



Universal Atrial Fibrillation Screening Using Electrocardiographic Artificial Intelligence: A Cost-Effective Approach in Rural Communities

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Abstract

Atrial fibrillation (AF) significantly contributes to the incidence of strokes. Screening for AF enhances its detection and effective management. However, universal AF screening in rural areas poses a challenge. This study evaluates the cost-effectiveness of artificial intelligence-enabled 12-lead electrocardiography (AI-ECG) model for AF screening in rural communities.

This cost-effectiveness analysis targeted individuals aged 65 or older, employing a lifelong decision analytic Markov model. AI-ECG model, trained and validated at three Taiwanese hospitals with 285,108 patients, achieved sensitivities of 97.8% and specificities of 99.1%. The study incorporated costs and efficacy of anticoagulant treatments, health status utilities, and clinical variables, derived from literature and Taiwan's epidemiological data. Outcomes were expressed in US dollars per quality-adjusted life year (QALY). The base-case analysis contrasted AI-ECG screening performed by nurses and physician evaluations using standard 12-lead ECGs against no screening, incorporating uncertainty through probabilistic sensitivity analysis. Results were compared with one GDP per capita in Taiwan ($\approx$ \$32,327 per QALY), a commonly cited willingness-to-pay (WTP) benchmark.

Both AI-ECG and physician-led screenings were costlier yet more effective compared with no screening. Although both methods showed comparable effectiveness in detecting AF and in QALYs gained, AI-ECG screening was less expensive (\$141 versus \$196). Based on 5,000 Monte Carlo simulations, AI-based screening is more cost-effective at lower thresholds (\$4,349 to \$6,132 per QALY), while physician-led screening becomes preferable beyond \$6,132 per QALY. Both strategies remained cost-effective relative to the WTP benchmark. Sensitivity analyses further identified the referral rate following a positive AI-ECG screening as a critical determinant of its cost-effectiveness.

AI-ECG screening for AF is a cost-effective alternative, particularly suitable for areas with limited medical resources.

Keywords Artificial intelligence · Atrial fibrillation · Cost-effectiveness analysis · Electrocardiogram · Rural area · Systematic screening

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Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia worldwide, with its prevalence increasing alongside an aging population. AF, often asymptomatic in its early stages, is associated with a heightened risk of stroke, heart failure, and mortality [1, 2]. Current guidelines endorse comprehensive AF management, particularly the use of oral anticoagulants for stroke prevention, which have been shown to reduce the risk of stroke by 60% and mortality by 25% [3, 4]. Screening for AF can enhance its detection and facilitate early management. Although the universal clinical benefits of AF screening are not firmly established [5], screening is considered reasonable in individuals aged 65 years and older or those with specific stroke risk factors, such as heart failure, hypertension, and diabetes mellitus [3, 4].

AF screening can be conducted through various methods, including pulse checks, automated blood pressure monitors, wearable devices, and single to multiple leads electrocardiograms (ECGs) [3]. These screening tools have demonstrated cost-effectiveness in different contexts [6]. However, in rural areas, challenges to AF screening are prevalent, often leading to inferior cardiovascular outcomes [7–9]. Limited access to medical resources and a scarcity of healthcare professionals render opportunistic AF screening during regular medical visits less accessible [9]. Systematic screening for all at-risk individuals in rural settings can be costlier, and the relatively low yield of screening tools might diminish participation. With AF occasionally presenting as paroxysmal AF, repeat screenings, which can quadruple detection rates, are challenging to implement in rural areas [10]. These barriers highlight the urgent need for an effective and economical method for AF screening in rural areas with limited medical resources.

Deep learning, a subfield of artificial intelligence (AI), has exhibited remarkable accuracy in interpreting ECGs, comparable to the expertise of cardiologists [11]. Studies have shown that AI-enabled ECG can enhance the diagnosis of left ventricular dysfunction and may be cost-effective for widespread screening [12–14]. AI-guided AF screening has also increased the detection of unrecognized atrial fibrillation [15]. Despite the potential of AI-enabled ECG for AF screening in rural areas, its cost-effectiveness compared with traditional physician-led screening requires further investigation. This study assesses the cost-effectiveness of AI-enabled 12-lead ECG (AI-ECG) relative to physician-led AF screening in a rural community.

Methods

Development of AI-ECG Model for AF Detection

The algorithm designed to detect AF from 12-lead ECGs underwent training using data from 155,122 patients, encompassing 345,619 ECGs, of which 16,604 were diagnosed with AF and 329,015 were AF-negative, sourced from a medical center for development and fine-tuning purposes. An 82-layer convolutional neural network was employed, with technical specifications paralleling those outlined in our previous study [16], detailed further in the Supplementary Methods. ECGs received annotations based on corresponding reports, covering sinus rhythm, AF, atrial flutter, and other rhythms, as provided by cardiologists. Here, the AF category included both AF and atrial flutter.

