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Left Atrial Appendage Occlusion Versus Lifelong Anticoagulation: Framing a Genuinely Preference-Sensitive Decision

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Abstract

Percutaneous left atrial appendage occlusion (LAAO) was developed on a simple premise: in non-valvular atrial fibrillation, the great majority of atrial thrombi form in the left atrial appendage, so mechanically sealing it might substitute for lifelong oral anticoagulation. Fifteen years of randomized trials have shown LAAO to be non-inferior to warfarin for stroke prevention, with a durable reduction in hemorrhagic stroke and post-procedural bleeding, and procedural safety has improved considerably across successive device generations and operator experience. What has been missing until very recently was a well-powered, direct comparison against modern direct oral anticoagulant (DOAC) therapy in a general atrial-fibrillation population, rather than against warfarin or in a bleeding-risk-enriched subgroup. Two such trials reported topline results within days of each other in March 2026: CHAMPION-AF, an industry-funded trial using a single modern device, met noninferiority and showed markedly less non-procedural bleeding with LAAO than DOAC therapy; CLOSURE-AF, a publicly funded, multi-device, European trial in an older and more bleeding-prone population, did not meet noninferiority and reported a higher cardiovascular death rate with LAAO. Reconciling these results requires attention to funding source, device protocol, and population selection rather than treating either as definitive. Current guidelines already draw a sharper distinction than headline device comparisons suggest: LAAO carries a stronger recommendation for patients with a genuine contraindication to long-term anticoagulation than for patients who could take a DOAC but would prefer not to. This review sets out that fifteen-year evidence base, the specific and still-relevant risk of device-related thrombus, and the case for framing the LAAO-versus-anticoagulation choice through structured shared decision-making rather than as a question with one correct default answer.

Keywords: *Left atrial appendage occlusion; Atrial fibrillation; Anticoagulation; Direct oral anticoagulants; Shared decision making; Stroke prevention*

Introduction

Non-valvular atrial fibrillation raises stroke risk primarily because blood stagnates and clots within the left atrial appendage (LAA), a narrow, trabeculated pouch off the main atrial cavity. In a compiled surgical and pathological series of 222 left atrial thrombi in non-rheumatic atrial fibrillation, 201, or 91%, were isolated to or originated in the appendage [1]. That anatomical concentration of risk is the entire rationale for percutaneous left atrial appendage occlusion (LAAO): if most of the clot risk sits in one blind pouch, mechanically sealing that pouch might substitute for lifelong systemic

anticoagulation rather than merely supplementing it.

Guideline-recommended stroke prevention in atrial fibrillation still starts with oral anticoagulation, chosen using a validated risk score such as CHA2DS2-VASc, for patients above a low-risk threshold [2,18]. Direct oral anticoagulants (DOACs) are now preferred over warfarin on both efficacy and safety grounds in most such patients [3]. But a substantial minority either cannot safely take a long-term anticoagulant — because of a prior life-threatening bleed, an intracranial hemorrhage, or a condition that makes bleeding risk unacceptable — or can take one but would strongly prefer not to, given the burden of a lifelong daily medication and its bleeding risk. LAAO devices were developed for exactly this population, and fifteen years of randomized trials, summarized in Figure 1, have progressively tested the device against warfarin, against another device, and, only very recently, directly against modern DOAC therapy in a general atrial-fibrillation population.

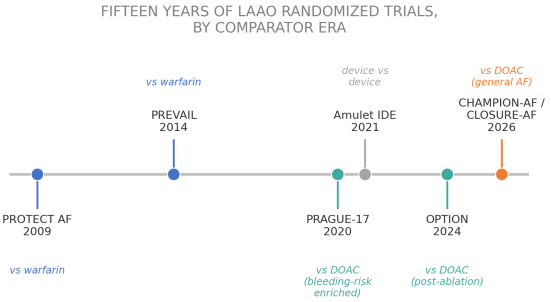

Figure 1: Fifteen years of randomized LAAO trials, by comparator era: warfarin (PROTECT AF, PREVAIL), device-versus-device (Amulet IDE), bleeding-risk-enriched or post-ablation DOAC comparisons (PRAGUE-17, OPTION), and, in 2026, two trials against DOAC therapy in a general atrial-fibrillation population (CHAMPION-AF, CLOSURE-AF) [4-11].

