

Mobile Cardiac Outpatient Telemetry Patch vs Implantable Loop Recorder in Cryptogenic Stroke Patients in the US – Cost-Minimization Model

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Purpose: The aim of this study was to compare costs and outcomes of mobile cardiac outpatient telemetry (MCOT) patch followed by implantable loop recorder (ILR) compared to ILR alone in cryptogenic stroke patients from the US health-care payors' perspective.

Patients and Methods: A quantitative decision tree cost-minimization simulation model was developed. Eligible patients were 18 years of age or older and were diagnosed with having a cryptogenic stroke, without previously documented atrial fibrillation (AF). All patients were assigned first to one then to the alternative monitoring strategies. Following AF detection, patients were initiated on oral anticoagulants (OAC). The model assessed direct costs for one year attributed to MCOT patch followed by ILR or ILR alone using a monitoring duration of 30 days post-cryptogenic stroke.

Results: In the base case modeling, the MCOT patch arm detected 4.6 more patients with AFs compared to the ILR alone arm in a cohort of 1000 patients (209 vs 45 patients with detected AFs, respectively). Using MCOT patch followed by ILR in half of the patients initially undiagnosed with AF leads to significant cost savings of US\$4,083,214 compared to ILR alone in a cohort of 1000 patients. Cost per patient with detected AF was significantly lower in the MCOT patch arm \$29,598 vs \$228,507 in the ILR only arm.

Conclusion: An initial strategy of 30-day electrocardiogram (ECG) monitoring with MCOT patch in diagnosis of AF in cryptogenic stroke patients realizes significant cost-savings compared to proceeding directly to ILR only. Almost 8 times lower costs were achieved with improved detection rates and reduction of secondary stroke risk due to new anticoagulant use in subjects with MCOT patch detected AF. These results strengthen emerging recommendations for prolonged ECG monitoring in secondary stroke prevention.

Keywords: ambulatory cardiac monitoring, Holter, atrial fibrillation, electrocardiography, economic evaluation, secondary prevention

Introduction

The fifth leading cause of death in the United States (US) is stroke. Annual incidence of stroke is 795,000 patients.¹ Stroke can be classified into two major subtypes: hemorrhagic, representing about 17% and ischemic, representing around 83% of patients. Of the ischemic strokes, approximately 15–40% are considered to be cryptogenic strokes, ischemic strokes with no identifiable etiology.^{1,2}

Identifying the cause of a stroke in the one-third of patients suffering cryptogenic stroke is essential for the implementation of appropriate secondary stroke prevention strategies.^{1,3–5} Newly diagnosed atrial fibrillation (AF) is only identified

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in $\approx 5\%$ of patients with stroke in the inpatient setting,⁶ but paroxysmal AF (PAF) may not be present at the time of the stroke or may escape detection during inpatient cardiac monitoring.⁷ Thus, outpatient cardiac monitoring is often used to improve the identification of PAF.

AF is defined as an episode of irregular heart rhythm, without detectable P waves, of any duration.^{8–10} AF is associated with an increase in the risk of stroke, cardiovascular morbidity and mortality, and significant increases in the total cost of care and impairment in quality of life (QoL).^{11,12} Among patients with AF, those with a history of stroke carry the highest risk of recurrent stroke, with a 15% risk during the first year after stroke (2.5 times higher than in those without a previous stroke).^{13,14} Management of stroke in the setting of AF is expensive, with one source citing an annual cost of approximately \$26 billion.¹⁵ Additionally, the major risks associated with undetected AF, both persistent and paroxysmal, are ischemic stroke and other thromboembolic events, which could be prevented by a prompt diagnosis of AF and consequent oral anticoagulant (OAC) therapy.^{16–19} Early identification of AF and treatment with OAC will reduce the risk of recurrent stroke and death in both the primary or secondary prevention setting.²⁰ The American Heart Association/American Stroke Association Guidelines recommend a confirmed diagnosis of AF following stroke before initiation of anticoagulant therapy whereas in the absence of proven AF, antiplatelet therapy is usually recommended.²¹