For validation purposes, an internal validation set from the medical center, an external validation set and an isolated validation set from two additional hospitals (a community hospital and one on an isolated island) were utilized, as depicted in Supplementary Fig. 1. Supplementary Table 1 details the baseline characteristics of each dataset. The AI-ECG model's performance was characterized by sensitivities ranging from 97.3% to 98.5%, specificities from 98.2% to 99.1%, and area under the receiver operating characteristic curve scores between 0.9955 and 0.9986 across the three validation sets, as illustrated in Supplementary Fig. 2. The model's positive predictive values varied from 69.7% to 77.0%, while maintaining a negative predictive value of 99.9%. These performance metrics are consistent with those reported in previous studies investigating AI models for AF detection [17, 18]. This study received approval from the Institutional Review Board at Tri-Service General Hospital, Taipei, Taiwan (C202105049).

Economic Model and Assumptions

To assess the cost-effectiveness of AI-ECG screening for AF compared with physician-led screening or no screening in a rural community, we utilized a decision analytic model featuring Markov processes. This model simulated a cohort of 65-year-old patients, tracking them over their remaining projected lifetime. Given the prevalence of the disease, risk of stroke, and health checkup policies in Taiwan, our analysis concentrated on individuals aged 65 as the base-case scenario. To further assess the cost-effectiveness of screening strategies in older age groups, additional analyses were conducted using screening ages of 75 and 85 years for comparison. The structure of this cost-effectiveness analysis draws upon methodologies established in previous literature [19–21], adopting the perspective of the healthcare payer.

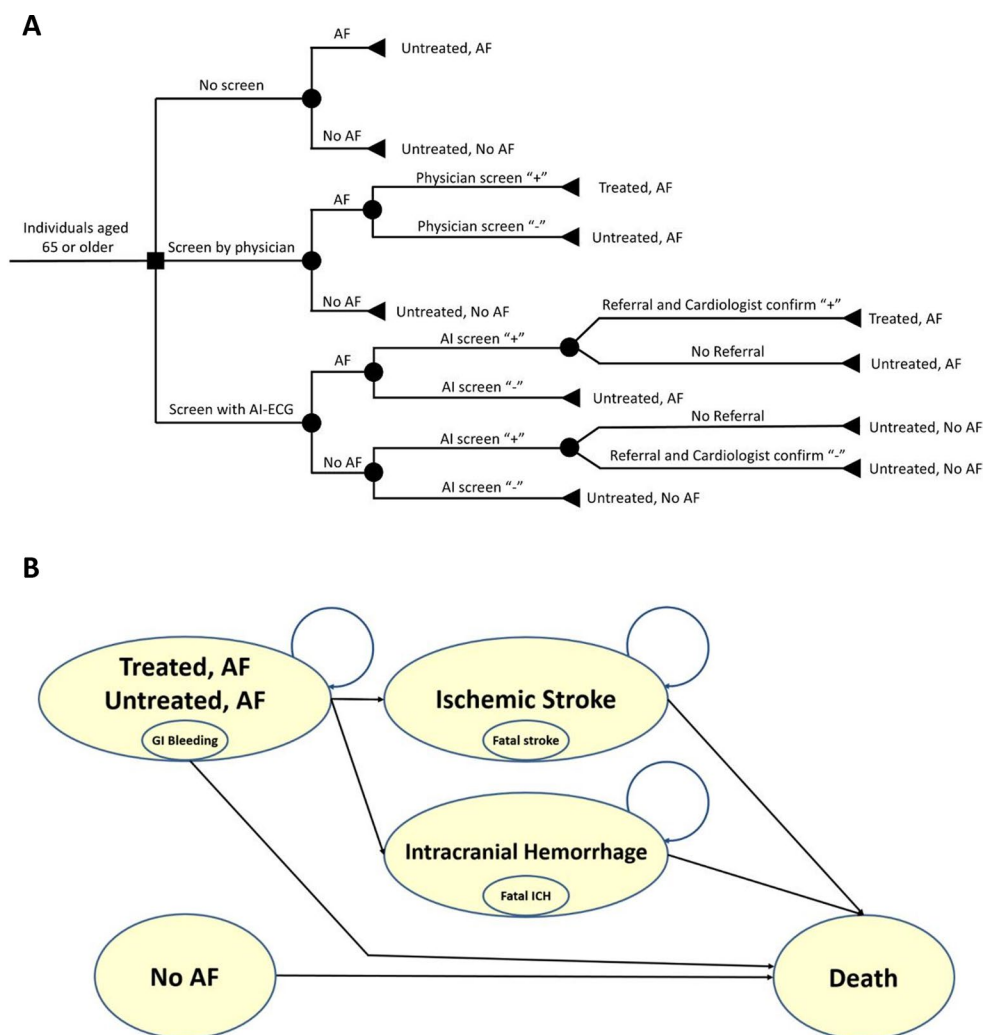
The decision analytic model comprises a decision tree and a Markov model.

