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ORIGINAL RESEARCH

Cost-Effectiveness of Monitoring Patients Post-Stroke With Mobile ECG During the Hospital Stay

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BACKGROUND: The effectiveness of a nurse-led in-hospital monitoring protocol with mobile ECG (iECG) was investigated for detecting atrial fibrillation in patients post-ischemic stroke or post-transient ischemic attack. The study aimed to assess the cost-effectiveness of using iECG during the initial hospital stay compared with standard 24-hour Holter monitoring.

METHODS AND RESULTS: A Markov microsimulation model was constructed to simulate the lifetime health outcomes and costs. The rate of atrial fibrillation detection in iECG and Holter monitoring during the in-hospital phase and characteristics of modeled population (ie, age, sex, CHA2DS2-VASc) were informed by patient-level data. Costs related to recurrent stroke, stroke management, medications (new oral anticoagulants), and rehabilitation were included. The cost-effectiveness analysis outcome was calculated as an incremental cost per quality-adjusted life-year gained. As results, monitoring patients with iECG post-stroke during the index hospitalization was associated with marginally higher costs (A$31 196) and greater benefits (6.70 quality-adjusted life-years) compared with 24-hour Holter surveillance (A$31 095 and 6.66 quality-adjusted life-years) over a 20-year time horizon, with an incremental cost-effectiveness ratio of $3013/ quality-adjusted life-years. Monitoring patients with iECG also contributed to lower recurrence of stroke and stroke-related deaths (140 recurrent strokes and 20 deaths avoided per 10 000 patients). The probabilistic sensitivity analyses suggested iECG is highly likely to be a cost-effective intervention (100% probability).

CONCLUSIONS: A nurse-led iECG monitoring protocol during the acute hospital stay was found to improve the rate of atrial fibrillation detection and contributed to slightly increased costs and improved health outcomes. Using iECG to monitor patients post-stroke during initial hospitalization is recommended to complement routine care.

Key Words: atrial fibrillation ■ cost-effectiveness analysis ■ iECG monitoring ■ stroke

Atrial fibrillation (AF) is associated with significantly increased risk of stroke. Among patients with established AF, patients with a history of stroke have the highest risk of future ischemic stroke.[1] Post-stroke patients with a diagnosis of AF are reported to carry a 15% risk over the first year of experiencing a recurrent stroke.[2,3] In contrast, patients with AF with no history of stroke only had a 6% risk of suffering from such an event.[2,3] AF thus is an important risk factor for stroke secondary prevention. However, a considerable proportion of patients with stroke might have paroxysmal, asymptomatic AF undetected, which places them at substantially increased risk of experiencing another ischaemic event. This under-diagnosis also precludes patients benefiting from new anticoagulants, which have proven to be significantly effective in reducing the risk of stroke recurrence by up to two thirds.[4–6] A systematic review and meta-analysis found that the AF

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CLINICAL PERSPECTIVE

What Is New?

- The potential health benefits in terms of number of recurrent strokes avoided, and long-term costs associated with nurse-led in-hospital monitoring for atrial fibrillation post-stroke were unknown.

What Are the Clinical Implications?

- The findings from this study showed the potential in identifying atrial fibrillation post-stroke could be translated into improved health outcomes accompanied with slightly increased cost, demonstrating values to complement routine practice.

Nonstandard Abbreviations and Acronyms

ICER	incremental cost-effectiveness ratio
iECG	smartphone-based handheld ECG device
NOAC	new oral anticoagulant

detection rate can be as high as 23.7% after 4 phases of sequential cardiac monitoring, while the diagnosis rate with in-hospital Holter monitoring was only 4.5%.[7]

The current stroke guidelines recommend that post-stroke patients should be monitored by an ECG for at least 24 hours,[8–10] and longer term monitoring was associated with greater detection rate of AF post-stroke or post-transient ischemic attack (TIA).[11,12] Adherence to these guidelines is suboptimal: an analysis of stroke registry data indicated that only 30% of patients received 24-hour Holter monitoring within 30 days of their stroke.[13]

To improve the detection rate of undiagnosed AF, several alternative devices are available to overcome the limitations of traditional Holter monitoring.[14] A recent observational study prospectively examined the diagnostic performance of a smartphone-based handheld ECG device (iECG) in patients hospitalized because of stroke or TIA.[15] It was found that the nurse-led iECG surveillance after stroke before hospital discharge was more effective than routine 24-hour Holter monitoring, by detecting AF earlier and changing subsequent management.[15]

Given the demonstrated clinical effectiveness of iECG, the next important question is whether offering this new model of cardiac monitoring represents value-for-money. This study aimed to undertake a modeled economic evaluation based on recently published clinical data to assess the cost-effectiveness of iECG in detecting AF for patients post-stroke or post-TIA during the acute in-hospital phase.

METHODS

Data Availability Statement

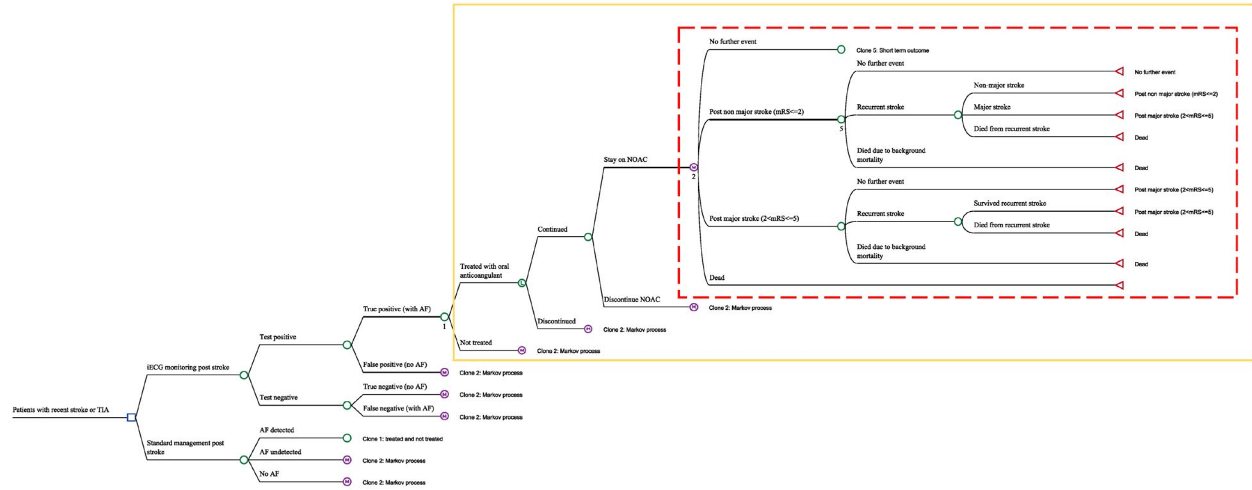
The data and methods that support the findings of this study are available from the corresponding author upon reasonable request.

