

Direct Oral Anticoagulants vs Vitamin K Antagonists in Atrial Fibrillation Patients with Bioprosthetic Aortic Valves: A Meta-Analysis of 12 Studies

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Introduction

Atrial fibrillation (AF) is common after bioprosthetic aortic valve replacement (BAVR), including transcatheter aortic valve replacement (TAVR), and requires long-term anticoagulation to prevent stroke and systemic embolism. Selecting the optimal agent remains challenging because patients differ in their risk profiles and the available evidence continues to evolve. Clinicians must balance protection from thromboembolic events with the risk of bleeding, which contributes to uncertainty in decision making.

Existing studies comparing direct oral anticoagulants (DOACs) with vitamin K antagonists (VKAs) in AF patients after TAVR are limited and often yield inconsistent results. Prior meta-analyses by Yan et al¹ and Oliveri et al² included mixed valve types, variable patient populations, and heterogeneous anticoagulation strategies. These methodological differences have produced conflicting findings, including modest mortality differences in some analyses but inconsistent effects on stroke and bleeding.

Although DOAC use has increased in clinical practice, there remains no clear consensus on the safest and most effective anticoagulant strategy for AF patients following bioprosthetic AVR. The predominance of observational evidence and the limited number of randomized trials focused on this population contribute to continued uncertainty. Broader reviews of DOAC use in valvular heart disease further emphasize the need for clearer guidance.³

Mechanical heart valves require warfarin based on established guidelines,⁴ so these patients were excluded from our analysis. Focusing on bioprosthetic valves allows a more accurate assessment of anticoagulation strategies in the population where ambiguity persists.

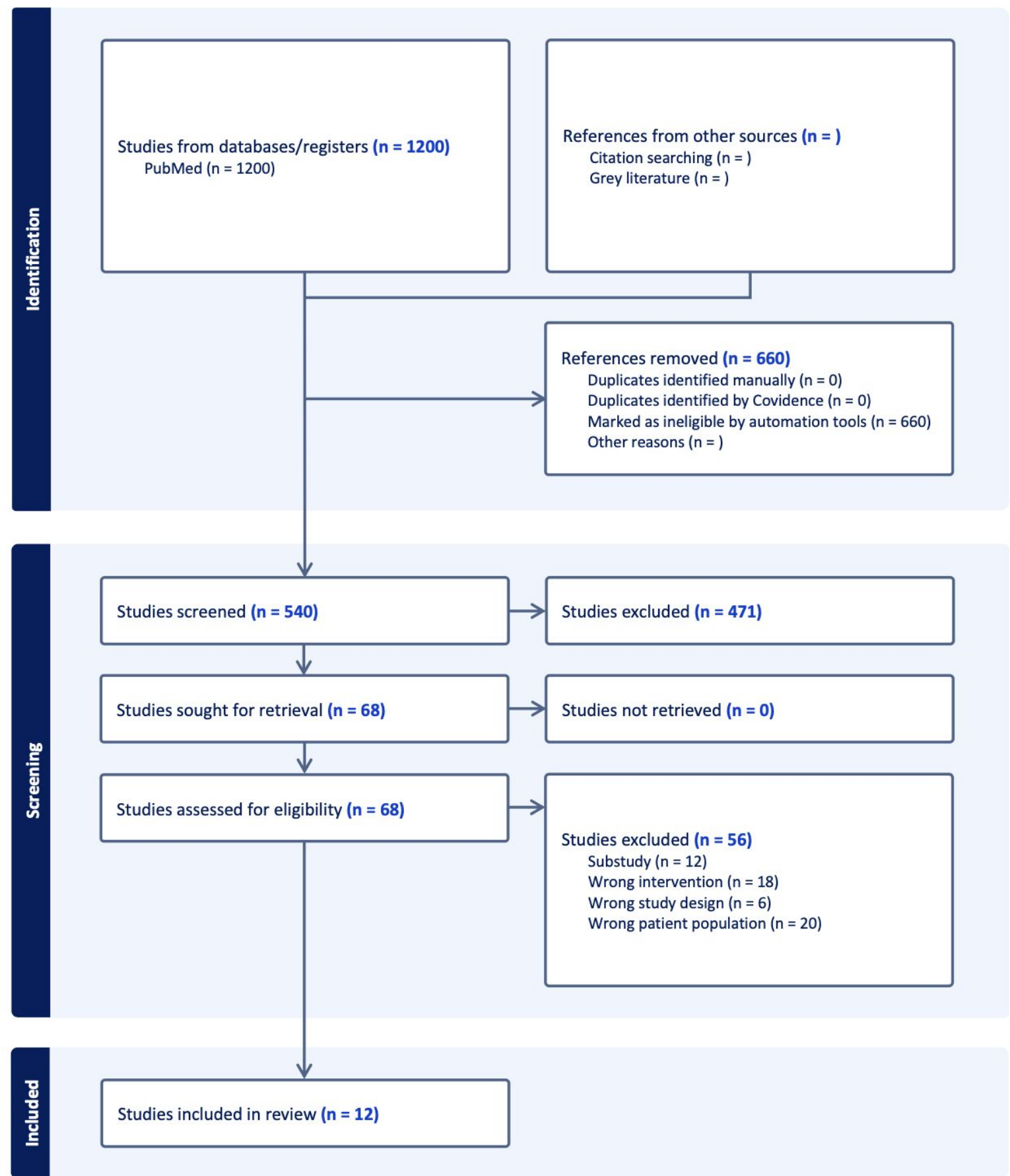
This study addresses an important gap in the literature by synthesizing contemporary randomized and observational evidence to directly compare DOACs and VKAs in AF patients following bioprosthetic AVR.

