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Original Article

Duration of Implantable Cardiac Monitoring and Detection of Atrial Fibrillation in Ischemic Stroke Patients: A Systematic Review and Meta-Analysis

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Background and Purpose Current guidelines do not provide firm directions on atrial fibrillation (AF) screening after ischemic stroke (IS). We sought to investigate the association of implantable cardiac monitoring (ICM) duration with the yield of AF detection in IS patients.

Methods We included studies reporting AF detection rates by ICM in IS patients with negative initial AF screening. We excluded studies reporting prolonged cardiac monitoring with devices other than ICM, not providing AF detection rates or monitoring duration, and reporting overlapping data for the same population. The random-effects model was used for all pooled estimates and meta-regression analyses.

Results We included 28 studies (4,531 patients, mean age 65 years). In meta-regression analyses, the proportion of AF detection by ICM was independently associated with monitoring duration (coefficient=0.015; 95% confidence interval [CI], 0.005 to 0.024) and mean patient age (coefficient=0.009; 95% CI, 0.003 to 0.015). No associations were detected with other patient characteristics, including IS subtype (cryptogenic vs. embolic stroke of undetermined source) or time from IS onset to CM implantation. In subgroup analyses, significant differences (P<0.001) in the AF detection rates were found for ICM duration (<6 months: 5% [95% CI, 3% to 6%]; ≥6 and ≤12 months: 21% [95% CI, 16% to 25%]; >12 and ≤24 months: 26% [95% CI, 22% to 31%]; >24 months: 34% [95% CI, 29% to 39%]).

Conclusions Extended duration of ICM monitoring and increased patient age are factors that substantially increase AF detection in IS patients with initial negative AF screening.

Keywords Atrial fibrillation; Stroke; Monitoring; Meta-analysis

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Introduction

Approximately one-third of all ischemic strokes (IS) are characterized as cryptogenic strokes (CS), due to the lack of a possible cause for the event or incomplete diagnostic work-up.[1-3] Atrial fibrillation (AF), either paroxysmal or chronic, represents a major risk factor for stroke and systemic embolism, and is associated with a 5-fold increase in IS risk.[4,5] Although paroxysmal AF appears to be implicated in at least 30% of patients with CS and in approximately 25% of patients with unselected IS,[6,7] current guidelines on secondary stroke prevention do not provide firm directions on AF screening after IS.

The American Heart Association/American Stroke Association (AHA/ASA) recommendations on secondary stroke prevention suggest that prolonged rhythm monitoring for approximately 30 days is reasonable for AF screening within 6 months after CS (Class IIa; Level of Evidence C),[8] while the recent AHA/ASA guidelines on the early management of IS patients indicate that the clinical benefit of prolonged cardiac monitoring to detect AF remains uncertain (Class of Recommendation: IIb, Level of Evidence: B).[9] However, clinical trials[6,10] suggest that implantable cardiac monitors (ICMs) substantially increase AF detection in IS patients, due to prolonged monitoring duration.

In the present systematic review and meta-analysis, we sought to investigate the association of ICM duration with the level of AF detection in IS patients. We also assessed whether IS subtype, patient characteristics, and elapsed time between IS onset and CM implantation may affect the probability of AF detection.

Methods

Search strategy and selection criteria

This study was conducted according to the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) statement.[11] We searched for studies reporting AF detection rates by ICM in patients with history of IS or transient ischemic attack (TIA). A literature search in MEDLINE, SCOPUS, and the Cochrane Central Register of Controlled Trials (CENTRAL) was performed, using the following terms in combination: "cardiac monitoring," "implantable loop recorder," "insertable loop recorder," "implantable cardiac monitor," "cryptogenic stroke," "embolic stroke of undetermined source," "ischemic stroke," "cerebral ischemia," "atrial fibrillation," and "atrial flutter." The complete algorithm used in the MEDLINE database search is available in the online Supplementary Methods. Eligible studies were also sourced from a manual search of key journals, conference proceedings and other (non-Cochrane) systematic reviews and meta-analyses. No language or other search restrictions were applied. The last literature search was performed on July 10, 2018.

We included all studies (randomized clinical trials [RCTs], prospective/retrospective cohort studies, case-control studies) reporting detection rates of AF by ICM in patients with history of IS or TIA. We excluded from further evaluation all case reports, case series, studies reporting cardiac monitoring with devices other than ICM, and studies not providing AF detection rate or monitoring duration with ICM. We also excluded studies reporting overlapping population data, and included only the study with the highest number of patients and/or more extended follow-up time. However, we retained publications providing data for distinct IS groups, including CS and embolic stroke of undetermined source (ESUS), despite the possibility of overlapping group data (ESUS overlapping with CS, and CS/ESUS overlapping with unselected IS/TIA). Reference lists of all articles that met the inclusion criteria, and of relevant review articles, were examined to identify studies that may have been missed by the initial database search. All retrieved studies were scanned independently by two reviewers (G.T. and A.H.K.). In case of disagreement regarding the literature search results between the two coauthors, the remaining coauthors were consulted, and disagreement was ultimately resolved with consensus. We used the Newcastle-Ottawa Scale to assess the quality of included studies that were published at the time of the literature search, and to identify potential sources of bias amongst eligible studies.[12] Quality control and bias identification were performed independently by the same authors who performed the literature search (G.T. and A.H.K.), and all potential disagreements were resolved after discussion and mutual consensus.

The minimum required AF duration, for diagnosing AF with ICM, was documented separately for each study protocol. We calculated the ICM AF detection rates for different ICM durations by dividing the number of events (patients with detected AF) by the total number of patients receiving ICM. After the overall analysis we performed meta-regression analyses for all study and patient characteristics that were available in 10 or more of the included studies.[13] We also conducted pre-defined subgroup analyses according to the study type (prospective or retrospective cohort), study population (CS, ESUS, unselected IS/TIA), the specific time threshold used for AF diagnosis (30 seconds, 2 minutes, 6 minutes), the monitoring duration (<6, ≥6 and ≤12, >12 and ≤24, >24 months), the ICM device used, and the elapsed time between IS/TIA onset and implantation of CM (≤1 and >1 month), provided that at least two studies were included in each subgroup. Finally, for all the aforementioned meta-regression and subgroup analyses, we performed additional sensitivity analyses after excluding studies that were

presented in conferences and had only abstracts publicly available at the time of the literature search. Data extraction was performed by two independent authors (A.H.K. and L.P.), and in cases of disagreement, a senior author (G.T.) was consulted.

For all proportion analyses we used the variance-stabilizing double arcsine transformation.[14] Pooled estimates in both the overall and subgroup analyses were calculated using the Hartung-Knapp-Sidik-Jonkman method.[15] Meta-regression analyses were performed under the random-effects model (method of moments). Variables with a threshold of $P<0.1$ in the initial univariate meta-regression analyses were used as covariates for multivariate meta-regression models. Due to the established relationship of age with AF incidence,[16] mean age was included as an *a priori* potential confounder in all multivariate models. The equivalent z test was performed for each pooled estimate and $P<0.05$ was considered statistically significant. We assessed heterogeneity between studies with the Cochran Q and I^2 statistics.[17] For all subgroup analyses we used a standard test for heterogeneity across subgroup results, to investigate for potential differences between subgroups, as previously described.[18] Small-study effect (i.e., publication bias) across individual studies was evaluated graphically using both funnel plot inspection and the Egger's linear regression test, at a significance level of 0.1.[19]

All statistical analyses were performed using Stata Statistical Software Release version 13 for Windows (StataCorp LP, College Station, TX, USA) and OpenMeta-Analyst software.[20]

Since the present work is a systematic review and meta-analysis of previously published studies, IRB approval was waived.

Results

The PRISMA flowchart summarizing the literature search process is shown in Supplementary Figure 1. MEDLINE and SCOPUS literature searches retrieved 375 and 417 results respectively, while comprehensive searches of key journals and conference proceedings identified 20 additional studies. Of all potentially eligible studies, 18 study protocols were excluded (Supplementary Table 1) due to overlapping data (n=4), the use of monitoring devices other than ICM (n=11), or unavailable information on ICM duration (n=3). Our literature search highlighted 28 studies for inclusion, comprising 4,531 patients (mean age 65 years, 52% male).[6,21-48] Protocols and patient characteristics of included studies are briefly summarized in Table 1 and Supplementary Table 2, respectively. Most studies were conducted in the USA (n=9) and Germany (n=8). The most common subgroup studied was cryptogenic IS/TIA (n=17), followed by ESUS (n=9). The mean/median elapsed time from IS/TIA onset to cardiac monitoring implantation ranged from 3 to 174 days, while the mean/median ICM duration ranged from 180 to 1,080 days (Table 1). Included studies were generally found to have a low risk of bias (Supplementary Table 3), except in cases not clearly stating consecutive enrollment of patients,[23,26,27,39,44-47] exclusion of AF with electrocardiogram or short-term non-invasive Holter monitoring prior to ICM impantation,[21,33] or no adjudication of ICM recordings by experienced cardiologists.[26-29,33,41,46,47]

In the overall analysis of all included studies, the cumulative AF detection rate in patients with ICM was 26% (95% confidence interval [CI], 22% to 30%), with significant heterogeneity among studies (I^2=83%, P for Cochran Q <0.001) (Supplementary Figure 2). No evidence for publication bias was identified by funnel plot inspection (Supplementary Figure 3) or by the Egger's statistical test (P=0.525). In univariate meta-regression analyses of all included studies (Table 2) the proportion of AF detection by ICM was positively associated with the duration of monitoring (coefficient=0.009; 95% CI, 0.005 to 0.013; $P<0.001$) (Figure 1A) and mean patient age (P=0.018) (Supplementary Figure 4A). No associations were detected with other patient characteristics (Supplementary Figures 5A and 9A), including sex (P=0.100) (Supplementary Figure 5A), hypertension (P=0.215) (Supplementary Figure 6A), diabetes mellitus (P=0.140) (Supplementary Figure 7A), mean patient CHA_2DS_2-VASc score (P=0.232) (Supplementary Figure 8A), or elapsed time from IS/TIA onset to cardiac monitor implantation (P=0.363) (Supplementary Figure 9A). In multivariate analyses, both monitoring duration (coefficient=0.015; 95% CI, 0.005 to 0.024; P=0.003) and mean patient age (coefficient=0.009; 95% CI, 0.003 to 0.015; P=0.004) were independently associated with the proportion of AF detection (Table 2).

In the sensitivity univariate meta-regression analyses of published studies (Supplementary Table 4) duration of ICM (coefficient=0.007; 95% CI, 0.001 to 0.014; P=0.049) (Figure 1B), history of hypertension (coefficient=0.005; 95% CI, 0.001 to 0.010; P=0.029) (Supplementary Figure 6B), and diabetes mellitus (coefficient=0.013; 95% CI, 0.001 to 0.024; P=0.033) (Supplementary Figure 7B) were positively associated with higher rates of AF detection, while no association was detected with other patient characteristics (Supplementary Figures 4B, 5B, 8B, and 9B). However, in multivariate analyses only monitoring duration (coefficient=0.009; 95% CI, 0.003 to 0.015; P=0.006) and mean patient age (coefficient=0.037; 95% CI, 0.013 to 0.062; P=0.007) were independently associated with the proportion of AF detection (Supplementary Table 4).

In subgroup analyses of all included studies (Table 3), there

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Table 1. Characteristics of included studies

Study	Country	No. of patients	Population	Device	Monitoring time (day)	Implantation after event (day)	Insertion to AF detection (day)	AF definition
Asaithambi et al. (2017)[21]*	USA	114	CS	NR	415 (268–557)	NA	53 (5–132)	NA
Carrazco et al. (2018)[22]	USA	100	CS	Reveal XT/ Reveal LINQ	240–540	4.2±2.6	34	>2 min
Ching et al. (2018)[23]*	USA	177	ESUS	Reveal LINQ	478±179	NA	NA	NA
Cotter et al. (2013)[24]	UK	51	CS	Reveal XT	229±116	174±134	48	>2 min
CRYSTAL-AF (2014)[6]	Multicenter	221	CS	Reveal XT	1,080	38.1±27.6	41 (14–84)	>30 sec
CRYSTAL-AF (2017)[25]*	Multicenter	122	ESUS	Reveal XT	NA	NA	NA	≥2 min
de Lera et al. (2016)[26]*	Spain	163	ESUS	NR	616±340	NA	NA	>2 min
Dion et al. (2010)[27]	France	24	CS	Reveal Plus ILR 9526	435	90±30.3	NA	>30 sec
Etgen et al. (2013)[28]	Germany	22	CS	Reveal XT	360	8.5 (6.5–10.5)	152.8 (61.6–244.1)	>6 min
Israel et al. (2017)[29]	Germany	123	ESUS	Reveal XT	381±165	20	108	>2 min
Jorfida et al. (2016)[30]	Italy	54	CS	Reveal XT	435 (261–675)	108±60	162 (30–540)	>5 min
Kamel et al. (2018)[31]*	USA	886	Unselected	NR	720	NA	NA	NA
Katz et al. (2017)[32]*	USA	45	Unselected	Reveal LINQ	264	10	162.7	NA
Kotlarz-Böttcher et al. (2018)[33]*	Germany	100	ESUS	Reveal LINQ	362	NA	NA	NA
Makimoto et al. (2017)[34]	Germany	146	ESUS	NR	387 (283–552)	NA	NA	>30 sec
Navarro Pérez et al. (2018)[35]*	Spain	37	CS	NR	337.95	226.6	82.5	NA
Noone et al. (2016)[36]*	Ireland	31	ESUS	NR	540	NA	90	>30 sec
Pallesen et al. (2017)[37]*	Germany	75	ESUS	Reveal LINQ	NA	NA	57	NA
Poli et al. (2016)[38]	Germany	74	CS	Reveal XT/ Reveal LINQ	311±251	27±24	105±135	>2 min
REVEAL-AF (2018)[39]*	Multicenter	79	Unselected	Reveal XT/ Reveal LINQ	540–900	-	-	>6 min
Ritter et al. (2013)[40]	Germany	60	CS	Reveal XT	382 (89–670)	13 (10–67)	64	>30 sec
Rodríguez-Campello et al. (2015)[41]*	Spain	28	ESUS	NR	180 (60–360)	5–7	12 (10–21)	NA
Rojo-Martinez et al. (2013)[42]	Spain	101	CS	Reveal XT	281±212	<30	102	>2 min
Sethi et al. (2017)[43]*	USA	197	CS	NR	454 (50–951)	3	NA	NA
SPIDER Registry (2015)[44]*	USA	64	CS	Reveal XT/ Reveal LINQ	223	NA	35	>10 sec
SURPRISE (2014)[45]	Denmark	85	CS	Reveal XT	569±310	107±117	109±48	>2 min
TRACK-AF (2018)[46]	Germany	105	CS	Reveal XT	217 (72.5–338)	0–28	NA	>30 sec
Ziegler et al. (2015)[47], (2017)[48]	USA	1,247	CS	Reveal LINQ	579±222	NA	112 (35–293)	>2 min

Values are presented as median (interquartile range), range, or mean±standard deviation.
AF, atrial fibrillation; CS, cryptogenic stroke; NA, not available; ESUS, embolic stroke of undetermined source; CRYSTAL-AF, Cryptogenic Stroke and underlying Atrial Fibrillation; REVEAL AF, Incidence of AF in High Risk Patients; SPIDER Registry, Stroke Prevention through the Improved Detection of AF registry; SURPRISE, Stroke Prior to Diagnosis of Atrial Fibrillation Using Long-term Observation with Implantable Cardiac Monitoring Apparatus Reveal; TRACK-AF, Follow-up of Kryptogenic Stroke Patients With Implantable vs. Non-invasive Devices to Detect Atrial Fibrillation.
*Conference proceedings abstracts.

were significant differences (*P* for subgroup differences <0.001) in the rates of AF detection in subgroups stratified by ICM duration (<6 months: 5% [95% CI, 3% to 6%]; ≥6 and ≤12 months: 21% [95% CI, 16% to 25%]; >12 and ≤24 months: 26% [95% CI, 22% to 31%]; and >24 months: 34% [95% CI, 29% to 39%]) (Supplementary Figure 10). No differences were

Table 2. Univariate and multivariate meta-regression analyses of the association of patient and study characteristics with the percentage of patients detected with atrial fibrillation after implantable loop recorder insertion

Variable	Univariate meta-regression analysis			Multivariate meta-regression analysis		
	Number	Coefficient (95% CI)	*P*	Number	Coefficient (95% CI)	*P*
Age	30	0.013 (0.002 to 0.024)	0.018	30	0.009 (0.003–0.015)	0.004
Male gender	29	–0.008 (–0.018 to 0.002)	0.100	-	-	-
Hypertension	19	0.003 (–0.002 to 0.008)	0.215	-	-	-
Diabetes mellitus	17	0.009 (–0.003 to 0.021)	0.140	-	-	-
CHA_2DS_2-VASc score	13	0.079 (–0.058 to 0.216)	0.232	-	-	-
Duration of monitoring	45	0.009 (0.005 to 0.013)	<0.001	30	0.015 (0.005–0.024)	0.003
Time from event to cardiac monitor implantation	19	0.001 (–0.001 to 0.002)	0.363	-	-	-

CI, confidence interval.