Model Structure

A Markov microsimulation model, consisting of no further events, post–non-major stroke (defined by modified Rankin scale (score ≤2), post-major stroke (modified Rankin scale score 3–5), and death (modified Rankin scale score=6), was constructed to simulate the long-term outcomes after an index stroke/TIA (Figure 1). Following the study outcome, a proportion of patients being diagnosed with AF via iECG (ie, true positives) and routine Holter surveillance would initiate the new oral anticoagulant (NOAC) treatment. Over a lifetime horizon, patients post-stroke/TIA may remain event-free or experience a recurrent stroke (non-major or major defined by modified Rankin scale score ≤2 or >2), or die from non-stroke causes. Non-major recurrent strokes were considered because of significant detection of clinically silent infarcts in patients with AF (15%).[16]

Population

A hypothetical cohort of Australian patients who had survived an ischemic stroke/TIA as defined by the characteristic from the primary study in 2017 was simulated. Briefly, a total of 1079 patients (median age of 66 years with predominantly male participants) were recruited for the study from 8 hospitals across China and Australia.[15] The total number of ischemic strokes and deaths from stroke were sourced from publicly available data.[17–19] CHA2DS2-VASc scores calculate the stroke risk for patients with AF. The post-stroke CHA2DS2-VASc score, age, and sex distribution of each simulated patient were defined by the patient-level data from the primary observational study,[15] and the CHA2DS2-VASc score was modified by increasing age over the timeframe of the simulation for patients with diagnosed AF. In the base case analysis, the simulated stroke survivors run through the Markov microsimulation model one-by-one and are followed for 20 years given the remaining life expectancy from corresponding general Australians. The AF detection rate by monitoring protocols was derived from patient-level data from the original study.[15] Ethics approval for



Red dashed rectangle represents the Clone 2: Markov process; Yellow continuous rectangle denotes the Clone 1: treated and not treated

Figure 1. Markov simulation model structure.
AF indicates atrial fibrillation; iECG, smartphone-based handheld ECG device; mRS, modified Rankin Scale; NOAC, new oral anticoagulant; and TIA, transient ischemic attack.

the primary study was obtained with patient consent waiver through the Melbourne Health Human Research Ethics Committee on March 25, 2015.

Transition Probability

The proportion of patients being diagnosed with AF using iECG or Holter monitoring was derived from the primary study (8.5% versus 2.8%). The annual probability of recurrent stroke for each hypothetical patient was derived directly from their CHA2DS2-VASc score if they were comorbid with AF.[20] It was conservatively assumed that most patients would have a non-major stroke in the event of a recurrent event,[21,22] even though AF-related stroke would be expected to be more disabling. The compliance and adherence with NOAC treatment was also considered (15% discontinued in the first year and 2% thereafter).[23] All the transition probabilities are presented inTable 1 [7,15,23–29] and Tables S1 to S2.

Costs

Costs relating to iECG monitoring, rehospitalization because of recurrent stroke, stroke management (ie, outpatient care with GP/specialist, medications, examinations, etc.), rehabilitation, NOAC, and adverse events because of NOAC (ie, gastrointestinal and intracranial bleeding) were included in the model (Table 2). It was assumed that formal diagnosis of AF in patients receiving iECG monitoring (ie, those who tested either true or false positive) would require a read over by a specialist referred by a GP for patients receiving iECG monitoring (equivalent to the cost of performing a 24-hour Holter recording) and removal of the cost for specialist overread was tested in the sensitivity analysis. For the patients classified as false negatives, the same costs related to the formal AF diagnosis were also applied. For the intervention cost, in addition to the device cost of iECG, the opportunity cost of nurse's time to deliver the iECG monitoring was also included (average 2.5 recordings per day for a duration of 4 days).[15] The distributions for key cost inputs are constructed to account for first-order uncertainty (Table S3).[30]

Utility Weights

Utility weights corresponding to each modeled health state (no further event, post–non-major stroke, and post-major stroke) were derived from the published literature. A disutility (utility decrement attributable to an event) was applied if a patient experienced a recurrent stroke and/or adverse event attributable to NOAC. Moreover, a utility decrement was applicable to all patients as per the monitoring strategy to account for the quality-of-life impact from either wearing a Holter or being monitored frequently by iECG. The utility weights and disutility are shown in Table 1.

Further details on methods are presented in Data S1.

Cost-Effectiveness Analysis

The primary outcome measure for the cost-effectiveness analysis was the quality-adjusted life-year (QALY) gained. Utility weights were assigned to the corresponding life-years lived. Current clinical practice (ie, Holter monitoring over the acute hospital stay) to identify AF in patients post-stroke was adopted as the comparator. The incremental cost-effectiveness

