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Budget Impact of Increasing Market Share of Patient Self-Testing and Patient Self-Management in Anticoagulation

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ABSTRACT

Background: Patient self-testing (PST) and/or patient self-management (PSM) might provide better coagulation care than monitoring at specialized anticoagulation centers. Yet, it remains an underused strategy in the Netherlands. **Methods:** Budget-impact analyses of current and new market-share scenarios of PST and/or PSM compared with monitoring at specialized centers were performed for a national cohort of 260,338 patients requiring long-term anticoagulation testing. A health care payer perspective and 1- to 5-year time horizons were applied. The occurrence of thromboembolic and hemorrhagic complications in the aforementioned patient population was assessed in a Markov model. Dutch-specific costs were applied, next to effectiveness data derived from a meta-analysis on PST and/or PSM. Sensitivity and scenario analyses were performed to assess uncertainty on budget-impact analysis results. **Results:** Increasing PST and/or PSM usage in the national cohort from the current 15.4% to 50% resulted in savings ranging from €8 million

after the first year to €184 million after 5 years. Further increases in the use of PST and/or PSM produced greater savings. Sensitivity analyses revealed budget-impact model sensitivity to the baseline and relative risks of thromboembolic complications. Unfavorable budget impact was found in scenarios exploring an increase in the use of PST alone as well as an increase in the market share of PST and PSM in patients with atrial fibrillation.

Conclusions: Overall study findings indicated that PST and PSM are more favorable alternatives to monitoring at specialized centers in patients without atrial fibrillation.

Keywords: anticoagulation, budget-impact analysis, patient self-management, patient self-testing, point-of-care devices.

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Introduction

Oral anticoagulation therapy (OAT) with vitamin K antagonists (VKAs) has been shown to reduce the risks of thromboembolic events in a number of clinical situations [1]. In the Netherlands, indications for OAT include patients with atrial fibrillation (AF), arterial diseases (e.g., cardiomyopathy, coronary syndromes and surgery, vascular surgery, and cerebral embolism), heart valve replacement, venous thromboembolism, and some other specific diseases [2]. Patients with AF represent most of the patients requiring OAT (i.e., 62% in the Netherlands). With the increase in the number of patients with AF, it is not surprising that the number of patients requiring OAT has increased as well over the past decades in Western countries [2]. Furthermore, the population of patients in need of OAT is projected to increase further in the coming decades [3,4]. This is partly due to the aging population in Western countries and the observation that both the incidence and the prevalence of AF increases with increasing age [5].

Although warfarin is commonly used worldwide, acenocoumarol and phenprocoumon (to a lesser extent) are the VKAs of first choice in the Netherlands. Prophylaxis with VKAs is an

effective strategy, but it has some shortcomings, including multiple interactions with food and other drugs as well as interindividual and intraindividual variability in pharmacodynamics [6,7]. As a result, regular monitoring is required to maintain the international normalized ratio (INR) within the therapeutic range. INR testing is typically performed at specialized anticoagulation testing centers, adding to the cumbersomeness of VKA use for the patients. Notably, point-of-care (PoC) devices allow for patient self-testing (PST), in which trained patients can perform the INR test but still inform his or her health care provider for subsequent advice on anticoagulant dosing, or even patient self-management (PSM), with trained patients performing the INR test, interpreting the results, and adjusting dosing accordingly.

In agreement with the increasing number of patients with indications for OAT, the number of patients using INR testing in the Netherlands has increased from approximately 320,000 in 2002 to 430,000 in 2012 [2]. Again, this trend is expected to continue in the coming years with the aging population. Also, between 2007 and 2011, the annual incidence of AF has steadily increased from less than 40,000 in 2008 to 56,000 in 2012 [2].

These figures, however, may still underrepresent the actual number of patients in need of OAT because many eligible

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patients do not receive anticoagulation because of concerns of the patients or concerns of their physicians of their INR values being outside the therapeutic range [8–12]. PoC testing may also address this issue. In line with international findings [13,14], PST and/or PSM might lead to better coagulation care in the Netherlands compared with regular monitoring in specialized anticoagulation centers [2]. This may be due in part to the convenience of use, resulting in more frequent testing, which is associated with greater time in therapeutic range (TTR) [15]. Also, findings from meta-analytical studies suggest that PST and/or PSM compared with regular monitoring have similar risks of bleedings but reduced risks of thromboembolic events and all-cause mortality [13]. Finally, it has been reported that the patient empowerment inherent in PoC strategies in itself already directly reduces the risks of complications and death even in the theoretical sheer absence of any measurable increase in the quality of the anticoagulation control [16]. Despite these positive results, the use of PST and/or PSM remains an underused strategy in the Netherlands.