Methods

We conducted a systematic review and meta-analysis comparing DOACs vs. VKAs in AF patients post-bioprosthetic AVR.

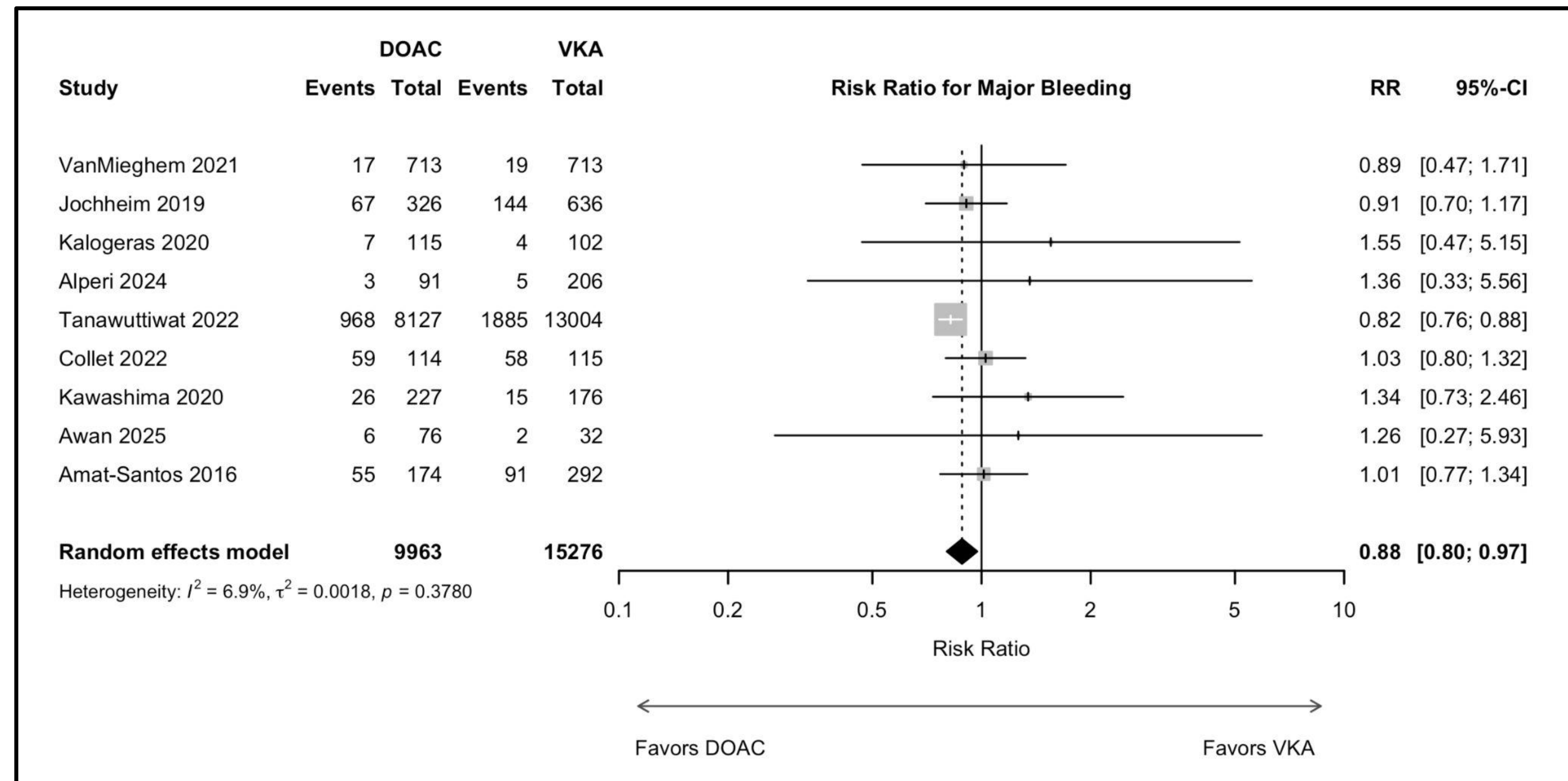
- Primary outcomes: all-cause mortality, stroke, major bleeding
- PubMed search (1,200 records) screened in Covidence (PRISMA compliant)
- Final inclusion: 12 studies (Figure 1)
 - 2 randomized controlled trials
 - 10 observational studies (prospective and retrospective cohorts)
- Excluded: mechanical valves, mitral valve replacements without stratified outcomes, mixed valve cohorts without AF-specific or aortic-specific data
- Extracted data: event-level outcomes and time-to-event outcomes
- Statistical approach:
 - Random-effects models (R version 4.5.1)
 - Risk ratios using DerSimonian–Laird
 - Hazard ratios using inverse variance weighting
 - Heterogeneity assessed with I²
- Risk of bias: Cochrane RoB 2.0 for RCTs and Newcastle–Ottawa Scale for cohort studies

