Cerebrovascular Diseases

Clinical Research in Stroke

Cerebrovasc Dis
DOI: 10.1159/000550005

Received: August 10, 2025
Accepted: November 26, 2025
Published online: December 12, 2025

Digital Health-Enabled Monitoring Strategies for Atrial Fibrillation Detection after Embolic Stroke of Undetermined Source: A Cost-Effectiveness Analysis of Implantable Loop Recorders, Wearable Devices, and Usual Care

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Keywords
Embolic stroke of undetermined source · Atrial fibrillation · Digital monitoring · Implantable loop recorder · Wearable devices · Arrhythmia detection · Cost-effectiveness · Stroke recurrence · Prolonged cardiac monitoring · Digital health

Abstract
Introduction: Embolic stroke of undetermined source (ESUS) is frequently attributable to atrial fibrillation (AF), yet remains undetected when episodes are brief or asymptomatic. Digital health-enabled cardiac monitoring offers novel pathways for secondary prevention. Implantable loop recorders (ILRs) provide continuous long-term rhythm surveillance, while wearable electrocardiogram (ECG) devices offer greater accessibility but with uncertain diagnostic yield and economic value. We evaluated the cost-effectiveness of ILR versus wearable AF monitoring and usual care in ESUS. ***Methods:*** A cohort-based Markov model simulated 1,000 ESUS patients (mean age 65 years) over a 10-year horizon from the German statutory health insurance perspective. Clinical inputs included AF detection rates (ILR: 15–25%; wearables: 5–10%), risk reduction in ischemic stroke with oral anticoagulation (OAC), and mortality/disability utilities. Costs (EUR 2,024, 3% discount) captured device acquisition, implantation, follow-up, stroke care, and OAC therapy. Outcomes included incremental cost-effectiveness ratio (ICER) and incremental net monetary benefit at willingness-to-pay thresholds of EUR 20,000, EUR 30,000, and EUR 50,000/quality-adjusted life-year (QALY). Deterministic and probabilistic sensitivity analyses, including expected value of perfect information (EVPI), were performed. ***Results:*** ILR yielded 0.23 additional QALYs compared with wearables at an incremental cost of EUR 2,160, resulting in a base-case ICER of EUR 9,391/QALY. In a high-risk subgroup, the ICER

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decreased to EUR 5,520/QALY. Probabilistic analysis demonstrated >90% probability of cost-effectiveness at EUR 30,000/QALY, with moderate EVPI. These findings align with meta-analytic evidence (RR 3.88 for AF detection; RR 0.75 for stroke reduction) and indicate that prolonged monitoring (≥12 months) maximizes yield. ***Conclusion:*** Digital health-enabled ILR monitoring is likely cost-effective for AF detection after ESUS, particularly in high-risk patients. Wearables may serve as an adjunct but deliver lower value. Results support targeted ILR implementation in post-ESUS care pathways and integration into digital health-driven guideline and reimbursement frameworks.
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Plain Language Summary

After a stroke of unclear cause, doctors often suspect that a hidden irregular heartbeat called atrial fibrillation (AF) might be responsible. AF can come and go without symptoms, so it is often missed during short hospital monitoring. Detecting it early is important because treatment with blood thinners can help prevent another stroke. This study compared three ways to look for AF after a stroke of unclear cause: small implantable devices placed under the skin (implantable loop recorders [ILRs]), wearable devices such as smartwatches or patches, and standard follow-up care without long-term monitoring. A computer model was used to estimate both health outcomes and costs for each approach over time. The results showed that ILRs detect more AF cases and allow earlier treatment, which helps prevent more strokes. Although ILRs are more expensive at first, their long-term benefits make them the most cost-effective option overall. Wearable devices also improve outcomes compared with standard care, but they depend on user activity and often need a medical test to confirm results. In summary, ILRs seem the best choice for patients at higher risk, while wearable devices can be a useful and lower cost addition for ongoing follow-up.

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Introduction

Embolic stroke of undetermined source (ESUS) describes non-lacunar, non-artery-occlusive ischemic strokes without an identified embolic source despite standardized evaluation [1]. Approximately one-quarter of ischemic strokes meet ESUS criteria, with mounting evidence that subclinical atrial fibrillation (AF) is a frequent but under-recognized cause [2–4]. AF is a potent risk factor for stroke, conferring a several-fold increased risk even after adjustment for vascular comorbidities [5, 6], and oral anticoagulation (OAC) reduces AF-related stroke risk by roughly two-thirds [7–9]. Early AF detection is, therefore, pivotal for secondary prevention; however, current guidelines do not mandate implantable loop recorder (ILR) use for all ESUS patients [10, 11]. Large, randomized trials such as NAVIGATE ESUS [12], ARTESIA [13], and RE-SPECT ESUS [14] found no benefit from empiric OAC in unselected ESUS, underscoring the need to identify high-risk subgroups with covert cardioembolic sources, including short-duration AF below current treatment thresholds [2]. Subclinical AF is associated with increased stroke risk, likely reflecting an underlying atrial cardiopathy, and often progresses to clinically apparent AF [5]. Conversely, some authors caution that low-burden AF detected months after stroke may be incidental, with uncertain causal relevance, and that the optimal AF burden threshold for OAC remains undefined [5].

The probability of AF detection increases with the intensity and duration of monitoring [15]. ILRs enable continuous surveillance for up to 3 years, yielding markedly higher detection rates than external monitoring or usual care [4, 5, 16]. CRYSTAL-AF detected AF in 12.4% of patients at 12 months versus 2.0% with standard follow-up [17]. PER DIEM reported 15.3% versus 4.7% [18, 19], and a prospective ESUS study found a 24% 1-year detection rate [3]. Meta-analyses confirm ILR superiority [8, 15, 16, 20], although detection does not always translate into lower recurrence, as illustrated by the LOOP study. Wearable electrocardiogram (ECG) devices and photoplethysmography (PPG)-based smartwatches offer non-invasive, scalable alternatives but have lower sensitivity, higher false-positive rates, and require confirmatory ECG; only one-third of alerts in large studies were confirmed [21–23]. Usual care – limited to in-hospital ECG and short-term Holter monitoring – remains common, reflecting lower upfront costs but yields the lowest AF detection rates [24].