Table 1. Probabilities and Utility Weights for the Markov Model Parameters

Variable	Base case	Range	Reference
Sensitivity of iECG	0.97	0.92–1.00	Lowers et al[24]
Specificity of iECG	0.92	0.89–0.93	Lowers et al[24]
Prevalence of AF after a stroke/TIA	0.0876		
Proportion of patients experienced gastro bleeding with anticoangulant treatment (per yearly cycle)	0.004	…	Connolly et al 2011[25]
Proportion of patients experienced intracranial bleeding with anticoangulant treatment (per yearly cycle)	0.006	…	Connolly et al 2011[25]
Probability of diagnosing AF using iECG	0.085	0.05–0.10	Yan et al 2020,[15] and Sposato et al 2015[7]
Probability of diagnosing AF not using iECG	0.028	…	Yan et al 2020[15]
Relative risk of background mortality for patients with AF and no AF	1.66	1.59–1.73	Miyasaka et al 2007[26]
Probability of treating with oral anticoagulant in the iECG group	0.44	…	Yan et al 2020[15]
Probability of treating with oral anticoagulant in the no iECG group	0.625	…	Yan et al 2020[15]
Probability of recurrent stroke without AF (per yearly cycle)	0.021	…	Mohan et al 2011[27]
Probability of having a non-major stroke	0.5	…	Assumption*
Relative risk of all-cause mortality for NOAC vs no NOAC	0.79	0.62–1.02	Connolly et al 2011[25]
Relative risk of stroke for NOAC vs no NOAC	0.37	0.25–0.55	Connolly et al 2011[25]
Discontinuation rate with NOAC			
First year	0.15	…	Garkina et al 2016[23]
Second year onwards	0.02	…	Garkina et al 2016[23]
Baseline utility	0.63	0.50–0.76	Sturm et al 2002[28]
Utility post a major stroke	0.35	…	Sturm et al 2002[28]
Utility post a non-major stroke	0.55	…	Sturm et al 2002[28]
Utility decrement from Holter monitoring	0.0203	…	Diekmann et al 2019[29]
Utility decrement from iECG monitoring	0.0020	…	Assumption

AF indicates atrial fibrillation; iECG, smartphone-based handheld ECG device; NOAC, new oral anticoagulant; and TIA, transient ischemic attack.
*Assuming equal probability of having a major and non-major stroke.

ratio (ICER) representing the ratio between incremental cost (ie, total costs related to iECG and Holter monitoring) and incremental QALYs (ie, total QALYs related to these 2 management groups) was calculated. Both costs and QALYs were discounted at a rate of 3%.[37] All the costs were expressed in Australian dollars valued for the 2018 reference year. An often cited willingness-to-pay per QALY threshold (A$50 000/QALY) was adopted to determine the cost-effectiveness of iECG surveillance compared with the usual care over a 20-year time horizon.[38]

Sensitivity Analyses

Both deterministic and probabilistic sensitivity analyses were performed to examine the model parameter uncertainty around the cost-effectiveness of iECG. For the deterministic sensitivity analyses, individual key model parameters were varied within a plausible range (informed by the published literature) one at a time to explore their impact on the ICER. A lifetime time horizon (ie, simulated until all patients were dead) was examined in the sensitivity analysis. The results from deterministic sensitivity analyses are presented in a Tornado diagram.

Probabilistic sensitivity analyses were undertaken which incorporated the distributions of main model parameters (ie, probabilities, utility weights, and costs) on the assumption that they were all independent of each other (eg the variation in transition probability was not correlated with changes in utility). Monte Carlo simulations randomly sampled 2000 parameters from a given distribution and then parameterised the Markov microsimulation model for each hypothetical patient (Table 1 and Table S4).

Estimation at the National Level

The 5-year budget impact of implementing this nurse-led AF monitoring protocol during the acute phase was further explored to examine its national impact. The number of ischemic stroke patients who survived an acute incident event and had no prior history of AF for the next 5 years from 2017 onwards were simulated. Costs were discounted at 3% per annum.[37]

RESULTS

The results of the observational study were reported in detail elsewhere.[15] Briefly, following screening in the stroke

Table 2. Unit Costs of Markov Model Parameters

Cost item	Unit cost	Reference
Gastrointestinal bleeding	$4777	AR-DRG G61A, G61B[31]
Intracranial bleeding	$23 648 ($19 060–28 235)	AR-DRG B70A[31]
Hospitalization for a major stroke	$17 724 ($14 212–21 235)	Cost weight 8.0 round 20 (2015–2016)[31]
Dying immediately from acute stroke	$11 541 ($9302–13 779)	Cost weight 8.0 round 20 (2015–2016)[31]
Hospitalization for a non-major stroke	$6666 ($5372–7959)	Cost weight 8.0 round 20 (2015–2016)[31]
Monitoring with iECG	$22	Orchard et al[32]
Nurse's time to administer iECG monitoring	$5.6	Calculated as 10 min (10 recordings ×1 min/recording) times with the average hourly wage (A$33.59) for a nurse
Monitoring with 24-h Holter	$170.15	MBS 11709
Specialist consultation	$86.85	MBS 104
GP consultation	$38.75	MBS 23
Management post a non-major stroke	$1559	Arona et al 2018[33]
Management post a major stroke	$11 368 ($9162–13 573)	Arona et al 2018[33]
Novel oral anticoagulant medication per year	$1273	PBS 10414D
Rehabilitation for a major stroke	$67 158 ($60 340–73 976)	Costing data from Royal Melbourne Hospital, Australia
Rehabilitation for a non-major stroke	$7170	Gao et al 2019[34]

MBS indicates Medicare Benefits Schedule Australia[35]; and PBS, Pharmaceutical Benefits Scheme Australia.[36]

ward, the study recruited 1079 patients who underwent iECG monitoring, and 294 patients who had both iECG and 24-hour Holter outcomes concurrently with a median CHA2DS2-VASc score of 4 (interquartile range, 3–5). During routine observations of vital signs (typically every 2 to 4 hours), trained nursing staff performed iECG recordings on patients up to the time of hospital discharge. AF was detected in 8.5% by iECG versus 2.8% by 24-hour Holter recording (P<0.001). Median time from stroke onset to AF detect was 3 days (interquartile range, 2–6) for iECG and 7 days (interquartile range, 6–10) for Holter (P=0.02). Among patients detected with AF, the anticoagulant treatment during the hospital stay was initiated for 44% versus 63% in the iECG and Holter monitoring groups, respectively (P>0.05).

In 2017, there were 56 000 stroke events in Australia with ≈80% being ischemic strokes; 80% survived this acute incident event. It was assumed that one third of patients with stroke had a prior history of AF. Therefore, in the baseline cohort, there were 25 088 stroke survivors modeled in 2017.