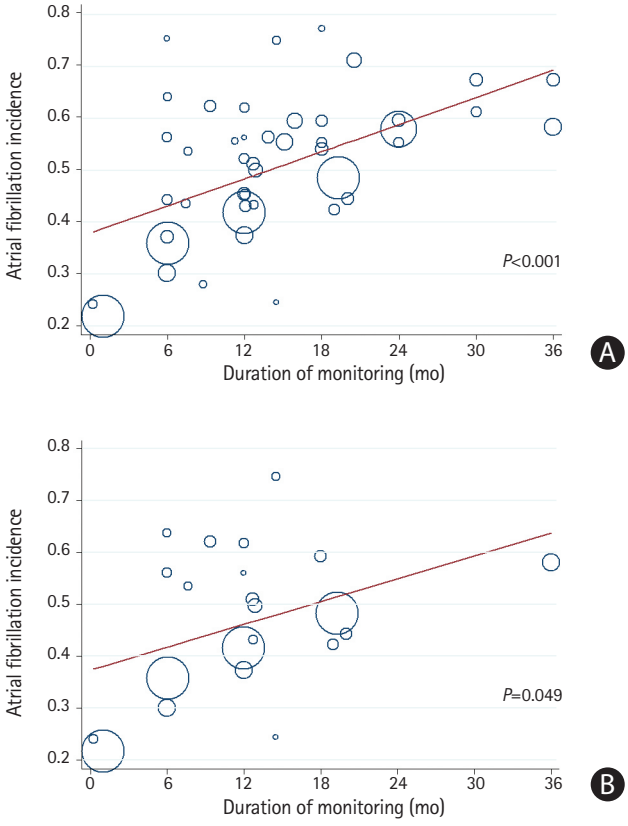

Figure 1. Meta-regression analysis of the association of monitoring duration with the rate of atrial fibrillation (AF) detection with implantable cardiac monitors reported, in (A) all included (abstracts and full publications) studies and (B) fully published studies. AF incidence was calculated using the double arcsine Freeman-Tukey transformation (FTT).

found in the subgroup analyses of all included studies stratified by study type (*P*=0.178) (Supplementary Figure 11), IS/TIA subgroup (*P*=0.093) (Supplementary Figure 12), the time threshold used for AF definition (*P*=0.234) (Supplementary Figure 13), the elapsed time from IS/TIA onset to cardiac monitor implantation (*P*>0.999) (Supplementary Figure 14) or the device used (*P*=0.174) (Supplementary Figure 15). Similarly, in the subgroup analysis of published studies (Supplementary Table 5) there were significant differences (*P* for subgroup differences <0.001) in AF detection rates in subgroups stratified by ICM duration (<6 months: 5% [95% CI, 3% to 6%]; ≥6 and ≤12 months: 22% [95% CI, 16% to 28%]; and >12 and ≤24 months: 22% [95% CI, 14% to 29%]) (Supplementary Figure 16). There were no differences in subgroup analyses of published studies stratified by IS/TIA subtype (*P*=0.429) (Supplementary Figure 17), the time threshold used for AF definition (*P*=0.149) (Supplementary Figure 18), the elapsed time from IS/TIA onset to cardiac monitor implantation (*P*=0.864) (Supplementary Figure 19), or the device used (*P*=0.174) (Supplementary Figure 20). In the aforementioned subgroup analyses, considerable heterogeneity was found within all subgroups (I^2>70%), except for the subgroup of studies reporting the 6 min interval as a threshold for AF detection (I^2=8%) and the subgroup of studies reporting more than 24 months of ICM duration (I^2=24%).

Finally, in a *post hoc* analysis of available studies, we found that among IS/TIA patients with AF detected during ICM, a total of 87% (95% CI, 78% to 96%) experienced asymptomatic AF episodes (Supplementary Figure 21), with no evidence of heterogeneity between studies (I^2=29%, *P* for Cochran Q=0.21).

Discussion

Our meta-analysis showed that AF detection in patients with history of IS/TIA is positively associated only with the duration of ICM and patient age. We failed to find any other independent association between AF detection rates and IS/TIA subtype, device type, other patient characteristics, or elapsed time between IS/TIA onset and cardiac monitor implantation. Approximately nine out of 10 patients, with positive ICM for AF, experienced asymptomatic AF episodes during the monitoring period.

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Table 3. Subgroup analyses of the association of baseline characteristics with the percentage of patients detected with atrial fibrillation after implantable loop recorder insertion

Subgroup	Number	AF detection (95% CI) (%)	Within subgroup heterogeneity, I^2 (%)	Subgroups difference, *P*
Monitoring duration (mo)				
<6	2	5 (3–6)	0	<0.001
≥6 and ≤12	19	21 (16–25)	81	
>12 and ≤24	20	26 (22–31)	82	
>24	4	34 (29–39)	24	
IS/TIA subtype				
CS	24	21 (17–25)	95	0.093
ESUS	14	29 (23–35)	84	
Unselected	7	23 (17–30)	84	
AF time threshold				
>30 sec	9	17 (9–26)	89	0.234
>2 min	18	25 (20–30)	97	
>6 min	6	25 (20–30)	8	
Time from IS/TIA onset to cardiac monitor implantation (mo)				
≤1	11	23 (16–30)	86	>0.999
>1	10	23 (15–31)	90	
Study type				
Prospective	43	24 (20–27)	95	0.178
Retrospective	2	30 (22–38)	0	
ICM device				
Reveal XT	10	27 (21–33)	75	0.174
Reveal LINQ	5	19 (12–27)	61	
Reveal XT/LINQ	4	28 (21–36)	87	

AF, atrial fibrillation; CI, confidence interval; IS, ischemic stroke; TIA, transient ischemic attack; CS, cryptogenic stroke; ESUS, embolic stroke of undetermined source; ICM, implantable cardiac monitor.

Our findings agree with a previously published systematic review and meta-analysis reporting improved AF detection with ICM, compared to wearable devices, in CS patients (23.3% [95% CI, 13.83% to 32.29%] vs. 13.6% [95% CI, 7.91% to 19.32%]; *P* for subgroup differences <0.05).[49] However, compared to the previous meta-analysis, we included a significantly higher number of studies and patients (seven studies with 774 patients vs. 28 studies with 4,531 patients). Moreover, we assessed the potential modifying effect of stroke subtype, baseline characteristics, and time interval between ischemic event and implantation.

AF detection rates in patients with IS/TIA were unrelated to any patient characteristics, except for mean patient age. Although increased age, increased stroke severity, left atrial enlargement, hypertension, congestive heart failure, and valvular heart disease have been associated with increased incidence of AF detection in IS patients,[50] proposed prediction scores including these parameters have limited diagnostic yield, especially at their middle grades.[51] Our meta-analysis also provides no further support to the theoretical concern regarding increased AF detection during the immediate post-IS period, due to stroke-induced sympathetic activation.[52] Finally, the results of subgroup analysis, regarding the time threshold used for AF definition, do not confirm the association of improved ICM performance with increased duration of AF episodes.[53]

Another intriguing finding was that we observed no differences in AF detection rates using ICM, between CS and ESUS patients. This observation challenges the notion that paroxysmal AF is the main underlying etiopathogenic mechanism of cerebral ischemia in ESUS patients[54] and is in line with the recently reported New Approach Rivaroxaban Inhibition of Factor Xa in a Global Trial versus ASA to Prevent Embolism in Embolic Stroke of Undetermined Source (NAVIGATE ESUS) trial, where the detection rate of symptomatic AF during an approximate 1-year follow-up period was only 3%.[55]

Several limitations of the present study need to be acknowl-

edged. Firstly, it should be noted that baseline characteristics of individual patients (Supplementary Table 2) and study protocol parameters (Table 1) were unavailable in a significant proportion of included studies, and particularly in abstracts from conference proceedings. Moreover, the presence of ecological bias cannot be excluded; thus, the associations of aggregate patient characteristics may not hold true also for individual patient characteristics. Secondly, since this is a study-level meta-analysis, we could not assess the influence of other parameters on AF detection rates that were not originally provided by included studies, e.g., the recently published hypertension, age, valvular heart disease, peripheral vascular disease, obesity, congestive heart failure, and coronary artery disease (HAVOC) score.[49] Thirdly, although meta-regression analyses did not provide evidence for any association bet=ween reported study characteristics (except for hypertension history) and AF detection rate, there is a possibility that heterogeneity in AF incidence could at least partially reflect inherent differences in the patient populations of included studies. Additionally, it should be highlighted that the lack of significant associations could be attributed to the low statistical power, especially for analyses including a low number of studies. Finally, it should be noted that in the present meta-analysis, we did not assess the number of AF episodes, false positive AF episodes, cumulative AF episode duration, or the impact of AF detection in patient management and long-term outcomes.[56]

Our findings challenge current AHA/ASA guidelines,[8,9] while further highlighting the indispensable role of prolonged rhythm monitoring, using ICM in the identification of a substantial portion of IS/TIA patients with occult AF. According to current recommendations, secondary CS prevention strategies are mainly based on antiplatelet therapy,[6] which is known to provide inadequate protection for patients with AF. In these patients, the systemic administration of anticoagulant therapy could contribute to an 8.4% annual absolute risk reduction of stroke recurrence, compared with antiplatelet therapy.[57] Also taking into account the negative results of the recent NAVIGATE ESUS trial, showing that rivaroxaban compared to aspirin increases major bleeding without reducing ischemic events in ESUS patients,[54] ICM emerges as an extremely useful diagnostic tool to identify those patients with occult AF within the heterogeneous group of ESUS or CS patients.[58] Therefore, prolonged monitoring could have a substantial impact on the secondary prevention of CS patients with underlying AF, leading to prompt anticoagulant initiation and lower stroke recurrence.[59] The Detection of Silent Atrial Fibrillation aFter Ischemic StrOke (SAFFO) study, guided by implantable loop recorder[60] and the AF detected by continuous electrocardiographic monitoring using implantable loop recorder to prevent stroke in individuals at risk (LOOP) study[61] are two ongoing, multicenter, open-label RCTs, that aim to evaluate health benefits, including reduction of recurrent ischemic events and cost-effectiveness of ICM in secondary stroke prevention. Results from these studies will further characterize the target population for ICM, the optimal threshold for AF definition and whether ICM monitoring results in lower stroke recurrence through anticoagulant initiation.

In conclusion, the results of the present meta-analysis support extended-duration ICM monitoring as a reasonable option for patients with IS or TIA, and initial negative screening for AF detection,[62] that may substantially enhance detection of predominantly subclinical AF episodes.

Supplementary materials

Supplementary materials related to this article can be found online at https://doi.org/10.5853/jos.2019.01067.

Disclosure

The authors have no financial conflicts of interest.

References

1. Sacco RL, Ellenberg JH, Mohr JP, Tatemichi TK, Hier DB, Price TR, et al. Infarcts of undetermined cause: the NINCDS Stroke Data Bank. *Ann Neurol* 1989;25:382-390.
2. Petty GW, Brown RD Jr, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Ischemic stroke subtypes: a population-based study of incidence and risk factors. *Stroke* 1999;30:2513-2516.
3. Kolominsky-Rabas PL, Weber M, Gefeller O, Neundoerfer B, Heuschmann PU. Epidemiology of ischemic stroke subtypes according to TOAST criteria: incidence, recurrence, and long-term survival in ischemic stroke subtypes: a population-based study. *Stroke* 2001;32:2735-2740.
4. Tsang TS, Petty GW, Barnes ME, O'Fallon WM, Bailey KR, Wiebers DO, et al. The prevalence of atrial fibrillation in incident stroke cases and matched population controls in Rochester, Minnesota: changes over three decades. *J Am Coll Cardiol* 2003;42:93-100.
5. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke* 1991;22:983-988.
6. Sanna T, Diener HC, Passman RS, Di Lazzaro V, Bernstein RA, Morillo CA, et al. Cryptogenic stroke and underlying atrial fibrillation. *N Engl J Med* 2014;370:2478-2486.

7. Sposato LA, Cipriano LE, Saposnik G, Ruíz Vargas E, Riccio PM, Hachinski V. Diagnosis of atrial fibrillation after stroke and transient ischaemic attack: a systematic review and meta-analysis. *Lancet Neurol* 2015;14:377-387.
8. Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2014;45:2160-2236.
9. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. 2018 Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2018;49:e46-e110.
10. Reiffel JA, Verma A, Kowey PR, Halperin JL, Gersh BJ, Wachter R, et al. Incidence of previously undiagnosed atrial fibrillation using insertable cardiac monitors in a high-risk population: the REVEAL AF Study. *JAMA Cardiol* 2017;2:1120-1127.
11. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol* 2009;62:e1-e34.
12. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality if nonrandomized studies in meta-analyses. The Ottawa Hospital Research Institute. http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm. 2019. Assessed July 3, 2019.
13. Deeks JJ, Higgins JP, Altman DG. Chapter 9.6.4: Meta-regression. In: Higgins JP, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions. Hoboken, NJ: Wiley, 2011. https://handbook-5-1.cochrane.org/chapter_9/9_6_4_meta_regression.htm. Assessed July 3, 2019.
14. Freeman MF, Tukey JW. Transformations related to the angular and the square root. *Ann Math Stat* 1950;21:607-11.
15. IntHout J, Ioannidis JP, Borm GF. The Hartung-Knapp-Sidik-Jonkman method for random effects meta-analysis is straightforward and considerably outperforms the standard DerSimonian-Laird method. *BMC Med Res Methodol* 2014;14:25.
16. Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution, and gender of patients with atrial fibrillation. Analysis and implications. *Arch Intern Med* 1995;155:469-473.
17. Deeks JJ, Higgins JP, Altman DG. Chapter 9: Analyzing data and undertaking meta-analyses. In: Higgins JP, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions. Hoboken, NJ: Wiley, 2011. https://handbook-5-1.cochrane.org/chapter_9/9_analysing_data_and_undertaking_meta_analyses.htm. Assessed July 3, 2019.
18. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Introduction to Meta-Analysis. Chichester, UK: John Wiley & Sons, 2008.
19. Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomized controlled trials. *BMJ* 2011;343:d4002.
20. Wallace BC, Dahabreh IJ, Trikalinos TA, Lau J, Trow P, Schmid CH. Closing the gap between methodologists and end-users: R as a computational back-end. *J Stat Softw* 2012;49:1-15.
21. Asaithambi G, Monita JE, Hanson SK. Abstract WP231: Predictors for early atrial fibrillation detection among cryptogenic stroke patients with insertable cardiac monitors: a single-center experience. *Stroke* 2017;48(Suppl 1):AWP231.
22. Carrazco C, Golyan D, Kahen M, Black K, Libman RB, Katz JM. Prevalence and risk factors for paroxysmal atrial fibrillation and flutter detection after cryptogenic ischemic stroke. *J Stroke Cerebrovasc Dis* 2018;27:203-209.
23. Ching MI, Zhang C, Vaughn C, Lail N, Leahy T, Kandel A, et al. Abstract WP199: Left atrial volume index and PR interval are independent predictors of atrial fibrillation in embolic stroke patients with insertable cardiac monitor. *Stroke* 2018;49(Suppl 1):AWP199.
24. Cotter PE, Martin PJ, Ring L, Warburton EA, Belham M, Pugh PJ. Incidence of atrial fibrillation detected by implantable loop recorders in unexplained stroke. *Neurology* 2013;80:1546-1550.
25. Passman RS, Rymer MM, Liu S, Ziegler PD. Abstract 78: Incidence of atrial fibrillation among patients with an embolic stroke of undetermined source. *Stroke* 2017;48(Suppl 1):A78.
26. de Lera M, Largaespada G, Cortijo E, Sandin M, Calleja A, García E, et al. AS18-008: Predictors of higher arrhytmic load in patients with cryptogenic stroke and covert atrial fibrillation detected by implantable loop recorders. *Eur Stroke J* 2016;1(1 Suppl):641.
27. Dion F, Saudeau D, Bonnaud I, Friocourt P, Bonneau A, Poret P, et al. Unexpected low prevalence of atrial fibrillation in cryptogenic ischemic stroke: a prospective study. *J Interv Card Electrophysiol* 2010;28:101-107.
28. Etgen T, Hochreiter M, Mundel M, Freudenberger T. Insertable cardiac event recorder in detection of atrial fibrillation after cryptogenic stroke: an audit report. *Stroke* 2013;44:2007-2009.
29. Israel C, Kitsiou A, Kalyani M, Deelawar S, Ejangue LE, Ro-