Atrial fibrillation can remain undetected in patients using the current standard of care (SoC) for AF detection – electrocardiogram (ECG) monitoring for at least 24h after a stroke.^{22–24} To detect AF, recommendations from the American Academy of Neurology suggest monitoring cardiac rhythm for prolonged periods, often for periods longer than 1 week, instead of shorter periods (ie, 24 hours) in patients with cryptogenic stroke without known AF.²⁵

Clinicians have several monitoring options offering different monitoring periods, detection rates and costs. Common monitoring solutions include: Holter monitors (short-term (24–48h) and long-term (1–2 weeks)), post-event recorders (non-looping recorders), external loop recorders (ELR), mobile cardiac outpatient telemetry (MCOT), and implantable loop recorders (ILR).²⁶ Due to variation in the costs and outcomes, an economic evaluation comparing some of these options would inform treatment choices and health system efficiency. Therefore, the

analysis described here focused on a post-stroke population in which options included monitoring with MCOT[®] patch (BioTelemetry Inc, a Philips company, Malvern, PA, USA) for 30 days possibly followed by ILR if AF is not diagnosed or ILR monitoring only with evaluation of up to the first 30 days of monitoring.

Materials and Methods

The aim of this economic analysis was to assess the costs associated with MCOT patch followed by ILR, compared to ILR alone in cryptogenic stroke patients from the US payors' perspective.

We designed a quantitative decision-tree simulation model with base values identified through targeted literature reviews. The analysis described will aid clinicians and hospital procurement staff to optimize patient outcomes and improve health system efficiency.

Several targeted literature searches were performed to obtain source data on costs, the probability of different events occurring, different model designs, modeling assumptions, current standard medical practice for monitoring cryptogenic stroke patients and different international medical guidelines. Search terms used to identify articles in PubMed included: disease terms (ischemic stroke, atrial fibrillation), intervention terms (cardiac monitoring, electrocardiography) and health economics terms (cost-minimization analysis, cost-effectiveness analysis, cost-benefit analysis, cost-utility analysis). Search strategies were restricted to publications written in English. There were no time restrictions for studies; however, most recently published studies were preferred. The main inclusion criteria were: cryptogenic stroke patients based in the USA wearing either MCOT or ILR.

Model Structure

Figure 1 illustrates the model structure used for quantifying costs and outcomes at every stage of monitoring and treatment. There are two diagnostic and monitoring arms in the model:

- MCOT patch arm: MCOT patch followed by ILR in undetected AF patients for 30 days;
- ILR arm: ILR alone evaluating first 30 days of monitoring.

Eligible patients were 18 years of age or older and were diagnosed with cryptogenic stroke, without previously documented AF at the time of index presentation or

following in-hospital Holter monitoring, and for whom additional cardiac monitoring would be desired to screen further for the possibility of paroxysmal AF.

A quantitative decision tree cost-minimization simulation model was developed in Microsoft Excel applying a one-year time horizon without discounting of costs or outcome.

Model Assumptions

Several assumptions were applied in the model consistent with previous studies, identified through a targeted literature review, reporting costs of stroke prevention in patients with AF:^{27,28}

1. All patients entered the model with “no underlying AF” or “occult AF not detected.” Depending on the diagnostic performance of the allocated ECG monitoring strategy, AF was subsequently detected, and patients were initiated on appropriate therapy (ie, anticoagulation with OACs).
2. The diagnostic yield of devices was constant for a 30-day period. The cumulative probability of diagnosis of post-stroke AF for MCOT was taken from a meta-analysis performed by Sposato et al 2015.²⁹ The cumulative probability of diagnosis of post-stroke AF for ILR was taken from the Ziegler et al 2015 study.³⁰
3. The selection of antithrombotic agents for secondary stroke prevention in patients who were found to have AF after cryptogenic stroke was at the discretion of their treating physician.
4. Absence of stroke implied that no additional costs other than monitoring were accrued. Therefore, we did not calculate any costs for those patients that did not have recurrent strokes and ongoing management costs.
5. AF was defined as AF of any duration based on study treatment protocol of a large number of cryptogenic stroke patients diagnosed with AF. These stroke patients, in whom AF of any duration was diagnosed, were all advised to begin anticoagulation unless clinical contraindications existed.³¹
6. The percentage of patients using oral anticoagulants and aspirin was the same. However, two scenarios were considered:
 - a. Base case: 100% for both aspirin and OAC – Assumption.
 - b. Scenario 1: 84% for both aspirin and OAC – based on Favilla et al 2015.³¹