Table 3. Base Case Results From the Cost-Effectiveness Analysis

	iECG	Usual care	Difference	ES*	ICER
Total cost	$31 196	$31 095	$101	0.002	
Management	$22 238	$22 240	−$3	…	
Rehabilitation	$5506	$5717	−$211	…	
Hospitalization	$2792	$2888	−$96	…	
NOAC	$563	$222	$342	…	
Adverse events	$70	$28	$43	…	
iECG device	$27	$0	$27	…	
No. of recurrent stroke†	0.344	0.358	−0.014	0.019	$7374
No. of stroke-related death†	0.064	0.066	−0.002	0.008	$56 275
QALY	6.697	6.663	0.034	0.012	$3013
LY	11.51	11.47	0.037	0.008	$2733

ES indicates effect size (calculated as standardized mean difference); ICER, incremental cost-effectiveness ratio; iECG, smartphone-based handheld ECG device; LY, life-year; NOAC, new oral anticoagulant; and QALY, quality-adjusted life-year.

*The average number of events across all simulated cohort since not all patients would experience an event over the modeled time horizon.

†Effect size <0.1 is considered trivial.

Cost-Effectiveness Analysis

Monitoring stroke survivors with iECG was associated with both higher cost and benefits (QALY): the total cost and QALYs of patients managed by iECG and 24-hour Holter were A$31 196 and 6.70 versus A$31 095 and 6.66, respectively. Increased costs related to the early initiation of NOAC (A$563 versus $222) and its associated adverse events (A$70 versus $28) could be partly offset by the cost savings resulting from lower costs of hospitalization (A$2792 versus A$2888), management (A$22 238 versus A$22 240), and rehabilitation (A$5506 versus A$5717). Not surprisingly, iECG-monitored patients also experienced fewer recurrent strokes over the lifetime horizon compared with those managed by 24-hour Holter (3440 versus 3580 per 10 000 stroke patients). Therefore, monitoring AF in patients post-stroke with iECG during the acute phase has an ICER of A$3013/QALY in comparison with traditional 24-hour Holter recording (Table 3).

Subgroup Cost-Effectiveness Analysis

In the subgroup of patients aged ≥65 years, the same rate of detection was 10.3% in the iECG and 4.0% in the 24-Holter recording groups (*P*<0.001). Similarly, iECG again led to higher costs and benefits. Results of the subgroup analysis are summarized in Table S5 and Data S2.

Sensitivity Analysis

The 1-way deterministic sensitivity analyses identified that the base case result was most sensitive to the increased relative risk for background mortality, the acquisition cost of NOAC, proportion of patients being treated with NOAC after AF detection, and cost of management for a major stroke (Figure 2).

The probabilistic sensitivity analysis showed that iECG monitoring has a 100% probability of being a cost-effective strategy to monitor AF in patients post-stroke using the $50 000/QALY willingness-to-pay threshold,

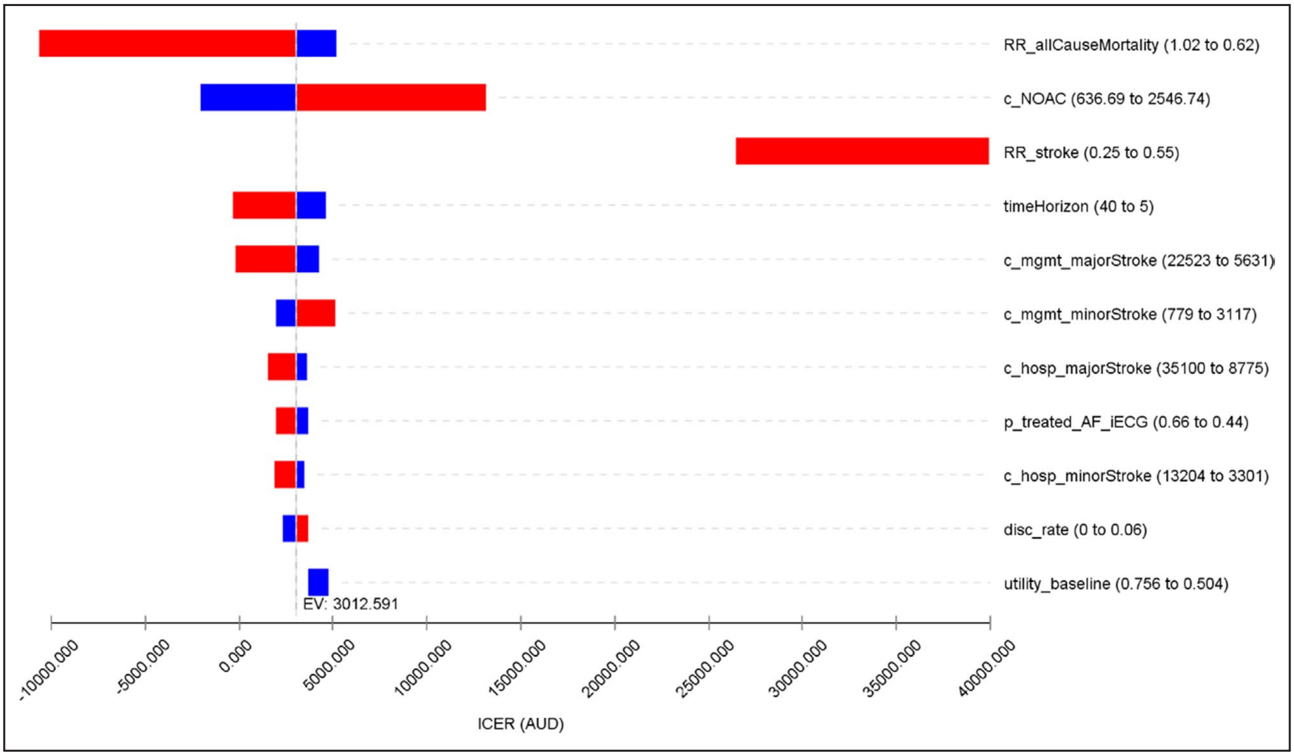


Figure 2. Tornado diagram for the 1-way deterministic sensitivity analyses.
Incremental net monetary benefit was calculated according to the willingness-to-pay/quality-adjusted life-year threshold of $50 000. The expected value at base case suggests that smartphone-based handheld ECG device (iECG) is associated with an incremental cost-effectiveness ratio of $3013/quality-adjusted life-year in the base case scenario. RR_stroke and utility_baseline do not align with the base case line as they both impact the results of iECG and standard care arms. c_NOAC indicates cost of new oral anticoagulant medications; c_hosp_majorStroke, cost of hospitalization for a major stroke; c_hosp_minorStroke: cost of hospitalization for a minor stroke; c_mgmt_majorStroke, annual management cost post a major stroke; c_mgmt_minorStroke, annual cost of management post a minor stroke; disc_rate, discount rate; EV, expected value; ICER, incremental cost-effectiveness ratio; p_treated_AF_iECG, probability of initiating oral anticoagulant treatment after AF detection by iECG; RR_allCauseMortality, relative risk of all cause mortality for oral anticoagulant treated vs non-oral anticoagulant treated patients; RR_stroke, relative risk of stroke for oral anticoagulant treated vs non-oral anticoagulant treated patients; timeHorizon, long-term modeled time horizon; and utility_baseline, utility weight for being post an ischemic stroke at baseline.