galewski A, et al. Detection of atrial fibrillation in patients with embolic stroke of undetermined source by prolonged monitoring with implantable loop recorders. *Thromb Haemost* 2017;117:1962-1969.
30. Jorfida M, Antolini M, Cerrato E, Caprioli MG, Castagno D, Garrone P, et al. Cryptogenic ischemic stroke and prevalence of asymptomatic atrial fibrillation: a prospective study. *J Cardiovasc Med (Hagerstown)* 2016;17:863-869.
31. Kamel H, Yaghi S, Passman R, Allred J, Sarkar S, Kohler J, et al. AS21-004: Comparison of atrial fibrillation diagnosis and oral anticoagulation utilization among ischemic stroke patients with vs. without insertable cardiac monitors. *Eur Stroke J* 2018;3(1 Suppl):452.
32. Katz JM, Gribko M, Jadonath R, Arora R, Salamon E, Garlitzki A, et al. Abstract WMP63: Prevalence of occult paroxysmal atrial fibrillation in non-cryptogenic ischemic stroke patients. *Stroke* 2017;48(Suppl 1):AWMP63.
33. Kotlarz-Böttcher MJ, Busch M, Frenzel M, Hummel A, Schminke U, von Sarnowski B. AS21-019: Risk factors for atrial fibrillation in patients with embolic stroke of undetermined source (ESUS). *Eur Stroke J* 2018;3(1 Suppl):457.
34. Makimoto H, Kurt M, Gliem M, Lee JI, Schmidt J, Müller P, et al. High incidence of atrial fibrillation after embolic stroke of undetermined source in posterior cerebral artery territory. *J Am Heart Assoc* 2017;6:e007448.
35. Navarro Pérez MP, Pérez Lázaro C, Pelegrín Díaz J, Rodrigo Trallero G, Sánchez Val A, Garcés Antón E, et al. AS21-031: Paroxysmal atrial fibrillation detection after cryptogenic stroke: a single center experience. *Eur Stroke J* 2018;3(1 Suppl):460.
36. Noone I, Meagher MK, Mc Creery C, Cassidy T. AS18-027: The role of loop recorders in embolic stroke of uncertain source (ESUS). *Eur Stroke J* 2016;1(1 Suppl):16.
37. Pallesen LPM, Mayer J, Barlinn K, Barlinn J, Prakapenia A, Sieppmann T, et al. Abstract WP230: Real-life detection rate of insertable cardiac monitors in patients with ESUS. *Stroke* 2017;48(Suppl 1):AWP230.
38. Poli S, Diedler J, Härtig F, Götz N, Bauer A, Sachse T, et al. Insertable cardiac monitors after cryptogenic stroke: a risk factor based approach to enhance the detection rate for paroxysmal atrial fibrillation. *Eur J Neurol* 2016;23:375-381.
39. Elkind MS, Wachter R, Verma A, Kowey PR, Halperin JL, Gersh BJ, et al. Abstract 189: Identifying patients at highest risk of developing atrial fibrillation and the role of remote prior stroke: insights from the REVEAL AF study. *Stroke* 2018;49 (Suppl 1):A189.
40. Ritter MA, Kochhäuser S, Duning T, Reinke F, Pott C, Dechering DG, et al. Occult atrial fibrillation in cryptogenic stroke: detection by 7-day electrocardiogram versus implantable cardiac monitors. *Stroke* 2013;44:1449-1452.
41. Rodríguez-Campello A, Cuadrado-Godia E, Ois A, Giralt-Steinhauer E, Jiménez-Conde J, Puig-Pijoan A, et al. ESOC-1467: Early detection of atrial fibrillation in embolic stroke of unknown origin (ESUS). *Int J Stroke* 2015;10:268-269.
42. Rojo-Martinez E, Sandín-Fuentes M, Calleja-Sanz AI, Cortijo-García E, García-Bermejo P, Ruiz-Piñero M, et al. High performance of an implantable Holter monitor in the detection of concealed paroxysmal atrial fibrillation in patients with cryptogenic stroke and a suspected embolic mechanism. *Rev Neurol* 2013;57:251-257.
43. Sethi P, Biby S, Allred J, Seiler A, Xu J. AS18-067: Surveillance for atrial fibrillation in patients with cryptogenic stroke using an implantable loop recorder during an inpatient hospitalization in a community hospital setting. *Eur Stroke J* 2017;2(1 Suppl):115.
44. Joseph K, Wanjiku S, Jumaa M, Richards M. Abstract W P194: Improved efficacy of ICM detection of atrial fibrillation in cryptogenic stroke patients with MRI-defined infarcts: preliminary results from the SPIDER registry. *Stroke* 2015;46(Suppl 1):AWP194.
45. Christensen LM, Krieger DW, Højberg S, Pedersen OD, Karlsen FM, Jacobsen MD, et al. Paroxysmal atrial fibrillation occurs often in cryptogenic ischaemic stroke. Final results from the SURPRISE study. *Eur J Neurol* 2014;21:884-889.
46. Reinke F, Bettin M, Ross LS, Kochhäuser S, Kleffner I, Ritter M, et al. Refinement of detecting atrial fibrillation in stroke patients: results from the TRACK-AF Study. *Eur J Neurol* 2018;25:631-636.
47. Ziegler PD, Rogers JD, Ferreira SW, Nichols AJ, Sarkar S, Koehler JL, et al. Real-world experience with insertable cardiac monitors to find atrial fibrillation in cryptogenic stroke. *Cerebrovasc Dis* 2015;40:175-181.
48. Ziegler PD, Rogers JD, Ferreira SW, Nichols AJ, Richards M, Koehler JL, et al. Long-term detection of atrial fibrillation with insertable cardiac monitors in a real-world cryptogenic stroke population. *Int J Cardiol* 2017;244:175-179.
49. Afzal MR, Gunda S, Waheed S, Sehar N, Maybrook RJ, Dawn B, et al. Role of outpatient cardiac rhythm monitoring in cryptogenic stroke: a systematic review and meta-analysis. *Pacing Clin Electrophysiol* 2015;38:1236-1245.
50. Kwong C, Ling AY, Crawford MH, Zhao SX, Shah NH. A clinical score for predicting atrial fibrillation in patients with cryptogenic stroke or transient ischemic attack. *Cardiology* 2017;138:133-140.
51. Andrade JG, Field T, Khairy P. Detection of occult atrial fibrillation in patients with embolic stroke of uncertain source: a work in progress. *Front Physiol* 2015;6:100.

https://doi.org/10.5853/jos.2019.01067

52. Katsanos AH, Korantzopoulos P, Tsivgoulis G, Kyritsis AP, Kosmidou M, Giannopoulos S. Electrocardiographic abnormalities and cardiac arrhythmias in structural brain lesions. *Int J Cardiol* 2013;167:328-334.
53. Lee R, Mittal S. Utility and limitations of long-term monitoring of atrial fibrillation using an implantable loop recorder. *Heart Rhythm* 2018;15:287-295.
54. Hart RG, Diener HC, Coutts SB, Easton JD, Granger CB, O'Donnell MJ, et al. Embolic strokes of undetermined source: the case for a new clinical construct. *Lancet Neurol* 2014;13:429-438.
55. Hart RG, Sharma M, Mundl H, Kasner SE, Bangdiwala SI, Berkowitz SD, et al. Rivaroxaban for stroke prevention after embolic stroke of undetermined source. *N Engl J Med* 2018;378:2191-2201.
56. Hart RG, Benavente O, McBride R, Pearce LA. Antithrombotic therapy to prevent stroke in patients with atrial fibrillation: a meta-analysis. *Ann Intern Med* 1999;131:492-501.
57. Katsanos AH, Bhole R, Frogoudaki A, Giannopoulos S, Goyal N, Vrettou AR, et al. The value of transesophageal echocardiography for embolic strokes of undetermined source. *Neurology* 2016;87:988-995.
58. Wechselberger S, Kronborg M, Huo Y, Piorkowski J, Neudeck S, Päßler E, et al. Continuous monitoring after atrial fibrillation ablation: the LINQ AF study. *Europace* 2018;20:f312-f320.
59. Tsivgoulis G, Katsanos AH, Mac Grory B, Köhrmann M, Ricci BA, Tsioufis K, et al. (AS25-022) Prolonged cardiac rhythm monitoring and secondary stroke prevention in patients with cryptogenic cerebral ischemia: a systematic review and meta-analysis. *Eur Stroke J* 2019;4(1 Suppl):178.
60. Toni D, Lorenzano S, Strano S; SAFFO Trial Investigators. Detection of Silent Atrial Fibrillation aFter Ischemic StrOke (SAFFO) guided by implantable loop recorder: multicentre Italian trial based on stroke unit network with paired cardio-arrhythmology units (Italian Neurocardiology Unit Network). *Int J Stroke* 2016;11:361-367.
61. Diederichsen SZ, Haugan KJ, Køber L, Højberg S, Brandes A, Kronborg C, et al. Atrial fibrillation detected by continuous electrocardiographic monitoring using implantable loop recorder to prevent stroke in individuals at risk (the LOOP study): rationale and design of a large randomized controlled trial. *Am Heart J* 2017;187:122-132.
62. Albers GW, Bernstein RA, Brachmann J, Camm J, Easton JD, Fromm P, et al. Heart rhythm monitoring strategies for cryptogenic stroke: 2015 diagnostics and monitoring stroke focus group report. *J Am Heart Assoc* 2016;5:e002944.

Supplementary Methods

Complete MEDLINE search algorithm

((("heart"[MeSH Terms] OR "heart"[All Fields] OR "cardiac"[All Fields]) AND monitoring[All Fields]) OR (insertable[All Fields] AND loop[All Fields] AND ("recorder"[All Fields]) OR (implantable[All Fields] AND cardiac[All Fields] AND monitoring[All Fields] AND ((cryptogenic[All Fields] AND ("stroke"[MeSH Terms] OR "stroke"[All Fields])) OR (("ischemia"[MeSH Terms] OR "ischemia"[All Fields] OR "ischemic"[All Fields]) AND ("stroke"[MeSH Terms] OR "stroke"[All Fields])) OR (("embolism"[MeSH Terms] OR "embolism"[All Fields] OR "embolic"[All Fields]) AND ("stroke"[MeSH Terms] OR "stroke"[All Fields]) AND undetermined[All Fields] AND ("Source Notes Hist Art"[Journal] OR "source"[All Fields])) OR ("cerebral ischemia"[All Fields] OR "cerebral infarction"[MeSH Terms] OR ("cerebral"[All Fields] AND "infarction"[All Fields]) OR "cerebral infarction"[All Fields] OR ("cerebral"[All Fields] AND "ischemia"[All Fields]) OR "cerebral ischemia"[All Fields] OR "brain ischemia"[MeSH Terms] OR ("brain"[All Fields] AND "ischemia"[All Fields]) OR "brain ischemia"[All Fields] OR ("cerebral"[All Fields] AND "ischemia"[All Fields]))) AND (("atrial fibrillation"[MeSH Terms] OR ("atrial"[All Fields] AND "fibrillation"[All Fields]) OR "atrial fibrillation"[All Fields]) OR ("atrial flutter"[MeSH Terms] OR ("atrial"[All Fields] AND "flutter"[All Fields]) OR "atrial flutter"[All Fields]))

Supplementary Table 1. Excluded studies with reasons for exclusion

Study	Reasons for exclusion
de Lera et al. (2017)[1]	Overlapping data
Favilla et al. (2015)[2]	Monitoring with device other than ICM
Friberg et al. (2014)[3]	Monitoring with device other than ICM
Giralt-Steinhauer et al. (2015)[4]	Monitoring with device other than ICM
Kitsiou et al. (2015)[5]	Overlapping data
Kitsiou et al. (2016)[6]	Overlapping data
Pedersen et al. (2016)[7]	Monitoring with device other than ICM
Prakapenia et al. (2017)[8]	Monitoring duration not available
Perera et al. (2016)[9]	Monitoring with device other than ICM
Rem et al. (1985)[10]	Monitoring with device other than ICM
Ricci et al. (2018)[11]	Monitoring with device other than ICM
Rizos et al. (2015)[12]	Monitoring with device other than ICM
Rodríguez-Campello et al. (2018)[13]	Monitoring duration not available
Rojo et al. (2015)[14]	Overlapping data
Schneider et al. (2016)[15]	Monitoring duration not available
Sposato et al. (2012)[16]	Monitoring with device other than ICM
Stahrenberg et al. (2010)[17]	Monitoring with device other than ICM
Yetim et al. (2016)[18]	Monitoring with device other than ICM

ICM, implantable cardiac monitor.

Supplementary Table 2. Characteristics of patients in included studies

Study	Stroke (%)	Age (yr)	Male (%)	HTN (%)	DM (%)	CHF (%)	VD (%)	HLP (%)	Previous stroke (%)	$CHADS_2$ score	CHA_2DS_2-VASc score	Asymptomatic (%)	Lost to follow-up (%)
Asaithambi et al. (2017)[19]*	NA	NA	NA	76	NA	NA	NA	NA	NA	NA	NA	NA	NA
Carrazco et al. (2018)[20]	100	66	47	78	27	4	NA	68	15	NA	NA	NA	NA
Ching et al. (2018)[21]*	100	70	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Cotter et al. (2013)[22]	100	51±14	54.9	NA	NA	NA	NA	NA	NA	2 (2–3)	3 (2–4)	92	0
CRYSTAL-AF (2014)[23]	90.5	62±11	64.3	65.2	15.4	NA	NA	56.6	16.7	3 (2–4)	NA	79	5.4
CRYSTAL-AF (2017)[24]*	100	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
de Lera et al. (2016)[25]*	100	67	55	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Dion et al. (2010)[26]	100	49±14	62.5	29.2	0	NA	NA	33.3	NA	NA	NA	100	0
Etgen et al. (2013)[27]	100	61.6	50	63.6	9.1	NA	NA	72.7	NA	NA	NA	67	0
Israel et al. (2017)[28]	100	65±9	61.1	82.9	24.4	NA	33.3	NA	NA	NA	4.5±1.3	NA	0
Jorfida et al. (2016)[29]	100	68±9	57.4	88.7	18.5	NA	NA	NA	27.8	3.4±0.8	4.5±1.2	76	0
Kamel et al. (2018)[30]*	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Katz et al. (2017)[31]*	NA	65	68.1	NA	NA	NA	NA	NA	NA	3.5	4.5	NA	NA
Kotlarz-Böttcher et al. (2018)[32]*	100	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Makimoto et al. (2017)[33]	100	62±12	58	73	16	NA	12	NA	NA	NA	4.1±1.3	NA	0
Navarro Pérez et al. (2018)[34]*	NA	74.4	56.8	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Noone et al. (2016)[35]*	100	NA	NA	41.7	7.5	NA	23.6	74.8	56.3	NA	NA	NA	NA
Pallesen et al. (2017)[36]*	100	61	64	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Poli et al. (2016)[37]	89	66±12	47	79	15	NA	36	NA	NA	NA	5 (4–6)	92	0
REVEAL-AF (2018)[38]*	100	-	-	-	-	-	-	-	-	-	-	-	-
Ritter et al. (2013)[39]	100	63 (48–72)	57	70	11.6	0	13.3	NA	NA	3 (2–3)	4 (3–5)	NA	1.6
Rodríguez-Campello et al. (2015)[40]*	100	75±9	60.7	64.3	NA	NA	NA	NA	NA	NA	NA	NA	NA
Rojo-Martinez et al. (2013)[41]	90.1	67±13	46.5	55.4	19.8	NA	20.9	52.5	NA	NA	4.51±1.54	NA	NA
Sethi et al. (2017)[42]*	100	67.9	53.6	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
SPIDER Registry (2015)[43]*	NA	67±13	59.4	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
SURPRISE (2014)[44]	72.3	57	55.1	45.3	6.9	NA	NA	NA	NA	2	3	100	8.4
TRACK-AF (2018)[45]	81.9	64±13	56.2	NA	NA	NA	NA	NA	NA	NA	4 (3–6)	NA	0
Ziegler et al. (2015)[46] (2017)[47]	NA	65±13	53	NA	NA	NA	NA	NA	NA	NA	NA	NA	0

Values are presented as mean±standard deviation or median (interquartile range).
HTN, hypertension; DM, diabetes mellitus; CHF, congestive heart failure; VD, vascular disease; HLP, hyperlipidemia; NA, not available; CRYSTAL-AF, Cryptogenic Stroke and underlying Atrial Fibrillation; REVEAL AF, Incidence of AF in High Risk Patients; SPIDER Registry, Stroke Prevention through the Improved Detection of AF registry; SURPRISE, Stroke Prior to Diagnosis of Atrial Fibrillation Using Long-term Observation with Implantable Cardiac Monitoring Apparatus Reveal; TRACK-AF, Follow-up of Kryptogenic Stroke Patients With Implantable vs. Non-invasive Devices to Detect Atrial Fibrillation.
*Available only as abstracts.