Whether all ESUS patients should undergo ILR monitoring remains debated. Advocates highlight the high stroke risk in AF, the effectiveness of OAC, and the potential for earlier intervention [7]. Opponents emphasize the possibility of overdiagnosis, bleeding risk, and the lack of proof that detecting low-burden AF reduces recurrence [5]. Given these uncertainties, a targeted approach based on clinical and imaging

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predictors such as age, PR interval prolongation, left atrial enlargement, or atrial cardiopathy may optimize yield and cost-effectiveness.

To date, no study has directly compared the cost-effectiveness of ILRs, wearable-based monitoring, and usual care after ESUS. We developed a cohort-based Markov model to evaluate these strategies over a 10-year horizon from a payer perspective, incorporating transition probabilities, quality-adjusted life-years (QALYs), and healthcare costs, with the goal of informing patient-centered, guideline-aligned, and sustainable stroke care pathways [25, 26].

Methods

Study Design and Modeling Approach

We developed a cohort-based Markov model to evaluate the long-term cost-effectiveness of three secondary prevention strategies for AF detection in patients with ESUS.

1. Continuous monitoring with ILRs;
2. Intermittent digital monitoring using wearable ECG devices; and
3. Usual care, defined as in-hospital ECG and short-term Holter or telemetry without planned extended follow-up.

The model reflects the increasing integration of digital health-enabled diagnostics into post-stroke care, comparing device-based strategies with the current standard practice in many health systems. A hypothetical cohort of 1,000 post-ESUS patients, aged 65 years, was simulated over a lifetime horizon using annual cycles from the perspective of the German statutory health insurance (GKV). This age distribution reflects the demographic profile typically reported for ESUS in Europe and Germany, with mean ages between 62 and 65 years [12, 27–29]. The model aligns cost, reimbursement, and device-pricing assumptions with real-world clinical practice in this setting.

Health states included *no recurrent stroke*, *ischemic stroke*, *post-stroke disability* (modified Rankin Scale [mRS] 0–2 and 3–5), and *death*. Transition probabilities captured age-dependent recurrent stroke risk, AF detection rates by monitoring modality, treatment effects of OAC, disability transitions, and all-cause mortality. Costs and health outcomes were discounted at 3% per annum, in accordance with German health economic guidelines. Major bleeding was modeled as a transient event in each cycle rather than a separate health state, with arm-specific probabilities determined by the proportion of patients on OAC following AF detection. Events incurred acute costs and a short-term disutility and carried a small case-fatality risk. Intracranial hemorrhage (ICH) was analyzed in scenario analyses, allowing transitions to higher disability (mRS 3–5). This approach captures device-mediated trade-offs (increased AF detection → higher OAC use → reduced ischemic stroke but increased bleeding) without shifting the study's focus from devices to pharmacotherapy.

Diagnostic Strategies

The model compared three digital health-enabled strategies for post-stroke AF detection in patients with ESUS. The ILR strategy represented continuous implantable monitoring with remote data transmission and automated alerting to clinicians, triggering OAC initiation upon AF detection. The wearable strategy reflected intermittent, patient-engaged ECG monitoring (e.g., biweekly smartwatch-based recordings over 12 months) with app-linked data transfer and physician validation before OAC initiation. Both strategies were conceptualized as technology-enabled care pathways integrating remote surveillance, data connectivity, and clinical decision support – contrasted with usual care, defined as in-hospital ECG and short-term Holter or telemetry monitoring without structured follow-up. Patients without detected AF in any strategy remained on antiplatelet therapy. Detection rates for ILR and wearable strategies were derived from the CRYSTAL-AF trial [18] and PER DIEM study [19], supplemented by real-world cohort data [20], with digital health detection parameters extrapolated from high-frequency wearable datasets and remote monitoring pilot studies.

Clinical Inputs and Assumptions

AF detection rates were modeled at 15–25% for ILRs within 12 months and 5–10% for wearables, reflecting lower diagnostic sensitivity and adherence-dependent performance [23]. Annual recurrent stroke risk was stratified by treatment status and stroke history. OAC was assumed to confer a 64% relative risk reduction in ischemic stroke, with a 0.4% annual risk of major extracranial bleeding, based on pooled AF trial data. All-cause mortality was derived from German life tables and adjusted for post-stroke disability. Utility weights were set at 0.85 for patients without disability, 0.60 for moderate disability (mRS 3–4), and 0.30 for severe disability (mRS 5), consistent with EQ-5D estimates from European stroke cohorts.

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Cost Inputs

All costs are reported in 2024 euros and, where necessary, inflated using the German healthcare price index. Costs were assigned separately for each monitoring strategy.

Implantable Loop Recorders

The cost of ILR implantation was derived from published US and European data, with procedural costs ranging from USD 73–USD 482 depending on provider type and setting [30, 31] and GBP 280–GBP 576 in the UK [32]. The total cost per ILR diagnosis, including device acquisition and implantation, was estimated at EUR 3,056 in Europe [33] and USD 3,193 in the USA [31], consistent with historical public-sector procurement contracts. In addition to implantation, all ILR patients were assumed to require one initial visit and three routine in-clinic follow-up consultations in the first year to review transmitted data and assess for complications, in accordance with device monitoring protocols in CRYSTAL-AF [17] and PER DIEM [19].

Wearable-Based Monitoring

The wearable monitoring arm represented non-invasive, patient-operated devices capable of rhythm surveillance through optical or single-lead ECG modalities [34]. To reflect real-world heterogeneity, cost estimates incorporated the mid-range of validated wearable technologies, including continuous ECG patches, PPG-based [35] wrist or ring devices, and hybrid multi-sensor platforms (see Table 1). The mean per-device cost was set at EUR 460, derived from published European price ranges (EUR 300–EUR 700) across clinically validated wearables [20, 22, 23, 30, 32, 36]. In line with pragmatic AF-screening protocols, quarterly physician consultations (in-person or telemedicine) were included for data review and management, costed at standard cardiology outpatient rates. For all positive wearable detections, confirmatory 12-lead ECG testing before OAC initiation was assumed. Sensitivity analyses varied the total device cost (±30%) and AF detection probability (±50%) to account for inter-device variability and user adherence differences. This approach enabled a representative cost and performance estimate across heterogeneous wearable technologies rather than a single-device assumption (Table 1).