Eligible patients for PST and/or PSM include all those on long-term OAT (regardless of indication) who have passed the required training. To date, the estimated number of patients on long-term OAT in the Netherlands is approaching 260,338. In the current situation, 15.4% of this population uses PST and/or PSM [2]. In this study, we assessed the budget impact of the current situation and new scenarios in which PST and/or PSM represent 50%, 75%, and 100% of INR monitoring in the Netherlands.

Methods

A budget-impact analysis (BIA) was performed using a patient cohort approach. Patients in the cohort may exit the model after death, but no new patients enter the model (closed model). The perspective of the study is that of a health care payer. In the present analysis, the patient cohort includes all patients who require anticoagulation monitoring for OAT for any clinical indication.

The design and reporting of study outcomes followed the recommendations of the International Society for Pharmacoeconomics and Outcomes Research for BIAs Task Force [17,18].

Model Structure

Patients indicated for OAT are at risk of hemorrhagic and thromboembolic events. To incorporate the course of disease in the BIA, a Markov model was developed. This model includes the following health states: no complications, thromboembolic complications, hemorrhagic complications, and death (see Appendix

Fig. 1 in Supplemental Materials found at <http://dx.doi.org/10.1016/j.jval.2015.12.017>). A cycle length of 1 year was used. The cumulative budget impact of the cohort was assessed each year up to 5 years. Patients enter the model in the “no complications” health state.

In the base-case analysis, transition probabilities for thromboembolic and hemorrhagic complications and death were based on a systematic review and meta-analysis of individual patient data on self-monitoring of oral anticoagulation by Heneghan et al. [14]. This study estimated the relative risks (RRs) of thromboembolic and hemorrhagic complications and death between testing at anticoagulation centers and PST and/or PSM for all indications of OAT (Table 1). To assign transition probabilities for each testing strategy, baseline risks for patients visiting anticoagulation centers/clinics were also needed. Data on the number of events and the duration of follow-up for this group were taken from studies by Menéndez-Jándula et al. [19], Fitzmaurice et al. [20], Matchar et al. [21], and Siebenfofer et al. [22] (see Appendix Table 1 in Supplemental Materials found at <http://dx.doi.org/10.1016/j.jval.2015.12.017>). These studies were selected because they were included in the study by Heneghan et al. [14]. To estimate baseline risks of complications and death, we conducted a meta-analysis on the aforementioned studies in the statistical program R 3.0.2, using the “metafor” package (Table 1) [19–24]. Because the study populations are not homogeneous across the studies and do not fit the assumption of a fixed-effect model, a random-effect model was applied.

Annual risks of complications and death for the PST and/or PSM group were calculated by taking the product of the RRs reported by Heneghan et al. [14] and the baseline risks were estimated through a random-effect model (Table 1). In addition, age-specific background mortality rates for the Netherlands for 2012 were used to estimate the transition from “no complications” to “death” [25].

Cost Parameters

Costs associated with thromboembolic and hemorrhagic complications were collected from published Dutch studies. All costs were inflated to 2013 levels using the harmonized index for consumer product for the health sector for the Netherlands [26]. Costs for thromboembolic events were derived from costs of ischemic stroke [27], myocardial infarction [28], and pulmonary embolism [29], with contributions of 71.43%, 24.32%, and 4.25%, respectively, to the overall estimate [30]. Cerebral hemorrhage [31], gastrointestinal bleeding [32], and other bleedings [32] were assumed to represent 10.66%, 30.46%, and 58.88% of the costs, respectively, associated with hemorrhagic complications [30]. For

Table 1 – Annual risks of clinical events for use in the Markov model—base-case and univariate sensitivity analyses.

Clinical events	Specialized center	PST and/or PSM	
	Annual baseline risk (%) [*]	Relative risk (%) [†]	Annual risk (%) [‡]
Thromboembolic event	3.22 (1.50–4.94)	0.44 (0.17–1.14)	1.42 (0.26–5.63)
Hemorrhagic event	2.84 (1.16–4.52)	0.91 (0.74–1.12)	2.58 (0.86–5.06)
Death	2.87 (1.01–4.74)	0.82 (0.52–1.28)	2.35 (0.53–6.07)

Note. 95% CI limits of risk estimates are shown in parentheses. Upper and lower 95% CI limits were used as inputs for univariate sensitivity analysis.