The short-term decision tree, depicted in Fig. 1A, evaluates the performance of AI-ECG screening for AF compared with physician-led screening or no screening. Literature suggests that paroxysmal AF may not be consistently detected through a single ECG screening. Research indicates that approximately 1.4% of the population aged 65 without prior AF diagnosis could be identified with AF via a single ECG screening [22]. Accordingly, a detection rate of 1.4% for 65-year-old individuals was integrated into the model. A positive AI screening result leads to a referral for a cardiologist outpatient visit to confirm true-positive cases or exclude false-positive AF instances by reviewing the screening ECG. Referral rates may vary substantially depending on healthcare resources and geographic barriers. Based on previous studies, a referral rate of 82% was applied in the model [23, 24]. Participating physicians were assumed to be adequately trained, proficient in AF identification, and would diagnose AF using a 12-lead ECG with

100% accuracy, in line with a cardiologist's capability at the same detection rate.

The hypothetical cohort transitions to the Markov model, entering one of three health states post-screening: (1) treated for AF if positively screened using the AI-ECG model and confirmed by a referral cardiologist, or by a frontline physician (true positive); (2) untreated for AF if the AI-ECG model failed to detect an existing condition (false negative); or (3) untreated without AF if the condition was absent. As illustrated in Fig. 1B, the Markov model includes four health states: stable AF; post-ischemic stroke; post-intracranial hemorrhage (ICH); and death. Both treated and untreated individuals for AF might experience gastrointestinal (GI) bleeding in the stable AF health state. Subsequently, individuals with AF could progress to experiencing a stroke or ICH. Except in the event of death, individuals would remain in the post-ischemic stroke or post-ICH states. Transitions to a deceased state could occur annually from any health condition, adhering to specific transition probabilities.

Fig. 1 Schematic of the decision analytic model. **(A)** The first part depicts a decision tree representing the screening outcomes. **(B)** The second part features a Markov structure simulating patients' costs and effects over the analyzed horizon. Abbreviations: AI, artificial intelligence; AF, atrial fibrillation; ECG, electrocardiogram; GI, gastrointestinal; ICH, intracranial hemorrhage



Health Outcomes, Costs and Discounting

Table 1 presents estimated values for various elements within the model, including AI-ECG model performance, health outcomes, costs, utilities, and other factors. For AI-ECG model performance in AF detection, data from the internal validation cohort was applied. The sensitivity of the AI-ECG model for detecting AF was 97.8% (standard error [SE]: 0.0035), and the specificity was 99.1% (SE: 0.0004). The prevalence of AF in 65-year-old individuals was set at 2.5%, in accordance with published literature [25]. The model assumes that simulated individuals receive AF treatment using non-vitamin K anticoagulants (NOACs), namely apixaban, dabigatran, edoxaban, and rivaroxaban following physician evaluation. To reflect real-world practice, prescription rates for each NOAC were incorporated: 42.3% of AF patients received no anticoagulant therapy, while 17.7% received edoxaban, 15.0% apixaban, 15.0% rivaroxaban, and 10.0% dabigatran [37].

Annual transition probabilities to stroke and treatment-related adverse events, including ICH and GI bleeding, for both treated and untreated patients, along with their utility scores, were primarily derived from data in four crucial trials on NOACs involving Asian populations, meta-analyses, and related literature [26–30]. Other bleeding events, such as those involving soft tissue or muscle, genitourinary sites, retroperitoneal spaces, or the respiratory tract, were not included in the model because they are infrequently reported and have a low incidence [38, 39]. Annual risks of ischemic stroke in patients on warfarin or NOACs, as reported in clinical trials, ranged from 0.8% to 2.2% [26–29]. Conversely, the annual risk of ischemic stroke in AF patients not receiving oral anticoagulants was higher, at 5.1%, based on a meta-analysis comparing the risk reduction in AF patients with and without anticoagulant therapy [30]. The average CHA₂DS₂-VASc score for AF patients in Taiwan was 4.14, reflecting the baseline stroke risk in the model [25]. The risks of GI bleeding and ICH in AF patients not on oral anticoagulants were similar to those on NOACs in our model, informed by lower incidences of bleeding events in specific NOAC trials [26, 27]. In the event of a stroke or ICH, cases were classified as mild (independent), moderate (moderate disability), severe (totally dependent), or fatal, according to functional severity, as their incidence, medical costs, and utility differ substantially. Real-world incidence data for stroke and ICH were incorporated to better reflect actual clinical conditions [31]. Transition probabilities from post-screening to death were calculated using age and sex-specific survival rates from the Taiwan life Table [34].

The cost of an AI-ECG screening was set equal to a standard electrocardiogram (\$4.96) in the base case, increasing

up to five times in the sensitivity analysis due to uncertainties in pricing AI-ECG screening. The costs of health resources, including cost per outpatient visit and annual cost of outpatient AF management were calculated based on the Taiwan National Health Insurance, as presented in Table 1. Both cost and effectiveness were discounted at a rate of 3%, accounting for the time preference that places a higher value on costs incurred or effectiveness gains realized now rather than later.