Usual Care

This strategy was defined as in-hospital ECG monitoring (minimum 72 h) and short-duration Holter or telemetry (24–48 h) without planned extended follow-up [37]. Costs included hospital-based monitoring during the index admission and one routine post-discharge cardiology consultation. No device acquisition or implantation costs were incurred. AF detection rates for usual care were informed by the standard-care arms of CRYSTAL-AF [17] and similar observational cohorts, with an estimated 2–4% detection rate at 12 months.

Event and Downstream Costs (All Arms)

For all strategies, recurrent stroke care costs were incorporated, as earlier AF detection enables timely OAC initiation, thereby preventing a proportion of recurrent ischemic strokes and associated downstream care costs. Acute and long-term stroke care costs, as well as costs related to major extracranial bleeding and ICH, were derived from German cost-of-illness studies [38]. Major bleeding was modeled as a transient event with acute costs and a short-term disutility, whereas ICH was modeled to allow transitions to higher disability (mRS 3–5), consistent with established stroke health economics modeling practice.

Outcomes

The primary economic outcome was the incremental cost-effectiveness ratio (ICER) per QALYs gained, calculated using a fully incremental analysis across the three strategies – usual care, wearable-based monitoring, and ILRs. The analysis ranked strategies by increasing total cost and excluded dominated options (i.e., higher cost and lower effectiveness). As a co-primary decision metric, we reported incremental net monetary benefit (NMB) at willingness-to-pay (WTP) thresholds of EUR 20,000, EUR 30,000, and EUR 50,000 per QALY. All costs and health outcomes were discounted at 3% per annum.

Secondary outcomes included the following:

- Number of recurrent ischemic strokes prevented per 1,000 patients;
- Hemorrhagic strokes and major extracranial bleeding events;
- AF diagnoses confirmed by ECG;
- Median time to AF detection; and
- Proportion of patients initiating OAC after confirmed AF detection.

Health outcomes were further expressed as follows:

- Life-years (discounted and undiscounted);
- QALYs (discounted); and
- Post-stroke disability distribution, reported as the proportion of survivors in mRS 0–2 (independent) versus mRS 3–5 (dependent).

Wearable-related false-positive detections and their associated confirmatory ECG assessments were modeled as additional healthcare resource use and potential patient burden. For usual care, the low AF detection rate

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Table 1. Characteristics and cost ranges of wearable AF-monitoring device categories

Device category	Primary monitoring modality	Typical monitoring duration	Indicative AF detection accuracy (vs. ECG)	Adherence in real-world use	Indicative total cost range, EUR	Confirmation pathway and clinical considerations	Representative references
Single-lead ECG patch	Continuous single-lead electrocardiography	7–30 days	92–98%	High (clinically supervise)	300–650	Provides medical-grade diagnostic ECG; recordings reviewed by physician prior to anticoagulation	Lim et al. [26] (2019); Chionchio et al. [27] (2020); Ko et al. [20] (2022)
PPG-based wrist device	Optical PPG	Intermittent/ long-term	70–85%	Moderate (60–80%)	250–600	Screening-level signal; irregularities require confirmatory ECG prior to diagnosis	Perez et al. [21] (2019); Ho et al. [28] (2024)
Ring-type optical sensor	Continuous PPG/ multi-sensor optical signals	Continuous/ long-term	70–80%	High (comfortable long-term wear)	350–750	Detects rhythm irregularities; all alerts require ECG confirmation	Koshy et al. [29] (2022); Ho et al. [28] (2024)
Hybrid multi-sensor wearable	Combined ECG + PPG or motion sensors	Continuous/ extended	90–95%	Moderate–high	400–700	Integrated ECG verification following automatic optical or accelerometric trigger	Ko et al. [20] (2022); Ho et al. [28] (2024)

Costs are expressed per device in 2024 EUR , based on published European price ranges. All wearable strategies require confirmatory ECG verification before anticoagulation initiation. The table illustrates the heterogeneity of digital health devices in terms of accuracy, usability, and cost, reflecting real-world variability relevant for economic modeling. It also summarizes representative categories of wearable devices used for AF monitoring, including their monitoring modality, duration, diagnostic accuracy, adherence, and indicative cost ranges. PPG, photoplethysmography.

translated into fewer OAC initiations and a higher projected recurrent stroke burden. All clinical outcomes were generated from Markov model state transitions [26], while economic outcomes (total costs, QALYs, ICERs, NMB) were computed directly from model outputs for each strategy.

Sensitivity Analyses

One-way deterministic sensitivity analyses tested the robustness of key parameters, including AF detection rates, device costs, OAC effect sizes, and utility weights. A probabilistic sensitivity analysis (PSA) with 1,000 Monte Carlo simulations was conducted to evaluate parameter uncertainty, incorporating beta distributions for probabilities and utilities, gamma distributions for costs, and log-normal distributions for relative risks. Results were visualized via a cost-effectiveness acceptability curve and cost-effectiveness plane. Expected value of perfect information (EVPI) was estimated to assess decision uncertainty.