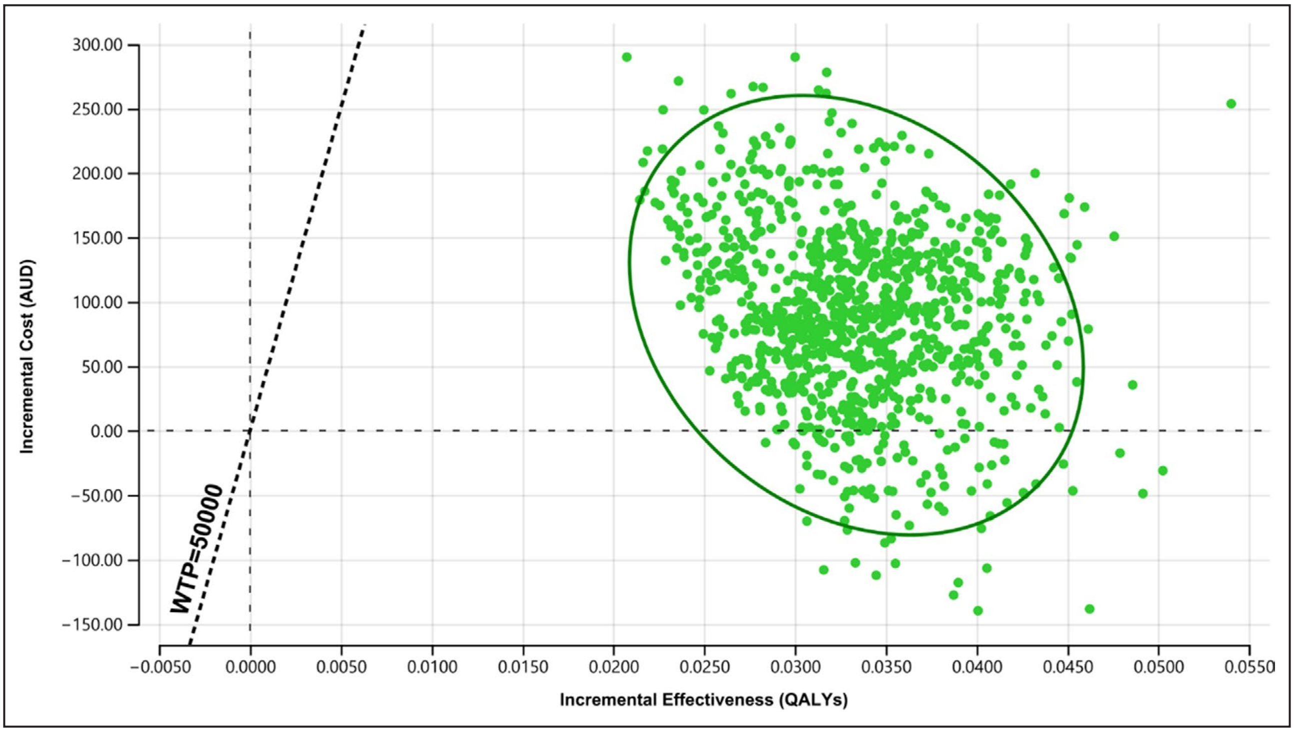


Figure 3. Incremental cost-effectiveness plane from the probabilistic sensitivity analysis.
One hundred percent of results suggesting smartphone-based handheld ECG device being the cost-effective monitoring strategy with 9.5% indicating less costly and more effective using the $50 000/quality-adjusted life-year willingness-to-pay threshold. AUD indicates Australian dollar; QALY, quality-adjusted life-year; and WTP, willingness-to-pay.

with 9.5% of results showing it was a dominant strategy (ie, less costly and more effective) (Figure 3).

For the subgroup of patients aged ≥65 years, a similar pattern was seen: the base case ICER was most sensitive to the variation in the relative risk for background mortality, relative risk of NOAC in preventing stroke, and the acquisition cost of NOAC (Figure S1). The probabilistic sensitivity analysis indicated that this nurse-led monitoring protocol had a 100% probability of being cost-effective using the $50 000/QALY willingness-to-pay threshold (Figure S2).

Estimation at the National Level

If rolled out to a national population, over 5 years, the total costs associated with iECG device (and time associated with iECG monitoring) and NOAC treatment (including related adverse events) were A$3.19 million and A$45.5 million. Meanwhile, the cost offset from avoided hospitalizations, rehabilitation, and long-term management was $36.6 million, which would result in a net cost to the health system of A$12.0 million over 5 years (Table S6).

DISCUSSION

A Markov microsimulation model was constructed to maximize the use of data from a key observational study and to reflect the heterogeneity of the patients with stroke. The results showed that monitoring patients post-stroke with iECG led to both higher health care costs and health benefits compared with 24-hour Holter recording, making iECG a highly cost-effective management strategy for secondary prevention of stroke using the $50 000/QALY willingness-to-pay threshold.