7. The cost analysis assumed 100% treatment compliance
8. The time horizon of the model was 1 year post cryptogenic stroke.
9. All four OACs (dabigatran, rivaroxaban, apixaban, edoxaban) applied in the model were considered to have the same/similar efficacy.
10. All patients with newly detected AF receiving OAC in the study would derive the same clinical benefit regarding secondary stroke prevention.
11. Cryptogenic stroke was assumed to be similar/same for all patients. Therefore, the size, severity of stroke and the risk of recurrent bleeding were not taken into account.

Perspective and Time Horizon

The economic analysis of this model was performed from a US payor perspective including only direct medical costs. The current model assesses the costs accrued with MCOT patch followed by ILR or ILR alone using a monitoring time of 30 days and a time horizon of one year post-cryptogenic stroke.

Input Parameters

The dosages of OACs were aligned with the dosages prescribed in the summary of product characteristics. The acquisition costs were obtained for the smallest pack size. In our model, all patients started treatment with aspirin. OACs were initiated only upon AF detection. Of those receiving anticoagulant therapy (dabigatran, rivaroxaban, apixaban, edoxaban), an average price of all four drugs was used. The costs were inflated from the published cost year to 2021 levels using the Medical Consumer Price Index as reported by the US Bureau of Labor Statistics.³² An overview of all cost inputs used in the model is provided in [Table 1](#).

Event Probabilities

Event probabilities used in the model are shown in [Table 2](#). Values were derived from published studies identified through targeted literature review. All-cause mortality rates were derived from Sawyer et al.³³

Depending on the diagnostic performance of the allocated monitoring strategy, AF was subsequently detected, and patients were initiated on appropriate therapy (ie, OACs). If subsequent testing for AF was non-diagnostic, patients received aspirin alone ([Figure 1](#)). To account for differences in costs, and post-stroke mortality, we further

Table I Model Input Parameters – Costs

Parameter	Value Used in the Model (Inflated to 2021 Values)	Original Value (Year)	Reference
DRUG COSTS – 1 month therapy			
Aspirin (108x81mg)	\$3.20	N/A	[40]
Dabigatran	\$320.96	\$296.06 (2018)	[41]
Rivaroxaban	\$335.64	\$309.60 (2018)	[41]
Apixaban	\$336.01	\$309.94 (2018)	[41]
Edoxaban	\$272.00	\$250.90 (2018)	[41]
Average price of OAC (dabigatran, rivaroxaban, apixaban, edoxaban)	\$316.15	N/A	Calculation
STROKE COSTS			
Recurrent mild stroke	\$14,657.50	\$12,398.00 (2015)	[42]
Recurrent moderate stroke	\$31,031.62	\$26,248.00 (2015)	[42]
Recurrent severe stroke	\$71,893.62	\$60,811.00 (2015)	[42]
Recurrent fatal stroke/death	\$35,123.37	\$29,709.00 (2015)	[42]
COST OF INFECTIONS			
Risk-adjusted cost for Superficial Surgical site infections	\$9,507.73	\$7,003.00 (2010)	[43]
BLEEDING COSTS			
Major bleeding	\$20,750.52	\$19,469.00 (2019)	[44]
CRNM bleed event	\$5,201.22	\$4,880.00 (2019)	[44]
MCOT COSTS			
Professional Fee	\$27.92	\$27.43 (2020)	CPT: 93,228 CMS Physician Fee Schedule 2020 (National Average) https://www.cms.gov/apps/physician-fee-schedule/search/search-criteria.aspx
Technical Fee	\$728.32	\$715.66 (2020)	CPT 93229
Total MCOT Cost:	\$756.24	\$743.09	

(Continued)

Table I (Continued).