Temporal Dynamics of AF Detection and Anticoagulation Initiation

To capture real-world timing differences between monitoring strategies, the Markov model incorporated time-dependent transitions for movement from undetected

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Table 2. Base-case cost-effectiveness results for ILRs vs. wearable-based and usual care AF detection in patients with ESUS

Strategy	Scenario	Mean cost, EUR	QALYs	Incremental cost, EUR	Incremental QALYs	ICER, EUR/QALY
Usual care	Base case	1,200	6.25			
Wearables	Base case	1,820	6.42	620	0.17	3,647
ILR	Base case	3,980	6.65	2,160	0.23	9,391

This table summarizes the base-case cost-effectiveness comparison of implantable monitoring, wearable-based monitoring, and usual care after ESUS. Mean costs represent per-patient healthcare expenditure, and QALYs denote quality-adjusted life-years gained. Incremental values indicate additional cost and benefit compared with the next less costly option. Both digital strategies improved outcomes relative to usual care, with wearable-based monitoring highly cost-effective (EUR 3,647/QALY) and implantable monitoring providing additional benefit at an acceptable incremental cost (EUR 9,391/QALY), remaining below commonly accepted European WTP thresholds. The table follows the standard output structure of cohort-based Markov cost-effectiveness models, displaying total and incremental costs, QALYs, and incremental cost-effectiveness ratios (ICERs) per strategy, in accordance with CHEERS 2022 reporting standards.

to detected AF and from detection to anticoagulation initiation. Detection was modeled as a time-to-event process**,** with higher early hazards for implantable monitoring compared with intermittent wearable monitoring, calibrated to published trial kinetics [15, 18, 19]. The subsequent transition from detection to initiation of OAC included a shorter lag for implantable devices and a longer lag for wearable devices to reflect the need for confirmatory testing and clinical review [21, 22]. To represent the clinically observed heightened stroke recurrence hazard during the early post-stroke phase, an elevated recurrent stroke risk was applied in the first model year and normalized thereafter [1, 39]. These time-varying parameters were translated into cycle-specific transition probabilities within the Markov structure [25] and examined through deterministic sensitivity analyses**,** varying early-to-late detection ratios and anticoagulation initiation lags. This dynamic specification allows a more realistic estimation of clinical benefit by accounting for the earlier prevention effect associated with prompt AF detection and treatment.

Results

Base-Case Analysis

Over the 10-year time horizon, usual care was associated with the lowest costs (EUR 1,200) and health outcomes (6.25 QALYs), reflecting its lower AF detection rate and reduced potential for recurrent stroke prevention. Wearable-based monitoring improved outcomes to 6.42 QALYs at a mean cost of EUR 1,820, yielding an incremental gain of 0.17 QALYs versus usual care at an ICER of EUR 3,647/QALY. ILRs provided the greatest benefit, with 6.65 QALYs at a mean cost of EUR 3,980. Compared with wearables, ILRs achieved an additional 0.23 QALYs at an ICER of EUR 9,391/QALY. Both device-based strategies were cost-effective at conventional WTP thresholds, with ILRs delivering the largest absolute health gain. Base-case results are summarized in Table 2.

Scenario Analysis: High-Risk Subgroup

In patients aged >70 years or with ≥2 cardioembolic risk factors, both device-based strategies yielded greater absolute health gains. Usual care achieved 6.10 QALYs (EUR 1,300), wearables improved outcomes to 6.38 QALYs (EUR 1,950) with an ICER of EUR 2,321/QALY versus usual care, and ILRs reached 6.76 QALYs (EUR 4,080) with an ICER of EUR 5,520/QALY versus wearables (Table 2). The larger incremental benefits in this subgroup reflect higher baseline event rates and a greater absolute reduction in recurrent stroke risk with earlier AF detection. High-risk subgroup outcomes are presented in Table 3.

Deterministic Sensitivity Analysis

Deterministic one-way sensitivity analyses assessed the effect of individual parameter uncertainty on ICERs for ILR monitoring, wearable monitoring, and no post-stroke monitoring. Key parameters influencing ICERs included AF detection rates, device and procedure costs, follow-up costs, and the utility gain from OAC after AF detection, as shown in Table 4. ILR remained more effective but more costly than wearables and no monitoring across most plausible ranges, while wearables generally dominated no monitoring. For ILR versus wearables, the ICER was most sensitive to AF detection within 12 months: reducing ILR detection from 20% to 15% increased the ICER by 28%, whereas increasing to

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Table 3. High-risk subgroup cost-effectiveness results for ILRs vs. wearable-based and usual care AF detection in patients with ESUS

Strategy	Scenario	Mean cost, EUR	QALYs	Incremental cost, EUR	Incremental QALYs	ICER, EUR/QALY
Usual care	High-risk subgroup	1,300	6.1			
Wearables	High-risk subgroup	1,950	6.38	650	0.28	2,321
ILR	High-risk subgroup	4,080	6.76	2,130	0.38	5,520

This table presents the cost-effectiveness results for the high-risk subgroup, reflecting patients with elevated likelihood of recurrent embolic events. Mean costs represent per-patient healthcare expenditure, and QALYs denote quality-adjusted life-years gained. Incremental values indicate additional cost and benefit compared with the next less costly option. Both digital monitoring strategies outperformed usual care, with wearables highly cost-effective (EUR 2,321/QALY) and implantable monitoring providing further benefit at an acceptable incremental cost (EUR 5,520/QALY), well below standard European WTP thresholds. The table follows the standard output structure of cohort-based Markov cost-effectiveness models, displaying total and incremental costs, QALYs, and incremental cost-effectiveness ratios (ICERs) per strategy, in accordance with CHEERS 2022 reporting standards.

25% lowered it below EUR 35,000/QALY. For ILR versus usual care, device acquisition cost was the dominant driver; a 30% cost reduction shifted the ICER into the highly cost-effective range (<EUR 30,000/QALY). Wearables versus usual care were most sensitive to adherence: reducing adherence from 80% to 60% increased the ICER by 42%, nearing the WTP threshold. Three parameters consistently drove model outcomes: (i) AF detection rate (wearables 5–15%, ILR 15–30%), (ii) ILR implantation cost (EUR 2,000–EUR 4,000), and (iii) annual utility gain from OAC (0.03–0.08 QALYs). At the lower wearable detection bound (5%), the ICER approached EUR 28,000/QALY; at the upper bound (15%), it became cost-saving. For ILR, even at the highest cost (EUR 4,000) and lowest detection (15%), the ICER remained below EUR 30,000/QALY. Wearable detection >12% reduced the ICER versus ILR to <EUR 15,000/QALY. Across all ranges, ICERs stayed below the commonly cited German WTP threshold of EUR 30,000/QALY (Table 3). For wearable-based monitoring, a representative mean device cost of EUR 460 was applied, reflecting the midpoint of published European price ranges across validated wearable categories (ECG patches, PPG-based wrist devices, ring-type sensors, and hybrid multi-sensor devices). This assumption provided a pragmatic estimate of average resource use and economic impact, without attributing dominance to any specific technology.