Cost-effectiveness analyses examining the economic credentials of other cardiac monitoring interventions in detecting AF post-stroke have been performed. A within-trial economic evaluation reported that the prolonged surveillance with 24-hour Holter recording for 10 days was associated with comparable costs and QALYs[39]; Kamel et al evaluated the long-term cost-effectiveness of 7-day outpatient cardiac surveillance for a cohort of patients (mean age of 70 years) with stroke history and reported an ICER of $13 000/QALY. The meta-analyzed AF detection rate for the surveillance strategy was 5.9% which is lower than the rate used in the current study.[40] Yong et al assessed the ambulatory cardiac surveillance after cryptogenic stroke for 7, 14, and 30 days and reported that, whilst 30 days monitoring was cost-effective, shorter term (7 or 14 or 7 days) monitoring was cost saving.[41] Another study evaluated the AF screening in the primary care setting for members of the general population (regardless of comorbidities) aged >65 years with a handheld, single-lead ECG device; they reported the screening program would save €764 and improve QALYs by 0.27 per participant.[42] For prolonged monitoring with an insertable device, generally it was considered cost-effective but not cost-saving because of the high acquisition and insertion cost of the device: an economic analysis based on the The Cryptogenic Stroke and Underlying AF trial reported it was cost-effective (ICER £13 926 and QALY gain of 0.15) in patients with cryptogenic stroke.[43] Another 3 modeled economic analyses also yielded similar conclusions in patients with cryptogenic stroke or high risk of stroke.[44–46] An Australian-based study that examined an opportunistic screening of AF in community pharmacies reported an ICER of A$5988 per QALY gained compared with the practice without such screening.[32] Although the results from these studies are not directly comparable, all indicated that cardiac monitoring for the purpose of AF detection in various settings is highly likely to be cost-effective or even cost-saving.

The results from this study have important implications for future clinical practice. It is a requirement for any new medical technology to demonstrate effectiveness, safety, and cost-effectiveness before receiving a public subsidy (ie, subsidized by the Commonwealth Department of Health in Australia). The evidence generated could inform policy making around post-stroke management during the index hospital stay. In the key observational study, cardiac monitoring was delivered by nurses during their routine work (ie, vital sign observation monitoring) and imposed no extra workload. Managing patients with iECG offers great potential to detect more patients with AF in a timely manner and to result in significant cost-savings in terms of hospitalization, rehabilitation, and management, and improved health outcomes for patients. It is possible that our nurse-lead in-hospital iECG monitoring protocol could become cost-saving with the current cost of NOAC having a moderate discount of 30% in the next 5 years. Moreover, in the current modeled analysis, the iECG device was costed for each individual patient. Since the surveillance was provided by stroke unit nurses, the number of devices required could be markedly reduced, meaning the estimated cost of devices is likely to be overestimated.

Some limitations warrant mentioning. First, the subsequent cost associated with false positives (patients without AF but incorrectly diagnosed by iECG) was not fully captured (only the cost of a following Holter to confirm the diagnosis was included). Even though the built-in algorithm allows the expedited diagnosis of AF, final diagnosis of AF would be established by a specialist. The false positives would have been ruled out. Second, the analysis did not take a societal perspective as recommended for gold standard evaluations. However, monitoring with iECG is likely to reduce the risk of recurrent stroke and to avoid potential disability because of stroke, thus the inclusion of the costs of productivity losses and informal care would further strengthen the cost-effectiveness profile of iECG in this setting. Thirdly, the cohort study on which the diagnostics yields of iECG were based upon may have inherent imbalance that confounds the results. However, the baseline characteristics in terms of age, sex, and comorbidities were well-balanced in the primary study. Lastly, the short-term in hospital monitoring might fail to identify some patients with AF, however there is insufficient clinical data to allow for that in the modeling.

CONCLUSIONS

iECG monitoring during the acute hospital stay by a nurse was found to significantly improve the rate of AF detection and was cost-effective, contributing to marginally increased costs and improved health outcomes. Using iECG to monitor patients post-stroke is recommended to complement the standard routine care.

ARTICLE INFORMATION

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None.

Supplemental Material

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Supplemental Material

Data S1.

Supplemental Methods

Transition probabilities

Mortality due to non-stroke causes by age and gender was sourced from the Australian Bureau of Statistics[47]. Since AF is associated with increased risk of death from other causes, a relative risk (RR) factor was applied to adjust this altered mortality[48]. For patients receiving NOAC treatment, the risk of having another recurrent event was reduced by applying the treatment effect of apixaban as a representative NOAC, whereas patients with undiagnosed AF (i.e. those who remain undiagnosed by Holter surveillance) would have unadjusted risk for such event.

Model assumptions

A key assumption was that patients from a post major stroke state could not return to the post non-major stroke state. A microsimulation approach was selected because it has the advantages of modelling for a heterogeneous population (i.e., subjects may vary in terms of baseline characteristics, thus with different transition probabilities of experiencing recurrent events) and tracking individual subjects over their lifetime. It enables the storing of event histories for each subject (i.e. the number of strokes occurring over the modelled time horizon, and the time point at which each event occurred).

Subgroup analysis

A subgroup analysis based on patients aged over 65 years was undertaken given the higher risk of AF in this aged cohort.

Example calculation for QALY gain

A utility weight of 0.5 (meaning the quality of life of 0.5 for a given health state) times 10 life years lived in that health state gives the equals 5 QALYs of 5.

Data S2.

Supplemental Results

Results of subgroup cost-effectiveness analysis (cohort aged over 65 years)

In the subgroup of patients aged 65 years and over, the same rate of detection was 10.3% in the iECG and 4.0% in the 24-Holter recording groups ($p<0.001$). Similarly, iECG again led to higher costs and benefits. Over the simulated time horizon, the total costs and QALYs were $26,119 vs. $25,888, and 5.603 vs. 5.565 in the iECG and usual care groups respectively. The corresponding ICER was $6052/QALY. Moreover, monitoring post stroke patients with iECG was associated with fewer numbers of recurrent strokes (2,860 vs 2,980) and stroke-related death (530 vs. 540) per 10,000 patients.

Comparison with other monitoring protocols

Further, ambulatory 7-day ECG monitoring also detected 5.7% of AF in patients with normal ECG and normal Holter[49]. Another study that extended the monitoring to 30-days using an event-triggered record yielded a significantly higher proportion of AF detection (16.1%) than that using a 24-hour Holter (3.2%) surveillance[50] in patients with cryptogenic stroke/TIA[51]. These results highlight the fact that using the traditional short-term cardiac surveillance protocol, a significant proportion of patients with unknown AF could be missed and therefore would not benefit from NOAC therapy. Monitoring post-stroke patients after hospital discharge for a longer timeframe may be able to detect a greater proportion of patients with AF, but it raises feasibility concerns (human resources, compliance, costs, etc.). Improving AF detection during the index hospital admission could overcome some of the issues especially with the evidence showing that early monitoring is important to identify the majority of AF[52,53].

Table S1. Probability of recurrent stroke by CHA2DS2-VASc score.