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Supplementary Table 3. Quality assessment of included studies

Study	Selection	Comparability	Outcome	Overall
Carrazco et al. (2018)[20]	3*	NA	3*	6/7
Cotter et al. (2013)[22]	3*	NA	3*	6/7
CRYSTAL-AF (2014)[23]	4*	NA	3*	7/7
Dion et al. (2010)[26]	3*	NA	2*	5/7
Etgen et al. (2013)[27]	3*	NA	2*	5/7
Israel et al. (2017)[28]	4*	NA	2*	6/7
Jorfida et al. (2016)[29]	4*	NA	2*	6/7
Makimoto et al. (2017)[33]	3*	NA	2*	5/7
Poli et al. (2016)[37]	4*	NA	3*	7/7
Ritter et al. (2013)[39]	3*	NA	3*	6/7
Rojo-Martinez et al. (2013)[41]	3*	NA	3*	6/7
SURPRISE (2014)[44]	3*	NA	3*	6/7
TRACK-AF (2018)[45]	3*	NA	3*	6/7
Ziegler et al. (2015)[46]	3*	NA	2*	5/7
Ziegler et al. (2017)[47]	46/56	NA	36/42	82/98

NA, not applicable; CRYSTAL-AF, Cryptogenic Stroke and underlying Atrial Fibrillation; SURPRISE, Stroke Prior to Diagnosis of Atrial Fibrillation Using Long-term Observation with Implantable Cardiac Monitoring Apparatus Reveal; TRACK-AF, Follow-up of Kryptogenic Stroke Patients With Implantable vs. Non-invasive Devices to Detect Atrial Fibrillation.
*Number of stars awarded for each category.

Supplementary Table 4. Univariate and multivariate meta-regression analyses of fully published studies on the association of monitoring duration and individual patient characteristics with the rate of atrial fibrillation detection using implantable cardiac monitoring

Variable	Univariate meta-regression analysis			Multivariate meta-regression analysis		
	Number	Coefficient (95% CI)	*P*	Number	Coefficient (95% CI)	*P*
Age	22	0.011 (–0.003 to 0.025)	0.110	16	0.037 (0.013 to 0.062)*	0.007
Male sex	22	–0.008 (–0.019 to 0.003)	0.136	-	-	
Hypertension	16	0.005 (0.001 to 0.010)	0.029	16	–0.006 (–0.019 to 0.007)	0.353
Diabetes mellitus	16	0.013 (0.001 to 0.024)	0.033	16	–0.001 (–0.007 to 0.005)	0.775
CHA_2DS_2VASc score	12	0.094 (–0.028 to 0.216)	0.118	-	-	
Duration of monitoring	22	0.007 (0.001 to 0.014)	0.049	16	0.009 (0.003 to 0.015)	0.006
Time from event to cardiac monitor implantation	16	0.001 (–0.001 to 0.002)	0.492	-	-	

CI, confidence interval.
*Mean patient age was included in the multivariate analysis as an *a priori* potential confounder.

Supplementary Table 5. Subgroup analyses of fully published studies on the association of monitoring duration and individual patient characteristics with the rate of atrial fibrillation detection using implantable cardiac monitors

Subgroup	Number	AF detection (95% CI) (%)	Within subgroup heterogeneity, I^2 (%)	Subgroup differences, *P*
Monitoring duration (mo)				
<6	2	5 (3–6)	0	<0.001
≥6 and ≤12	10	22 (16–28)	87	
>12 and ≤24	9	22 (14–29)	80	
IS/TIA subtype				
CS	20	20 (15–26)	95	0.429
ESUS	2	23 (18–28)	0	
AF time threshold				
>30 sec	8	15 (9–21)	88	0.149
>2 min	11	21 (16–27)	97	
Time from IS/TIA onset to cardiac monitor implantation (mo)				
<1	8	22 (15–29)	84	0.864
>1	9	23 (14–32)	91	
ICM device				
Reveal XT	9	26 (19–32)	70	0.174
Reveal XT/LINQ	2	32 (25–39)	0	

AF, atrial fibrillation; CI, confidence interval; IS, ischemic stroke; TIA, transient ischemic attack; CS, cryptogenic stroke; ESUS, embolic stroke of undetermined source; ICM, implantable cardiac monitor.

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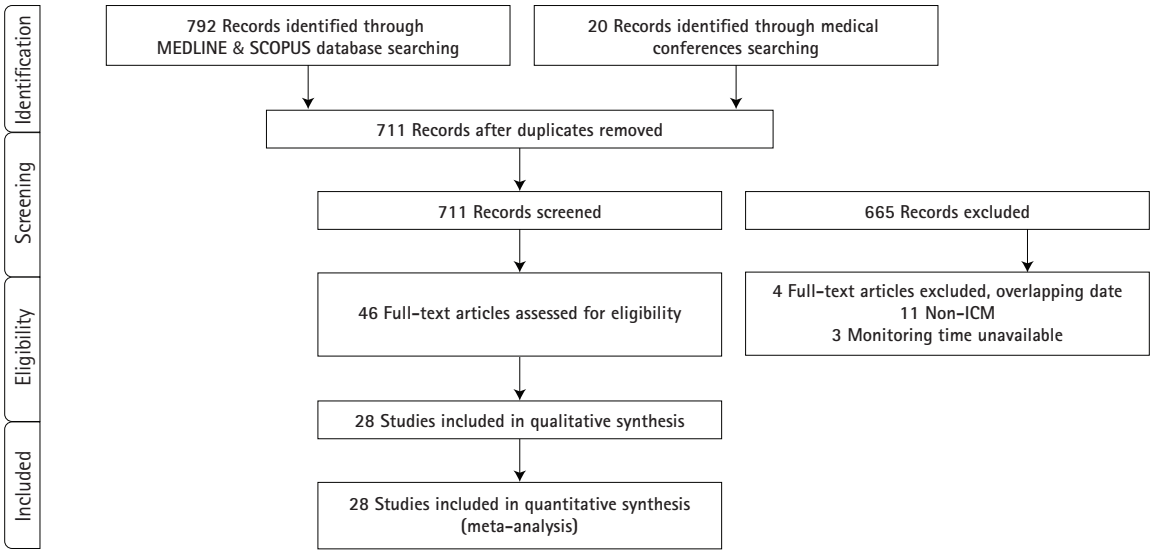
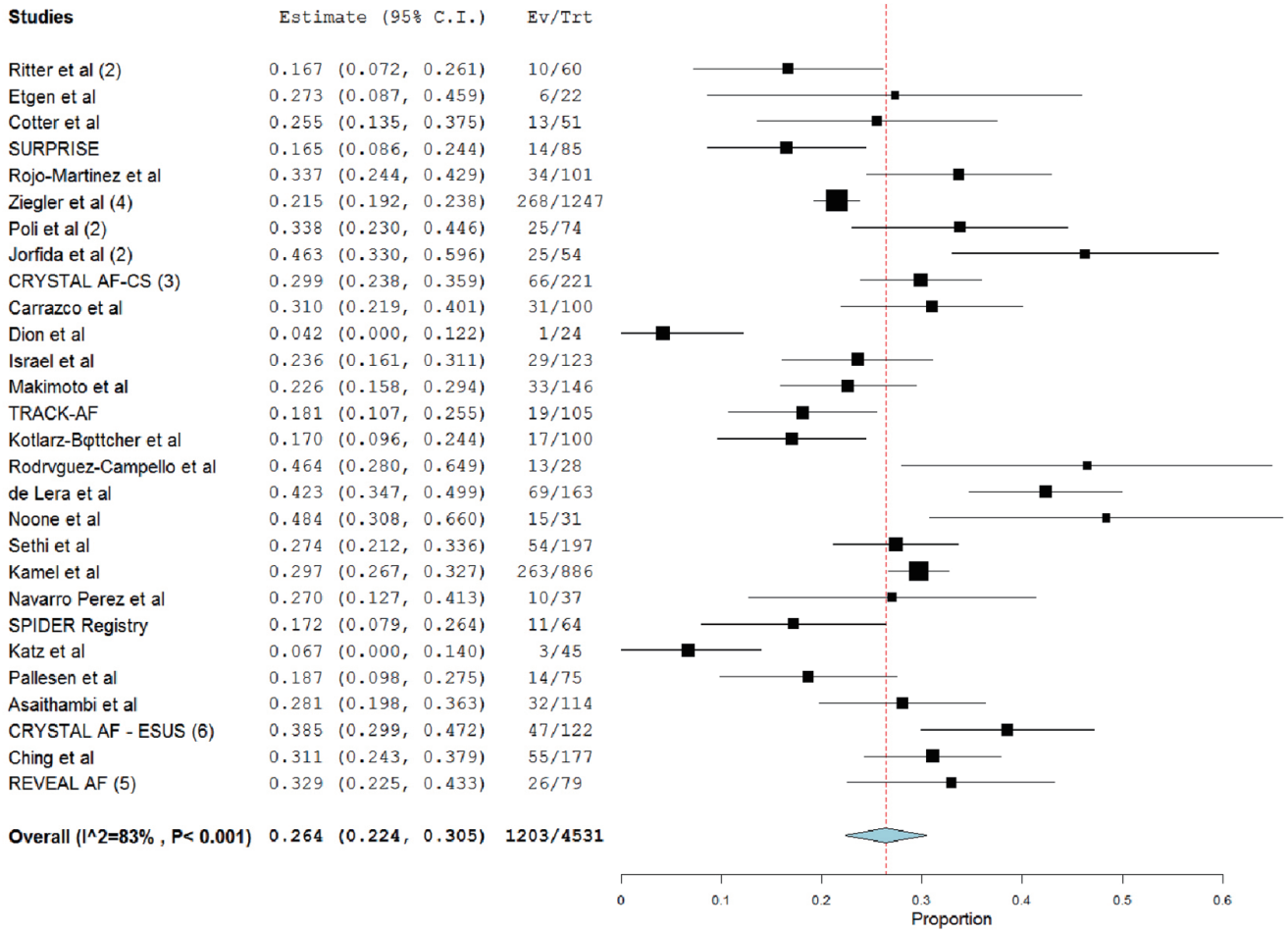
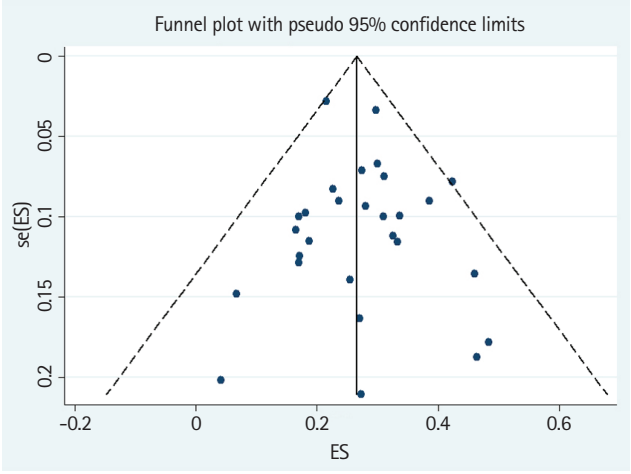


Supplementary Figure 1. Flow chart summarizing the selection procedure for eligible studies. ICM, implantable cardiac monitor.



Supplementary Figure 2. Overall analysis of the cumulative rate of atrial fibrillation detection with implantable cardiac monitors. CI, confidence interval; EV/Trt, events/treated.



Supplementary Figure 3. Funnel plot of publication bias assessment. SE, standard error; ES, effect estimate.

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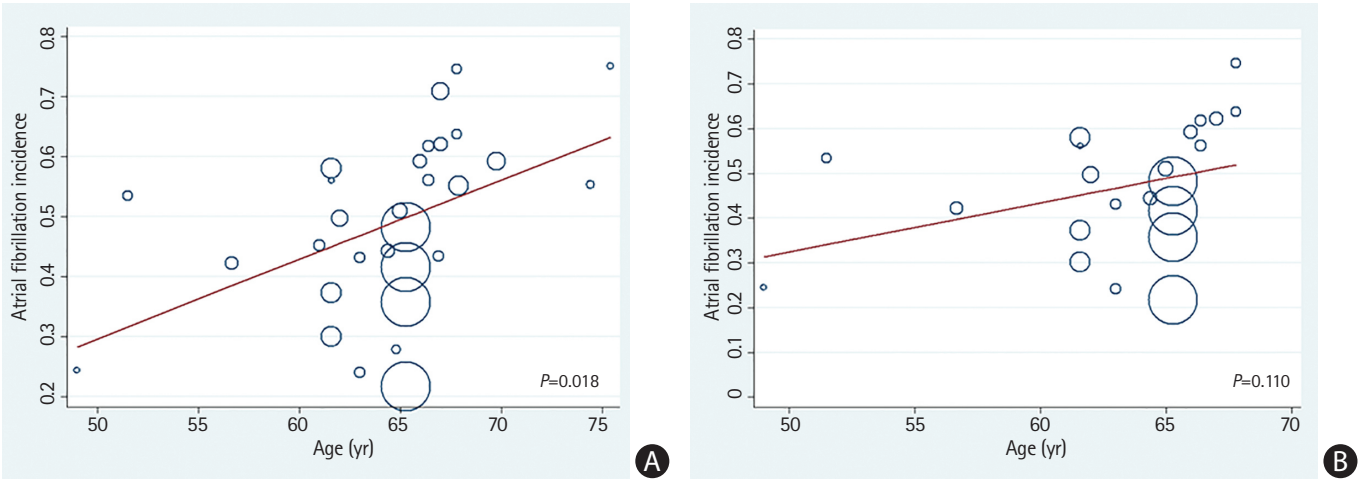
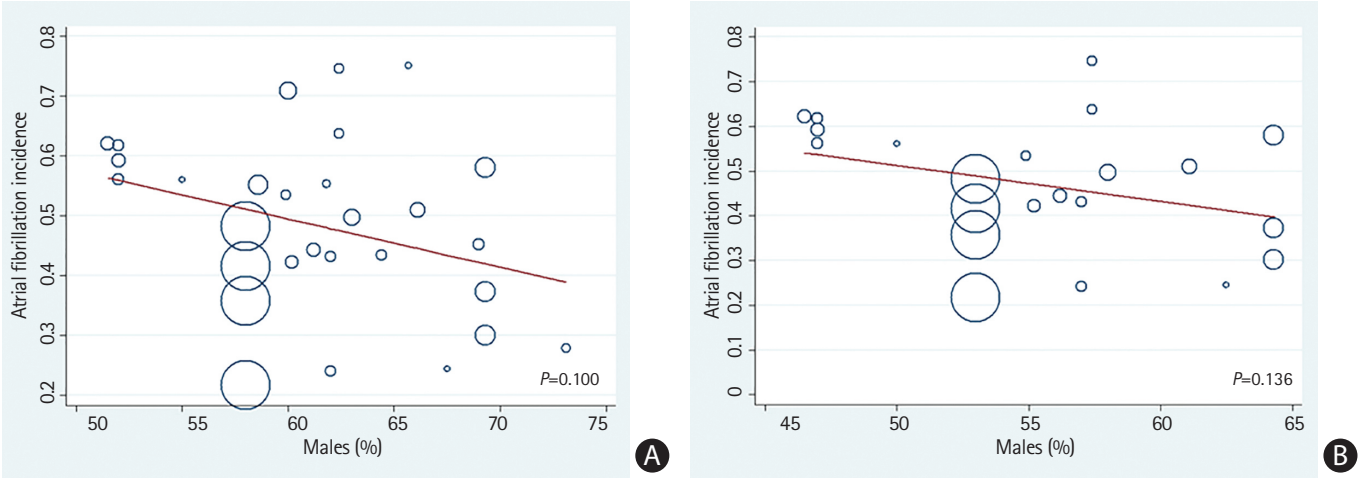
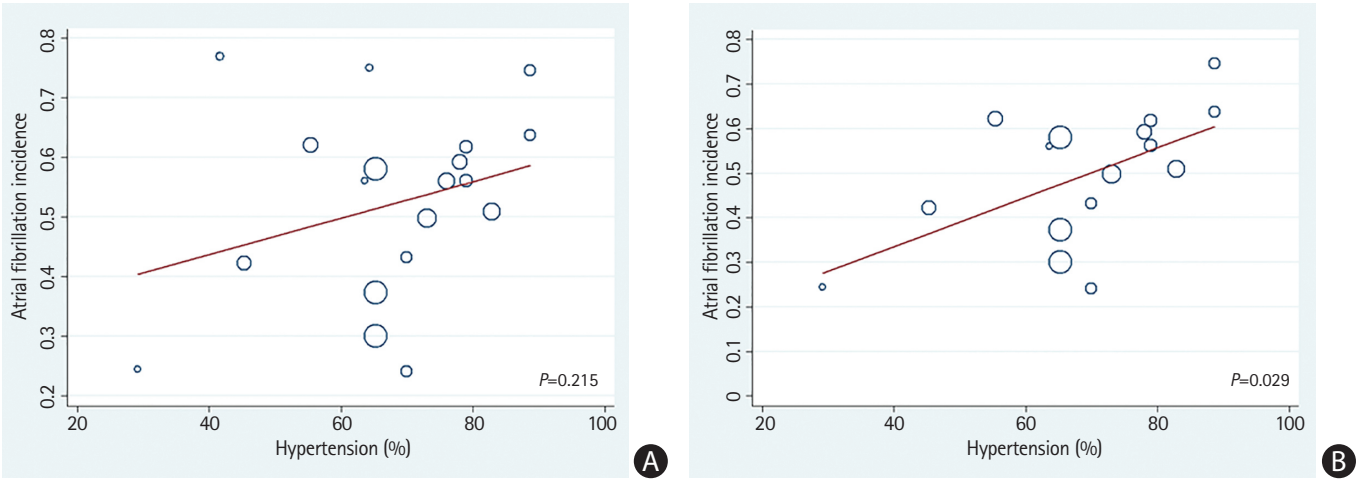