PRISMA Diagram (Figure 1)

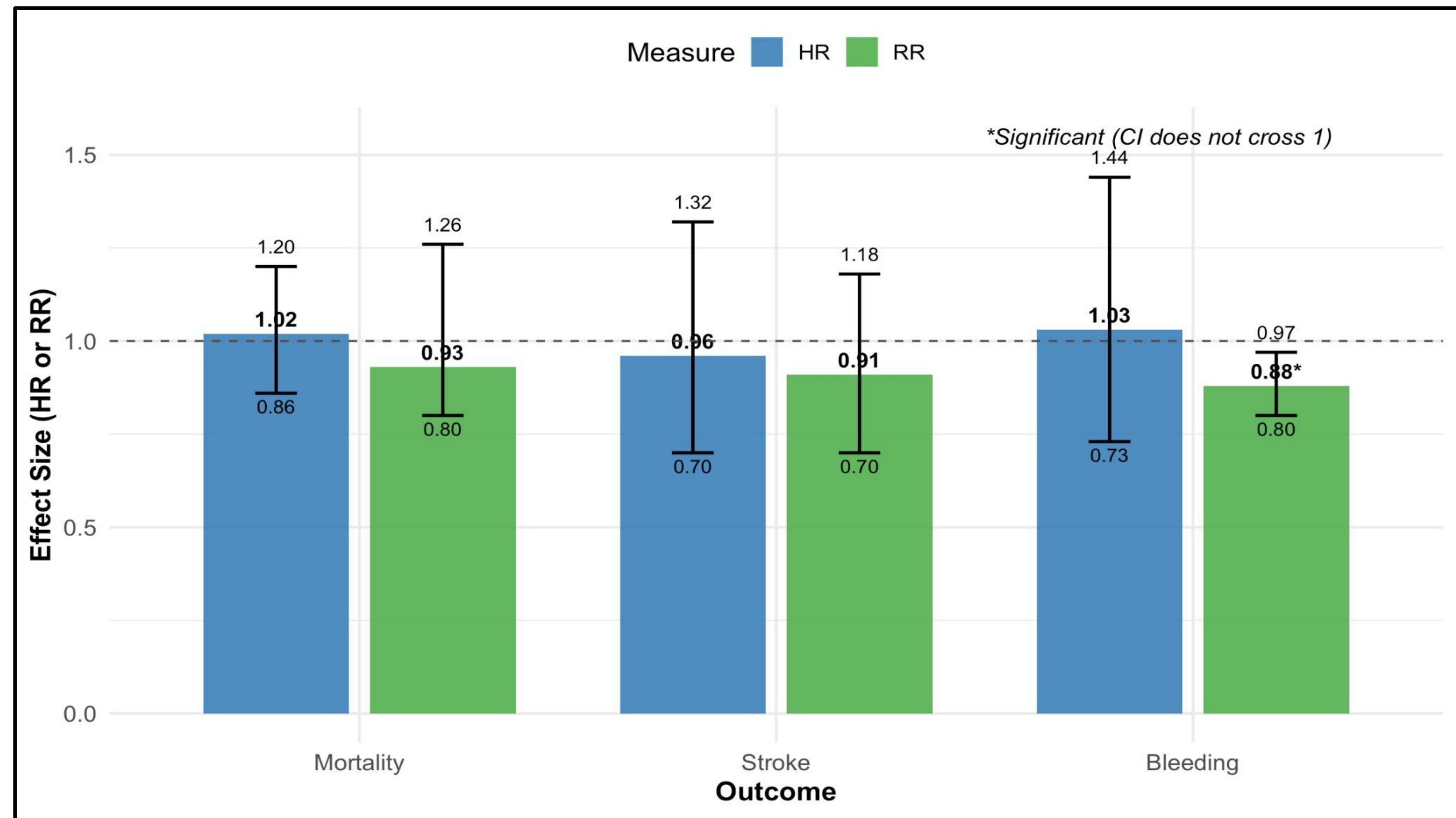


Results

Bleeding Risk by Anticoagulant Class (Figure 2)



Effect of DOACs vs VKAs Across Clinical Outcomes (Figure 3)



Study Characteristics (Figure 4)

Twelve studies were included (N = 36,112; DOAC = 13,030; VKA = 23,082, Figure 4).

Major bleeding

- DOACs were associated with a significantly lower risk of major bleeding than VKAs (Figure 2)
- RR = 0.88 (95% CI 0.80–0.97)
- Hazard ratio was not significant: HR ≈ 1.03 (95% CI 0.73–1.44)

All-cause mortality

- No significant difference between DOACs and VKAs (Figure 3).
- RR ≈ 0.93
- HR ≈ 1.02 (95% CI 0.86–1.20)

Stroke

- No significant difference between groups was seen (Figure 3).
- RR ≈ 0.91
- HR ≈ 0.96 (95% CI 0.70–1.32)

Author	Year	Location	Study Design	N (DOAC)	N(VKA)	Follow Up (months)	Outcomes Reported	HR/RR Reported	Bias Risk
VanMieghem	2021	North America, Europe	Randomized Controlled Trial	713	712	17.8	Mortality, Stroke, Bleeding	HR, RR	Low
Jochheim	2019	Germany	Prospective	326	636	12	Mortality, Stroke, Bleeding	HR, RR	Moderate
Butt	2021	Germany	Prospective	1078	219	14.5	Mortality, Stroke, Bleeding	HR	Low
Kalogeras	2020	UK, Greece, Japan	Retrospective	115	102	15.1	Mortality, Bleeding	HR, RR	Moderate
Alperi	2024	Spain	Prospective	91	206	12	Stroke, Bleeding	HR	Low
Tanawuttiwat	2022	United States	Retrospective	8127	13004	12	Mortality, Stroke, Bleeding	HR, RR	Low
Collet	2022	North America, Europe	Randomized Controlled Trial	114	115	12	Mortality, Stroke, Bleeding	HR, RR	Low
Kawashima	2020	UK, Greece, Japan	Retrospective	227	176	18.7	Mortality, Stroke, Bleeding	HR, RR	Moderate