CI, confidence interval; PSM, patient self-management; PST, patient self-testing.

^{*} Estimated through a random-effects meta-analysis of annual risks for patients using anticoagulation testing centers.

[†] Adapted from the meta-analysis of individual patient data on self-monitoring of oral anticoagulation by Heneghan et al. [14].

[‡] Estimated by taking the product of the relative risks reported by Heneghan et al. [14] and the baseline annual risks estimated by the authors' random-effects meta-analysis of annual risks for patients using anticoagulation testing centers.

each complication, costs were differentiated between first and subsequent years in the analysis, given the different nature of complications between these years. No subsequent-year cost was assumed for pulmonary embolism and bleeding events though. Furthermore, death was not associated with any additional cost. The weighted costs of thromboembolic complications were €41,866 for the first year and €8,750 for subsequent years. For hemorrhagic complications, the weighted averages were €9748 and €1263 for first and subsequent years, respectively (Table 2).

The acquisition cost of VKAs and anticoagulation monitoring are presented in Table 2. The cost of VKAs was estimated as a weighted average cost of acenocoumarol 1mg and phenprocoum on 3mg on the basis of their usage in the Netherlands (i.e., 80%:20%,

respectively). The annual cost of VKAs was estimated at €16.06 [33]. Anticoagulation testing at centers may involve blood sampling at the centers or at home. For blood sampling and measurement at testing centers, 21.1 INR tests per patient per year were assumed [2]. In addition, there were 8.6 home blood samplings per patient per year for the same patient group as those tested in the center [2]. The annual cost of monitoring at testing centers is the same for each year and estimated to be €248 [34].

The first-year cost of PST and/or PSM consisted of the costs of the device and one initial training session and three supervision sessions. Subsequent years of use required quarterly supervision sessions. The costs of the first and subsequent years were estimated to be €958 and €749, respectively [34]. Here, no additional costs were assumed for dosing given that these patients receive information for possible adjustments in their dose by e-mail or specific software.

Table 2 – Cost parameters applied in the model (€2013 per patient).

Parameter	First year	Subsequent years
Stroke [27]	50,828	11,800
Myocardial infarction [28]	22,015	1,338
Pulmonary embolism [29]	5,244	0
Weighted average thromboembolic event [†]	41,866	8,750
Cerebral hemorrhage [27,31] [‡]	38,417	11,800
Gastrointestinal bleeding [32]	7,120	0
Other major bleeding [32]	5,884	0
Weighted average hemorrhagic event [§]	9,748	1,263
Testing strategy		
VKA [33]	16	16
Specialized centers	248	248
Blood sampling & INR measurements at centers [34]	181	181
Additional tariff for blood sampling at home [34] [¶]	67	67
PST and/or PSM	958	749
Initial training & instruction [34]	396	0
Monitoring & supervision [34] [#]	562	749
Additional tariff for phone consultation for PST only [32] ^{**}	210	210

INR, international normalized ratio; PSM, patient self-management; PST, patient self-testing; VKA, vitamin K antagonist.

* Cost estimate of pulmonary embolism from the original source was corrected to exclude the cost of INR testing and coumarines.

† On the basis of the assumption that the cost of a thromboembolic event will be a composite of the costs related to stroke, myocardial infarction, and pulmonary embolism, with contributions of 71.4%, 24.3%, and 4.2%, respectively, to the overall estimate.

‡ Cost estimate of cerebral hemorrhage from the original source was corrected to exclude the costs of home help and private transportation costs.

§ On the basis of the assumption that the cost of a hemorrhagic event will be a composite of the costs related to cerebral hemorrhage, gastrointestinal bleeding, and other major bleeding, with contributions of 10.7%, 30.5%, and 58.9%, respectively, to the overall estimate.

|| Assuming 21.1 tests per year [2].

¶ Assuming 8.6 home blood samplings per year [2].

Assuming three supervision sessions in the first year and four supervision sessions in the subsequent years.