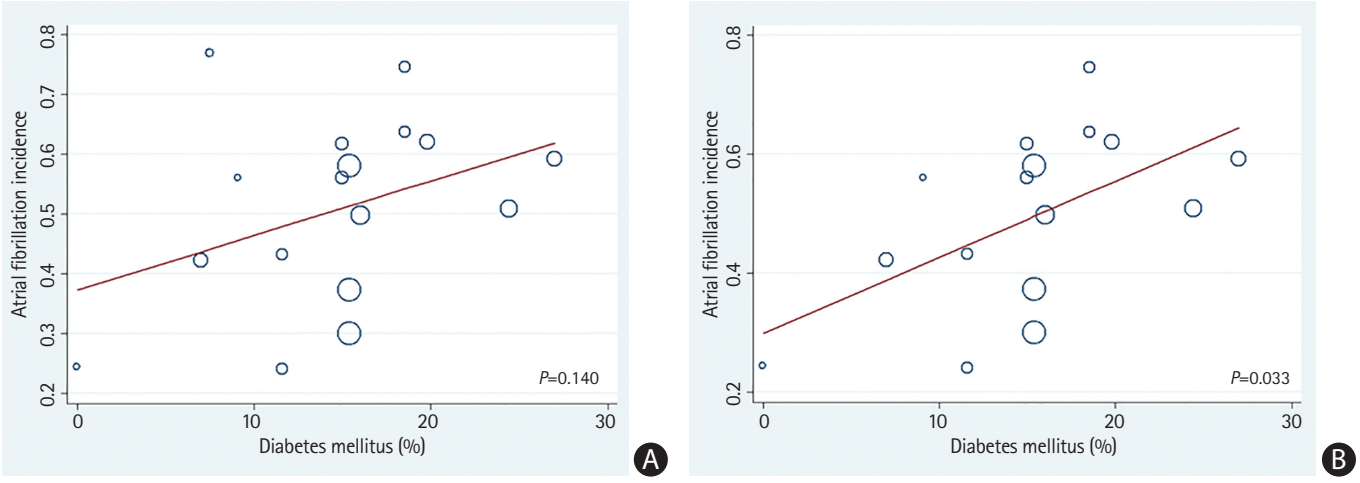
Supplementary Figure 4. Meta-regression analysis of the association of mean patient age with the rate of atrial fibrillation detection with implantable cardiac monitors reported in (A) all included (abstracts and full publications) studies and (B) fully published studies. Atrial fibrillation incidence was calculated using the double arcsine Freeman-Tukey transformation.



Supplementary Figure 5. Meta-regression analysis of the association of sex with the rate of atrial fibrillation detection with implantable cardiac monitors reported in (A) all included (abstracts and full publications) studies and (B) fully published studies. Atrial fibrillation incidence was calculated using the double arcsine Freeman-Tukey transformation.



Supplementary Figure 6. Meta-regression analysis of the association of hypertension with the rate of atrial fibrillation detection with implantable cardiac monitors reported in (A) all included (abstracts and full publications) studies and (B) fully published studies. Atrial fibrillation incidence was calculated using the double arcsine Freeman-Tukey transformation.



Supplementary Figure 7. Meta-regression analysis of the association of diabetes mellitus with the rate of atrial fibrillation detection with implantable cardiac monitors reported in (A) all included (abstracts and full publications) studies and (B) fully published studies. Atrial fibrillation incidence was calculated using the double arcsine Freeman-Tukey transformation.

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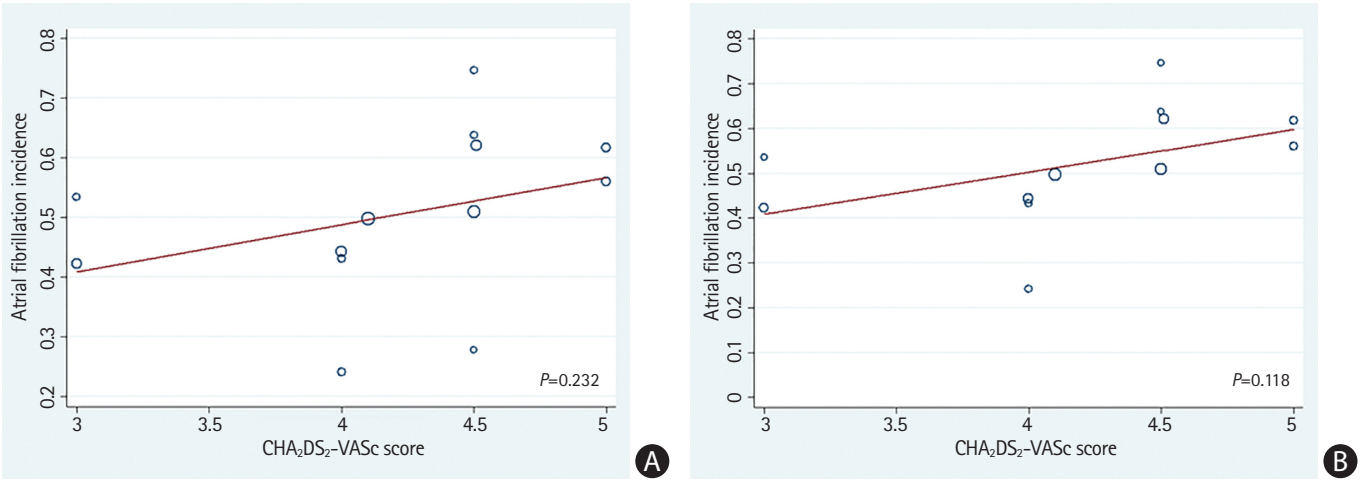
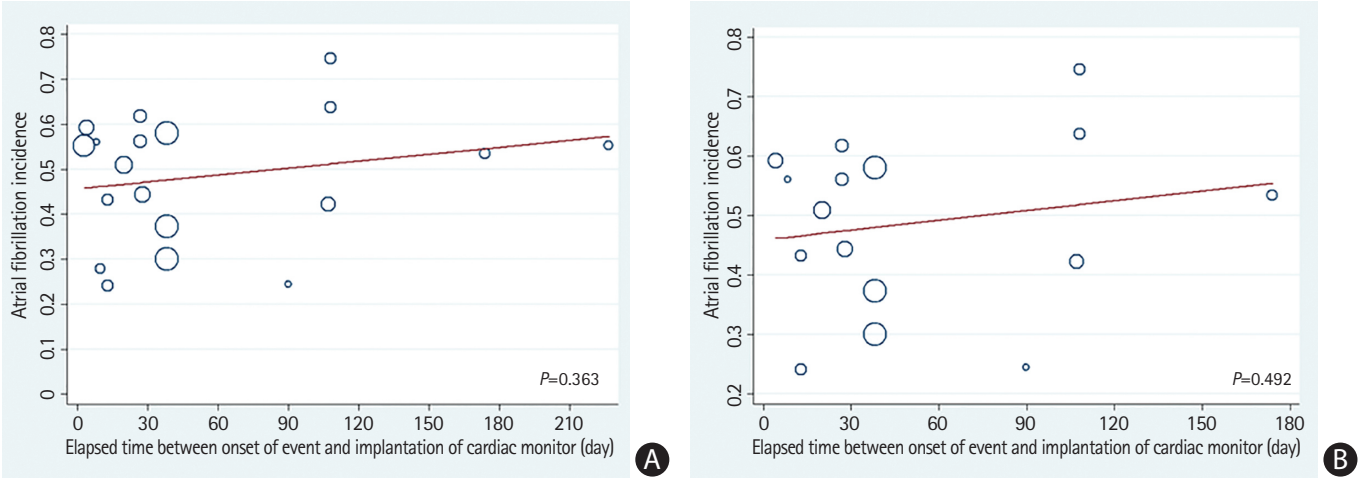
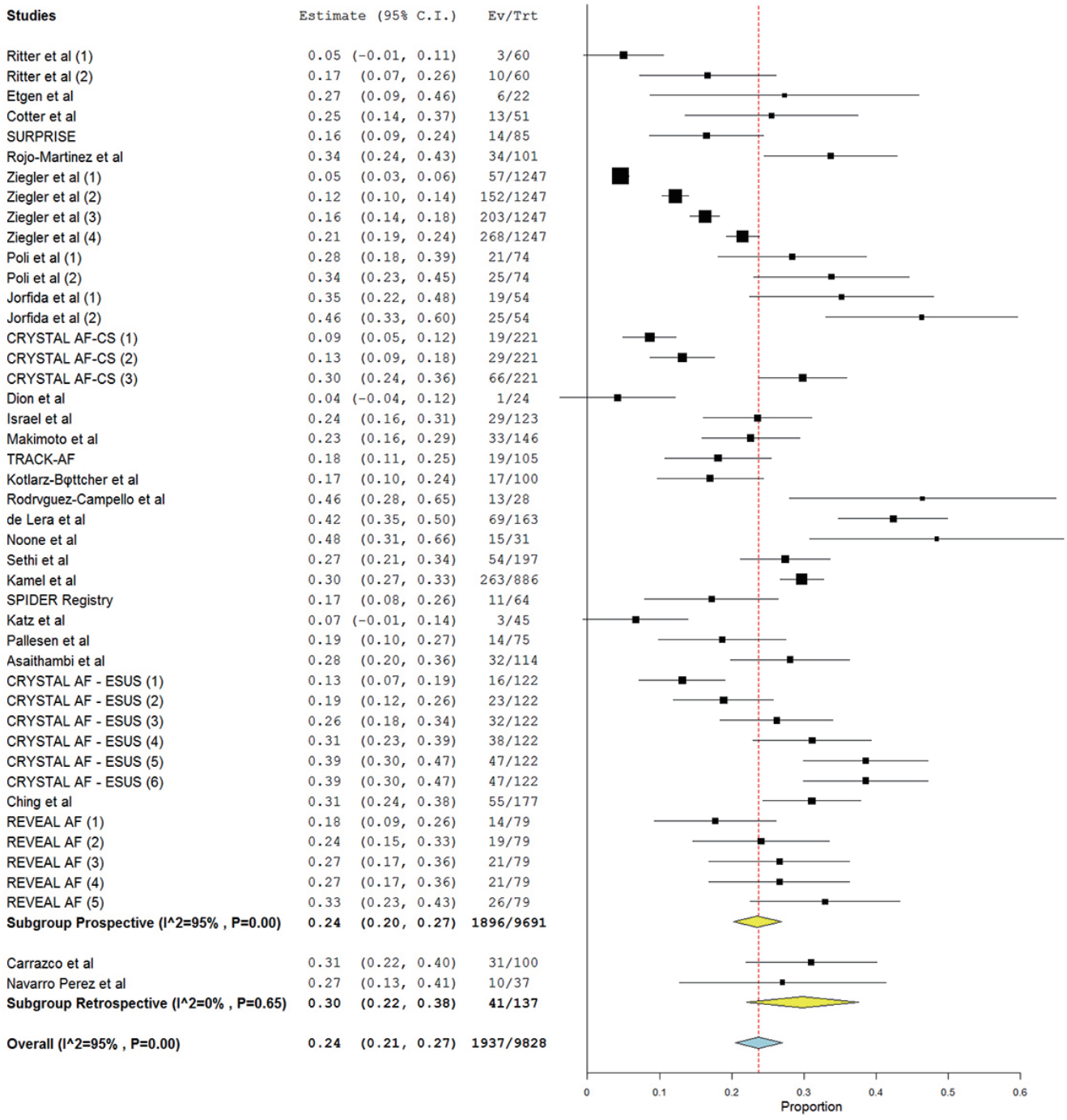


Supplementary Figure 8. Meta-regression analysis of the association of mean patient CHA_2DS_2VASc score with the rate of atrial fibrillation detection with implantable cardiac monitors reported in (A) all included (abstracts and full publications) studies and (B) fully published studies. Atrial fibrillation incidence was calculated using the double arcsine Freeman-Tukey transformation.



Supplementary Figure 9. Meta-regression analysis on the association of mean elapsed time from ischemic stroke or transient ischemic attack onset to cardiac monitor implantation, with the rate of atrial fibrillation detection with implantable cardiac monitors reported in (A) all included (abstracts and full publications) studies and (B) fully published studies. Atrial fibrillation incidence was calculated using the double arcsine Freeman-Tukey transformation.



Supplementary Figure 10. Subgroup analysis of the rate of atrial fibrillation detection with implantable cardiac monitors, stratified by study type (prospective or retrospective cohort), in all included studies. CI, confidence interval; EV/Trt, events/treated.