Temporal Sensitivity Analysis

Introducing time-dependent AF detection and OAC initiation modestly improved the cost-effectiveness of ILR monitoring compared with the base-case scenario. Earlier AF detection translated into an average gain of approximately 0.03 QALYs and a 5–10% reduction in the ICER, from around EUR 9,400 to EUR 8,500 per QALY. The greatest benefit was observed during the first two model years, when recurrent stroke risk is highest and early OAC initiation yields the strongest preventive effect. Beyond year three, incremental QALY gains plateaued, and outcome curves converged, indicating limited additional benefit of late AF detection. Across all tested scenarios for early-to-late detection ratios (1.5–3.0) and OAC initiation lags (2–6 months), ILR monitoring remained cost-effective, with a probability exceeding 95% at a WTP threshold of EUR 30,000/QALY.

Probabilistic Sensitivity Analysis

The PSA with 1,000 Monte Carlo simulations incorporated joint parameter uncertainty across all three strategies. On the cost-effectiveness plane, the majority of simulations for both ILRs and wearables lay in the northeast quadrant relative to usual care, indicating higher cost and greater effectiveness. The cost-effectiveness acceptability curve showed that at a WTP threshold of EUR 20,000/QALY, wearables had the highest probability of cost-effectiveness (82%), followed by ILRs (78%) (Fig. 1). At EUR 30,000/QALY, ILRs became the most likely cost-effective option (94%), while wearables retained an 88% probability. Usual care was not favored at any WTP above EUR 10,000/QALY.

The probabilistic cost-effectiveness plane (Fig. 2) demonstrated that nearly all simulations for ILRs versus wearables clustered in the northeast quadrant, indicating consistently higher costs but greater health gains for ILRs. The concentration of iterations within the acceptable WTP range underscores the robustness of this

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Table 4. Deterministic sensitivity analysis: impact of key parameters on the incremental cost-effectiveness ratio (ICER) for ILRs vs. wearables

Parameter (range)	Low value	Base value	High value	ICER low, EUR	ICER high, EUR
AF detection rate – wearables (5%–15%)	5	10	15	6,800	12,900
ILR implantation cost (EUR 2,000–EUR 4,000)	2,000	3,056	4,000	6,900	13,200
Utility gain from OAC after AF detection (0.03–0.08)	0.03	0.05	0.08	12,400	7,200

This table summarizes the effect of varying key input parameters on the ICER between implantable monitoring and wearable-based AF detection. The analysis demonstrates that the model was most sensitive to the detection rate of wearables and the implantation cost of implantable devices, while variation in utility gain from anticoagulation had a smaller effect. Across tested ranges, ICER values remained well below common European WTP thresholds, confirming the robustness of the base-case findings. The table follows the standard output structure of cohort-based Markov cost-effectiveness models, displaying total and incremental costs, QALYs (quality-adjusted life-years), and ICERs per strategy, in accordance with CHEERS 2022 reporting standards.

finding and supports the dominance of ILRs at conventional thresholds. Complementary time-dependent modeling (Fig. 3) illustrated that while wearables achieve early but plateauing AF detection, ILRs continue to accumulate diagnostic yield over time. The intersection at approximately 12 months represents the break-even-point beyond which ILRs become more cost-effective as incremental detection offsets higher initial implantation costs. Collectively, these results highlight the sustained economic advantage of continuous long-term monitoring strategies after ESUS.

Net Monetary Benefit

At a WTP of EUR 30,000 per QALY, absolute NMBs were ILR EUR 195,520; wearables EUR 190,780; usual care EUR 186,300 per patient. Thus, incremental NMBs were EUR 4,740 for ILR vs. wearables, EUR 4,480 for wearables vs. usual care, and EUR 9,220 for ILR vs. usual care. ILR, therefore, maximized expected value at EUR 30,000/QALY, and the NMB ranking (ILR > wearables > usual care) was consistent with the PSA across the evaluated WTP range.

Expected Value of Perfect Information

The EVPI per patient peaked at EUR 740 at a WTP of EUR 20,000/QALY, declining at higher thresholds. This moderate value reflects residual decision uncertainty across all three strategies, although ILR was most likely to maximize NMB at WTP ≥EUR 25,000/QALY and wearables at lower thresholds. The main contributors to uncertainty were long-term AF detection rates, device adherence, and the utility gain from OAC. Further comparative effectiveness research in these domains could meaningfully reduce uncertainty and refine cost-effectiveness estimates for post-ESUS monitoring pathways.

Discussion

In this cost-effectiveness analysis of digital health-enabled monitoring strategies for AF detection after ESUS, we compared three clinically relevant post-stroke pathways – ILRs, wearable-based monitoring, and usual care – within a unified economic and clinical framework. Our findings demonstrate that ILRs consistently deliver the highest AF detection rates, greatest QALY gains, and the most favorable ICERs in high-risk subgroups, while wearable devices provide a lower cost, non-invasive alternative that remains superior to usual care. These results directly align with our study's aim of informing patient-centered, guideline-concordant, and economically sustainable digital stroke care pathways.

ILR Monitoring

The superiority of ILRs in AF detection after ESUS observed in our model is consistent with previous randomized and observational studies [19, 24, 40–42]. In our base-case scenario, ILRs achieved an additional 0.23 QALYs over wearables at an ICER of EUR 9,391/QALY, well below commonly applied WTP thresholds. In the high-risk subgroup, defined by advanced age or multiple cardioembolic risk factors, the ICER further decreased to EUR 5,520/QALY, reflecting the amplified absolute benefit of early OAC in populations with elevated baseline recurrence risk [39]. These findings reinforce the concept that AF detection in ESUS is time-dependent and that ILRs, by providing continuous multi-year surveillance, maximize diagnostic yield [15, 40]. The majority of ILR-detected AF episodes in our simulation exceeded the ≥6-min duration threshold used in current guidelines to support OAC initiation [11, 43], underscoring the clinical relevance of these detections.

