

Trends and Variation in Oral Anticoagulant Choice in Patients with Atrial Fibrillation, 2010-2017

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January 23, 2018



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of PUBLIC HEALTH

Acknowledgments

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Funding

- This work is part (Aim 1) of the project “Personalized Decision Making for Oral Anticoagulant Choice in Atrial Fibrillation” supported through the Agency for Healthcare Research and Quality K01HS024737 (PI: Zhu)

Outline

- Background on atrial fibrillation and oral anticoagulants
- Study objectives
- Methods
- Results
- Conclusions
- Next steps

Atrial Fibrillation (AF)

- The most common cardiac arrhythmia, affecting over 2.7 million Americans
- Increase the risk of ischemic stroke five-fold
- AF-related stroke is more likely to cause severe disability and death than other types of stroke

Oral Anticoagulants (OACs)

- Warfarin
 - Cornerstone of stroke prevention in AF for decades
 - Limitations: a narrow therapeutic window, need for frequent monitoring and a restricted diet
- Non-vitamin K antagonist oral anticoagulants (NOACs) approved by the U.S. FDA for preventing stroke in patients with nonvalvular AF since 2010
 - Dabigatran: 10/19/2010
 - Rivaroxaban: 11/4/2011
 - Apixaban: 12/28/2012
 - Edoxaban: 1/8/2015

AHA/ACC/HRS Guideline

- The 2014 American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Rhythm Society (HRS) Guideline recommends the use of either warfarin or a NOAC for preventing stroke in AF

Prior Literature

- Younger age, male sex, white race, fewer comorbidities, lower stroke or bleeding risk, and prescription by a cardiologist have been shown to be associated with higher odds of choosing a NOAC over warfarin
- Most studies focused on dabigatran and rivaroxaban and used data from 2012 and earlier
- Few studies examined patient characteristics associated with choice among NOACs

Study Objectives

- To examine temporal trends in choice among warfarin, dabigatran, rivaroxaban, and apixaban from October 2010 through March 2017
- To examine the associations of patient demographic characteristics (e.g., age, sex) and clinical factors (e.g., ischemic stroke risk, prescribing specialty) with choice of a NOAC vs warfarin
- To examine the associations of patient demographic and clinical characteristics with choice among NOACs.

Methods

- Study design
- Data
- Eligible cohort & exclusion criteria
- Outcomes of interest
- Independent variables
- Statistical analysis

Study Design

- Retrospective, serial, cross-sectional study
- Data: OptumLabs claims data
- Sample: patients aged ≥ 18 years with nonvalvular AF who had a new fill of warfarin, dabigatran, rivaroxaban, or apixaban between October 2010 and March 2017

Data

- De-identified medical and pharmacy claims from the OptumLabs™ Data Warehouse (OLDW) in 2009-2017
- Longitudinal health information on commercial and Medicare Advantage enrollees of all ages and racial/ethnic groups from geographically diverse regions in a large, private, U.S. health plan
- Extensive service-level data for physician, hospital, and prescription drug services

Eligible Cohort & Exclusion Criteria

Initial sample: 805 104 users of an OAC between 10/2010-3/2017

- No continuous medical or pharmacy coverage at baseline: 397 622
- Not AF: 215 110
- Valvular heart disease at baseline: 13 225
- Aged <18 years at the index date: 522
- Deep vein thrombosis or pulmonary embolism at baseline: 19 297
- Total hip or knee replacement surgery within 6 weeks before the index date: 2 102
- Filled an OAC at baseline: 44 807
- Filled edoxaban: 167
- Missing values in gender and region: 65

Eligible cohort: 112 187

Outcomes of Interest

- Choice of warfarin vs a NOAC (dabigatran, rivaroxaban, or apixaban) at the index date
- Choice among the three NOACs at the index date

