# Effectiveness and Safety of Direct Oral Anticoagulants Versus Warfarin in Patients with Atrial Fibrillation and Cancer: A Target Trial Emulation from SEER-Medicare Database

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## INTRODUCTION

- Direct oral anticoagulants (DOACs) are preferred over warfarin in patients with atrial fibrillation (AFib). However, their safety and effectiveness in patients with AFib and cancer are inconclusive.
- In this study, we implemented a target trial framework to compare the effectiveness and safety profiles of DOACs and warfarin among newly diagnosed AFib patients with cancer.

## METHODS

- Study design and data source: retrospective, population-based cohort study using the SEER-Medicare database 2011-2019
- Study components of emulation are described in **Table 1**

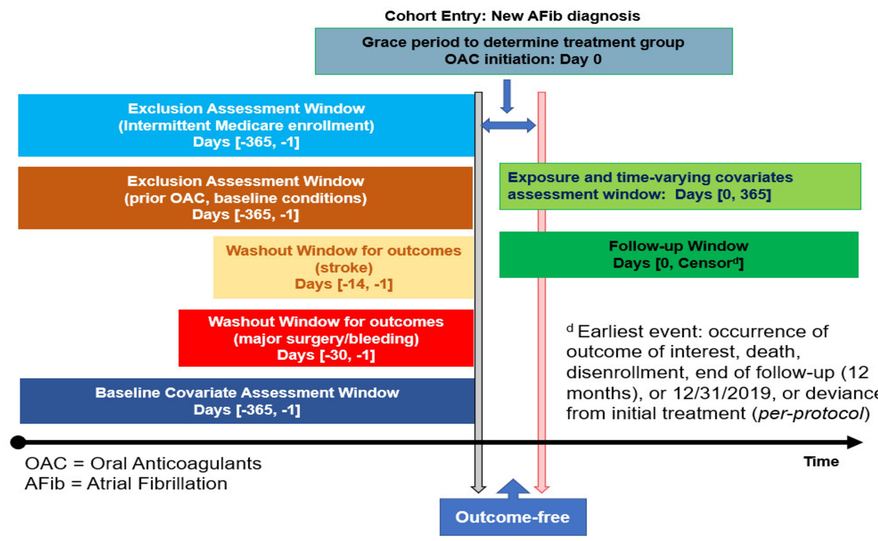


**Figure 1**. Study design and timeline

- Confounder: a set of 37 time-fixed baseline covariates and 7 time-varying covariates.
- Statistical analysis:
  - Inverse probability treatment weights and inverse probability censoring weights were used to adjust imbalanced patient and disease characteristics and loss to follow-up between the two groups.
  - Weighted pooled logistic regression were used to estimate treatment effect with hazard ratios (HRs) and 95% confidence interval (95% CIs).
  - Subgroup analyses: cancer type (breast, lung, prostate), cancer status at baseline (active, history), cancer stage (local, regional, and distant), and tumor grade (I, II, and III).
  - Sensitivity analyses: (1) 6-month grace period, (2) including individuals with all levels of baseline $CHA_2DS_2$-VASc score, (3) 36-month follow-up, (4) removing patients with metastatic cancer at baseline, (5) removing patients with thrombocytopenia, (6) truncated stabilized weights at 95th percentile.

## ADDITIONAL INFORMATION

Bang Truong is currently an AbbVie employee and received AbbVie travel fund for ISPOR 2024. This study was conducted before his employment. The authors did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Table 1**. Protocol for a target trial and emulation procedure using the SEER-Medicare database