Parameter	Value Used in the Model (Inflated to 2021 Values)	Original Value (Year)	Reference
ILR COSTS			
Professional Fee	\$28.65	\$28.15	CPT: 93,298 CMS Physician Fee Schedule 2020 (National Average) https://www.cms.gov/apps/physician-fee-schedule/search/search-criteria.aspx This accounts for 1/12th of the fee (for 1 month only)
Technical Fee	\$280.26	\$275.39	CPT: G2066 G2066 is Carrier Priced. Above rate is based on NY Locality 2 Physician Fee Schedule [LINK] This accounts for 1/12th of the fee (for 1 month only)
Insertion of ILR	\$5,250.64	\$5,159.37	CPT: 33,285 This accounts for the whole fee.
Removal of ILR	\$139.93	\$137.50	CPT: 33,286 This accounts for the whole fee.
Total ILR Cost:	\$5,699.48	\$5,600.41	

Abbreviations: CMS, Centers for Medicare & Medicaid Services; CPT, current procedural terminology; GI, gastrointestinal; ILR, implantable loop recorder; MCOT, mobile cardiac outpatient telemetry; OAC, oral anticoagulant.

stratified the patients based on mild, moderate, or severe post-stroke classified by the Modified Rankin Scale (mRS). The mild, moderate, and severe cases were defined as a mRS score of 0–2, 3–4, and 5, respectively.

At any point, there was a risk that patients experience an adverse event, such as bleeding as a side-effect of OAC therapy. Bleeding events incorporated into the model included major bleeding and clinically relevant non-major (CRNM) bleeds.

Analyses

The analysis quantifies the cumulative one-year costs following the initial treatment choice between MCOT and ILR and the incremental cost difference.

The results of the model will be presented for the base case and 3 different scenario analyses. An overview of the differences among base case and scenarios can be found in Table 3.

Parameter uncertainty was explored by use of deterministic one-way sensitivity analyses (OWSAs). Fundamental clinical input parameters were individually varied as $\pm 25\%$ (user-modifiable) of the point estimate for event probabilities.

Model Outcomes

The primary model outcome was the difference in total costs between MCOT patch and ILR only arms for the whole cohort of 1000 patients. Relevant secondary outcomes included: difference in costs per AF detected, average cost per one patient monitored, incremental recurrent strokes avoided and incremental infections avoided using MCOT patch vs ILR only arms.

Results

Base Case Results

The results of the base case economic analysis (per diagnosis arm and incremental results) are displayed in Tables 4 and 5.

Using the MCOT patch followed by ILR as the first choice for diagnosing AF after cryptogenic stroke leads to significant cost savings compared to ILR alone. The MCOT patch arm detected 4.6 times more patients with AF compared to the ILR alone arm based on a cohort of 1000 patients (209 vs 45 patients with detected AF respectively). The number of bleeding events was higher in the MCOT patch arm because more

Table 2 Model Input Parameters – Event Probabilities

Parameter	Value Used in the Model	Reference
Stroke-related probabilities		
Recurrent mild stroke	42%	[33]
Recurrent moderate stroke	26%	[33]
Recurrent severe stroke	10%	[33]
Recurrent fatal stroke/death	22%	[33]
Recurrent stroke in 1st year without OAC	15%	[13,14]
Recurrent stroke in 1st year with OAC	7.50%	[24]
Infection rate ILR		
Infection rate after ILR	0.7%	[45]
Extrusion rate ILR		
Extrusion rate after ILR	2.25%	[45]
Bleedings		
Annual bleeding rate combined (average from dabigatran, rivaroxaban, apixaban, edoxaban)	2.9%	[46]
Major bleeding	2.02%	[44]
CRNM bleed event	4.18%	[44]
Detection rates		
Detected AF MCOT	19.10%	[29]
No AF/Undetected AF [MCOT]	80.90%	Calculation based on Sposato et al 2015 ²⁹
Detected AF ILR	4.60%	[30]
No AF/Undetected AF [ILR]	95.40%	Calculation based on Ziegler et al 2015 ³⁰
No AF/Undetected AF [ILR] - After extrusion	100.00%	Assumption
Drug usage probabilities		
OAC usage post-detection of AF (base case)	100%	Assumption
Aspirin usage (base case)	100%	Assumption
OAC usage post-detection of AF (scenario analysis)	84%	[31]
Aspirin usage (scenario analysis)	84%	[31]
Other		
Percentage of patients getting ILR after MCOT and undetected AF or No AF	50–60%	KOL opinion

Abbreviations: AF, atrial fibrillation; CMS, Centers for Medicare & Medicaid Services; CPT, current procedural terminology; CRNM, clinically relevant non-major; GI, gastrointestinal; ILR, implantable loop recorder; MCOT, mobile cardiac outpatient telemetry; OAC, oral anticoagulant.