** Assuming 12 phone consultations on dosing per year for patients who only self-test.

Budget-Impact Analysis

In the analysis, a cohort population size was evaluated at 260,338. This cohort size represents an estimate of all patients requiring long-term anticoagulation testing for OAT for any indication on a national level for the Netherlands. Using estimates from the Federation of Dutch Thrombosis Services (“Federatie Nederlandse Trombosediensten”) Report 2012, the current share of PST and/or PSM among patients on long-term monitoring was assumed to be 15.4% [2]. This current situation was evaluated against potential new market penetration scenarios of 50%, 75%, and 100% for PST and/or PSM. The BIA was evaluated for each year up to 5 years. Costs were not discounted as recommended by the International Society for Pharmacoeconomics and Outcomes Research Task Force for BIAs [17].

Sensitivity Analysis

To examine the impact of uncertainty in key model parameters (i.e., baseline risks and RRs of complications and death and cost parameters), univariate sensitivity analyses were performed on 5-year BIA results considering a market penetration scenario of 50% in Dutch patients on long-term OAT. Here, each parameter was varied over the 95% confidence interval (CI) while holding all other parameters constant. Where CI or standard error was unavailable, the standard error was assumed to be 25% of the mean.

Scenario Analyses

Three scenario analyses were conducted to investigate the impact of increasing the market share of PST and/or PSM up to 50% under different decision analytic settings. Scenario 1 explored a linear increase in the uptake of PST and/or PSM from the current 15.4% to the expected 50% in 5 years. In scenario 2, an increase in the market share of PST alone from the current 6.16% (i.e., 40% of all patients with PoC devices) to 50% was explored. Here, transition probabilities for thromboembolic and hemorrhagic complications in the Markov model were based on the RRs of using PST alone compared with testing at specialized centers reported by Heneghan et al., and the baseline risks estimated through a random-effect model (see Appendix Table 2 in Supplemental Materials found at <http://dx.doi.org/10.1016/j.jval.2015.12.017>). In this scenario, the costs of PST alone were assumed to be associated with an additional €210 per year compared with the PST and PSM strategy, reflecting consultations for dosing regimen adjustments.

Finally, the BIA of increasing the market share of PST and/or PSM from the assumed 15.4% to 50% in patients with AF was explored in scenario 3. In this scenario, it was assumed that 62% of the patients on long-term OAT are affected with AF; thus, a cohort population size was evaluated at 161,410 patients. Here,

transition probabilities in the Markov model were based on the RRs of events for PST and/or PSM compared with testing in anticoagulation centers, assessed in patients with AF (see Appendix Table 2).

Results

Base-Case Results

The allocation of total costs per patient associated with INR monitoring in specialized anticoagulation centers and with PoC devices in a time horizon of 1 to 5 years is detailed in Appendix Table 3 in Supplemental Materials found at <http://dx.doi.org/10.1016/j.jval.2015.12.017>. Monitoring-related costs were higher than event-related costs only in the first year in patients conducting INR testing with PoC devices. Costs associated with thromboembolic and hemorrhagic events were responsible for the vast majority of total costs with PoC devices in the longer time horizons and in all time horizons in patients conducting testing in specialized centers. Expanding the aforementioned findings to a Dutch national cohort of 260,338 patients using long-term anticoagulation testing, a current situation of 15.4% using PST and/or PSM with PoC devices resulted in cumulative costs of €486 million, €1.00 billion, €1.54 billion, €2.11 billion, and €2.70 billion in the first, second, third, fourth, and fifth year, respectively (Fig. 1). On increasing the use of PST and/or PSM to 50% in the first year, a cost saving of €8 million from the health care budget could be observed. The savings increased exponentially each year, reaching an estimated saving of €184 million after the fifth year. Similarly, increasing PST and/or PSM market penetration to 75% and 100% produced correspondingly greater 5-year cumulative savings of €317 and €450 million, respectively. Although it is not likely that PST and/or PSM will completely replace INR testing at specialized anticoagulation centers, this latter scenario illustrates the potential maximum savings in long-term utilization.

Sensitivity Analysis

The results of the univariate sensitivity analyses show the impact of uncertainty surrounding the key model parameters, illustrating that the RR and the baseline risk of thromboembolic complications had the highest impact on the BIA results (Fig. 2). Specifically, when the RR of thromboembolic complications would drop to the lower limit of the 95% CI, BIA results would indicate savings of €382 million. At risks increasing to the upper limits of 95% CIs, an expenditure of €302 million from the health care budget would be observed. The univariate sensitivity analyses also found that the BIA results were sensitive to the uncertainty around the cost parameters. Yet, these results generally favored an increasing market penetration of PST and/or PSM.

