To Treat or Not to Treat: Comparing Oral Anticoagulant Outcomes among U.S. Nursing Home Residents with Atrial Fibrillation

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BACKGROUND

- Anticoagulants are effective in reducing the risk of cardioembolic stroke due to atrial fibrillation but increase bleeding risk
- Net clinical benefits of oral anticoagulants (OACs) may diminish among nursing home residents with advanced age and complicated clinical comorbidities
- Evidence on the effectiveness and safety of oral anticoagulants (OACs) in older nursing home residents with atrial fibrillation (AF) is limited, as this population is excluded from most clinical trials

OBJECTIVES

To compare the effectiveness and safety of OAC users versus OAC non-users among nursing home residents with atrial fibrillation and to compare the effectiveness and safety of OAC use versus non-use by OAC class (warfarin and direct-acting oral anticoagulants (DOACs)).

METHODS

- **Data sources (2011-2016):**
  - Minimum Data Set (MDS) 3.0
  - Master Beneficiary Summary file, Medicare Part D, Medicare Part A (MedPAR)
- **Study design**: Retrospective cohort study. The index date for new OAC users was the first OAC prescription date since July 1, 2011 and the index date for OAC non-users (no use in prior 6 months) was a randomly selected MDS assessment date during July 1, 2011 and December 31, 2016
- **Study population**
  - The study included 517,660 records of Medicare fee-for-service beneficiaries (each resident could contribute up to one record each to the exposed and unexposed groups).
  - Aged ≥ 65 years old; non-comatose; not on hospice; alive on the index date.
  - Continuously enrolled in Medicare fee-for-service Parts A and Part D during 6 months pre-index
  - Diagnosed with atrial fibrillation or flutter on Part A or MDS during 12 months prior to index date;
- **Study outcomes (time from index to the earliest Part A hospitalization claim for the following):**
  - Primary effectiveness outcome: ischemic stroke or systemic embolism
  - Primary safety outcome: intracranial bleeding or extracranial bleeding
  - Secondary outcomes:
    - Death
    - Net clinical benefit outcome (1): primary effectiveness or primary safety outcome
    - Net clinical+ death outcome (2): primary effectiveness, primary safety, or death
- **Covariates**
  - Demographic information, clinical conditions including CHA_2DS_2-VASc ischemic stroke risk score and ATRIA bleeding risk score components); other medications used
- **Instrumental Variable: Facility Prescribing Preference**
  - Mixed effect logistic regression estimated facility level prescribing preference (random facility effect) for OACs as an instrumental variable, while adjusting for resident characteristics using propensity scores, and the instrumental variable was ranked in quartiles
- **Statistical Analysis**
  1. Cox proportional hazards models estimated the associations between OAC use (overall and stratified by OAC class) and time to primary and secondary outcomes
  2. Two-stage logistic and Cox proportional hazards models estimated associations between OAC use and study outcomes among residents in the top and bottom of quartiles of the instrument

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SUMMARY OF RESULTS

- Among 512,467 residents, 9.4% were OAC users. The median age among OAC users was 83 years and that of OAC non-users was 87 years. The mean $CHADS_2$-VASc score was 5 in both groups.
- Among OAC users, the incidence of the primary effectiveness outcome was 0.86 per 100 person-years and the incidence of primary safety outcome was 2.31 per 100 person-years. Among OAC non-users, the incidence of primary effectiveness outcome was 1.73 per 100 person-years and that of the primary safety outcome was 1.75 per 100 person-years.
- OAC use was associated with a lower risk of the primary effectiveness outcome (aHR: 0,67; 95% confidence interval (CI): 0.61- 0.74), higher risk of the primary safety outcome (aHR: 1.68; 95% CI: 1.57- 1.80) and a lower risk of the net clinical+death outcome (aHR: 0.60; 95% CI; 0.59- 0.61).
- The direction and magnitude of associations from instrumental variable analyses were generally aligned with Cox modeling results for the effectiveness, safety, and mortality outcomes.
- DOAC users had lower rates of the net clinical benefit outcome versus non-users (aHR: 0.89; 95% CI: 0.81-0.89) while warfarin did not (aHR: 1.03; 95% CI: 0.97-1.10). Both drug classes had lower rates of stroke and death compared with non-users.