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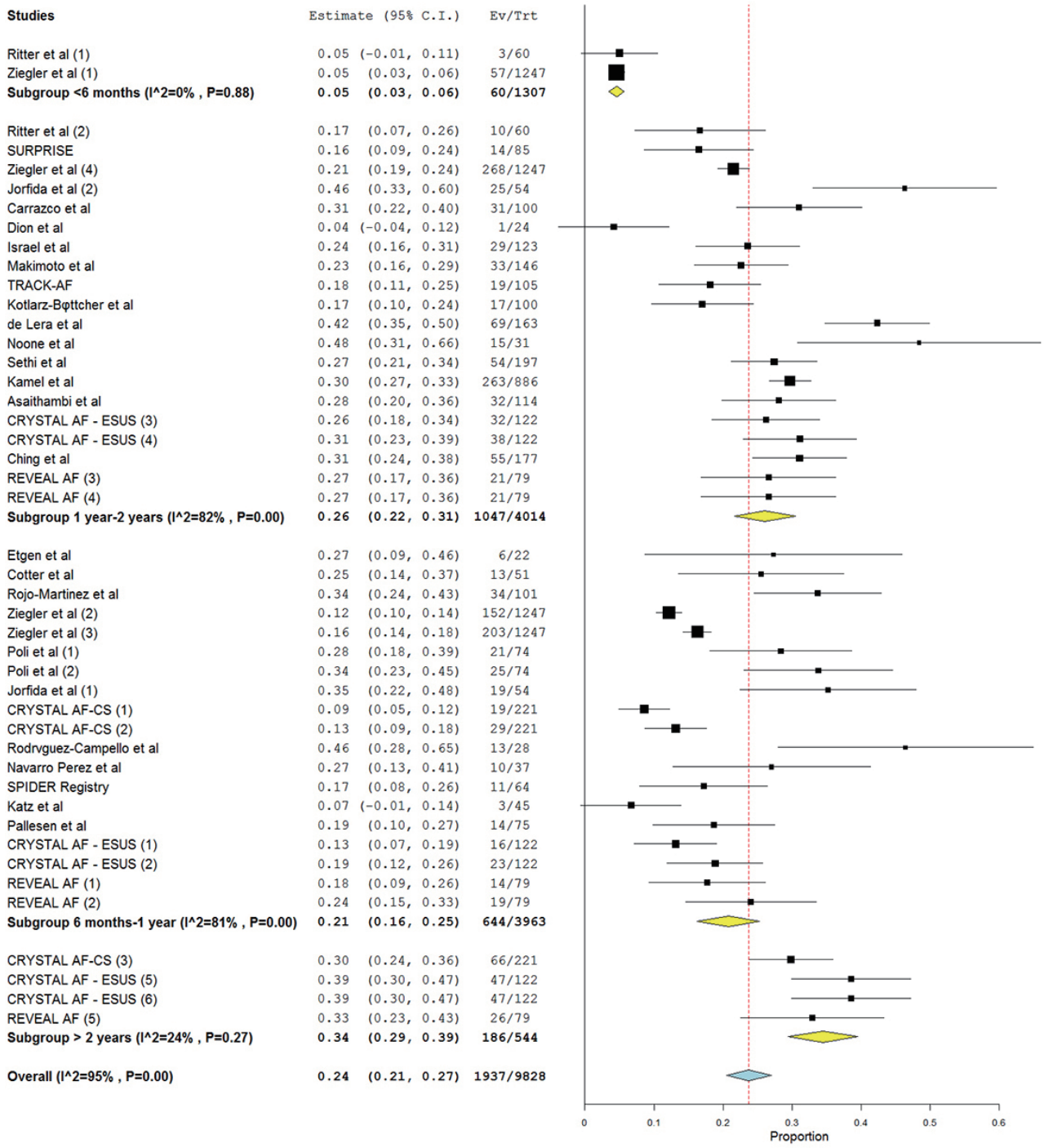
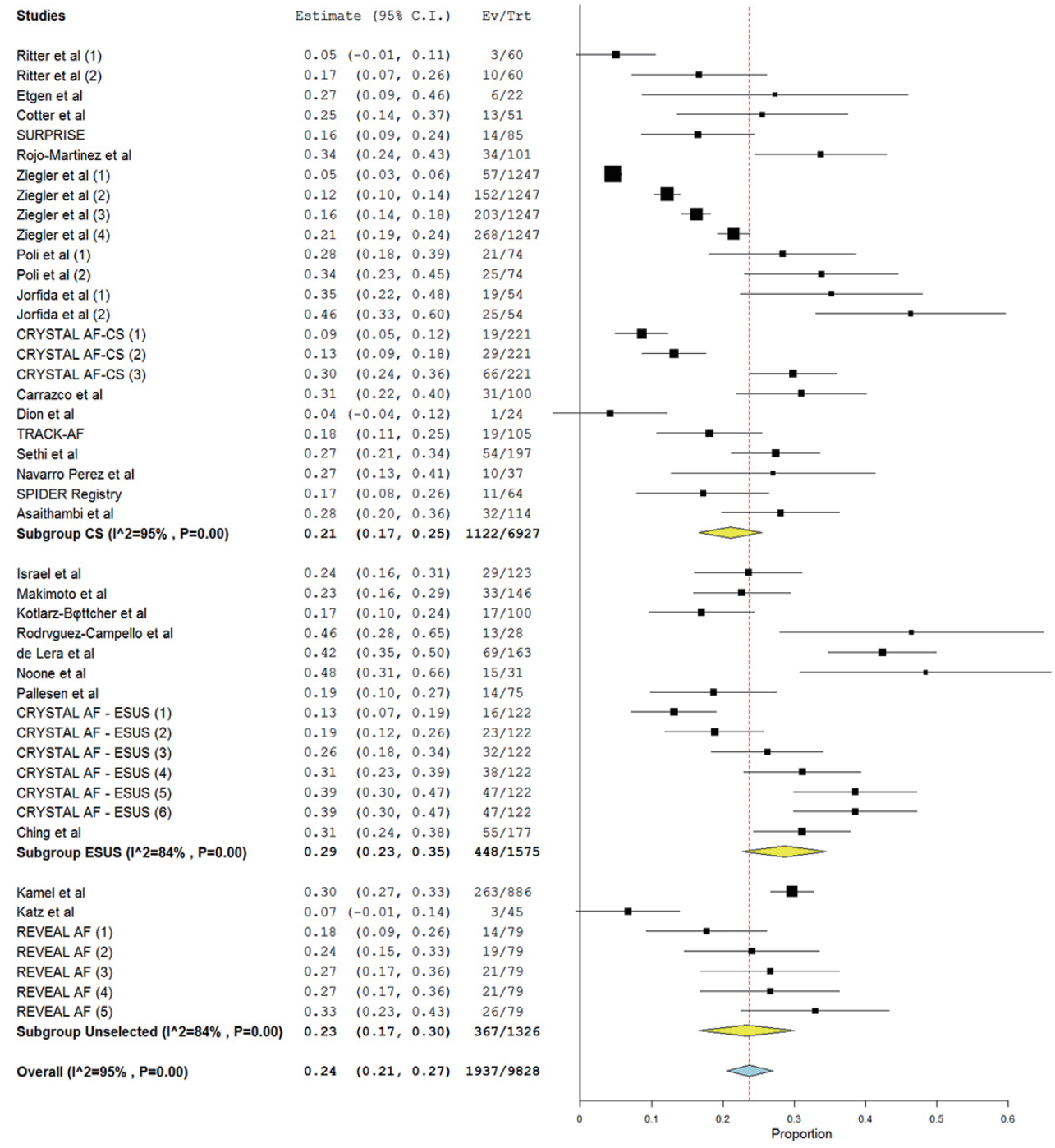


Supplementary Figure 11. Subgroup analysis of the rate of atrial fibrillation detection with implantable cardiac monitors, stratified by monitoring duration (<6, ≥6 and ≤12, >12 and ≤24, and >24 months), in all included studies. CI, confidence interval; EV/Trt, events/treated.



Supplementary Figure 12. Subgroup analysis of the rate of atrial fibrillation detection with implantable cardiac monitors, stratified by ischemic stroke subtype (cryptogenic stroke [CS], embolic stroke of undetermined source [ESUS], unselected ischemic stroke/transient ischemic attack), in all included studies. CI, confidence interval; EV/Trt, events/treated.

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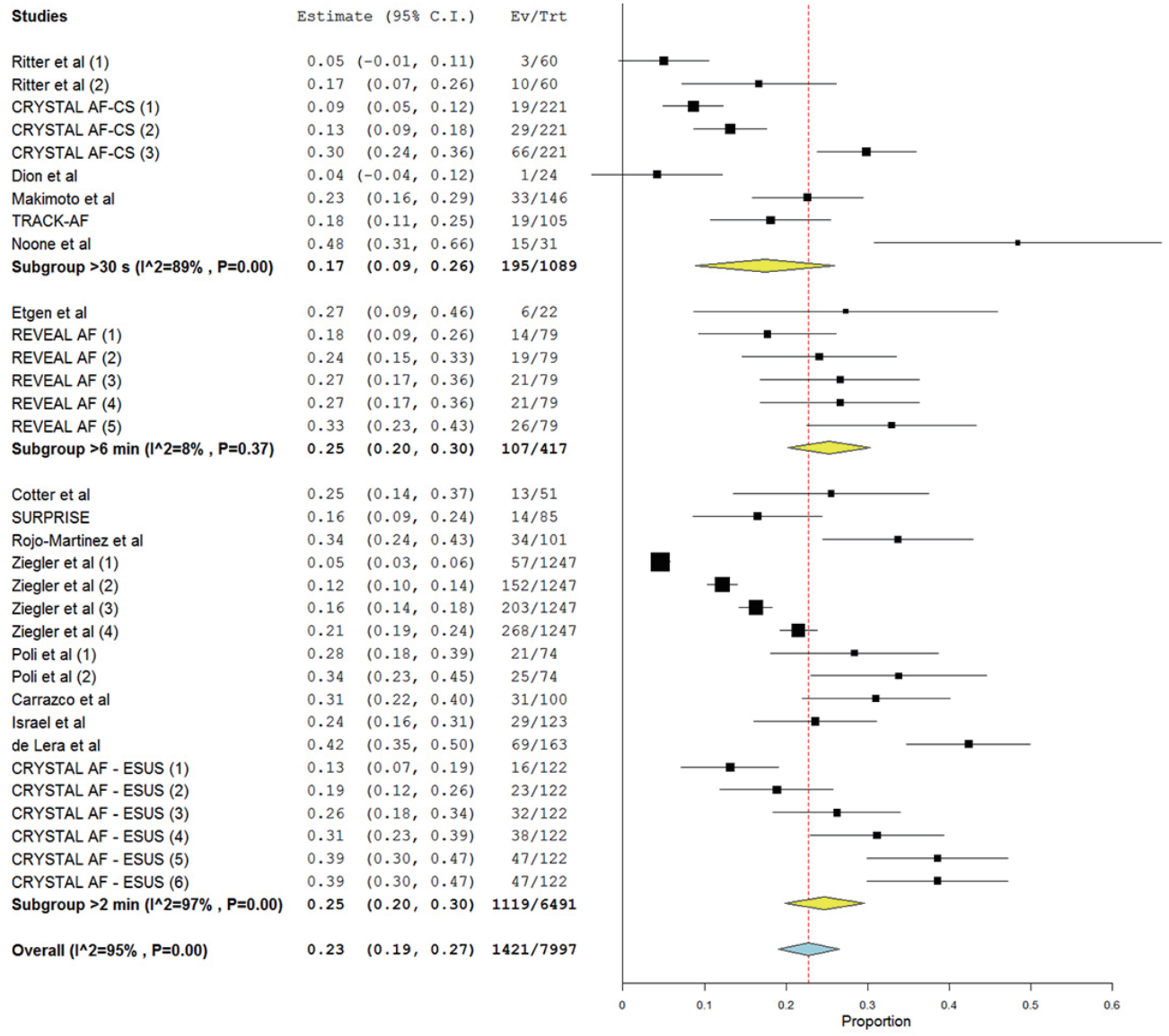
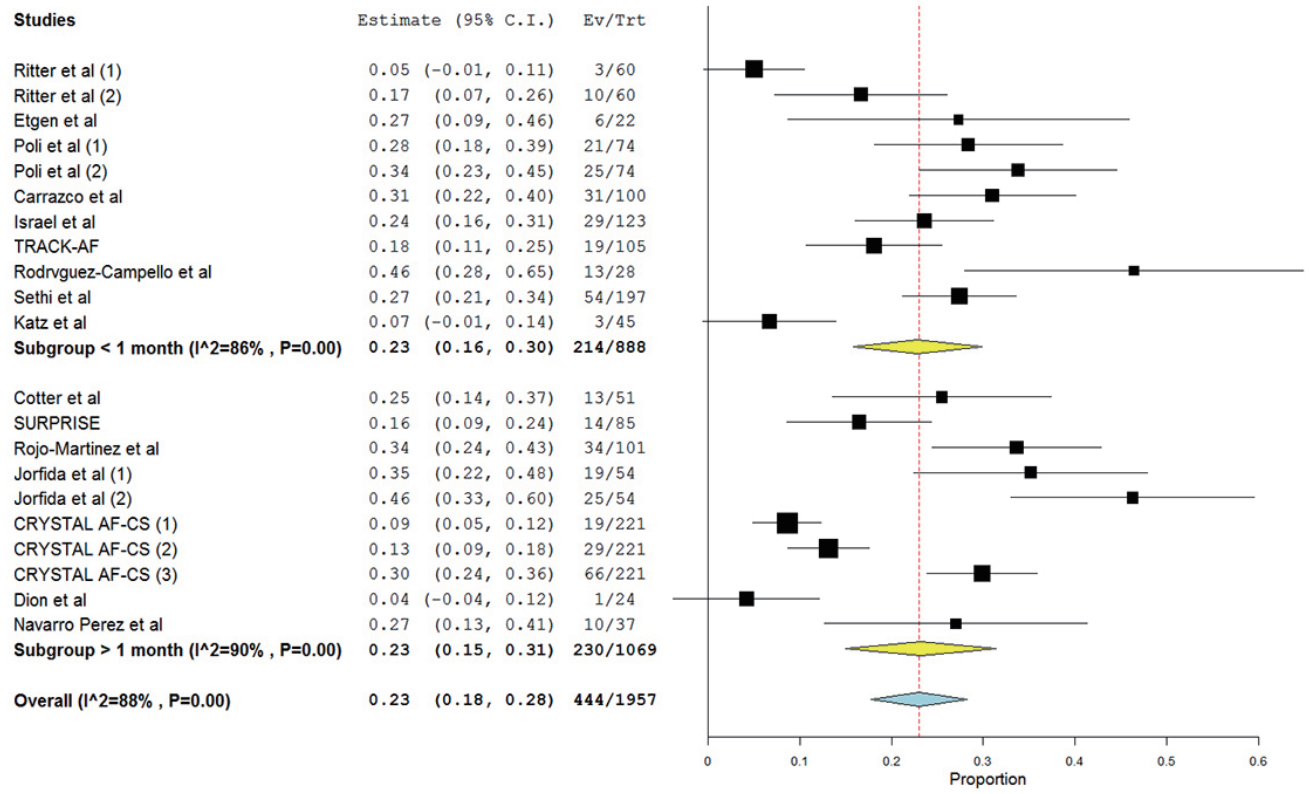
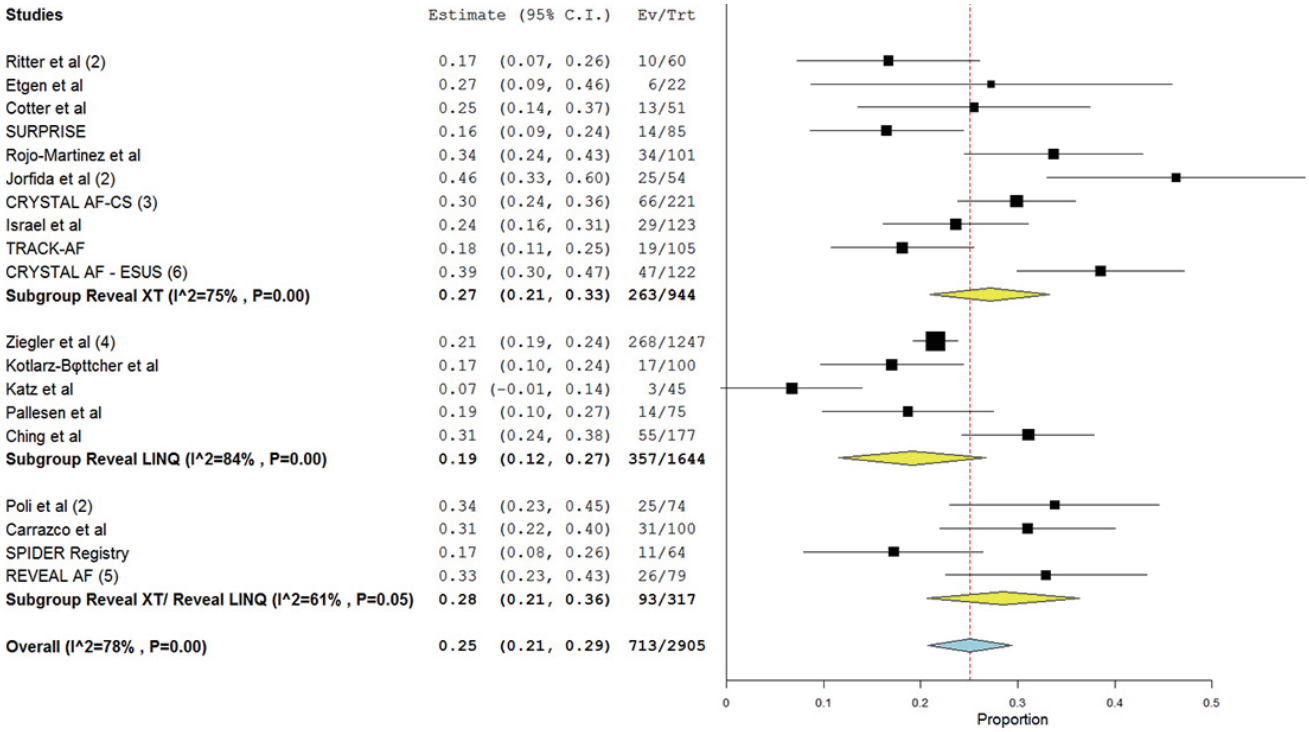


Supplementary Figure 13. Subgroup analysis of the rate of atrial fibrillation detection with implantable cardiac monitors, stratified by the time threshold used for atrial fibrillation diagnosis (30 seconds, 2 minutes, 6 minutes), in all included studies. CI, confidence interval; EV/Trt, events/treated.