That final comparison matters because it is the one clinicians and patients actually face most often: not "device versus warfarin" for a patient who cannot take an anticoagulant at all, but "device versus a modern DOAC" for a patient who could take either. Two trials answering that exact question reported topline results within days of each other in March 2026, and reached opposite headline conclusions. This review sets out the fifteen-year evidence base leading up to that moment, the specific and still-relevant procedural and device-related risks of LAAO, and why the honest reading of the current evidence is that this is a genuinely preference-sensitive decision rather than one with a single correct default.

Material and Methods

This is a narrative review, not a systematic review or a new meta-analysis. The literature was assembled by searching for randomized trials of percutaneous LAAO, their published long-term follow-up analyses, the National Cardiovascular Data Registry (NCDR) LAAO Registry, and the current American and European atrial-fibrillation guideline documents, supplemented by each named trial's own registration and, where the full peer-reviewed paper was not yet available at the time of writing, its topline announcement or conference presentation as reported by specialist cardiology news outlets [4,9,10,12].

Every percentage, rate and hazard ratio reproduced here is taken directly from the cited source; none was recalculated by the present authors. Where two trials use different definitions for a nominally similar endpoint — annualized rate per 100 patient-years versus cumulative percentage over the trial's follow-up period, for example — that difference is stated explicitly rather than treated as directly comparable, and Table 1 sets out each trial's own definition alongside its result. The left atrial anatomy schematic and the decision-factors schematic appearing later in this review are illustrative diagrams built to explain a mechanism and a framework, not reproductions of any imaging study or decision-aid instrument.

Results

Fifteen years of randomized evidence: from warfarin to a direct DOAC comparison

PROTECT AF was the first randomized trial of percutaneous LAAO, comparing the first-generation Watchman device against warfarin in patients able to tolerate short-term anticoagulation after implantation. The device met its primary efficacy composite of stroke, systemic embolism and cardiovascular or unexplained death with a rate of 3.0 events per 100 patient-years versus 4.9 with warfarin [4]. A subsequent 4-year follow-up of the same trial cohort found the device arm's advantage widen rather than narrow over time, with a lower primary composite event rate (2.3% versus 3.8% per year) and lower all-cause and cardiovascular mortality than warfarin [19]. PROTECT AF nonetheless carried a higher rate of periprocedural safety events at the outset, chiefly pericardial effusion, and the U.S. Food and Drug Administration required a second randomized trial, PREVAIL, using a refined implant technique and more experienced operators, before approval [5]. PREVAIL's primary composite result was closely matched between arms (6.4% device versus 6.3% warfarin over 18 months) and its confidence interval did not meet the pre-specified noninferiority margin on that particular endpoint, but its all-complications safety rate fell to 4.5% from PROTECT AF's 8.7%, and a second, late-ischemic-endpoint analysis did meet noninferiority [5]. Figure 2 sets the primary composite results of both trials, and of the trials described below, side by side; a later figure traces the safety-event rate specifically within the Watchman device family across four successive trials.

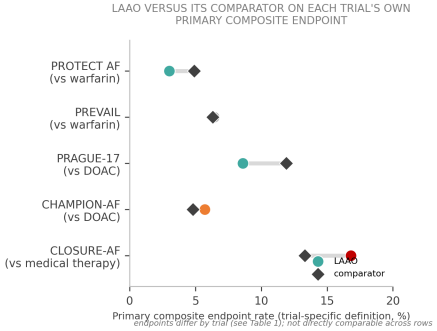

Figure 2: LAAO versus its comparator on each trial's own primary composite endpoint. Definitions differ by trial — some report annualized rates per 100 patient-years, others cumulative percentages over the trial's follow-up period; see Table 1 — so rows are not directly comparable to one another [4,5,7,10,11].

A pooled, patient-level five-year follow-up of PROTECT AF and PREVAIL together, covering 1,114 patients and 4,343 patient-years, found 41% lower cardiovascular or unexplained mortality and 27% lower all-cause mortality with the device, alongside 80% lower hemorrhagic stroke and 52% less frequent post-procedure major bleeding; combined stroke and systemic embolism did not differ significantly between arms [6]. That long-term profile — materially less bleeding and a durable mortality signal, without excess combined thromboembolism — is the foundation on which every subsequent trial has built.