Analytical Methods

One-way deterministic sensitivity analyses were performed to evaluate the model's robustness in relation to the performance of the AI, the referral rate after AI-ECG screening, the costs associated with AI-ECG screening, nurse-conducted AI-ECG screenings, and outpatient AF management. Additionally, to thoroughly examine covariate uncertainty, a probabilistic sensitivity analysis was performed. For each input variable, probability distributions were assigned, incorporating the mean values, standard errors, and distribution types. Probabilities and utilities employed beta distributions, appropriate for values between 0 and 1. Costs were modeled using gamma distributions, which are suitable for representing non-negative, right-tailed distributions typically associated with cost modeling.

Point estimates for the incremental cost-effectiveness ratio (ICER) were generated through a Monte Carlo simulation encompassing 5,000 iterations, drawing parameters from their respective probability distributions. In line with the WHO guidelines and local expert opinion, 1 Gross Domestic Product (GDP) per capita was considered a suitable threshold for assessing cost-effectiveness in Taiwan [40]. Accordingly, the willingness-to-pay (WTP) threshold was set at \$32,327 per quality-adjusted life year (QALY) gained, based on Taiwan's published 2023 GDP per capita. The percentage of iterations where AI-ECG screening achieved an ICER below the \$32,327 WTP threshold was used to construct the cost-effectiveness acceptability curve, indicating the likelihood of AI-ECG screening being a cost-effective strategy compared with its alternatives.

The model was developed and analyzed using TreeAge Pro version 2024. Costs were converted to USD based on the exchange rate from the Bank of Taiwan as of January 16, 2023. To demonstrate compliance with established reporting standards, the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist was employed, ensuring adherence to the key elements specified in the CHEERS guidelines [41] (Supplementary Table 2).

Table 1 Summary of model and parameter estimates

Factor	Estimate (SE)	Distribution modelled	Source
Atrial fibrillation		Uniform	
Prevalence			Chao et al. [25]
Age 60–69	0.025		
Age 70–79	0.051		
Age 80–89	0.059		
Age ≥ 90	0.063		
Annual incidence			Chao et al. [25]
Age 60–69	0.0021		
Age 70–79	0.0061		
Age 80–89	0.0139		
Age ≥ 90	0.0254		
Detection rate	0.014		Lowres et al. [22]
Probabilities and outcomes			
Sensitivity of AI	0.978 (0.0035)	Beta	
Specificity of AI	0.991 (0.0004)	Beta	
Referral rate after AI screen	0.82	Uniform	Chen et al. and Orchard et al. [23, 24].
Risk of stroke		Beta	
- Apixaban	0.021 (0.005)		Asian ARISTOTLE [26]
- Dabigatran	0.016 (0.003)		Asian RE-LY [27]
- Edoxaban	0.008 (0.003)		Asian ENGAGE AF-TIMI 48 [28]
- Rivaroxaban	0.021 (0.007)		Asian ROCKET AF [29]
- Untreated	0.051 (0.007)		Hart et al. [30]
Severity of stroke		Uniform	
- Mild (treated; untreated)	0.580; 0.400		Chang et al. [31]
- Moderate	0.160; 0.180		Chang et al. [31]
- Severe	0.020; 0.080		Chang et al. [31]
- Fatal	0.250; 0.350		Chang et al. [31]
Risk of ICH		Beta	
- Apixaban	0.007 (0.003)		Asian ARISTOTLE [26]
- Dabigatran	0.003 (0.001)		Asian RE-LY [27]
- Edoxaban	0.007 (0.003)		Asian ENGAGE AF-TIMI 48 [28]
- Rivaroxaban	0.006 (0.003)		Asian ROCKET AF [29]
- Untreated	0.008 (0.001)		Hart et al. [30]
Severity of ICH		Uniform	
- Mild	0.080; 0.140		Chang et al. [31]
- Moderate	0.090; 0.150		Chang et al. [31]
- Severe	0.320; 0.390		Chang et al. [31]
- Fatal	0.520; 0.330		Chang et al. [31]
Risk of GI bleeding		Beta	
- Apixaban	0.020 (0.004)		Asian ARISTOTLE [26]
- Dabigatran	0.025 (0.004)		Asian RE-LY [27]
- Edoxaban	0.029 (0.007)		Asian ENGAGE AF-TIMI 48 [28]
- Rivaroxaban	0.034 (0.008)		Asian ROCKET AF [29]
- Untreated	0.026 (0.002)		Hart et al. [30]
Mortality rate		Beta	
- Apixaban	0.029 (0.005)		Asian ARISTOTLE [26]
- Dabigatran	0.044 (0.005)		Asian RE-LY [27]
- Edoxaban	0.017 (0.005)		Asian ENGAGE AF-TIMI 48 [28]
- Rivaroxaban	0.048 (0.026)		Asian ROCKET AF [29]
- Untreated	0.049 (0.005)		Hart et al. [30]
Annual mortality post-stroke	0.260 (0.003)	Beta	Fang et al. [32]
Annual mortality post-ICH	0.181 (0.012)	Beta	Ponamgi et al. [33]
Age-specific mortality	Taiwan Life Table [34]		
Utility		Beta	
Utility score for having AF	0.81 (0.067)		Sullivan et al. [35]

Table 1 (continued)