Supplementary Figure 14. Subgroup analysis of the rate of atrial fibrillation detection with implantable cardiac monitors, stratified by the elapsed time between ischemic stroke/transient ischemic attack onset and implantation of cardiac monitor (≤1 and >1 month), in all included studies. CI, confidence interval; EV/Trt, events/treated.



Supplementary Figure 15. Subgroup analysis of the rate of atrial fibrillation detection with implantable cardiac monitors, stratified by the type of device used, in all included studies. CI, confidence interval; EV/Trt, events/treated.

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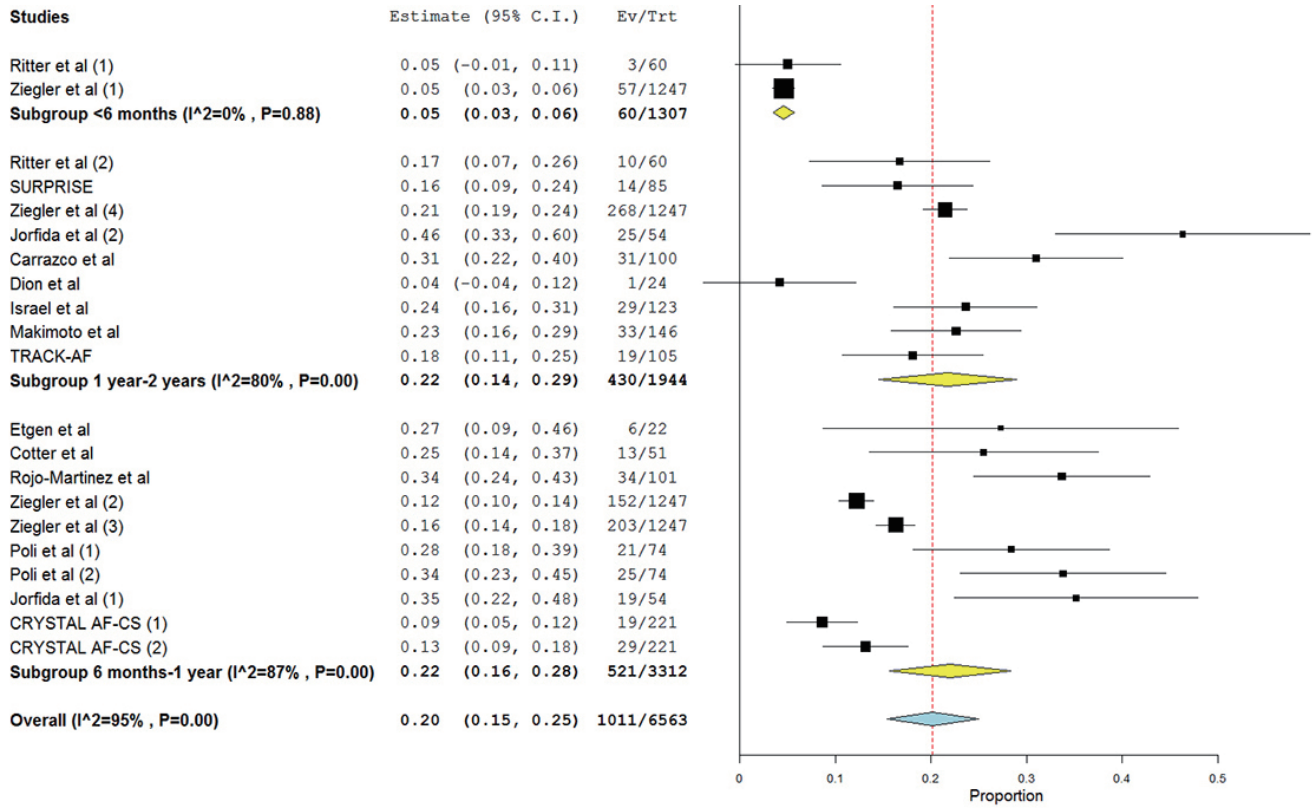
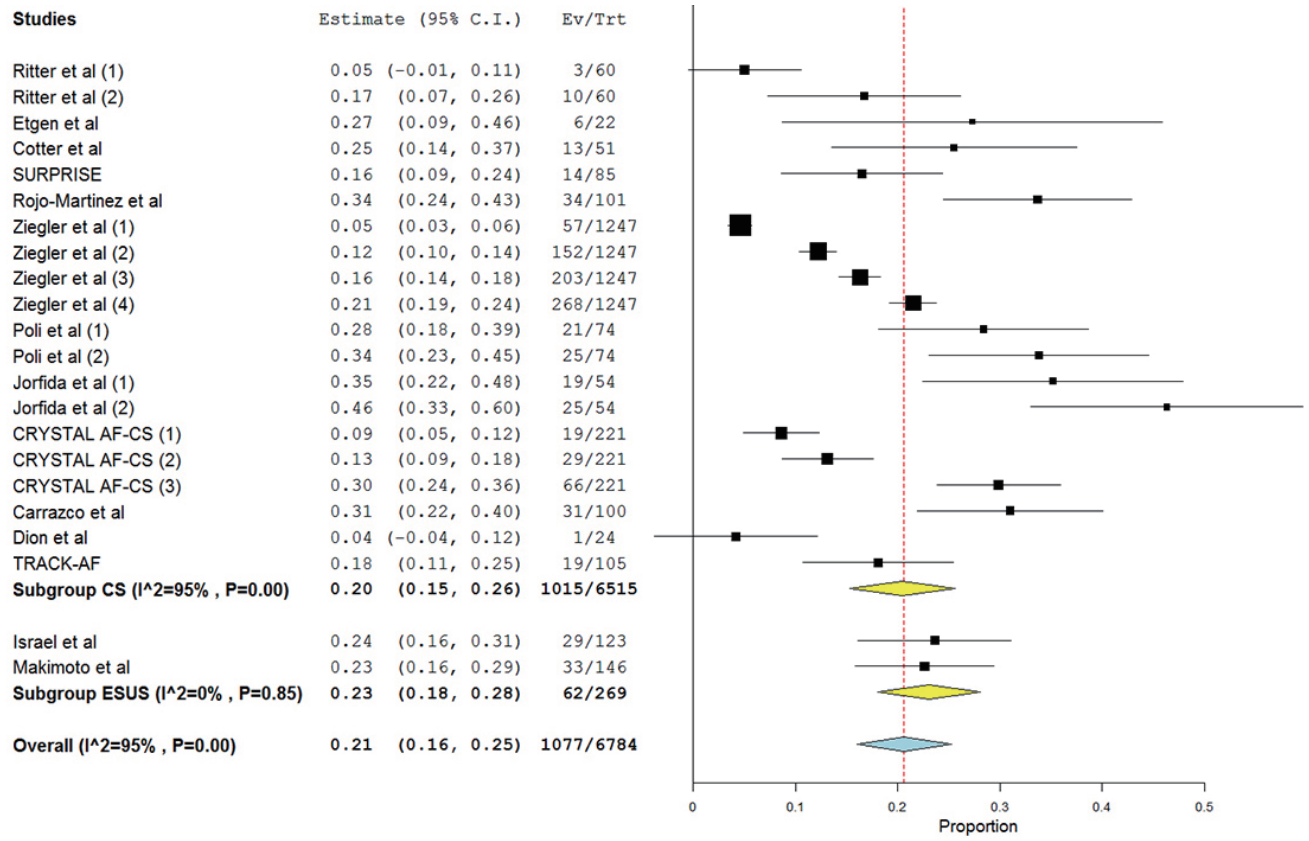


Supplementary Figure 16. Subgroup analysis of the rate of atrial fibrillation detection with implantable cardiac monitors, stratified by monitoring duration (<6, ≥6 and ≤12, >12 and ≤24 months), in fully published studies. CI, confidence interval; EV/Trt, events/treated.



Supplementary Figure 17. Subgroup analysis of the rate of atrial fibrillation detection with implantable cardiac monitors, stratified by ischemic stroke subtype (cryptogenic stroke [CS], embolic stroke of undetermined source [ESUS]), in fully published studies. CI, confidence interval; EV/Trt, events/treated.

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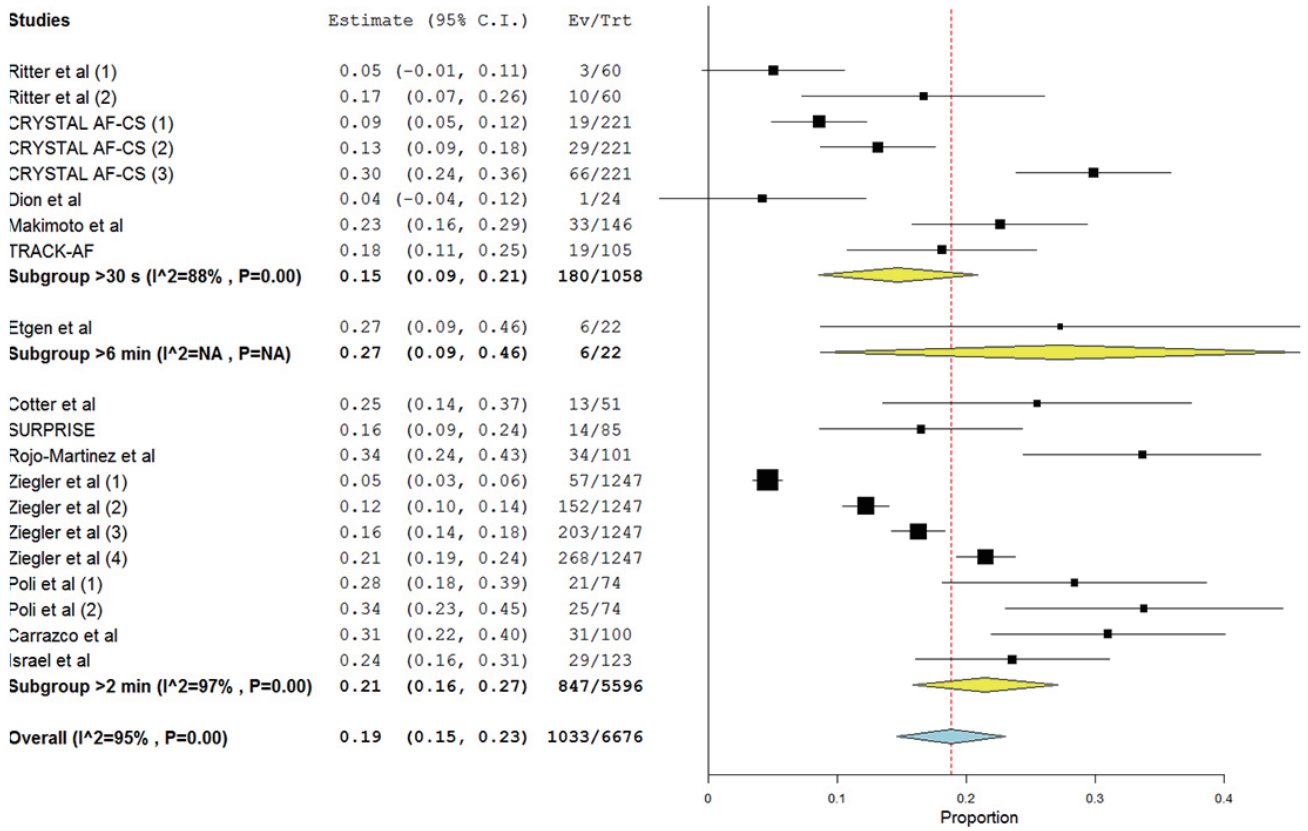
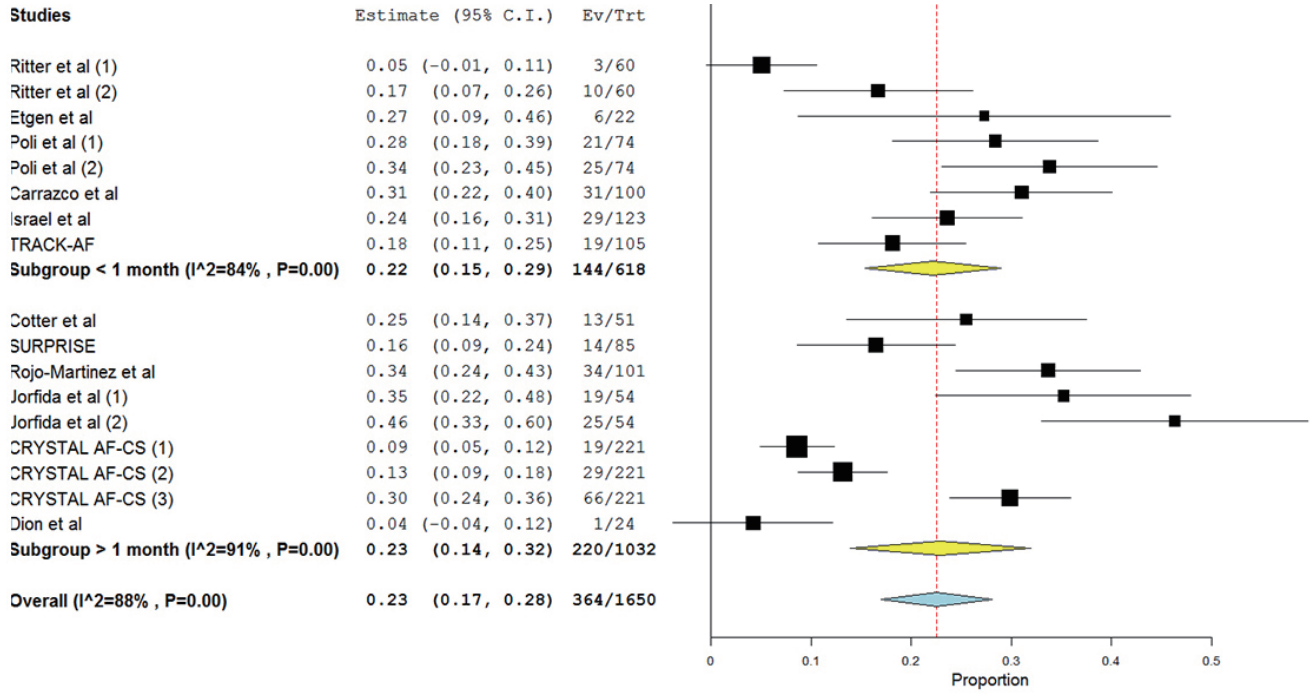
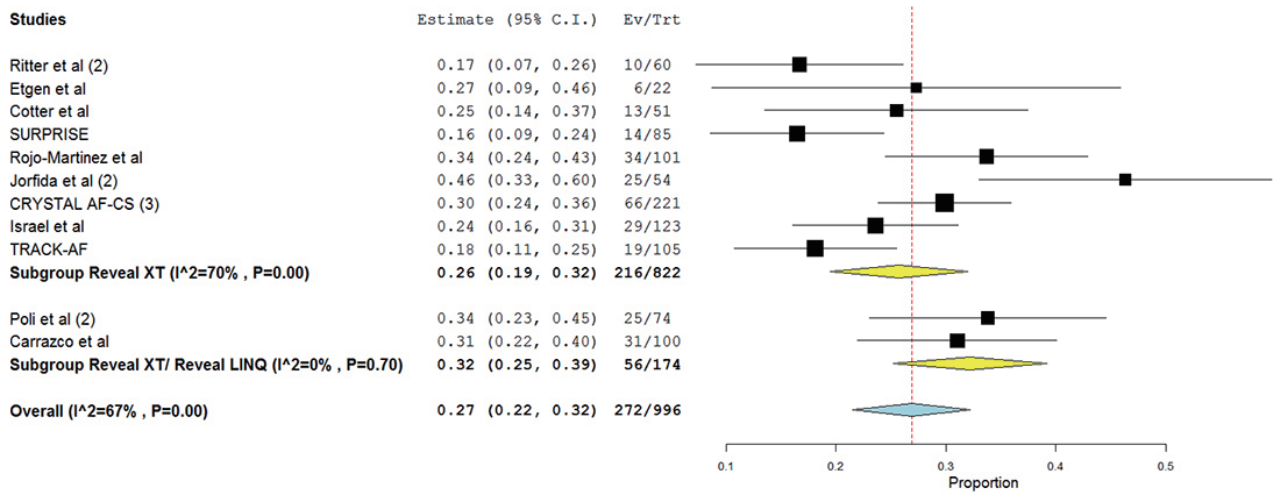