Trial (year)	Comparator	Endpoint definition	Result
PROTECT AF (2009)	Warfarin	Composite, per 100 patient-years	3.0 (device) vs 4.9 (warfarin)
PREVAIL (2014)	Warfarin	Composite, cumulative at 18 months	6.4% vs 6.3%
PRAGUE-17 (2020/2022)	DOAC, bleeding-risk enriched population	Annualized composite	8.6% vs 11.9%
CHAMPION-AF (2026)	DOAC, general AF population	Cumulative composite	5.7% vs 4.8%
CLOSURE-AF (2026)	Medical therapy, bleeding-prone population	Composite, per 100 patient-years	16.8 vs 13.3

Table 1: Primary composite results across five randomized LAAO trials, with each trial's own endpoint definition. Cumulative percentages and annualized per-100-patient-year rates are not interchangeable, which is why Figure 2 keeps them as separate rows rather than a single ranked comparison [4,5,7,10,11].

Later trials moved beyond the warfarin comparison. PRAGUE-17 randomized patients at elevated bleeding risk to LAAO or a DOAC and, in its longer-term follow-up with a median 3.5 years of observation, found an annualized primary composite rate of 8.6% with LAAO versus 11.9% with a DOAC, meeting noninferiority [7,8]. Amulet IDE compared two devices directly, the Amplatzer Amulet against the Watchman 2.5, rather than testing LAAO as a strategy against anticoagulation at all, and both met their respective noninferiority margins for stroke or systemic embolism [9]. OPTION, reported in 2024, addressed a narrower and increasingly common scenario: patients who had just undergone catheter ablation for atrial fibrillation, randomized to LAAO or continued DOAC therapy. At 36 months, the primary efficacy composite was 5.3% with LAAO versus 5.8% with DOAC therapy (meeting noninferiority), and non-procedure-related major or clinically relevant bleeding was substantially lower with LAAO, 8.5% versus 18.1% [12].

Procedural safety has improved, but device-related thrombus remains a distinct and relevant risk

Figure 3 illustrates what the device actually does: a self-expanding occluder is deployed across the ostium of the appendage, sealing it from the main atrial cavity so that any residual thrombus formed within the excluded pouch cannot embolize.

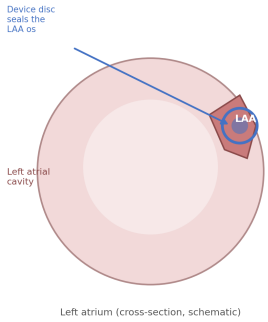

Figure 3: Schematic cross-section of the left atrium: a self-expanding device disc seals the ostium of the left atrial appendage, the site of origin of the great majority of atrial thrombi in non-valvular atrial fibrillation [1].

Implantation itself carries a periprocedural risk that has fallen substantially since PROTECT AF. Figure 4 traces the all-complications safety-event rate within the Watchman device family specifically, from 8.7% in PROTECT AF, to 4.5% in PREVAIL, to 2.5% in the Watchman 2.5 comparator arm of Amulet IDE, to 2.3% in CHAMPION-AF's Watchman FLX arm [4,5,9,10]. Real-world U.S. registry data are broadly consistent with this trend: the NCDR LAAO Registry, covering 38,158 Watchman implants at 495 hospitals between 2016 and 2018, reported a 2.16% in-hospital major complication rate and 98.3% acute procedural success, at a point in the device's adoption curve comparable to the later trials rather than the first [13].

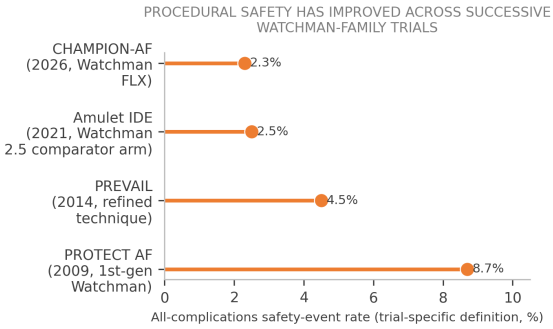

Figure 4: All-complications periprocedural safety-event rate across four successive trials within the Watchman device family, from first-generation PROTECT AF through Watchman FLX in CHAMPION-AF. Endpoint definitions are each trial's own composite of implant-related and short-term adverse events [4,5,9,10].

A successful implant does not eliminate risk at the device itself. A pooled analysis of 1,739 patients across four PROTECT AF- and PREVAIL-related studies found device-related thrombus (DRT) — clot forming on the atrial-facing surface of the device rather than being excluded by it — in 3.7% of patients, and DRT was independently associated with a more than three-fold higher rate of subsequent stroke or systemic embolism (adjusted rate ratio 3.55; 7.46 versus 1.78 events per 100 patient-years) [14]. DRT is uncommon but not negligible, typically prompts a return to anticoagulation once detected, and means that LAAO, even when successful, is not a risk-free alternative to anticoagulation but a different risk profile that trades a systemic bleeding risk for a smaller, localized, device-related one.