Factor	Estimate (SE)	Distribution modelled	Source
Decrement for GI bleeding	0.181 (0.013)		Sullivan et al. [35]
Utility score for mild stroke/ICH	0.750 (0.040)		Gage et al. [36]
Utility score for moderate stroke/ICH	0.390 (0.036)		Gage et al. [36]
Utility score for severe stroke/ICH	0.110 (0.024)		Gage et al. [36]
Costs (2022 USD)			
Screening with AI-ECG model	4.92	Uniform	NHIRD
Cost per outpatient visit	13.11	Uniform	NHIRD
Annual cost of outpatient AF management	65.57 (32.79)	Gamma	NHIRD
Cost per GI bleeding event	7,371 (3,686)	Gamma	NHIRD
Screening by a physician & nurse	17.08	Uniform	NHIRD; assumption
Screening by a nurse	2.05	Uniform	NHIRD; assumption
Annual costs of NOAC treatment		Uniform	
- Apixaban	755		NHIRD
- Dabigatran	1,050		NHIRD
- Edoxaban	944		NHIRD
- Rivaroxaban	744		NHIRD
Cost for stroke, one-time event		Gamma	
- Mild	2,380 (1,190)		Chang et al. [31]; NHIRD
- Moderate	12,427 (6,214)		Chang et al. [31]; NHIRD
- Severe	17,208 (8,604)		Chang et al. [31]; NHIRD
- Fatal	8,820 (4,410)		Chang et al. [31]; NHIRD
Cost for ICH, one-time event		Gamma	
- Mild	6,342.3 (3,171)		Chang et al. [31]; NHIRD
- Moderate	11,416 (5,708)		Chang et al. [31]; NHIRD
- Severe	15,222 (7,611)		Chang et al. [31]; NHIRD
- Fatal	7,404 (3,702)		Chang et al. [31]; NHIRD
Annual costs for post-stroke		Gamma	
- Mild	1,098 (549)		Chang et al. [31]; NHIRD
- Moderate	1,795 (898)		Chang et al. [31]; NHIRD
- Severe	2,016 (1,008)		Chang et al. [31]; NHIRD
Annual costs for post-ICH		Gamma	
- Mild	844 (422)		Chang et al. [31]; NHIRD
- Moderate	1,756 (878)		Chang et al. [31]; NHIRD
- Severe	2,379 (1,190)		Chang et al. [31]; NHIRD
Discounting			
Costs	3%	Uniform	Assumption
Outcomes	3%	Uniform	Assumption

Abbreviations: AI, artificial intelligence; AF, atrial fibrillation; GI, gastrointestinal; ICH, intracranial hemorrhage; NHIRD, National Health Insurance Research Database of Taiwan

Results

Base-Case Analysis

Figure 2A illustrates the number of AF patients detected among every 5,000 individuals, offering a visual comparison between the screened and non-screened groups over their remaining lifetimes. This figure highlights the diminishing gap in detected AF cases over time following the screening. In Fig. 2A, the orange and blue lines represent the numbers of AF patients identified through physician-led screening and AI-ECG screening, respectively, while the grey line indicates the count in the absence of screening. Initially,

physician screening identified 74 patients with AF, whereas AI-ECG screening identified 59 patients. The no-screening arm reflected the natural incidence of AF without intervention. As the model included only living patients, these numbers gradually declined in the later years of the simulation as some of the identified AF patients died. Overall, the simulation reveals that both AI-ECG and physician-led screenings result in earlier and more frequent AF detection.

Figure 2B details the annual costs for both the AI-ECG and physician-led screening groups. Notably, the costs associated with physician-led screening are higher, largely due to the upfront costs inherent in this approach. The annual cost declined markedly approximately 17 years

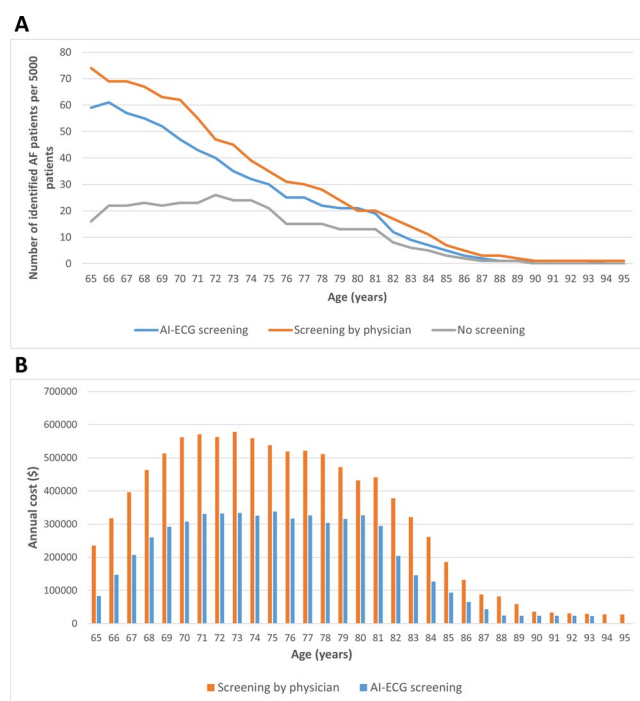


Fig. 2 (A) Number of identified AF patients per 5,000 patients in AI-ECG screening, screening by physician, and non-screening groups during 30 years after screening. (B) Annual cost in USD of 5,000 patients undergoing AF screening with A-ECG screening compared with screening by physician. The costs over time were higher for the screening by physician groups due to the physician's upfront cost. Abbreviations: AI-ECG, artificial intelligence-enabled electrocardiogram; AF, atrial fibrillation

after screening, reflecting the reduced survival rate of participants beyond their 80s. Over the lifetime horizon of the simulation, the total costs related to AF management for the cohort of 5,000 patients were approximately \$7.0 million for the AI-ECG group, compared with \$9.7 million for the physician-led group.