Table 3 Overview of Model Scenarios

	Base Case	Scenario 1	Scenario 2	Scenario 3
Percentage of patients getting ILR after MCOT and undetected AF or No AF	50%	50%	60%	60%
OAC usage post-detection of AF	100%	84%	100%	84%
Aspirin usage	100%	84%	100%	84%

Abbreviations: AF, atrial fibrillation; ILR, implantable loop recorder; MCOT, mobile cardiac outpatient telemetry; OAC, oral anticoagulant.

Table 4 Base Case – Clinical Results for a Cohort of 1000 Patients

	MCOT Patch Followed by ILR*	ILR	Difference MCOT Patch - ILR
Number of patients with detected AFs in a cohort of 1000 patients	209	45	164
Strokes			
Number of Recurrent Mild Strokes	30.9	61.6	-30.7
Number of Recurrent Moderate Strokes	19.1	38.1	-19.0
Number of Recurrent Severe Strokes	7.4	14.7	-7.3
Number of Recurrent Fatal Strokes/Deaths	16.2	32.3	-16.1
Total number of Recurrent Strokes	73.6	146.6	-73.0
Bleedings			
Number of Major bleedings	4.2	0.9	3.3
Number of CRNM bleed events	8.7	1.9	6.9
Total Number of bleedings	13.0	2.8	10.2
Infections/extrusions			
Number of infections	2.83	7.00	-4.17
Number of extrusions	9.10	22.50	-13.40

Note: *Percentage of undetected AF patients in MCOT patch group receive ILR for diagnosis.

Abbreviations: AF, atrial fibrillation; CRNM, clinically relevant non-major; ILR, implantable loop recorder; MCOT, mobile cardiac outpatient telemetry.

detected AF patients were started on OACs (13 vs 2.8 bleeding events, respectively, on a cohort of 1000).

We estimate that 16 fatal strokes were avoided in a cohort of 1000 patients annually for those diagnosed with MCOT compared to ILR.

The cost per patient with detected AF was significantly lower in the MCOT patch arm than in the ILR arm (\$29,598 vs \$228,507, respectively). The average cost per patient monitored with MCOT followed by ILR compared to ILR alone was \$6,192 vs \$10,275, respectively.

Model Uncertainty

Varying important clinical parameters in the model influenced the incremental cost savings between both treatment arms (Figure 2). The incremental cost savings was most sensitive to the percentage of undetected AF in patients receiving ILR after MCOT and undetected AF, followed by recurrent stroke without OAC (when only aspirin is given). Varying the proportion of infection rates, major bleeding with ILR and CRNM bleeding had limited influence on the conclusions of the base case analysis.

Table 5 Base Case – Economic Results for a Cohort of 1000 Patients

	MCOT Patch Followed by ILR*	ILR	Difference MCOT Patch - ILR
Device	\$3,061,680	\$5,699,480	-\$2,637,800
Fatal strokes/Death	\$568,995	\$1,133,013	-\$564,018
Recurrent strokes	\$1,576,819	\$3,139,845	-\$1,563,026
Infections	\$26,921	\$66,554	-\$39,633
Bleeding events	\$133,163	\$28,623	\$104,540
Aspirin costs	\$30,399	\$36,712	-\$6,313
OAC costs	\$793,625	\$170,590	\$623,035
Total costs	\$6,191,602	\$10,274,816	-\$4,083,214
Cost per patient with detected AF	\$29,598	\$228,507	-\$198,909
Cost per 1 patient monitored	\$6,192	\$10,275	-\$4,083

Note: *Percentage of undetected AF patients in MCOT patch group receive ILR for diagnosis.