Scenario Analyses

The results of scenario analyses are presented in Table 3. In scenario 1, a linear increase in the uptake of PST and/or PSM from the current 15.4% to the expected 50% indicated savings ranging from €2 million after the first year to €184 million cumulatively after the fifth year. Increasing the market share of PST alone from the current 6.16% to 50% resulted in expenditures from €57 million after the first year to €123 million cumulatively after the fifth year (scenario 2). Finally, increasing the market share of PST and/or PSM in a cohort of 161,410 patients with AF indicated an expenditure of €15 million after the first year, but resulted in cumulative savings of €2 million after 5 years (scenario 3).

Discussion

Our study presents a BIA of the current situation and new varying market penetration scenarios of anticoagulation monitoring with PST and/or PSM compared with monitoring at specialized anticoagulation centers in the Netherlands. Our findings in the base-case analysis indicated that increasing PST and/or PSM usage for

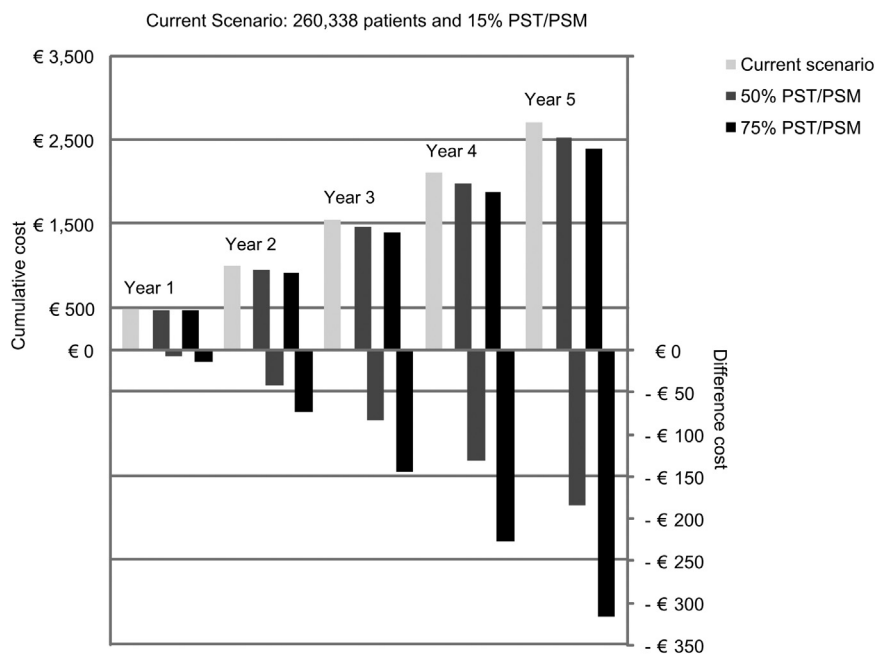


Fig. 1 – Budget-impact analysis from year 1 to year 5 of current and new market share scenarios for PST and/or PSM (in millions). Bars above the horizontal axis present cumulative costs of current (i.e., 15%) and new market-share scenarios for PST and/or PSM (i.e., 50% and 75%). Bars below the horizontal axis present the differences in cost between new and current market-share scenarios. PSM, patient self-management; PST, patient self-testing.