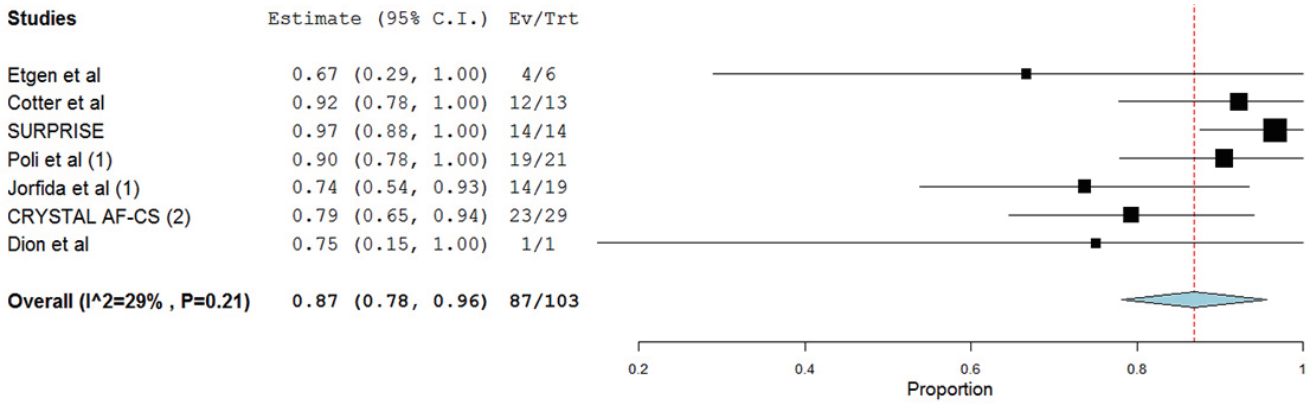
Supplementary Figure 18. Subgroup analysis of the rate of atrial fibrillation detection with implantable cardiac monitors, stratified by the time threshold used for atrial fibrillation diagnosis (30 seconds and 2 minutes) in fully published studies. CI, confidence interval; EV/Trt, events/treated; NA, not available.



Supplementary Figure 19. Subgroup analysis of the rate of atrial fibrillation detection with implantable cardiac monitors, stratified by the elapsed time between ischemic stroke/transient ischemic attack onset and implantation of cardiac monitor (≤1 and >1 month), in fully published studies. CI, confidence interval; EV/Trt, events/treated.



Supplementary Figure 20. Subgroup analysis of the rate of atrial fibrillation detection with implantable cardiac monitors, stratified by the type of device used, in all included studies. CI, confidence interval; EV/Trt, events/treated.



Supplementary Figure 21. Pooled analysis of the proportion patients with episodes of asymptomatic atrial fibrillation, among patients with episodes of atrial fibrillation (both asymptomatic and symptomatic) detected with implantable cardiac monitoring. CI, confidence interval; EV/Trt, events/treated.

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Supplementary References

1. de Lera M, Bulnes LR, Cortijo E, Bombín S, Calleja AI, García-Morán E, et al. AS18-066: Predictors of arrhytmic load in patients with cryptogenic stroke and covert atrial fibrillation detected by implantable loop recorders. *Eur Stroke J* 2017;2(1 Suppl):115.
2. Favilla CG, Ingala E, Jara J, Fessler E, Cucchiara B, Messé SR, et al. Predictors of finding occult atrial fibrillation after cryptogenic stroke. *Stroke* 2015;46:1210-1215.
3. Friberg L, Rosenqvist M, Lindgren A, Terént A, Norrving B, Asplund K. High prevalence of atrial fibrillation among patients with ischemic stroke. *Stroke* 2014;45:2599-2605.
4. Giralt-Steinhauer E, Cuadrado-Godia E, Soriano-Tárraga C, Ois Á, Jiménez-Conde J, Rodríguez-Campello A, et al. New-onset paroxysmal atrial fibrillation diagnosis in ischemic stroke patients. *Eur Neurol* 2015;74:211-217.
5. Kitsiou A, Kalyani M, Ekosso Ejangue L, Hagemeister C, Manegold J, Israel C, et al. ESOC-0735: Atrial fibrillation detection in patients with an implantable loop recorder after acute embolic stroke of unknown source (ESUS). *Int J Stroke* 2015;10(2 Suppl):273.
6. Kitsiou A, Kalyani M, Ekosso Ejangue L, Hagemeister C, Manegold J, Israel C, et al. Abstract TP216: Atrial fibrillation detection in patients with an implantable loop recorder after acute embolic stroke of unknown source (ESUS). *Stroke* 2016;47(Suppl 1):ATP216.
7. Pedersen KB, Chemnitz A, Madsen C, Sandgaard NCF, Bak S, Brandes A. Low incidence of atrial fibrillation in patients with transient ischemic attack. *Cerebrovasc Dis Extra* 2016;6:140-149.
8. Prakapenia A, Pallesen LP, Mayer J, Barlinn J, Barlinn K, Siepmann T, et al. AS18-059: Detection rate of insertable cardiac monitors is not influenced by embolic pattern in neuroradiological imaging. *Eur Stroke J* 2017;2(1 Suppl):113.
9. Perera KS, Vanassche T, Bosch J, Swaminathan B, Mundl H, Giruparajah M, et al. Global survey of the frequency of atrial fibrillation-associated stroke: embolic stroke of undetermined source global registry. *Stroke* 2016;47:2197-2202.
10. Rem JA, Hachinski VC, Boughner DR, Barnett HJ. Value of cardiac monitoring and echocardiography in TIA and stroke patients. *Stroke* 1985;16:950-956.
11. Ricci B, Chang AD, Hemendinger M, Dakay K, Cutting S, Burton T, et al. A simple score that predicts paroxysmal atrial fibrillation on outpatient cardiac monitoring after embolic stroke of unknown source. *J Stroke Cerebrovasc Dis* 2018;27:1692-1696.
12. Rizos T, Quilitzsch A, Busse O, Haeusler KG, Endres M, Heuschmann P, et al. Diagnostic work-up for detection of paroxysmal atrial fibrillation after acute ischemic stroke: cross-sectional survey on German stroke units. *Stroke* 2015;46:1693-1695.
13. Rodríguez-Campello A, Giralt-Steinhauer E, Ois A, Jiménez-Conde J, Avellaneda-Gómez C, Serra-Martínez M, et al. AS21-027: Atrial fibrillation detection and stroke recurrence in patients with early insertable cardiac monitor. A case-control study. *Eur Stroke J* 2018;3(1 Suppl):459.
14. Rojo E, Sandín-Fuentes M, Calleja AI, Largaespada G, Cortijo E, García-Morán E, et al. Abstract T MP57: Coexisting cerebrovascular disease and risk of occult atrial fibrillation in patients with embolic stroke of undetermined source. *Stroke* 2015;46(Suppl 1):ATMP57.
15. Schneider JS, Burshtein RD, Golyan D, Kahen M, Arora R, Salamon E, et al. Abstract 209: High yield of long-term implantable cardiac monitoring following cryptogenic ischemic stroke. *Stroke* 2016;47(Suppl 1):A209.
16. Sposato LA, Klein FR, Jáuregui A, Ferrúa M, Klin P, Zamora R, et al. Newly diagnosed atrial fibrillation after acute ischemic stroke and transient ischemic attack: importance of immediate and prolonged continuous cardiac monitoring. *J Stroke Cerebrovasc Dis* 2012;21:210-216.
17. Stahrenberg R, Weber-Krüger M, Seegers J, Edelmann F, Lahno R, Haase B, et al. Enhanced detection of paroxysmal atrial fibrillation by early and prolonged continuous holter monitoring in patients with cerebral ischemia presenting in sinus rhythm. *Stroke* 2010;41:2884-2888.
18. Yetim E, Topcuoglu MA, Canpolat U, Gocmen R, Oguz KK, Ozer N, et al. Nonsustained atrial fibrillation in ischemic stroke patients and stroke-free controls from the perspective of stroke pathophysiology. *J Am Heart Assoc* 2016;5:e004021.
19. Asaithambi G, Monita JE, Hanson SK. Abstract WP231: Predictors for early atrial fibrillation detection among cryptogenic stroke patients with insertable cardiac monitors: a single-center experience. *Stroke* 2017;48(Suppl 1):AWP231.
20. Carrazco C, Golyan D, Kahen M, Black K, Libman RB, Katz JM. Prevalence and risk factors for paroxysmal atrial fibrillation and flutter detection after cryptogenic ischemic stroke. *J Stroke Cerebrovasc Dis* 2018;27:203-209.
21. Ching MI, Zhang C, Vaughn C, Lail N, Leahy T, Kandel A, et al. Abstract WP199: Left atrial volume index and PR interval are independent predictors of atrial fibrillation in embolic stroke patients with insertable cardiac monitor. *Stroke* 2018;49(Suppl 1):AWP199.
22. Cotter PE, Martin PJ, Ring L, Warburton EA, Belham M, Pugh PJ. Incidence of atrial fibrillation detected by implantable loop recorders in unexplained stroke. *Neurology* 2013;80:

1546-1550.
23. Sanna T, Diener HC, Passman RS, Di Lazzaro V, Bernstein RA, Morillo CA, et al. Cryptogenic stroke and underlying atrial fibrillation. *N Engl J Med* 2014;370:2478-2486.
24. Passman RS, Rymer MM, Liu S, Ziegler PD. Abstract 78: Incidence of atrial fibrillation among patients with an embolic stroke of undetermined source. *Stroke* 2017;48(Suppl 1):A78.
25. de Lera M, Largaespada G, Cortijo E, Sandin M, Calleja A, García E, et al. AS18-008: Predictors of higher arrhythmic load in patients with cryptogenic stroke and covert atrial fibrillation detected by implantable loop recorders. *Eur Stroke J* 2016;1(1 Suppl):641.
26. Dion F, Saudeau D, Bonnaud I, Friocourt P, Bonneau A, Poret P, et al. Unexpected low prevalence of atrial fibrillation in cryptogenic ischemic stroke: a prospective study. *J Interv Card Electrophysiol* 2010;28:101-107.
27. Etgen T, Hochreiter M, Mundel M, Freudenberger T. Insertable cardiac event recorder in detection of atrial fibrillation after cryptogenic stroke: an audit report. *Stroke* 2013;44:2007-2009.
28. Israel C, Kitsiou A, Kalyani M, Deelawar S, Ejangue LE, Rogalewski A, et al. Detection of atrial fibrillation in patients with embolic stroke of undetermined source by prolonged monitoring with implantable loop recorders. *Thromb Haemost* 2017;117:1962-1969.
29. Jorfida M, Antolini M, Cerrato E, Caprioli MG, Castagno D, Garrone P, et al. Cryptogenic ischemic stroke and prevalence of asymptomatic atrial fibrillation: a prospective study. *J Cardiovasc Med (Hagerstown)* 2016;17:863-869.
30. Kamel H, Yaghi S, Passman R, Allred J, Sarkar S, Kohler J, et al. AS21-004: Comparison of atrial fibrillation diagnosis and oral anticoagulation utilization among ischemic stroke patients with vs. without insertable cardiac monitors. *Eur Stroke J* 2018;3(1 Suppl):452.
31. Katz JM, Gribko M, Jadonath R, Arora R, Salamon E, Garlitzki A, et al. Abstract WMP63: Prevalence of occult paroxysmal atrial fibrillation in non-cryptogenic ischemic stroke patients. *Stroke* 2017;48(Suppl 1):AWMP63.
32. Kotlarz-Böttcher MJ, Busch M, Frenzel M, Hummel A, Schminke U, von Sarnowski B. AS21-019: Risk factors for atrial fibrillation in patients with embolic stroke of undetermined source (ESUS). *Eur Stroke J* 2018;3(1 Suppl):457.
33. Makimoto H, Kurt M, Gliem M, Lee JI, Schmidt J, Müller P, et al. High incidence of atrial fibrillation after embolic stroke of undetermined source in posterior cerebral artery territory. *J Am Heart Assoc* 2017;6:e007448.
34. Navarro Pérez MP, Pérez Lázaro C, Pelegrín Díaz J, Rodrigo Trallero G, Sánchez Val A, Garcés Antón E, et al. AS21-031: Paroxysmal atrial fibrillation detection after cryptogenic stroke: a single center experience. *Eur Stroke J* 2018;3(1 Suppl):460.
35. Noone I, Meagher MK, Mc Creery C, Cassidy T. AS18-027: The role of loop recorders in embolic stroke of uncertain source (ESUS). *Eur Stroke J* 2016;1(1 Suppl):16.
36. Pallesen LPM, Mayer J, Barlinn K, Barlinn J, Prakapenia A, Sieppmann T, et al. Abstract WP230: Real-life detection rate of insertable cardiac monitors in patients with ESUS. *Stroke* 2017;48(Suppl 1):AWP230.
37. Poli S, Diedler J, Härtig F, Götz N, Bauer A, Sachse T, et al. Insertable cardiac monitors after cryptogenic stroke: a risk factor based approach to enhance the detection rate for paroxysmal atrial fibrillation. *Eur J Neurol* 2016;23:375-381.
38. Elkind MS, Wachter R, Verma A, Kowey PR, Halperin JL, Gersh BJ, et al. Abstract 189: Identifying patients at highest risk of developing atrial fibrillation and the role of remote prior stroke: insights from the REVEAL AF study. *Stroke* 2018;49(Suppl 1):A189.
39. Ritter MA, Kochhäuser S, Duning T, Reinke F, Pott C, Dechering DG, et al. Occult atrial fibrillation in cryptogenic stroke: detection by 7-day electrocardiogram versus implantable cardiac monitors. *Stroke* 2013;44:1449-1452.
40. Rodríguez-Campello A, Cuadrado-Godia E, Ois A, Giralt-Steinhauer E, Jiménez-Conde J, Puig-Pijoan A, et al. ESOC-1467: Early detection of atrial fibrillation in embolic stroke of unknown origin (ESUS). *Int J Stroke* 2015;10:268-269.
41. Rojo-Martinez E, Sandín-Fuentes M, Calleja-Sanz AI, Cortijo-García E, García-Bermejo P, Ruiz-Piñero M, et al. High performance of an implantable Holter monitor in the detection of concealed paroxysmal atrial fibrillation in patients with cryptogenic stroke and a suspected embolic mechanism. *Rev Neurol* 2013;57:251-257.
42. Sethi P, Biby S, Allred J, Seiler A, Xu J. AS18-067: Surveillance for atrial fibrillation in patients with cryptogenic stroke using an implantable loop recorder during an inpatient hospitalization in a community hospital setting. *Eur Stroke J* 2017;2(1 Suppl):115.
43. Joseph K, Wanjiku S, Jumaa M, Richards M. Abstract W P194: Improved efficacy of ICM detection of atrial fibrillation in cryptogenic stroke patients with MRI-defined infarcts: preliminary results from the SPIDER registry. *Stroke* 2015;46(Suppl 1):AWP194.
44. Christensen LM, Krieger DW, Højberg S, Pedersen OD, Karlsen FM, Jacobsen MD, et al. Paroxysmal atrial fibrillation occurs often in cryptogenic ischaemic stroke. Final results from the SURPRISE study. *Eur J Neurol* 2014;21:884-889.
45. Reinke F, Bettin M, Ross LS, Kochhäuser S, Kleffner I, Ritter

https://doi.org/10.5853/jos.2019.01067

M, et al. Refinement of detecting atrial fibrillation in stroke patients: results from the TRACK-AF Study. *Eur J Neurol* 2018;25:631-636.

46. Ziegler PD, Rogers JD, Ferreira SW, Nichols AJ, Sarkar S, Koehler JL, et al. Real-world experience with insertable cardiac monitors to find atrial fibrillation in cryptogenic stroke. *Cerebrovasc Dis* 2015;40:175-181.
47. Ziegler PD, Rogers JD, Ferreira SW, Nichols AJ, Richards M, Koehler JL, et al. Long-term detection of atrial fibrillation with insertable cardiac monitors in a real-world cryptogenic stroke population. *Int J Cardiol* 2017;244:175-179.