The significant increase in the average cost per patient in the cases of complication occurrence, noted in both methods, produces adverse macro- and microeconomic consequences. In the private sector, the economic benefit deriving from the use of self-monitoring versus the traditional method in the cases of complications

reaches €258 per patient for a five-year period. If, according to the opinion of the experts, it is estimated that 60% of users (12,000 patients) receive medical care in the private sector, this means that for the total of 972 patients presenting complications there is a decrease in private expenditure of approximately €250,776. Respectively, for the 11,028 patients who would not present complications, the decrease in private expenditure amounts to €3,096,000 over the five-year period, a sum that until now has been borne directly by the patients' private or family income. Within this framework, the saving in public health expenditure is also significant and worth noting, and is estimated at €2,473,317 over five years.

Study limitations

In carrying out this study, the research team faced methodological problems due to the lack of epidemiological data, patient records, and clinical guidelines regarding the management of patients under OAT in Greece. This was the reason for choosing the particular methodology (consensus panel) in spite of the disadvantages that have been reported concerning the objectivity of opinions and the reliability of data.²⁸ Nevertheless, in similar cases this method is considered to be the method of choice.^{21,30} The lack of data and the inability to compare with relevant international sources ruled out the possibility of applying the technique of meta-analysis, by which the research team could more accurately assess the incidence density and the cumulative incidence of complications.³¹ For this reason the research team compared the opinions of the experts with the findings of international studies related to the incidence of complications and submitted the study findings to sensitivity analysis in order to test the accuracy of the results. In any case, since this is not a randomised study, the findings should be interpreted with caution.

Another weakness of the study lies in the fact that the research hypothesis did not include the case of anticoagulant therapy being followed up in specialised clinics. In many countries such units have been widely established,^{18,26,27} and the frequency of complications in patients is less than with the traditional method, but remains greater than with self-monitoring (Table 2). Given the fact that in Greece these facilities are very few in number,¹ it was considered expedient to omit them from the research hypothesis. According to the opinions of the experts, the cumulative incidence in this method is 3.4%, approaching the advantage of the self-

monitoring method (2.4%), in comparison to the probability of occurrence of complications with the traditional method (8.1%). As a result, in spite of the positive picture presented by the specialised clinic-unit method, the idea of extending them throughout the country should be examined closely, since expansion would also require development of the relevant infrastructure. Additionally, the use of self-monitoring would require a one-time group training of patients,³² of maximum duration two hours. The associated cost of this was not included in the total cost, since training is usually undertaken by the companies and the cost does not fall on insurance funds or the public health system as a whole.

Finally, the use of shadow prices is an additional weakness, but at the same time it allows estimation of the actual cost in the public sector with greater accuracy and reliability.²¹ Taking into account the actual cost per service provided, as well as the official reimbursement prices, helped avoid cost underestimation, a fact that is corroborated by the relatively high *per diem* cost of hospitalisation that appears in the public sector prices in the study.

Conclusions

The results of the analysis highlight the fact that the savings accruing to the health system with the use of the self-monitoring method are significant, and that the further use of this technology can contribute to the proper allocation of healthcare resources. Carrying out such studies allows for the creation of epidemiological, clinical, and economic data, which are necessary for the better documentation of the outcome produced by the different methods of resource allocation. In this way, the economic evaluation of health-related technology can undoubtedly contribute to proper decision making, using the criteria of effective and efficient use of healthcare resources.

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