CHA2DS2-VASc score	Probability of recurrent stroke per annual
0	0
1	0.013
2	0.022
3	0.032
4	0.04
5	0.067
6	0.098
7	0.096
8	0.125
9	0.152

CHA2DS2-VASc scores calculates the stroke risk for patients with AF.
Reference 20

Table S2. Background mortality.

Age	Mortality rate_noAF_male	Mortality rate_noAF_female	Mortality rate_AF_male	Mortality rate_AF_female
64	0.00929	0.00538	0.015421	0.008931
65	0.0101	0.0059	0.016766	0.009794
66	0.01099	0.00653	0.018243	0.01084
67	0.012	0.00725	0.01992	0.012035
68	0.01317	0.00805	0.021862	0.013363
69	0.01449	0.00891	0.024053	0.014791
70	0.01602	0.00988	0.026593	0.016401
71	0.01776	0.01098	0.029482	0.018227
72	0.01972	0.01223	0.032735	0.020302
73	0.02191	0.01367	0.036371	0.022692
74	0.0243	0.0153	0.040338	0.025398
75	0.02699	0.01717	0.044803	0.028502
76	0.03006	0.01931	0.0499	0.032055
77	0.03358	0.02179	0.055743	0.036171
78	0.03758	0.02467	0.062383	0.040952
79	0.04216	0.028	0.069986	0.04648
80	0.04752	0.0319	0.078883	0.052954
81	0.05366	0.03646	0.089076	0.060524
82	0.06054	0.04178	0.100496	0.069355
83	0.06828	0.04793	0.113345	0.079564
84	0.07722	0.05503	0.128185	0.09135
85	0.08735	0.06311	0.145001	0.104763
86	0.09862	0.07221	0.163709	0.119869
87	0.1109	0.08258	0.184094	0.137083
88	0.12427	0.09437	0.206288	0.156654
89	0.13867	0.10778	0.230192	0.178915
90	0.15409	0.1229	0.255789	0.204014
91	0.17078	0.13957	0.283495	0.231686
92	0.18851	0.15789	0.312927	0.262097
93	0.20688	0.17768	0.343421	0.294949
94	0.22531	0.19844	0.374015	0.32941
95	0.23916	0.21042	0.397006	0.349297
96	0.25101	0.23459	0.416677	0.389419
97	0.26474	0.25393	0.439468	0.421524
98	0.28313	0.27387	0.469996	0.454624
99	0.31095	0.29699	0.516177	0.493003
100	0.34231	0.31683	0.568235	0.525938

Australian Bureau of Statistics, Table 1.9 Life Tables, Australia, 2015-2017

Table S3. Distributions for first-order uncertainty examined in the simulation model.

Variables	Distribution	Parameters	Range (AUD)
Cost of rehospitalisation			
Major stroke	Gamma	Alpha 95.80 Lambda 0.0055	$14,212-21,235
Non-major stroke	Gamma	Alpha 99.99 Lambda 0.0015	$5,372-7,959
Cost of management post a major stroke	Gamma	Alpha 100.0 Lambda 0.0089	$9,162-13,573
Cost of intracranial haemorrhage due to NOAC	Gamma	Alpha 100 Lambda 0.0043	$19,060-28,235
Cost of dying immediately from acute stroke	Gamma	Alpha 100 Lambda 0.0087	$9,302-13,779
Cost of rehabilitation post of major stroke	Gamma	Alpha 425.48 Lambda 0.0064	$60,340-73,976

NOAC: new oral anticoagulant.; AUD: Australian dollar.

Due to the absence of evidence to inform the distribution, we adopted the distribution recommended for costs in the book entitled Decision Modelling for Health Economic Evaluation - Handbooks in Health Economic Evaluation Series

Table S4. Distributions examined in the probabilistic sensitivity analyses.

Variable	Distribution	Parameters	Reference
Probability of recurrent stroke (no AF patients)	Beta	Alpha 24.4774; beta 1193.304	Expert opinion
RR of stroke for patients treated with NOAC vs no NOAC	Beta	Alpha 3.3115; Beta 5.6384	Connolly et al. 2011
RR of all-cause mortality for patients treated with NOAC vs no NOAC	Beta	Alpha 2.3593; Beta 0.6272	Connolly et al. 2011
Baseline utility post Stroke/TIA	Beta	Alpha 8.62; beta 5.0625	Expert opinion

AF: atrial fibrillation; NOAC: new oral anticoagulant; TIA: transient ischemic attack; RR: relative risk

Beta distribution is characterised by alpha and beta parameters ranging from zero to one.

Table S5. Results of cost-effectiveness analysis for the subgroup (aged 65 years and over).

	iECG	Usual care	Difference	ICER
Total cost	$26,119	$25,888	$230	
· **Management**	$18,299	$18,190	$109	
· **Rehabilitation**	$4,780	$4,930	-$150	
· **Hospitalisation**	$2,387	$2,474	-$86	
· **NOAC**	$555	$262	$293	
· **Adverse events**	$70	$33	$37	
· **iECG device**	$27	$0	$27	
Number of recurrent stroke*	0.286	0.298	-0.012	$19,599
Number of stroke-related death*	0.053	0.054	-0.001	$200,252
QALY	5.603	5.565	0.038	$6,052
LY	9.610	9.562	0.048	$4,759

*the average number of events across all simulated cohort since not all patients would experience an event over the modelled time horizon.

Table S6. Results from national impact.

Calendar year	Cost of devices	Cost-offset	Cost of NOAC and AEs
2017	$677,376	-$7,777,280	$9,658,880
2018	$657,055	-$7,543,962	$9,369,114
2019	$637,343	-$7,317,643	$9,088,040
2020	$618,223	-$7,098,113	$8,815,399
2021	$599,676	-$6,885,170	$8,550,937
Total	$3,189,673	-$36,622,168	$45,482,370
		Net cost	**$12,049,875**

A total of 56,000 stroke occurred in 2017 with an estimated 25,088 patients survived without no prior atrial fibrillation.

NOAC: new oral anticoagulant; AEs: adverse events.

Figure S1 Tornado diagram for the one-way sensitivity analysis_ patients aged over 65 years.