Abbreviations: AF, atrial fibrillation; ILR, implantable loop recorder; MCOT, mobile cardiac outpatient telemetry; OAC, oral anticoagulant.

Scenario Analyses

Scenario analyses were performed to investigate the impact on the total cost difference and number of detected patients with AF by varying the following parameters:

- Percentage of patients getting ILR after MCOT and undetected AF from 50% to 60% (Scenarios 2 and 3; [Table 3](#));
- Changing OAC and aspirin usage from 100% in the base case to 84% based on Favilla et al 2015 study (Scenarios 1 and 3; [Table 3](#)).³¹

An overview of the clinical results of the difference between the MCOT patch arm and the ILR arm is presented in [Table 6](#). Total cost differences between the two arms are also presented in [Table 6](#) for all three scenarios. The highest impact on the total cost difference is an increase in the percentage of patients getting ILR after MCOT and undetected AF from 50% to 60%. However, this increase in costs did not lead to significantly more patients with detected AF and led to >10% increase in costs per patient with detected AF.

To summarize, base case results were confirmed by all three scenarios. Therefore, the results showed that 30-day ECG monitoring and diagnosis of AF in cryptogenic stroke patients with an MCOT patch arm, as the first choice, is cost-saving compared to ILR only arm.

Discussion

Conducting a cost analysis of AF poses technical and operational challenges as higher detection rates will lead to increased costs. In the analysis described here, the acquisition costs of MCOT are less than ILR; however, the improved detection rate with MCOT leads to higher costs associated with stroke prevention, but lower costs associated with stroke events. As is often the case in healthcare, investments in one technology can generate other health system costs and savings. This highlights the importance of conducting a comprehensive cost analysis taking into consideration the full range of costs and consequences. The success of a diagnostic and monitoring strategy is determined by the performance of the diagnostic tool and by the impact that an accurate and timely diagnosis can have on treatment and subsequent health events. In our model, we used AF episodes of any duration. As described here, the MCOT patch is associated with an approximate four-fold higher rate of patients with AF detection compared with ILR over 30 days of monitoring. This could be due to the studies showing a delay in the start of ILR monitoring as compared to the start of cardiac monitoring.²⁹ Additionally, it could be affected by AF detection criteria as AF episodes less than 2 minutes in duration are not detected by the ILR algorithm.³⁰ In the model, this resulted in more patients with detected AF, fewer recurrent strokes and fewer deaths