The honest complication: two trials against modern DOAC therapy, opposite headline results

Every trial described so far compared LAAO against warfarin, against another device, or against a DOAC in a selected high-bleeding-risk or post-ablation subgroup. The comparison clinicians most need — a well-powered trial of LAAO against a modern DOAC in a general atrial-fibrillation population — did not exist until March 2026, when two such trials reported topline results within roughly two weeks of each other and reached opposite conclusions. CHAMPION-AF, an industry-funded, 3,000-patient trial using a single modern device (Watchman FLX) at predominantly high-volume U.S. centers, met noninferiority on its primary composite of cardiovascular death, stroke or systemic embolism (5.7% LAAO versus 4.8% DOAC), and reported markedly less non-procedural major or clinically relevant bleeding with LAAO than DOAC therapy, 10.9% versus 19.0%; combined bleeding including procedural events was similar between arms, 5.9% versus 6.4% [10]. Figure 5 sets out that bleeding result in full.

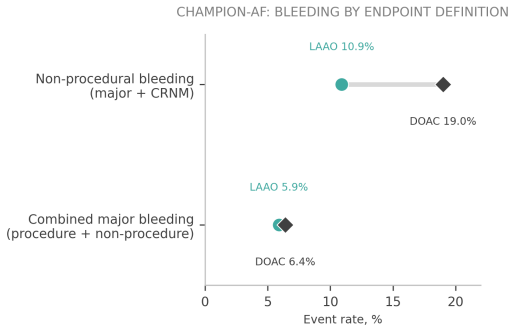

Figure 5: CHAMPION-AF bleeding results by endpoint definition: LAAO showed substantially less non-procedural bleeding than DOAC therapy, while combined bleeding including procedure-related events was similar between arms [10].

CLOSURE-AF, reported within days of CHAMPION-AF, asked a closely related question in a different way: 912 patients at 42 German centers, publicly funded through the German Centre for Cardiovascular Research, randomized to LAAO using a mix of devices or to continued medical therapy, in an older and more bleeding-prone population than CHAMPION-AF's. Over a median three years of follow-up, LAAO did not meet noninferiority on the primary composite of stroke, systemic embolism, cardiovascular or unexplained death, or major bleeding: 16.8 versus 13.3 events per 100 patient-years, driven substantially by a higher cardiovascular or unexplained death rate with LAAO (9.5 versus 7.7 per 100 patient-years), while stroke rates themselves were essentially identical between arms [11]. Table 2 sets these two trials directly side by side.

Feature	CHAMPION-AF	CLOSURE-AF
Funding	Industry (device manufacturer)	Public (national research funding)
Device protocol	Single device (Watchman FLX)	Mixed devices
Population	General AF, n=3,000, predominantly U.S. centers	Older, more bleeding-prone, n=912, German centers
Primary result	Noninferiority met	Noninferiority not met
Notable driver	Large bleeding reduction with LAAO	Higher cardiovascular death rate with LAAO

Table 2: CHAMPION-AF and CLOSURE-AF, reported within roughly two weeks of each other in March 2026, asked closely related questions in different populations, with different devices and different funding sources, and reached opposite headline conclusions [10,11].

An editorial published alongside these results attributed the divergence to design rather than to either trial being wrong: an industry-run, single-device trial in a higher-volume, U.S.-weighted population produced a favorable result, while a publicly funded, multi-device trial in an older, more bleeding-prone European population, with more variable real-world operator experience, did not [15]. Neither trial's full peer-reviewed dataset was available at the time of writing; both are discussed here on the basis of their topline announcements.

Where guidelines currently stand, and why a preference-sensitive framing fits

Current guidance already distinguishes between two populations that are easy to conflate in headline device-versus-DOAC comparisons. The 2023 American College of Cardiology/American Heart Association/American College of Chest Physicians/Heart Rhythm Society atrial fibrillation guideline gives percutaneous LAAO a Class 2a recommendation, meaning it is reasonable, specifically for patients at moderate-to-high thromboembolic risk who have a genuine contraindication to long-term anticoagulation, an upgrade from the more cautious Class 2b recommendation in the prior focused update [2]. For patients who could take a DOAC but carry a high bleeding risk on it, and for whom PRAGUE-17 is the closest matching trial, the same guideline gives LAAO a more cautious Class 2b recommendation, positioning it as an alternative rather than a default. The 2024 European Society of Cardiology atrial fibrillation guideline is similarly cautious, giving percutaneous LAAO a Class 2b recommendation and explicitly citing, at the time it was written, a lack of solid randomized-trial data against modern DOAC therapy in a general population — the exact gap CHAMPION-AF and CLOSURE-AF were designed to fill, and which their divergent results have not yet resolved [16].