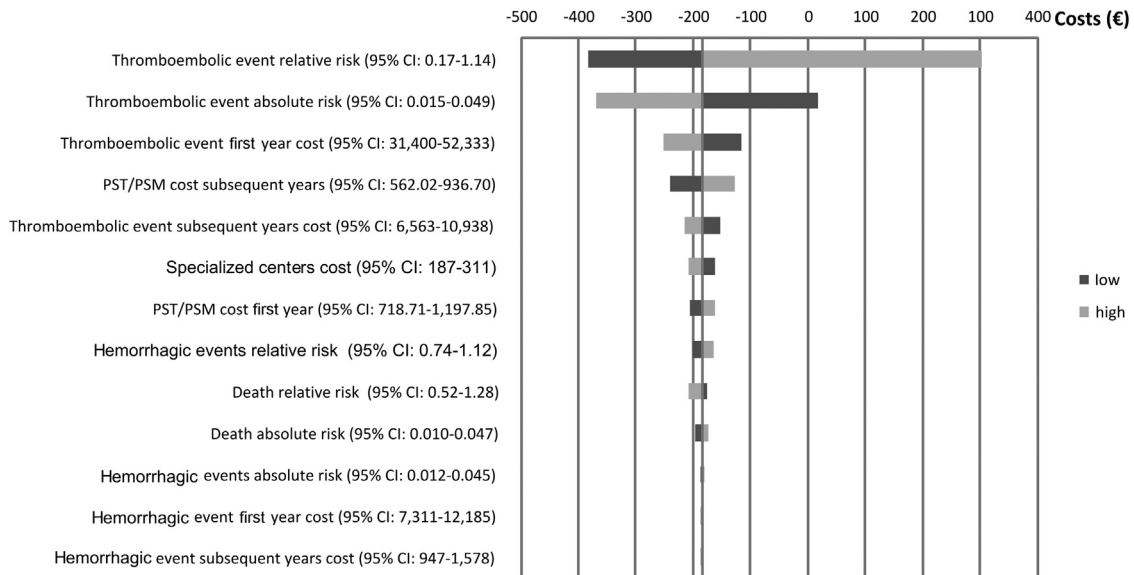


Fig. 2 – Tornado diagram illustrating results from sensitivity analyses for budget-impact analysis in a 5-year horizon considering a market penetration scenario of 50% for PST and/or PSM in a Dutch cohort of 260,338 patients (in millions). Gray bars denote the influence of the high value of the 95% confidence interval (CI) range, and black bars denote the influence of the low value for parameters investigated. PSM, patient self-management; PST, patient self-testing.

anticoagulation testing from the current 15.4% to 50%, 75%, and 100% would lead to significant savings in all analyzed scenarios. Even though INR testing is 3.9 times and 3.0 times more costly for PST and/or PSM compared with testing at specialized anticoagulation centers during the first year and subsequent years, cost saving was still observed when considering total direct medical costs due to considerably higher event-related costs in later years. This is due to the greater risk reductions of

thromboembolic and hemorrhagic complications associated with high medical costs. In fact, increasing the number of patients switching from conventional testing to PST and/or PSM by increasing market penetration produced even greater savings in the time horizon of 5 years. For example, considering a national-level cohort population, potential maximum savings of €450 million over the current situation may be observed in 5 years. However, this is under the unlikely scenario of 100% adoption of

Table 3 – Results of scenario analyses on uptake of PST and/or PSM (€, in millions*).

Scenario	Year	Population size	PST and/or PSM share	PST alone share	New scenario	Current scenario	Difference
Scenario 1		260,338	15.4%–50%	0%			
	1				485	486	–2
	2				983	1000	–17
	3				1493	1543	–50
	4				2007	2112	–105
Scenario 2		260,338	NA	6.16%–50%			
	1				555	497	57
	2				1113	1030	83
	3				1697	1595	102
	4				2301	2186	115
Scenario 3		161,410 [†]	15.4%–50%	0%			
	1				325	310	15
	2				652	638	15
	3				996	985	11
	4				1354	1348	6
	5	1723	1725	–2			

Note. Scenario 1 explores a linear increase in the uptake of PST and/or PSM from the current 15.4% to the expected 50% in 5 y. Scenario 2 explores an increase in the market share of PST alone from 6.16% to 50%. Scenario 3 explores an increase in the market share of PST and/or PSM in patients with AF from 15.4% to 50%.

AF, atrial fibrillation; NA, not applicable; PSM, patient self-management; PST, patient self-testing.

* Values are rounded.

[†] Patients with AF only.

PST and/or PSM. Yet, even if PST and/or PSM would only represent 50% of all patients requiring long-term INR testing—a figure that is quite attainable in the coming years—savings range from €8 million after the first year to €184 million after 5 years. These analyses demonstrated the value of PST and/or PSM strategy with PoC devices in the Netherlands. Univariate sensitivity analyses revealed the major impact of uncertainty in baseline and relative thromboembolic risk on the BIA results. The relevance of the uncertainty in the baseline thromboembolic risk can be directly attributed to its impact on the occurrence of stroke, myocardial infarction, and pulmonary embolism events and their related costs of treatment reaching in the first year and follow-up years a weighted average cost of €41,866 and €8,750 per patient, respectively.