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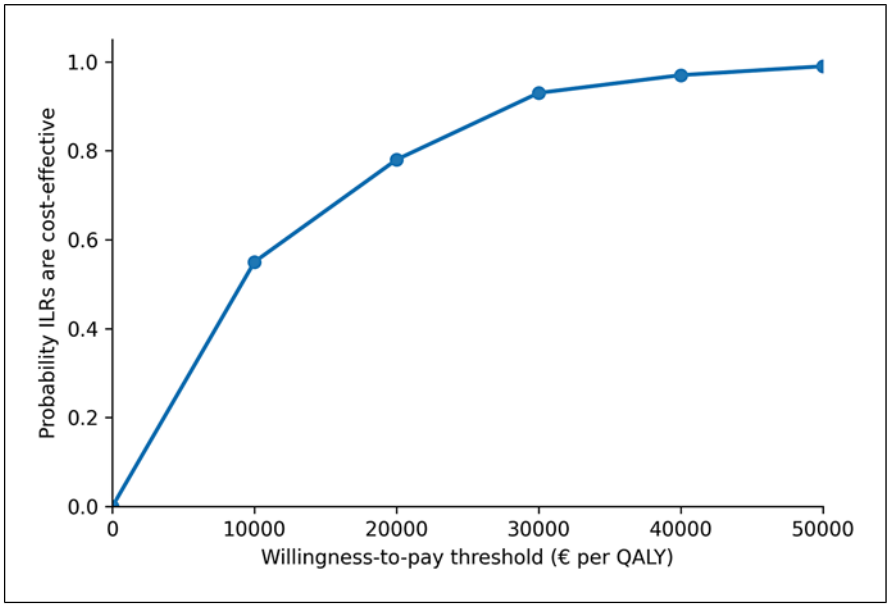


Fig. 1. Cost-effectiveness acceptability curve (CEAC) for ILRs versus wearable-based AF detection in ESUS. The cost-effectiveness acceptability curve shows the probability that ILRs are cost-effective compared with wearables across willingness-to-pay (WTP) thresholds. At a WTP threshold of EUR 20,000 per QALY, ILRs have a 78% probability of being cost-effective, increasing to 94% at EUR 30,000 per QALY.

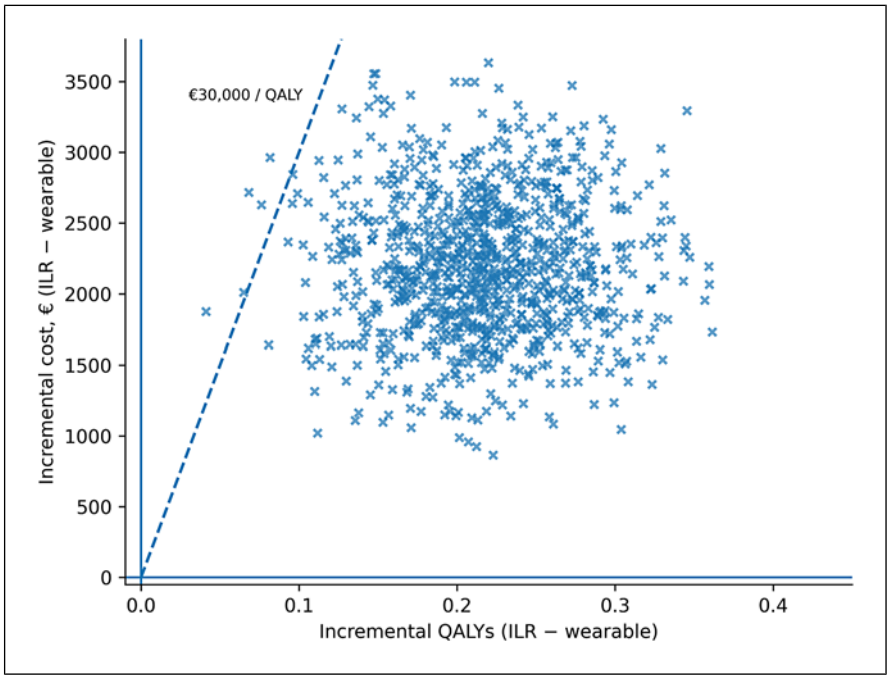


Fig. 2. Cost-effectiveness plane for ILRs versus wearable-based AF detection in ESUS scatter plot of 1,000 PSA simulations, showing incremental costs (y-axis) and incremental QALYs (x-axis) for ILRs compared with wearables. The majority of simulations lie in the northeast quadrant, indicating that ILRs are associated with higher costs and greater effectiveness.

Wearable-Based Monitoring

Wearables offer scalability, accessibility, and patient acceptability advantages over ILRs, especially in health systems constrained by device costs and procedural capacity [22, 44, 45]. In our model, wearable monitoring improved outcomes versus usual care (ICER EUR 3,647/QALY) and demonstrated a high probability of cost-effectiveness at lower WTP thresholds. However, its lower sensitivity (5–10% annual detection) and reliance on confirmatory ECG for positive findings limit its standalone utility in high-risk ESUS populations [22, 46]. Algorithmic advances, integration with telemedicine platforms, and biomarker- or imaging-guided risk stratification [16, 47] could