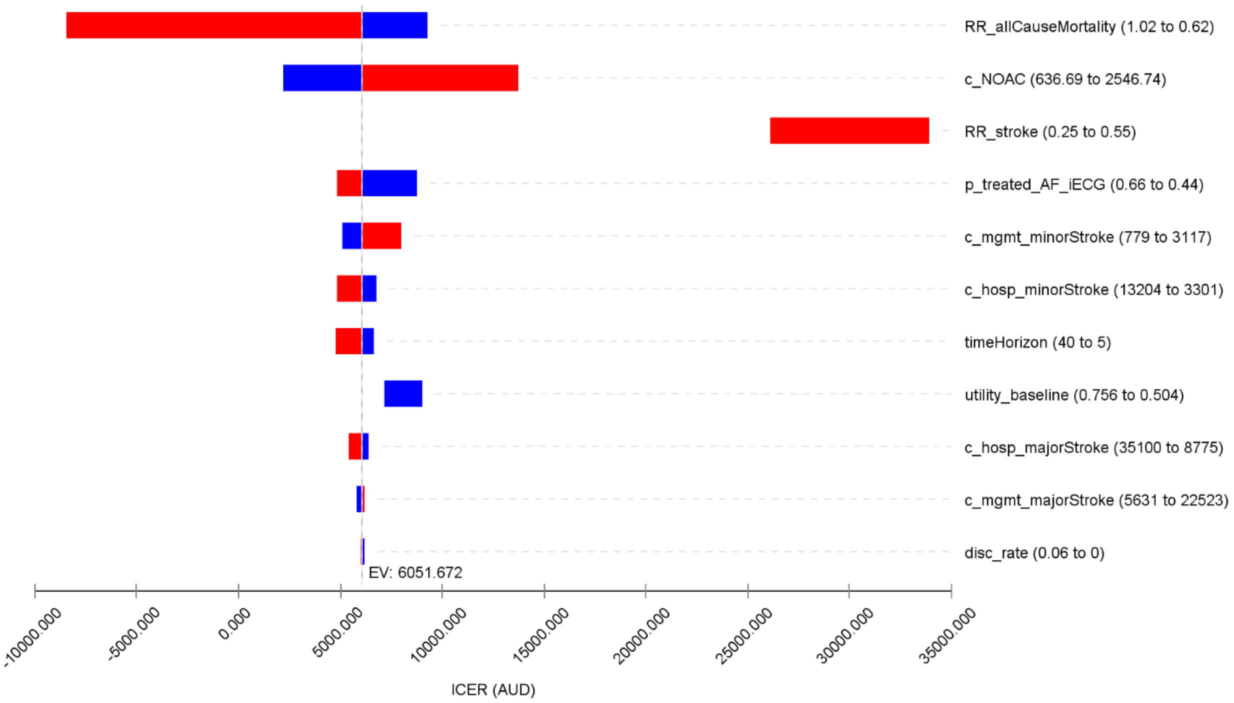
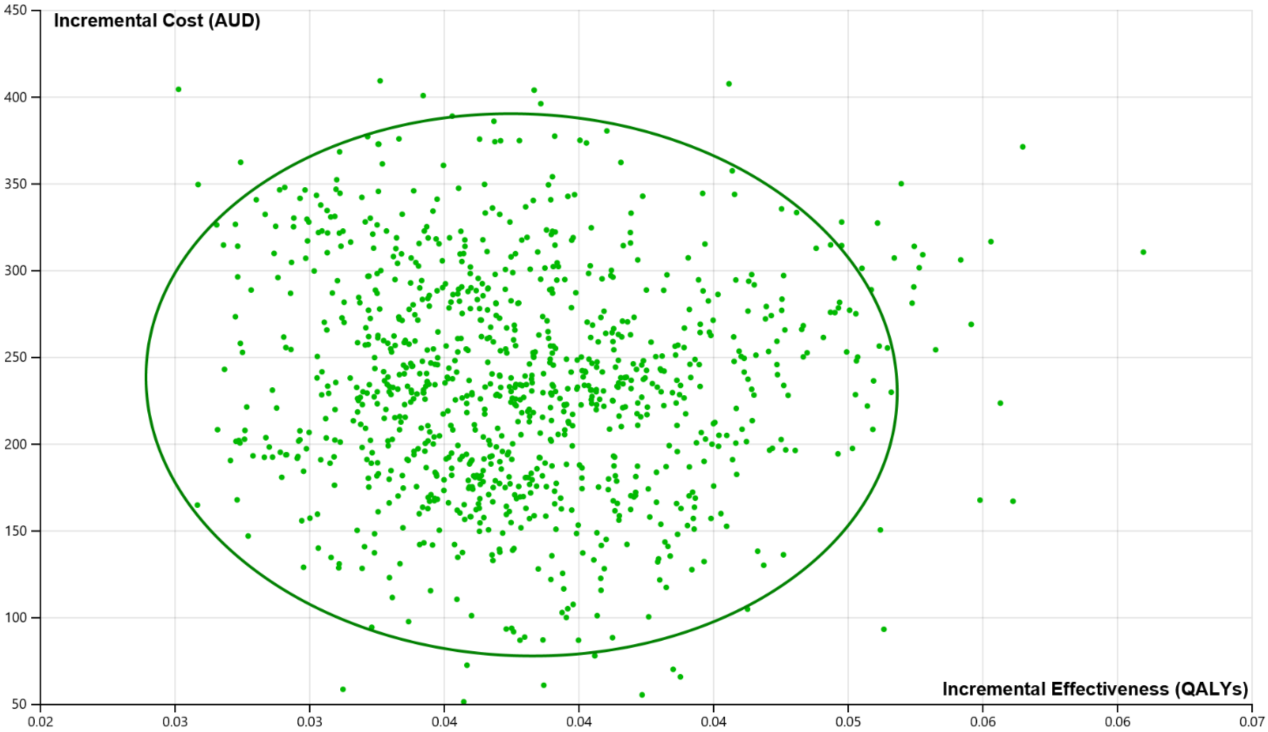


Figure S2. Incremental cost-effectiveness plane from the probabilistic sensitivity analysis_ patients aged over 65 years,



AUD: Australian dollar; QALY: quality-adjusted life year

Probability of being cost-effective is 100% using the $50,000/QALY WTP threshold. Red dots represent the results suggesting cost-ineffective (none in the figure above) whereas green dots denote the results indicating cost-effective.