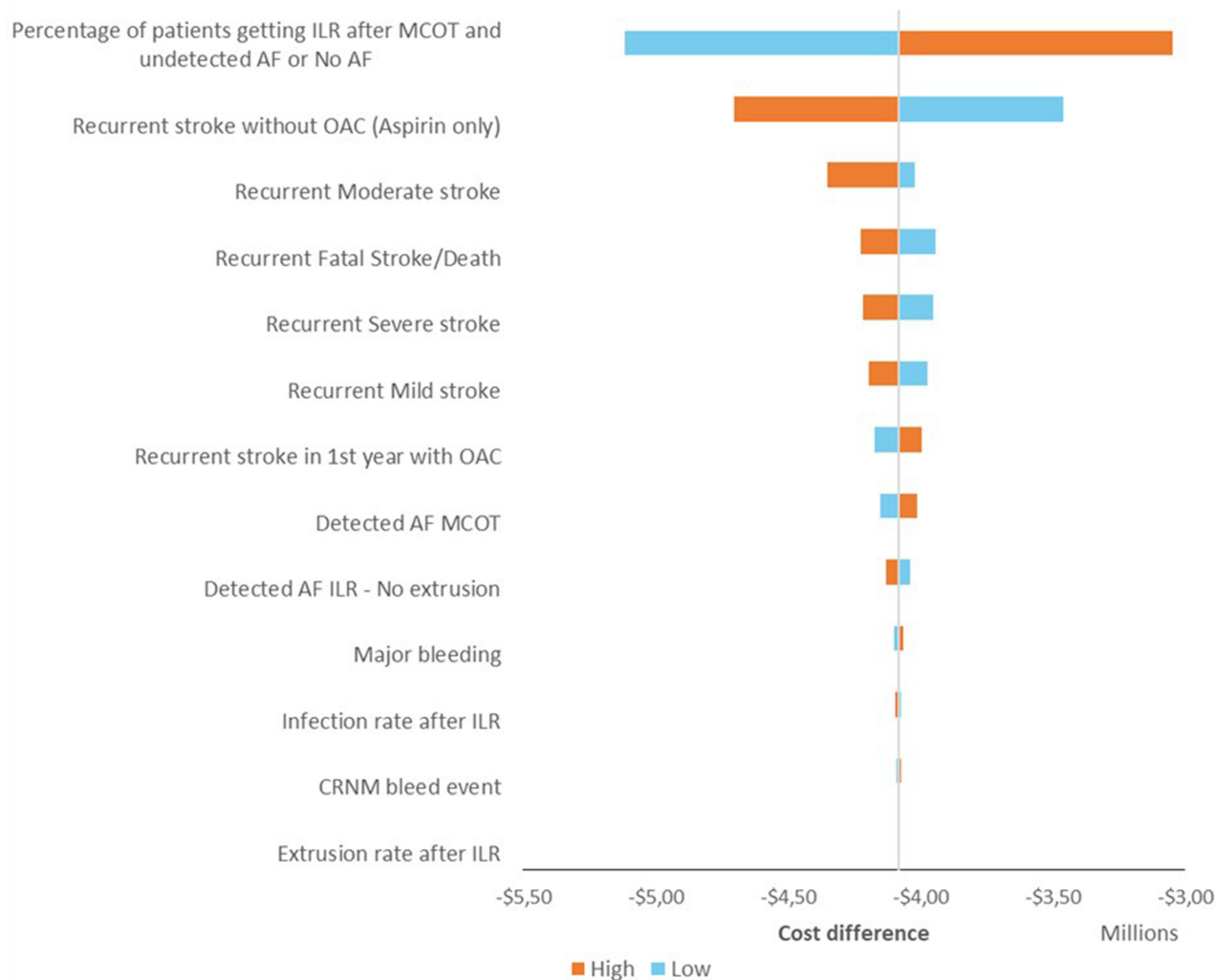


Figure 2 Incremental results one-way sensitivity analysis - Base case.

Abbreviations: AF, atrial fibrillation; CRNM, clinically relevant non-major; ILR, implantable loop recorder; MCOT, mobile cardiac outpatient telemetry; OAC, oral anticoagulant.

compared with ILR. Consequently, due to improved AF detection, the costs associated with oral anticoagulants and bleeding events were higher in the MCOT managed subjects due to increased oral anticoagulant usage. These costs were offset by savings associated with a reduction in recurrent stroke events and lower device costs. All patients with newly detected AF (regardless of duration) receiving any of the available OAC in the study would derive the same clinical benefit regarding secondary stroke prevention. In the real-world setting, this assumption would need to be validated and tested.

Other studies have examined the cost-effectiveness of ILR but have used a time horizon of over a lifetime,^{24,33–35} which is not relevant to our one-year timeframe. No prior

modeling study has examined the costs of MCOT from the US perspective. However, study by Tsang et al 2014 conducted a retrospective database analysis comparing MCOT to Event or Holter monitors in the US.³⁶ This study came to the similar conclusion like our study that hospitals should be promoting the use of MCOT over Event or the Holter monitors.³⁶ Another study, Kaura et al 2016, examined the costs of MCOT from the UK perspective.³⁷ One study, Yong et al 2016, compared different monitoring durations from Canadian perspective.³⁸ The conclusion from Yong et al's 2016 study is in line with our conclusion, meaning that in patients after a cryptogenic stroke, 30-day ECG monitoring is likely to be cost-effective for preventing recurrent strokes.³⁸ Our study is unique in that it

Table 6 Clinical and Economic Results (Difference MCOT Patch – ILR) for a Cohort of 1000 Patients – Scenarios 1, 2 and 3