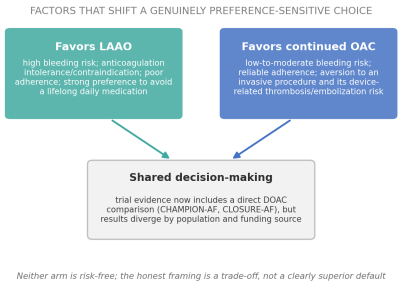

Figure 6: Factors that shift a genuinely preference-sensitive choice between LAAO and continued oral anticoagulation, converging on shared decision-making given that trial evidence now includes a direct DOAC comparison but with diverging results by population and funding source.

Neither guideline treats "patient could take a DOAC but would prefer not to" the same way as "patient cannot safely take a DOAC at all," and the two trials reported in March 2026, taken together rather than separately, support that distinction rather than undermining it. This is precisely the kind of decision that structured shared decision-making frameworks were designed for: a choice between two reasonable, evidence-supported options whose relative merits genuinely depend on an individual patient's bleeding risk, ability to adhere to daily medication, and personal weighting of a one-time procedural risk against an ongoing pharmacological one. The widely used "three-talk" model of shared decision-making — choice talk, option talk, and decision talk — was developed for exactly this kind of preference-sensitive scenario, where guidelines can bound the reasonable options but cannot select the correct one for a given patient [17]. Figure 6 sets out the factors that characteristically push a given patient toward one option or the other.

Discussion

Fifteen years of trials establish that percutaneous LAAO is noninferior to warfarin for stroke prevention, carries a durable reduction in hemorrhagic stroke and bleeding, and has become considerably safer to implant as devices and operator experience have matured [4-6,9,13]. What that evidence base did not establish until very recently was how LAAO compares against the anticoagulant most patients are actually offered today. CHAMPION-AF and CLOSURE-AF answer that question in opposite directions, and the honest response is not to declare one correct and the other flawed, but to notice they were never quite the same trial: different devices, different funding, and, most importantly, different populations, with CLOSURE-AF's more bleeding-prone and older cohort plausibly shifting the balance against a procedure that itself carries a small periprocedural hazard and an ongoing device-related thrombus risk [10,11,14,15].

That context-dependency is itself the finding worth acting on. Guidelines already encode something close to it, reserving a stronger recommendation for patients who cannot safely anticoagulate at all and a more cautious one for patients

weighing LAAO against a tolerable DOAC [2,16]. The March 2026 results sharpen rather than resolve that distinction: "LAAO versus modern DOAC therapy" has no single population-wide answer, which argues for structuring the individual conversation around a patient's own bleeding risk, adherence and preferences rather than around one headline trial result [17].

Study limitations

This is a narrative synthesis, not a systematic review, and the search followed no pre-registered protocol. CHAMPION-AF and CLOSURE-AF are reported here from topline announcements; the full peer-reviewed manuscripts were not available at the time of writing and may refine the comparison in Table 2 [10,11,15]. The trials compared throughout differ substantially in population, era, device and endpoint definition, a difference kept explicit in Table 1 and Figure 2 rather than collapsed into a single ranked comparison. No attempt is made here to adjudicate why CLOSURE-AF's cardiovascular death rate was higher with LAAO; that awaits the full published analysis.

Conclusion

Percutaneous left atrial appendage occlusion has accumulated fifteen years of randomized evidence supporting its use as an alternative to anticoagulation in appropriately selected patients, with procedural safety that has improved considerably across device generations [4,5,9,13]. The first direct, well-powered comparisons against modern DOAC therapy in a general atrial-fibrillation population, reported within days of each other in March 2026, reached opposite conclusions, and the most defensible reading of that divergence is that population, device protocol and funding source each mattered rather than that either trial was simply wrong [10,11]. Current guidelines already draw a sharper distinction than either headline result alone suggests, favoring LAAO more strongly where anticoagulation is truly contraindicated and more cautiously where it is merely undesired [2,16]. For that latter, larger group of patients, the accurate message is that this is a genuinely preference-sensitive decision between two reasonable options, best made through structured shared decision-making rather than by extrapolating a single trial's headline result to every patient [17].

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