Finally, this study observed potential unfavorable budget impact of increasing market shares of PST alone, as well as increasing market shares of PST and/or PSM in patients with AF on long-term OAT (scenarios 2 and 3). Greater expenditures associated with increasing market shares of PST alone in scenario 2 are due to not only the higher cost of PST strategy compared with PST and PSM combined but also costs associated with the lower number of prevented complications in comparison to the base-case scenario. The findings in scenario 3 may be attributed to the lower number of thromboembolic complications prevented in comparison to the base-case scenario, and the greater number of hemorrhagic complications with PST and/or PSM than with monitoring in specialized centers, which are associated with high costs.

Comparison with Other Studies

To our knowledge, published economic evaluations of PST and/or PSM compared with monitoring at specialized anticoagulation centers or with routine clinic-based care are all cost-effectiveness analyses (CEAs). This hampers a direct comparison of our study findings with the ones from these other studies. Yet, there is a general agreement in the conclusions of the available CEAs with our study results regarding the preference for PST and/or PSM for long-term use. However, all those CEAs indicate higher cost of PST and/or PSM compared with testing in anticoagulation centers, routine clinics, or by physicians. Specifically, Regier et al. [35] found the self-managed anticoagulation to be a more cost-effective alternative compared with physician-managed anticoagulation from the Canadian health care payer perspective in a 5-year time horizon with an incremental cost-effectiveness ratio (ICER) of Can\$14,129 per quality-adjusted life-year (QALY) [35]. In the same study, when the use of self-management was limited to a 1-year time horizon, an ICER of Can\$236,667 per QALY was estimated [35]. Furthermore, in the study by Lafata et al. [36], self-testing in a US setting was found to be a cost-effective alternative to testing in anticoagulation clinics, with an ICER of \$24,818 per event avoided in a 5-year time horizon. Finally, Jowett et al. [37] found PSM compared with routine clinic-based monitoring unlikely to be cost-effective from the UK health care system perspective in a 1-year time horizon (i.e., ICER of £32,716 per QALY). The key driving parameters of cost across these CEAs are detailed in Appendix Table 4 in Supplemental Materials found at <http://dx.doi.org/10.1016/j.jval.2015.12.017>. The results of CEAs may be mainly attributed to greater local costs of the PST/PSM strategy compared with the alternative testing strategy and sources of effectiveness data. Across all the aforementioned studies, the total cost of testing with PST and/or PSM outweighed the cost of alternative strategy. These findings were mainly driven by the effectiveness data used to estimate the number of thromboembolic and hemorrhagic complications and death, their associated costs, and costs of testing strategies. In particular, Jowett et al. used patient-level data from a randomized controlled

trial (RCT) by Fitzmaurice et al. [20] that if summarized (Heneghan et al. [14]) indicate greater RRs of thromboembolic and hemorrhagic events for PST and/or PSM compared with the alternative testing strategy. In the studies by Regier et al. and Lafata et al., the number of thromboembolic and hemorrhagic events occurring while using the investigated testing strategies was estimated on the basis of the TTR achieved (i.e., 71.8% vs. 63.2% and 89% vs. 65%, respectively, on PST/PSM vs alternative testing) and the risk of those events conditional on the TTR. This estimation resulted in a relatively low number of events avoided with PST and/or PSM compared with the alternative testing strategy. Regier et al. found only 0.72 thrombotic and 0.17 hemorrhagic events avoided per 100 patients with PST and/or PSM in the first year, while after 5 years this summed up to 3.5 and 0.79 events avoided, respectively. Similarly, Lafata et al. observed in total 4.9 events avoided per 100 patients with PST and/or PSM compared with the alternative testing strategy over a 5-year time horizon.

Strengths and Limitations

Inferences drawn from BIAs are related to the quality of the evidence that goes into the model. One point of strength of the current analysis is that effectiveness inputs are based on a consistent synthesis of evidence [14]. In the hierarchy of evidence pyramid, evidence synthesis of multiple trials resides above evidence from a single RCT [38,39]. Yet, it must be pointed out that no studies investigating the effectiveness of PST and/or PSM have been conducted in the Netherlands. In the present analysis, effectiveness measures were derived from studies investigating PST and/or PSM versus specialized testing centers for all OAT indications [19–22]. Because of the heterogeneity between the studies, a random-effect model was used to establish baseline risks for thromboembolic and hemorrhagic complications for patients using anticoagulation testing centers. To estimate risks of complications for patients using PST and/or PSM, RR reduction was applied as reported by Heneghan et al. [14]. In addition, an advantage of this approach over relying on data from a single RCT is that all indications for OAT were considered. This reflects a more complete assessment of the impact of different strategies on costs of anticoagulation testing. Also, we examined the impact of uncertainty surrounding the key model parameters on BIA results. Finally, to explore the impact of increasing market shares of PoC devices on the health care budget in specific settings, such as the use of PST alone and the use of PoC in patients with AF, scenario analyses were conducted.

