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.

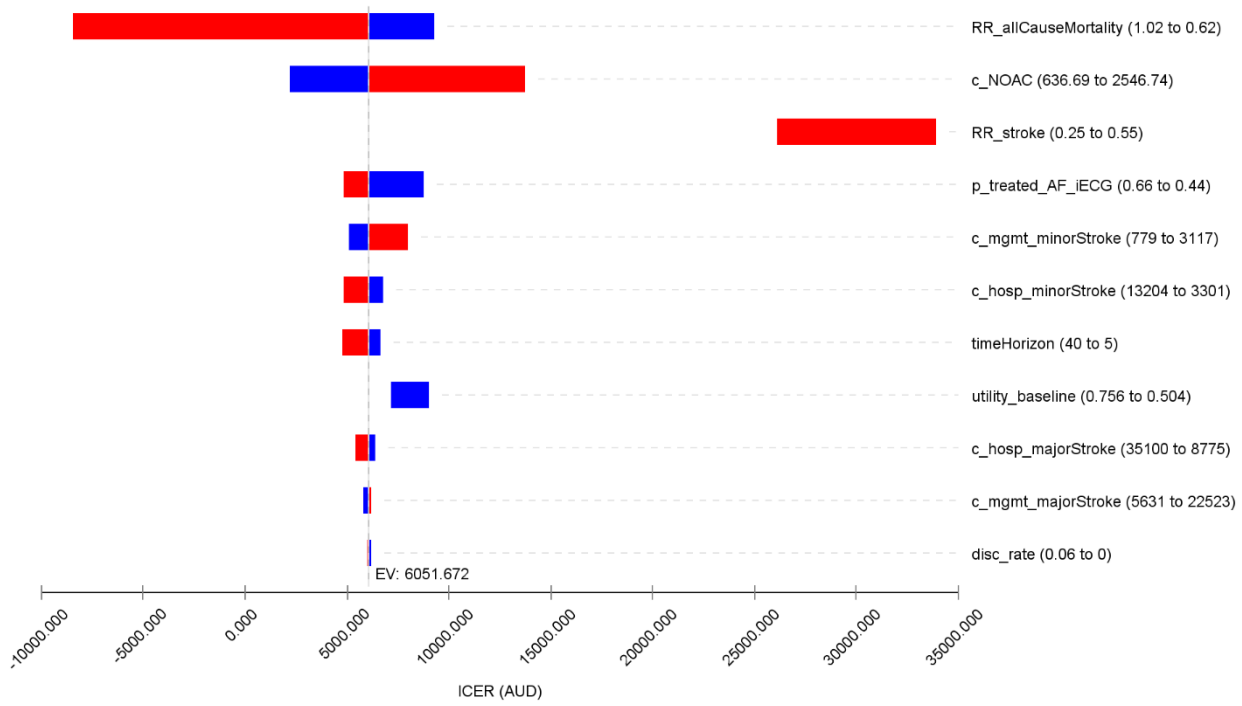
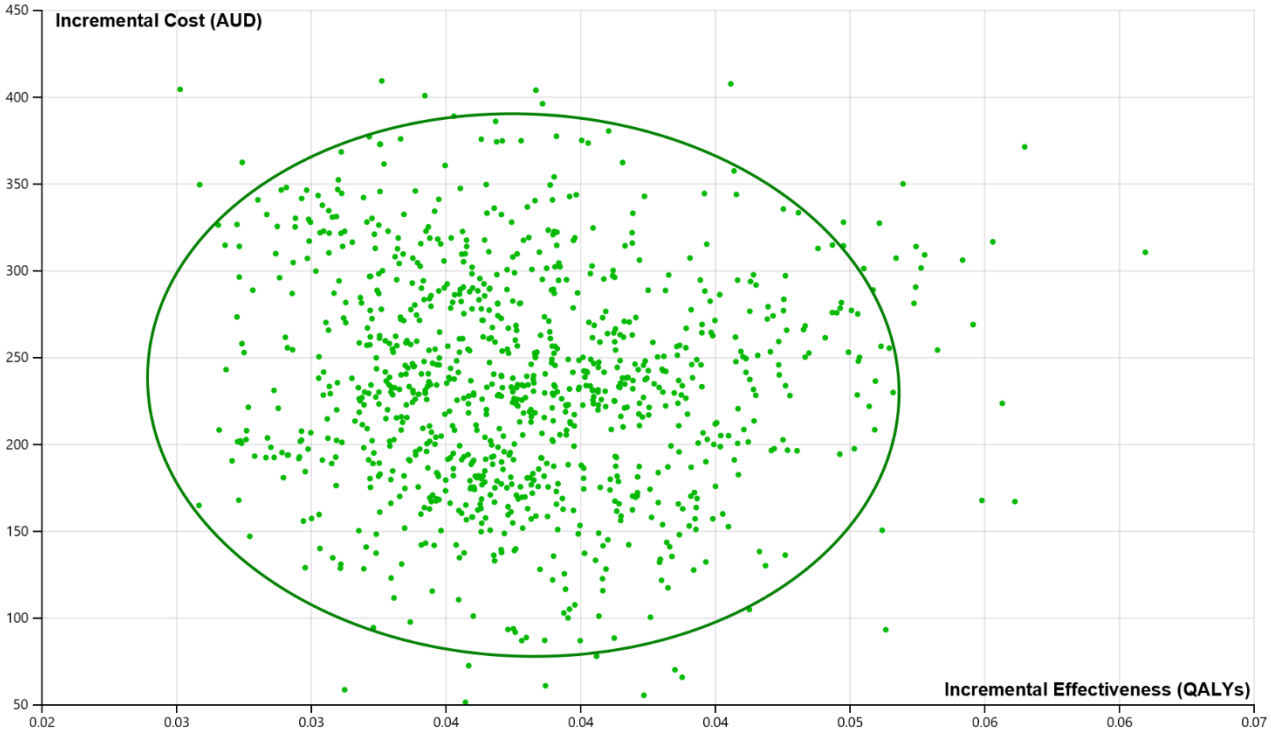


Figure S2. Incremental cost-effectiveness plane from the probabilistic sensitivity analysis_ patients aged over 65 years,



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.