Seeger	2017	Germany	Prospective	141	131	12	Mortality, Stroke	HR	Low
Mannacio	2022	United States	Retrospective	76	32	49.5	Stroke, Bleeding	HR	Low
Awan	2025	Saudi Arabia	Retrospective	76	32	27	Mortality, Stroke, Bleeding	HR, RR	Moderate
Amat-Santos	2016	France	Prospective	174	247	3	Mortality, Stroke, Bleeding	HR, RR	Low

Discussion

This meta-analysis of 12 studies including 27,798 patients with AF following bioprosthetic AVR found that DOACs significantly reduced major bleeding compared with VKAs, while mortality and stroke outcomes were similar. These findings build upon previous observational and randomized studies, including POPular-TAVI⁵ and ATLANTIS,⁶ which demonstrated comparable thromboembolic outcomes but variable bleeding profiles.

By evaluating only AF patients after bioprosthetic AVR, this analysis provides focused insight into a population that has historically lacked clear guidance on anticoagulation. Concerns regarding DOAC use have persisted, particularly after the GALILEO trial,⁷ which reported adverse outcomes with rivaroxaban in certain TAVR populations. However, the present findings do not show an increased risk of stroke or mortality with DOACs, supporting their use in carefully selected patients.

These results also point to the need to reassess current anticoagulation guidelines, which continue to favor VKAs despite accumulating evidence supporting the safety and practicality of DOACs in AF patients with bioprosthetic valves.⁴ The alignment of outcomes across multiple systematic reviews¹² further reinforces the growing role of DOACs in this setting.

References

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