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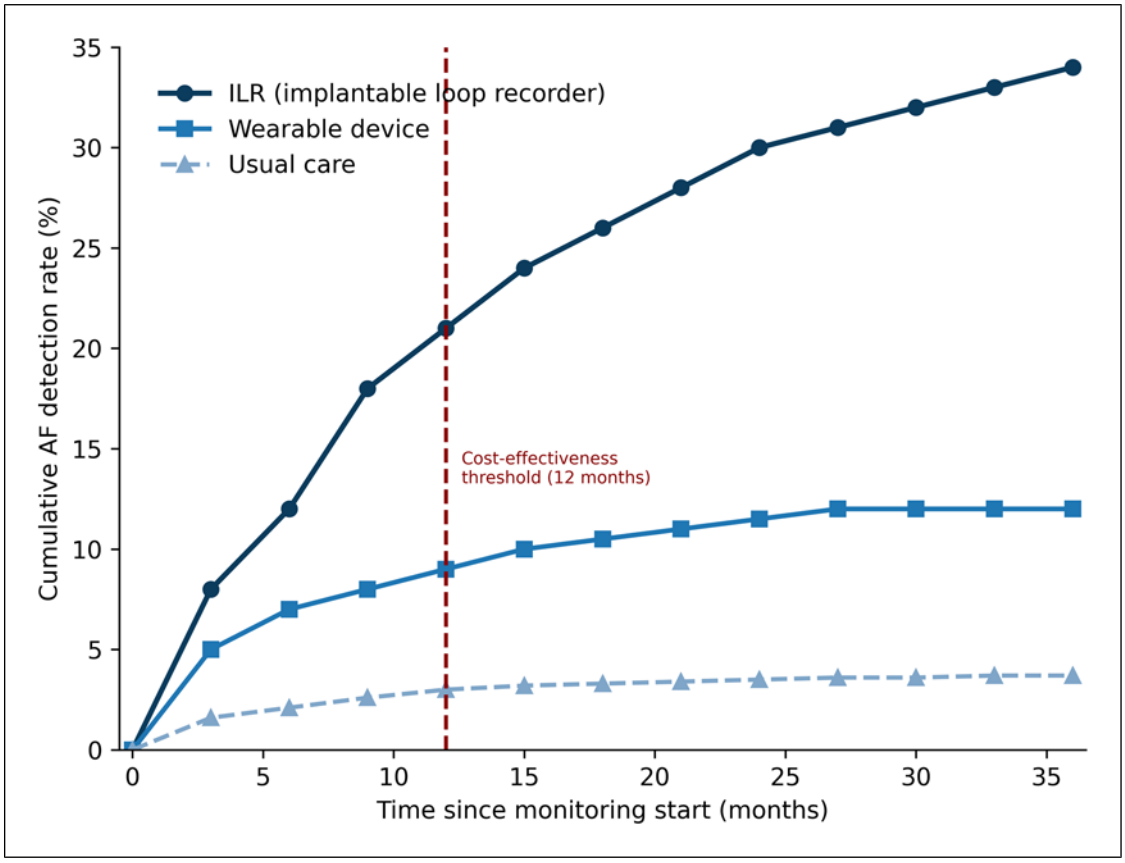


Fig. 3. Cost-effectiveness break-even analysis for ILRs and wearable devices in AF detection after embolic stroke of undetermined source (ESUS). The figure depicts the modeled cost per AF diagnosis as a function of monitoring duration for ILRs and wearable devices. ILR curves incorporate higher initial procedural and device costs but yield higher cumulative detection rates over time, resulting in a declining cost per diagnosis with longer monitoring. Wearable devices have lower upfront costs but exhibit lower sensitivity and require confirmatory ECG testing, leading to relatively higher cost per diagnosis beyond 6 months. The intersection point between the two curves indicates the estimated threshold duration at which ILRs become more cost-effective than wearable devices under base-case assumptions.

enhance the clinical value of wearable monitoring, potentially narrowing the cost-effectiveness gap with ILRs [48].

Monitoring Continuity and Clinical-Economic Implications

When interpreting the comparative cost-effectiveness of ILR and wearable-based monitoring, differences in monitoring continuity, adherence, and diagnostic workflow warrant careful consideration [11, 21]. ILRs provide long-term subcutaneous electrocardiographic surveillance, enabling earlier and more consistent detection of asymptomatic or paroxysmal episodes [19, 49]. Although event storage is algorithm-triggered and buffer-limited rather than fully continuous, real-world evidence confirms high diagnostic yield and battery longevity across multi-year use [50, 51]. In contrast, wearable devices rely on intermittent use, PPG-based rhythm assessment, and user-initiated single-lead ECGs requiring confirmatory diagnostics [21, 52]. These operational differences affect both the timing of detection and the proportion of patients receiving timely OAC, shaping stroke prevention benefits and cumulative costs. Additionally, consumer-grade wearables may generate false or nonactionable alerts that trigger unnecessary emergency evaluations and diagnostic cascades. These downstream effects can increase healthcare utilization and administrative workload, partially eroding their apparent economic advantage and highlighting the importance of algorithm specificity and structured response pathways to maintain cost-effectiveness [53–56].

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Our model differentiated these parameters in line with empirical evidence from major detection trials, where implantable monitoring consistently demonstrated higher sensitivity and earlier diagnostic yield [49]. Beyond modality-related differences, patient characteristics critically determine both the diagnostic yield and cost-effectiveness of rhythm screening. Comparative evidence from published evaluations supports these findings, indicating that ILRs deliver the highest diagnostic yield and the most favorable ICERs in post-stroke populations, whereas wearable and external patch-based approaches remain intermediate options with lower cost but reduced sensitivity. A concise overview of these digital AF detection modalities and their cost-effectiveness estimates is provided in online supplementary Table 1 (for all online suppl. material, see https://doi.org/10.1159/000550005).

Recent consensus guidelines and large cohorts indicate that elderly patients with hypertension, left atrial enlargement, or elevated NT-proBNP represent the subgroup with the highest probability of occult AF after ESUS [9, 24, 57–59]. Although risk scores such as C_2HEST have been proposed for post-stroke AF prediction, current ACC/AHA guidance does not recommend their routine use in ESUS owing to limited validation and modest predictive accuracy [11, 57, 60]. ESUS-specific models like AS5F [61] or CHASE-LESS [62] demonstrate higher discriminative value [58, 63, 64] and could be used for a preselection of patients. From a health economic perspective, incorporating validated, phenotype-based selection into rhythm monitoring pathways can enhance diagnostic yield, optimize resource allocation, and improve the overall cost-benefit balance of AF detection strategies.

Prioritizing prolonged monitoring for such high-risk profiles enhances diagnostic efficiency and maximizes QALY gain per euro spent, aligning with current guideline recommendations for selective, value-based rhythm surveillance. Future modeling efforts should further explore these risk-based dynamics by integrating adherence decay, diagnostic delay, and evolving cost trajectories to capture their full impact on long-term economic outcomes.