| Protocol component | Hypothetical target trial | Emulation in SEER-Medicare |
|---|---|---|
| **Eligibility criteria** | ▪ Patients aged ≥66, newly diagnosed with non-valvular AFib within 12 months before enrollment and history or active breast, lung, prostate cancer between 01/01/2012 and 12/31/2019, continuously enrolled in Medicare part A, B, D, and without Medicare Advantage for 12 months before the diagnosis.<br>▪ Baseline $CHA_2DS_2$-VASc score ≥2<br>▪ No history of OAC use; no history of mitral valve disease, heart valve repair or replacement, deep vein thrombosis, pulmonary embolism, or joint replacement<br>▪ Without any diagnosis of stroke within the previous 14 days<br>▪ Without any conditions associated with an increased risk of bleeding, including major surgery within the previous month, history of intracranial, intraocular, spinal, retroperitoneal or atraumatic intra-articular bleeding, gastrointestinal hemorrhage within the last 30 days<br>▪ Without renal impairment stage 5 or end-stage renal diseases within the last 12 months | Same as target trial |
| **Treatment strategies** | Eligible individuals are randomly assigned to warfarin or DOACs within a grace period of 3 months. | Participants are randomly assigned conditioning on baseline covariates |
| **Follow-up** | The follow-up of target trials starts when the patients initiated their treatment within a grace period. End of follow-up = the occurrence of a specific study outcome, the end of administrative censoring (12 months after baseline), death, loss to follow-up, or December 31, 2019, whichever came first. | Same as target trial |
| **Outcomes** | Primary outcomes: ischemic stroke, major bleeding<br>Secondary outcomes: VTE, intracranial bleeding, gastrointestinal bleeding, and non-critical site bleeding | Same as target trial, identified by diagnosis and procedure codes |
| **Causal contrast** | Intention-to-treat effect, per-protocol effect | Observational analog of intention-to-treat and per-protocol effect |

## RESULTS

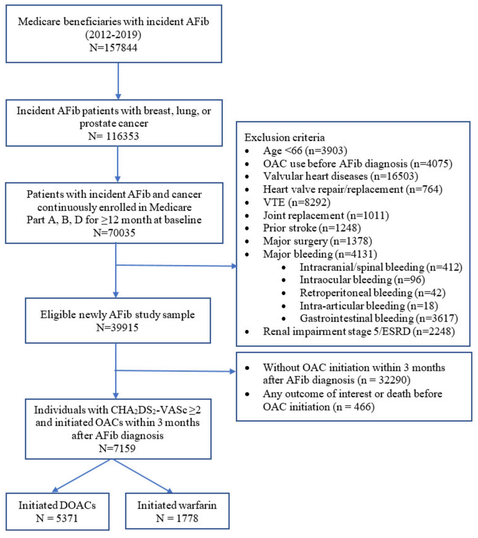


**Figure 2**. Study sample flowchart

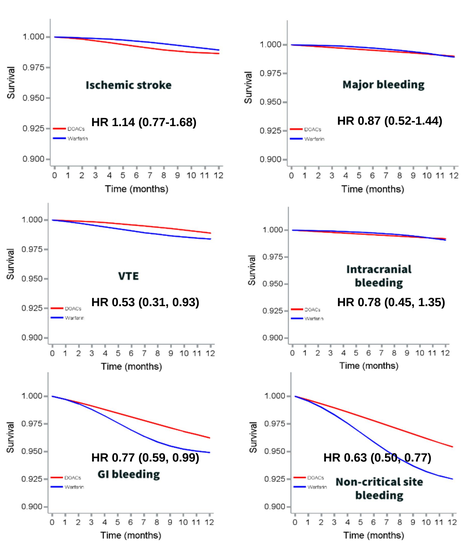


**Figure 3**. Weighted survival curves for ITT analysis

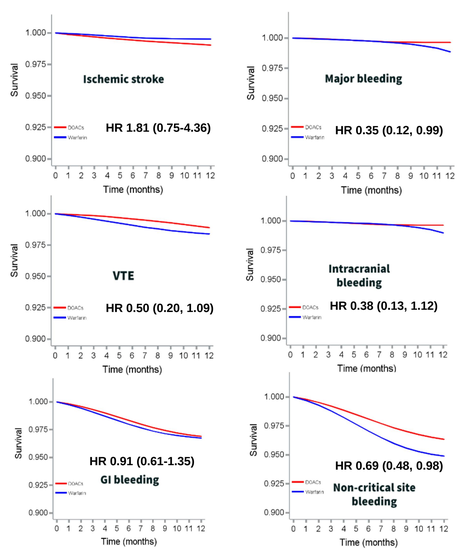


**Figure 4**. Weighted survival curves for PP analysis

- Study sample include 5371 DOAC initiators (3264 apixaban, 314 dabigatran, 1786 rivaroxaban, 7 edoxaban) and 1788 warfarin initiators
- DOACs initiators had a higher socio-economic and lower comorbidity burden compared to those initiated warfarin. Patients with breast or prostate cancer were more likely to receive DOACs while more patients with lung cancer were on warfarin.
- Sensitivity and subgroup analyses: Results remained consistent across subgroups and robust in sensitivity analyses.

## CONCLUSION

DOACs are safe and effective alternatives to warfarin in the management of patients with AFib and cancer.