The age pattern in the no-screening arm (rising detections from the late 60s to the mid-70s and tapering thereafter with mortality) is consistent with published epidemiology of AF in older Asian populations [25, 34]. In addition, the model's relative findings, with earlier yield and higher upfront costs for physician-led screening and similar detection at lower cost for AI-ECG screening, align with prior AF screening models that compared handheld single-lead ECG strategies with no screening [42]. These consistencies support the external face validity of our model.

In the base-case scenario, outlined in Table 2, screenings conducted by AI-ECG and physicians were more expensive but also more effective than no screening. The average cost per patient was higher for those screened and referred for AF detection through AI-ECG screening compared with no screening (\$141 versus \$39). This led to an incremental gain of 0.02 QALYs, resulting in a relatively low ICER of \$4,349. Although both strategies showed comparable effectiveness, AI-ECG screening was less costly than physician-led screening (\$141 versus \$196). In the comparison of AI-ECG screening with physician-led screening, AI-ECG screening was associated with an average cost reduction of \$55 per patient and a minor difference in quality-adjusted life expectancy (0.009 QALYs gained per patient), leading to an ICER of \$6,132. These results indicate that both AI-ECG and physician-led screenings are more effective than no screening, with AI-ECG screening proving to be cost-effective across various ages ranging from 65 to 85 years, as detailed in Table 2. As the screening age increased to 75 and 85 years, both incremental QALYs and subsequent medical costs after screening decreased. Screening with AI-ECG at age 75 yielded a higher ICER compared with screening at 65 or 85, primarily due to the relatively smaller QALY gain in relation to the associated medical costs.

Table 2 Cost, effect, and incremental cost-effectiveness ratio of screening with AI-ECG versus screening by physician and no screening for atrial fibrillation according to different age groups

Strategy	Cost (\$)		QALY		Sequential ICER	
	Mean	95% CrI	Mean	95% CrI	Mean	95% CrI
Starting age=65 years old (base-case)						
No screening	39	32–49	16.49	16.47–16.51		
Screening with AI-ECG and referral	141	131–153	16.52	16.49–16.54	4349	3318–6214
Screening by physician	196	184–210	16.53	16.50–16.55	6132	5031–7862
Starting age=75 years old						
No screening	53	43–64	8.65	8.61–8.68		
Screening with AI-ECG and referral	123	114–134	8.66	8.62–8.69	6095	4624–8868
Screening by physician	169	159–181	8.66	8.63–8.69	9225	7689–11,674
Starting age=85 years old						
No screening	25	21–31	4.60	4.58–4.62		
Screening with AI-ECG and referral	69	65–75	4.61	4.59–4.63	5966	4711–8027
Screening by physician	108	103–113	4.61	4.59–4.63	11,229	9648–13,902

Abbreviations: AI-ECG, artificial intelligence-enabled electrocardiogram; CrI, credible interval; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life years

Fig. 3 Tornado diagram for the deterministic sensitivity analyses of physician-led screening for atrial fibrillation vs. AI-ECG screening. Base case: \$6132. The red bar corresponds to the upper range, and the blue bar with the lower range of an input. Abbreviations: AI-ECG, artificial intelligence-enabled electrocardiogram; AF, atrial fibrillation; ICER, incremental cost-effectiveness ratio; ICH, intracranial hemorrhage heart failure; WTP, willingness-to-pay