Our study has several limitations. First, only direct medical costs were considered in our analyses and no costs related to productivity loss were included. Costs related to productivity loss may be reduced for patients using PST and/or PSM because they may miss less work as a result of greater effectiveness in the prevention of complications (Table 1). Also, testing at home with a PoC device avoids work time lost because it eliminates the need for travel and waiting time at testing centers. Yet, one caveat in considering productivity loss among patients indicated for OAT is that many are elderly patients, such as those with AF, and may already be retired. Notably, although the current estimates on cost savings in the 5-year time horizon applied are substantial, they may still reflect an underestimation of the true savings in the patient groups in whom accounting for productivity loss is considered to be appropriate (i.e., patients <65 years of age). Second, our model design may also be a factor for underestimation. In this analysis, clinical events and associated costs were followed for a cohort of patients for up to 5 years. An alternative approach is to dynamically add new patients each year as estimated by annual incidence rates. Such an approach would include more patients in the analysis because the incidence rates

are expected to continue to rise in the coming decades [3]. Third, the recent introduction of novel oral anticoagulants, such as dabigatran, rivaroxaban, and apixaban, in the Dutch market for use in patients with some of the indications for OAT was not accounted for in our study [40,41].

Currently, such a comparison between novel oral anticoagulants and VKAs managed with PST and/or PSM is hampered given the lack of RCTs between the two comparators as well as data on the current use of novel oral anticoagulants in clinical practice in the Netherlands. Fourth, future uptake of the PST and/or PSM strategy (i.e., 50%, 75%, and 100%) in this study was based on an assumption. Yet, it may be more informative to estimate this in relation to the factors influencing its current low market share, for example, because of patients' preferences. In particular, there are indications by some Dutch experts that some patients prefer to have more regular contact with hospitals/anticoagulation centers rather than to self-manage. In addition, they indicate that an increase in the uptake of PoC strategies could be achieved if these strategies would be actively offered to patients as an alternative to management in the clinics, which currently is not the case. Finally, because of data limitations, estimates of the baseline risks used in this study could not be supported by local real-life data. Such information is needed given that the baseline information used from the RCTs is commonly based on highly selected patient populations whose characteristics may deviate from the usual practice.

The potential deviation from the Dutch patient population indicated for long-term OAT may concern eligibility and exclusion criteria for PST and/or PSM. For example, one of the RCTs included only those patients who were 60 years or older [22], and another study excluded patients who failed to attend a training for PST/PSM [19]. This differs from the Dutch practice in which patients are eligible for PST and/or PSM if they are on long-term OAT and have passed the required training. Furthermore, the TTR observed at 1 year for patients visiting anticoagulation centers/clinics in the RCTs was in range from 61% to 68.8%. In the Dutch health care system, the quality of anticoagulation care performed by specialized anticoagulation testing centers is considered high, with approximately 80% of the patients having their measurements within the INR limits [2]. This study did not aim to model a possible association between the proportion of TTR with bleeding and thromboembolic risk, and one could expect that such an association would lead to lower baseline risk in Dutch patients and consequently greater expenditure for patients switching to PST and/or PSM. In conclusion, overall study findings indicated that compared with regular anticoagulation testing at specialized centers, PST and PSM with PoC devices can lead to cost savings in patients without AF. In addition, our study indicated that using PoC devices solely for PST resulted in greater expenditures compared with testing in anticoagulation clinics; thus, this strategy may need to be disregarded. Further research is needed to explore this strategy in other indications and confirm the aforementioned findings with local real-life data.

Given the increasing number of patients with indications for OAT and high treatment costs of thromboembolic events, the choice of the optimal monitoring and managing strategy is of high importance, both regarding the costs considered here and the health effects. Further research should be directed at performing formal CEAs comparing the two strategies in specific indications (AF, deep vein thrombosis, etc.). This would provide additional insights into both societal costs and long-term effects of those strategies on health, such as expressed in terms of QALYs.

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Supplemental Materials

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