	Scenario 1	Scenario 2	Scenario 3
Number of patients with detected AFs	164	168	168
Strokes			
Number of Mild Strokes	-30.7	-25.7	-25.7
Number of Moderate Strokes	-19.0	-15.9	-15.9
Number of Severe Strokes	-7.3	-6.1	-6.1
Number of fatal strokes/deaths	-16.1	-13.4	-13.4
Total number of strokes	-73.0	-61.1	-61.1
Bleedings			
Number of Major bleedings	2.8	3.4	2.8
Number of CRNM bleed events	5.8	7.0	5.9
Total Number of bleedings	8.6	10.4	8.7
Infections/extrusions			
Number of infections	-4.17	-3.60	-3.60
Number of extrusions	-13.40	-11.58	-11.58
Economic results			
Device	-\$2,637,800	-\$2,176,712	-\$2,176,712
Fatal strokes/Death	-\$564,018	-\$472,357	-\$472,357
Recurrent strokes	-\$1,563,026	-\$1,309,012	-\$1,309,012
Infections	-\$39,633	-\$34,249	-\$34,249
Bleeding events	\$87,814	\$106,856	\$89,759
Aspirin costs	-\$2,815	-\$6,453	-\$3,430
OAC costs	\$523,350	\$636,836	\$534,942
Total costs	-\$4,196,128	-\$3,255,091	-\$3,371,059
Cost per patients with detected AF	-\$198,789	-\$195,524	-\$195,406
Cost per 1 patient monitored	-\$4,196	-\$3,255	-\$3,371

Abbreviations: AF, atrial fibrillation; CRNM, clinically relevant non-major; ILR, implantable loop recorder; MCOT, mobile cardiac outpatient telemetry; OAC, oral anticoagulant.

compares two diagnostic strategies that have not been compared previously from the US cost perspective in a cost-minimization analysis.

Despite applying standard methodological approaches to our analysis, the study had several limitations that are worth taking into consideration when applying our results in practice. Firstly, the cost analysis considered only a 1-year time horizon for calculating costs and event rates. As strokes can occur after 1-year, extending the

analysis to future years would influence the results. Secondly, monitoring period for ILR is 30-days, but this technology is worn for much longer. Limiting the monitoring period for ILR was done to ensure consistency in monitoring time across technologies. Thirdly, the selection of antithrombotic agent for secondary stroke prevention in patients who were found to have AF after cryptogenic stroke was at the discretion of their treating physician. The analysis did not consider any drug-specific differences

in efficacy which could influence the results described here. Cryptogenic stroke was assumed to be similar/same for all patients. Therefore, the size, severity of stroke and the risk of recurrent bleeding were not taken into account. Furthermore, use of a payor perspective means that our model does not capture the societal costs of recurrent strokes from lost productivity. The inclusion of lost productivity would have a significant impact on our results considered the likely work loss and carer time associated with caring for people with strokes.³⁹

Our findings have implications for both clinicians and policymakers that can improve health system efficiency. Cryptogenic stroke patients are common in everyday stroke practice.³⁸ With practice guidelines now recommending longer than 1 week of monitoring cardiac rhythm to detect AF after cryptogenic stroke,²⁵ our results support the recommendation that 30-day MCOT monitoring be made available to cryptogenic stroke patients. Use of MCOT as the first-line evaluation of cryptogenic stroke patients would further the goal of optimizing secondary stroke prevention by identifying as many patients with atrial fibrillation as possible at the lowest cost per identifiable AF and at the highest quality of life for these patients.

Conclusion

The results of this cost-minimization analysis indicate that 30-day ECG monitoring and diagnosis of AF in cryptogenic stroke patients with MCOT patch arm as an initial diagnostic strategy is cost-saving compared to proceeding directly to ILR only. Cost-savings were achieved due to improved detection rates and subsequent prevention of future strokes in subjects monitored with MCOT patch. These results strengthen emerging recommendations for prolonged ECG monitoring in secondary stroke prevention.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

GM, JL, VN, MW, BAM and WMD are the employees of Philips. MW is the Chief Medical Officer for Biotelemetry, a producer of MCOT. NK and MPC are the employees of Global Market Access Solutions LLC. Global Market Access Solutions LLC received funding from Philips to build cost-minimization model and write the manuscript. The authors report no other conflicts of interest in relation to this work.

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