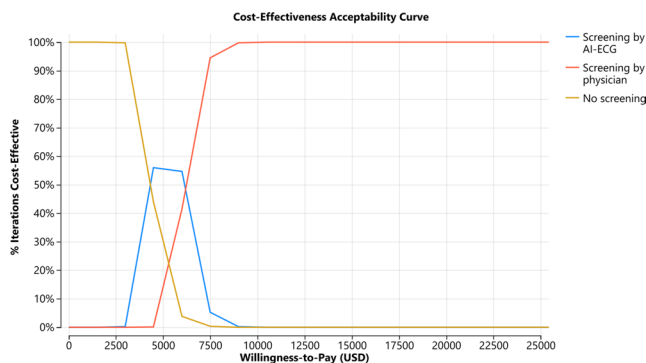
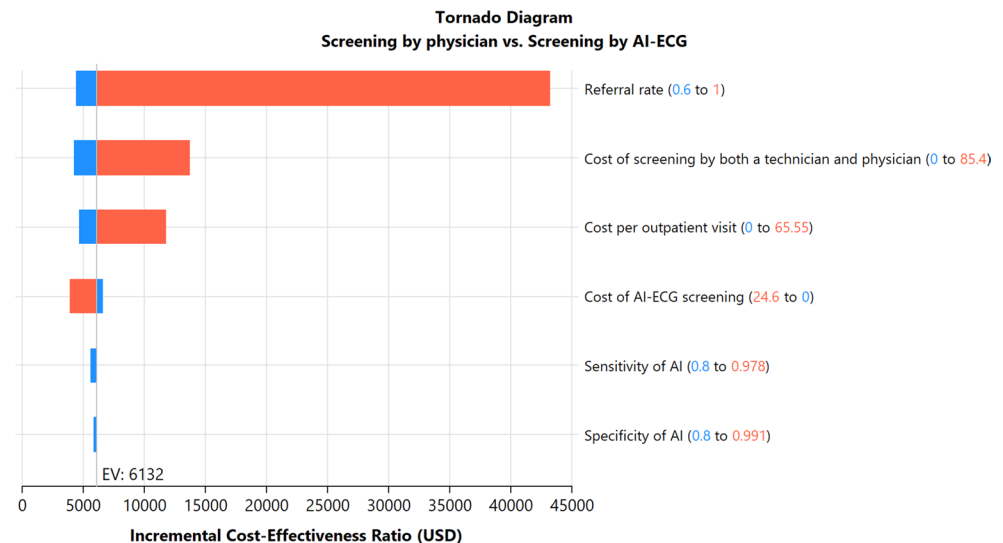


Fig. 4 Cost-effectiveness acceptability curves. The blue curve represents the probability of AI-ECG screening being cost-effective, while the red and yellow lines correspond to the probabilities for physician-led screening and no screening, respectively. Abbreviations: AI-ECG, artificial intelligence-enabled electrocardiogram

Sensitivity Analyses

Figure 3 presents the outcomes of deterministic sensitivity analyses that compare the cost-effectiveness of AI-ECG screening with physician-led screening. To address uncertainties related to healthcare service costs and healthcare professionals' wages in various settings, the costs in the model were adjusted to be five times higher than in the base case. The ICERs for physician-led screening relative to AI-ECG screening were found to be sensitive to variations in referral rate after AI-ECG screening. The analysis revealed that as the referral rate increases to 100%, physician-led screening becomes less likely to be cost-effective under the established WTP threshold of \$32,327, which corresponds to one GDP per capita in Taiwan. Other factors influencing the cost-effectiveness of AI-ECG screening to physician-led screening or no screening were also examined in the sensitivity analyses, with results displayed in Fig. 3, Supplementary Tables 3 and Supplementary Fig. 3.

To further understand the uncertainty of the results, a probabilistic sensitivity analysis was conducted with 5,000 iterations. The outcomes of this analysis are illustrated in the cost-effectiveness acceptability curves shown in Fig. 4. These curves indicate that AI-ECG screening is the most cost-effective strategy at lower cost-effectiveness thresholds, ranging from \$4,349 to \$6,132 per QALY gained. AI-ECG screening for AF is a cost-effective alternative, particularly suitable for areas with limited medical resources.

Discussion

This study evaluates the cost-effectiveness of AI-enabled screening compared with physician-led screening for elderly individuals in rural areas, focusing on AF detection. Our findings suggest that AI screening is more cost-effective for individuals aged 65, with the cost per QALY gained ranging from \$4,349 to \$6,132. Sensitivity analyses reveal consistent cost-effectiveness of AI-ECG screening across various age groups. A key factor influencing the overall value of AI-ECG screening is the referral rate following a positive test result. The study highlights the potential of AI-ECG screening in reducing healthcare disparities.

The debate over AF screening strategies continues, particularly regarding their applicability to specific populations. Opportunistic screening methods during routine medical visits are generally preferred over systematic approaches, primarily due to their cost-effectiveness and comparable effectiveness, as shown in previous studies [43, 44]. However, the burden of undetected AF might be more pronounced in rural areas, where routine detection is less common [45]. Systematic screening in these areas improves access for asymptomatic, at-risk individuals. A survey indicated that general physicians in rural areas are willing to

participate in AF screening, provided they have additional time and staff [46]. These findings highlight the practicality of AI-ECG model as an efficient screening tool in rural settings.