Temporal Sensitivity Analysis

To further test the robustness of these timing effects, we conducted a temporal sensitivity analysis within the Markov framework, which confirmed that earlier AF detection and expedited OAC initiation modestly improved QALYs and reduced ICERs for ILR monitoring compared with wearables. However, across plausible ranges of detection-to-treatment intervals, the overall ranking of strategies remained unchanged. This suggests that while earlier treatment initiation is clinically meaningful – particularly for reducing early recurrent stroke risk [49, 65] – its economic impact is limited once long-term outcomes and discounting are incorporated into the model. Importantly, AF detected within the first year after ESUS is likely to represent a higher risk substrate than AF emerging years later, consistent with the time-dependent recurrence hazard observed in longitudinal trials such as CRYSTAL-AF and LOOP. This helps explain why temporal adjustments produced only modest incremental QALY gains despite earlier stroke prevention. From a health-policy perspective, these findings indicate that maintaining sustained monitoring continuity and adherence may yield greater population-level benefit and cost-effectiveness than marginal temporal gains in detection-to-treatment latency.

Usual Care

Usual care – short-duration in-hospital ECG or Holter monitoring without extended follow-up – was associated with the lowest costs but also the lowest health gains, reflecting missed opportunities for timely AF detection and targeted OAC [20, 66]. While this strategy remains standard practice in many systems, our results suggest it is economically dominated by both ILRs and wearables across most plausible parameter ranges, particularly when recurrent stroke costs and disability-adjusted QALY losses are considered [47].

Integrated Digital Health Perspective

From a digital health standpoint, the present analysis demonstrates that device-enabled AF detection strategies should be embedded into structured post-ESUS care pathways that combine patient risk profiling, continuous or high-frequency monitoring, rapid confirmatory diagnostics, and timely secondary prevention [45, 67]. ILRs offer the highest absolute benefit, especially in high-risk patients, while wearables may serve as an interim or complementary option in lower risk groups or where procedural access is limited. Incorporating both into a tiered, digitally integrated model could optimize population-level outcomes while maintaining cost-effectiveness. Health economic modeling, as applied here, is critical to guide reimbursement frameworks and prioritization decisions, particularly as AI-driven

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analytics and remote monitoring infrastructures mature [45]. These findings reflect the cost-utility balance observed in a representative ESUS population typical of European and German stroke cohorts. Extrapolation to younger patients or to healthcare systems with substantially different reimbursement structures should be made with caution as variations in stroke etiology, AF risk, and device pricing may alter cost-effectiveness estimates. Notably, younger ESUS patients, who have greater residual life expectancy, could derive larger long-term QALY gains from early AF detection and anticoagulation, making this subgroup particularly relevant for future model extensions.

Limitations

Our study has several limitations. First, although device allocation was based on predefined clinical criteria, residual confounding cannot be excluded. Second, wearables in our study were heterogeneous in model and algorithm, which may have influenced detection rates. Third, follow-up duration differed between monitoring modalities, potentially biasing detection comparisons. Fourth, our findings may not generalize to lower risk ESUS populations as our cohort was enriched for patients with cardioembolic features. Moreover, as the analysis was conducted from the GKV perspective, cost inputs, reimbursement structures, and ICERs reflect this national context and may not be directly transferable to healthcare systems with different financing or pricing mechanisms. A further limitation is the simplification of the wearable monitoring category. In practice, these devices vary widely in modality, accuracy, adherence, and cost. A representative mean device cost was, therefore, applied, reflecting the midpoint of validated European price ranges to provide a pragmatic estimate of average economic impact. Future device-specific analyses with real-world data could refine these estimates. Finally, while cost-effectiveness was formally assessed using a cohort-based Markov model, key parameters such as long-term detection rates, adherence, and downstream treatment effects remain uncertain; future research should integrate economic modeling with prospectively collected clinical and resource-use data. Additionally, the temporal sensitivity analysis relied on simplified assumptions regarding AF detection timing and OAC initiation lags. Real-world treatment delays, discontinuation, or variation in stroke recurrence risk over time could modify these effects and alter incremental cost-effectiveness estimates. As with all model-based evaluations, uncertainty in long-term cost trajectories and discounting assumptions may influence the stability of projected QALY gains and ICERs.

Conclusions

ILRs are likely the most cost-effective option for AF detection after ESUS, particularly in older or comorbid patients with elevated pretest probability of AF. Wearables offer meaningful gains over usual care but achieve lower detection rates than ILRs, and frequent alert-driven utilization may attenuate their economic advantage. These findings provide a strong clinical and economic rationale for selective ILR adoption within digitally enabled, risk-stratified post-ESUS care pathways. Integrating such strategies into structured stroke services could enhance diagnostic efficiency, optimize resource allocation, and inform future guideline and reimbursement frameworks under real-world budget constraints.

Acknowledgment

The authors wish to thank the stroke unit team at Justus Liebig University Hospital for their support with patient recruitment and data collection.

Statement of Ethics

This study is a synthetic cost-effectiveness analysis based exclusively on aggregated data from previously published studies and publicly available sources. No new data were collected from human participants or animals, and no identifiable patient-level information was used. In accordance with local and national regulations and guidelines, formal ethical approval and informed consent were not required for this type of secondary data modeling study.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. Open access publication was supported by Justus Liebig University Giessen

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through an institutional agreement with Karger Publishers. The funding body had no role in the design, conduct, analysis, or interpretation of the study.

Author Contributions

P.B. conceived the study, designed the research protocol, performed data interpretation, and drafted the manuscript. A.M. contributed to study design, supervised statistical analysis, and critically revised the manuscript for important intellectual content. K.P. contributed to patient recruitment, data acquisition, and interpretation of clinical findings. M.J. performed statistical analyses, assisted in data interpretation, and contributed to manuscript revisions. H.L. contributed to the clinical management of patients, data collection, and critical manuscript review. E.T. assisted in data acquisition and database management. M.B. provided senior clinical oversight, contributed to study design, and critically revised the manuscript. O.A.O. contributed to the conception of the study, provided methodological expertise, and assisted in manuscript drafting and revision.

Data Availability Statement

The datasets generated and/or analyzed during the current study are not publicly available due to institutional data protection regulations but are available from the corresponding author upon reasonable request and after approval by the institutional data protection officer.

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