Table 1. Characteristics of nursing home residents with atrial fibrillation by to OAC use (N=517,660)

	OAC users n=48,093	OAC non-users n=469,567
Demographics		
Age in years, median (Q1, Q3)	83 (76, 89)	87 (80, 92)
Women, %	67.6	67.4
BMI, median (Q1, Q3)	27.1 (23.2, 32.3)	24.6 (21.1, 28.9)
Comorbidities		
Heart failure, %	40.7	38.2
Cancer, %	3.9	7.6
Diabetes Mellitus, %	42.4	35.7
Hypertension, %	81.6	85.7
Anemia, %	32.0	40.4
Venous thromboembolism, %	4.9	1.8
Peripheral vascular disease, %	12.0	13.4
Coronary artery disease, %	24.7	30.3
Acute myocardial infarction, %	3.8	2.1
Stroke, %	24.3	19.4
End-Stage renal disease, %	10.4	15.3
Liver disease, %	2.8	2.3
Alzheimer's disease and related dementias, %	50.3	60.4
2+ hospital admissions in prior year, %	46.5	24.4
Moderate to severe cognitive impairment, %	32.3	48.3
High or moderate level of dependency in ADL, %	57.4	65.8
Select prescription medications, %		
NSAIDs	15.9	13.1
Antiplatelet	19.5	17.9
Statin	49.1	39.7
CHA_2DS_2-Vasc Score (≥ 5), %	61.5	59.0
ATRIA Bleeding Risk Score high risk (5-10), %	46.8	48.4
Using more than 10 medications, %	68.8	57.1

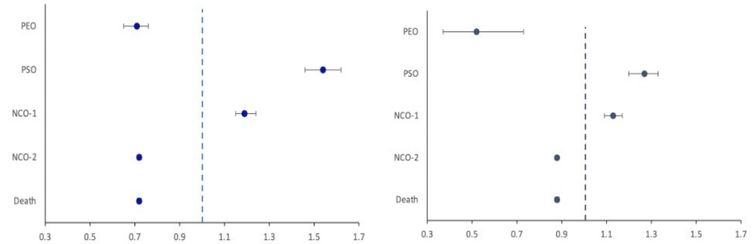
Abbreviations: activities of daily living (ADL), nursing home (NH), body mass index(BMI), non-steroidal anti-inflammatory drugs (NSAIDs)

Table 2. Incidence Rates Per 100 Person-Years for Primary and Secondary Outcomes Overall between OAC users and OAC non-users (N=517,660)

	All OAC users	OAC non-users
Effectiveness	0.86 (0.78- 0.95)	1.73 (1.69- 1.77)
Safety	2.31 (2.18- 2.45)	1.75 (1.71- 1.80)
Net clinical	3.19 (3.03- 3.35)	3.50 (3.44- 3.56)
Death	43.57 (42.99- 44.15)	77.94 (77.66- 7823)
Net clinical + death	44.68 (44.09- 45.28)	79.45 (79.16- 79.74)

*** N represented the number of records**

Figure 1. Adjusted Hazard Ratios[a] of Primary and Secondary Outcomes For OAC Users versus Non-Users using Conventional (Left) and Two-Stage IV Modeling (Right)[*]



[a] Hazard Ratio were adjusted by age, sex, race/ethnicity, BMI, ADL, cognitive impairment level, rejection of care, history of falling, cancer, Alzheimer's disease and related dementia, number of hospital admission, CHA_2DS_2-Vasc Score ATRIA score, use of NASIDs, use of antiplatelet, use of statin

Table 3. Prevalence of outcomes among warfarin and DOAC users and Incidence Rates Per 100 Person-Years for Primary and Secondary Outcomes among Warfarin Users versus OAC Non-users and DOAC Users versus OAC Non-users (N [warfarin]=500,462; N[DOAC]=486,765)

	IR (warfarin users vs non-users)	IR (DOAC users vs non-users)	Warfarin aHR	DOAC aHR
PEO	0.86 (0.77- 0.97)	0.86 (0.72- 1.02)	0.70 (0.62- 0.78)	0.62 (0.52- 0.74)
PSO	2.42 (2.26- 2.59)	2.08 (1.86- 2.32)	1.78 (1.65- 1.93)	1.40 (1.25- 1.58)
Net clinical	3.30 (3.11- 3.49)	2.95 (2.69- 3.24)	1.03 (0.97- 1.10)	0.89 (0.81- 0.98)
Death	43.89 (43.20- 44.59)	42.84 (41.81- 43.89)	0.69 (0.68- 0.70)	0.68 (0.67- 0.70)
Net clinical +death	45.13 (44.42- 45.85)	43.66 (42.62- 44.73)	0.70 (0.69- 0.71)	0.68 (0.67- 0.70)

CONCLUSIONS

- OAC use was associated with decreased risk of ischemic stroke or systemic embolism, lower rates of all-cause mortality, and increased risk of intracranial or extracranial bleeding.
- Findings were generally consistent in stratified analyses by warfarin or DOAC use, although only DOACs were associated with a lower rates of the net clinical benefit outcome for stroke and bleeding.
- Our results support a continued benefit of OAC use to prevent ischemic strokes among older residents with atrial fibrillation, while highlighting the need for a resident-centered shared decision-making process to weigh the apparent benefits against elevated risk for bleeding