Several mobile health tools are available for AF screening, including photoplethysmography (PPG), pulse variability, and ECG-based devices. Each method has its limitations. The majority of these tools have shown excellent discriminative performance in detecting AF, with sensitivities and specificities exceeding 90.0%, compared with the 12-lead ECG, the diagnostic gold standard [3, 47]. While abnormal results from PPG or pulse variability devices cannot confirm an AF diagnosis, further confirmation through methods such as the 12-lead ECG or longer-duration ECG recording devices is necessary. Paroxysmal AF may not always be detected during these confirmatory tests, which may necessitate repeat examinations. In contrast, ECG-based devices, such as the 30 s single lead ECG or the 10 s 12-lead ECG, can serve as both screening tools and confirmatory tests. Healthcare professionals can diagnose AF based on screening test results, allowing for the immediate initiation of anticoagulant therapy. The 12-lead ECG has demonstrated superior performance in detecting AF compared with the single lead ECG. Advancements in AI technology have enabled AI-enhanced 12-lead ECGs to identify arrhythmias at a level comparable to that of cardiologists [11]. While screening with ECG poses minimal harm to participants, abnormal results may cause anxiety, and misinterpretation could lead to unnecessary further examinations and treatments [5]. Therefore, the use of an accurate screening tool, such as AI-enhanced 12-lead ECGs in our study, is essential for the effective and widespread implementation of AF screening.

Previous research has established the cost-effectiveness of systematic AF screening, although the screening methods and target populations have varied. Aronsson et al. conducted a study comparing screening with a handheld single-lead ECG to no screening in individuals aged 75 and 76, revealing a relatively low ICER of €4,365 [48]. Lyth et al. examined screening using the handheld single-lead ECG twice daily for two weeks against no screening in a hypothetical population modeled after the STROKESTOP trial [49]. This trial demonstrated a superior AF detection rate with repeated single-lead ECGs, resulting in cost savings compared with no screening. These studies suggest that AF screening is cost-effective compared with no screening, aligning with conventional criteria and advocating for the implementation of such screening programs to enhance patient outcomes. However, approaches to AF screening have differed across various regions and healthcare systems. Therefore, our study further evaluates the cost-effectiveness of AI-ECG screening compared with physician-led

screening. AI-ECG screening is not only more effective but also incurs lower costs than physician-led AF screening, with an ICER of \$6,132 per QALY gained. Although this ICER is relatively low in economic terms, the practical challenges of implementing physician-led AF screening in rural areas highlight the significance of AI-ECG screening.

Although AI-ECG screening may serve as a low-cost alternative to physician-led programs, successful referral after a positive AI-ECG screening result is essential for ensuring cost-effectiveness. Barriers to adequate AF care in rural areas include the high cost of medication, limited awareness of the importance of AF management, and restricted access to medical resources when needed [50]. Patients with AF in rural settings are less likely to receive comprehensive care, such as regular outpatient follow-up and guideline-directed anticoagulant therapy [51]. As a result, they more frequently present to the emergency department with AF-related complications and experience higher in-hospital mortality [51]. AI-based tools integrated with telemedicine hold promise for bridging disparities in AF care between rural and urban populations; however, challenges such as inadequate infrastructure and limited digital literacy must be overcome [52]. Initiatives promoting the adoption of novel technologies in rural areas have the potential to reduce health inequities and enhance the quality of AF care.

This study is subject to several limitations. First, the transition probabilities in our economic model are derived from clinical trials, which generally emphasize short-term clinical outcomes within the initial years. Consequently, extrapolating these results to predict long-term follow-up outcomes may not accurately represent real-world scenarios. Second, the observed risks of GI bleeding were similar between patients on NOACs and those without treatment, which is contrary to the expected increased bleeding risks associated with NOACs. This discrepancy was considered in our sensitivity analysis and was also noted in the cost-effectiveness analysis of the STROKESTOP trial [53]. Third, in our model, patients who experienced a stroke or ICH did not return to the baseline health state, as the risk of recurrent events differs substantially from patients without prior events. Although stroke and ICH were stratified by functional severity (mild, moderate, severe, or fatal) and assigned corresponding long-term utility values, this approach may not fully capture the dynamic recovery process that some patients undergo after the acute phase. Consequently, utility may be slightly underestimated in patients who experience functional improvement over time. Fourth, the cost-effectiveness of AI-ECG screening for AF may be influenced by several factors, including the referral rate after a positive screening result, labor costs, anticoagulation therapy rates, AF prevalence, and the sensitivity of the AI-ECG model. Therefore, our results should be interpreted

with caution when applied to different healthcare settings. Finally, while repeated rhythm checks have been proven to improve AF detection rates, our base strategy involved only a single AI-ECG screening. This approach was chosen to favor simplicity in rural areas with limited medical resources. Future research is needed to evaluate the effectiveness of consecutive or periodic AI-ECG screenings and their potential for broader implementation.

In conclusion, our study emphasizes the potential of AI-ECG model for universal AF screening in elderly individuals in rural areas, offering comparable effectiveness to physician-led screening but at a lower cost, and remaining cost-effective under the WTP benchmark of \$32,327 per QALY in Taiwan. This innovative technology could enhance healthcare accessibility and reduce regional disparities.

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Data Availability Access to the original data will necessitate a data-sharing agreement, but summary data can be made available upon reasonable request.

Declarations

Human Ethics and Consent to Participate Declarations The authors confirm that patient consent is not applicable to this article. This research obtained approval from the Institutional Review Board of Tri-Service General Hospital, Taipei, Taiwan (IRB No. C202105049). Given that we utilized encrypted and de-identified data from the hospital, the data controller granted a waiver for informed consent for this study.

Competing interests The authors declare no competing interests.

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