Independent Variables

- Patient age, sex, race/ethnicity, education status, household net worth, region of residence, comorbidity (Charlson index), ischemic stroke risk (CHA₂DS₂-VASc score), bleeding risk (HAS-BLED score), use of antiplatelets and nonsteroidal anti-inflammatory drugs (NSAIDs), prescriber specialty, calendar quarter
- CHA₂DS₂-VASc: Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes, Stroke/transient ischemic attack/thromboembolism, Vascular disease, Age 65-74 years, Sex category (female)
- HAS-BLED: Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly (≥ 65 years), Drugs/alcohol use

Statistical Analysis

- Multivariable logistic regression - choice of a NOAC vs warfarin
 - October 2010-2012 (the period prior to the FDA approval of apixaban)
 - 2013-2014 (the early period when all three NOACs were available)
 - 2015-March 2017
- Multinomial logistic regression - choice among NOACs
 - 2013-2014
 - 2015-March 2017

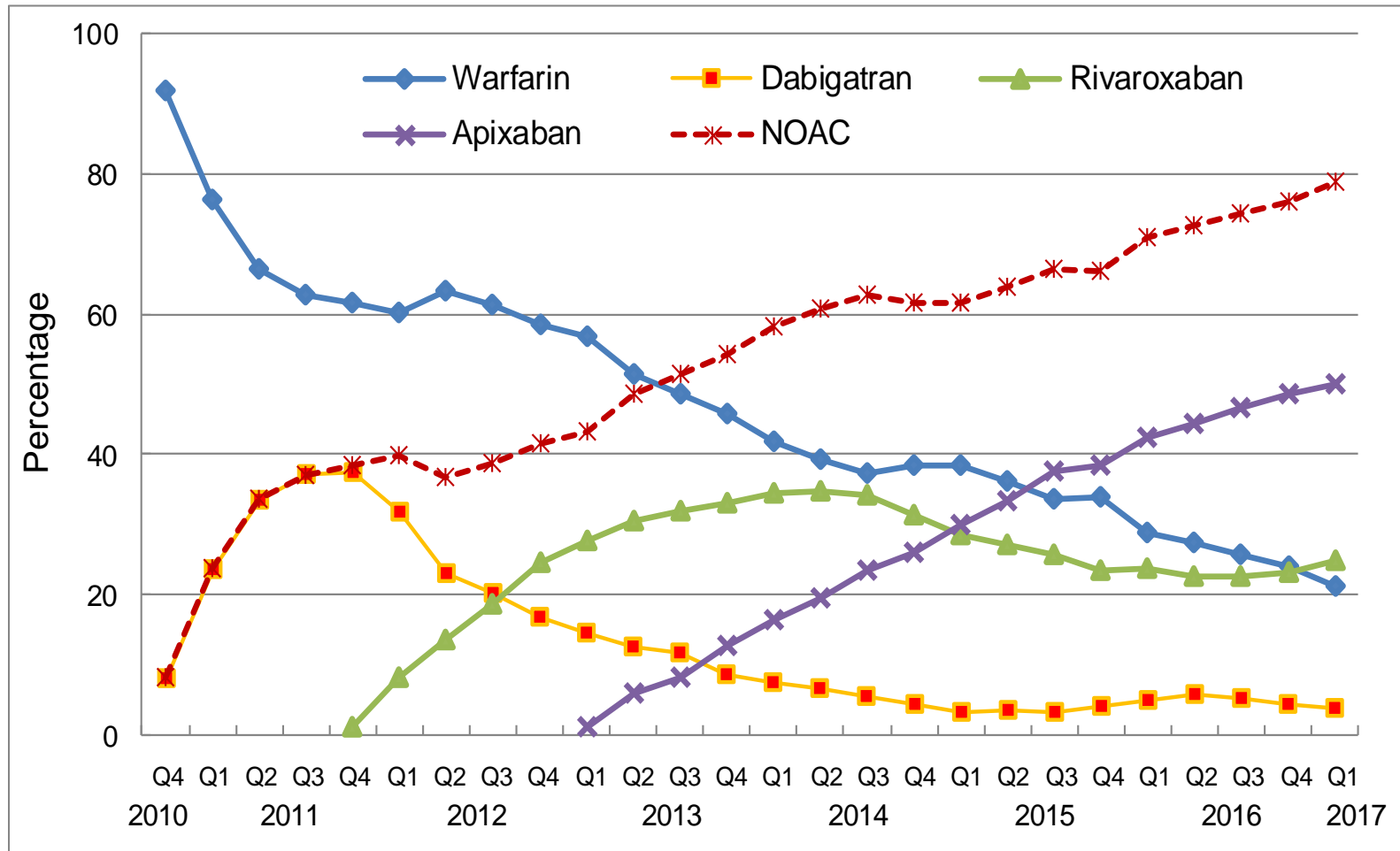
Results

- Baseline characteristics
- Quarterly trends in oral anticoagulant choice
- Factors associated with choice of NOACs vs warfarin
- Factors associated with choice among NOACs

Baseline characteristics of patients with AF by OAC choice, October 2010 to March 2017 (N=112 187)

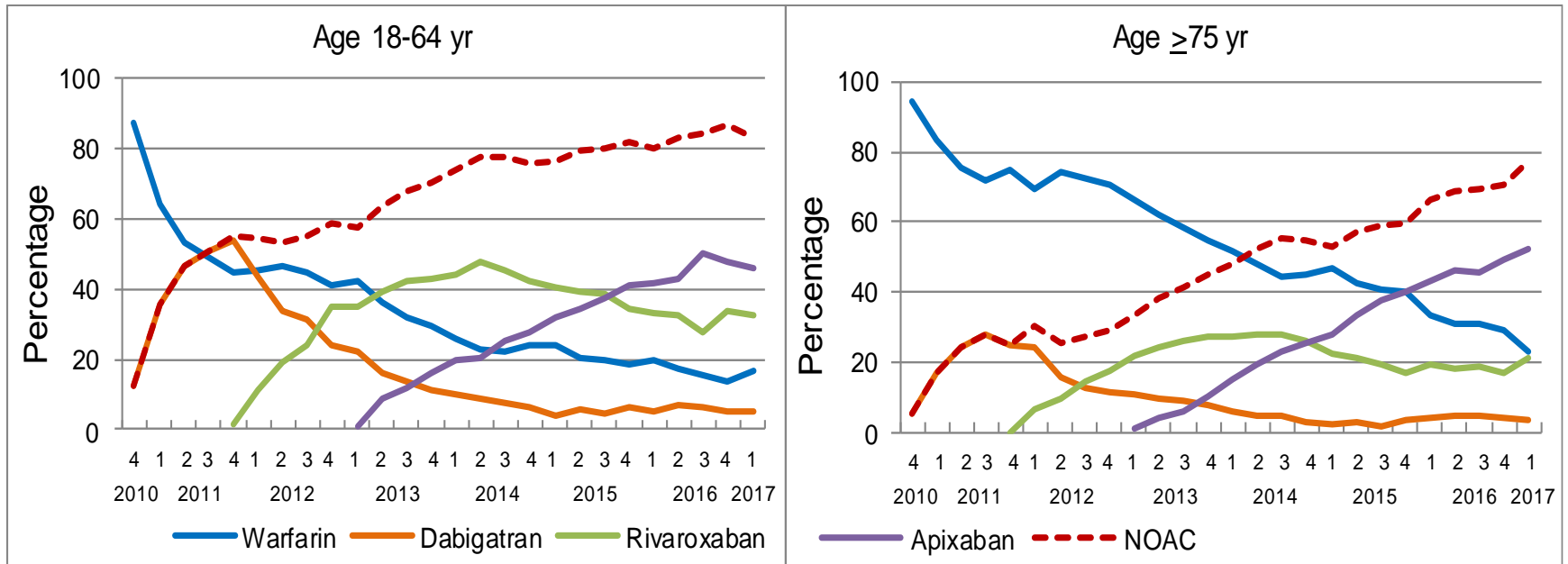
	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Total
Sample size	50,713	13 776	24 188	23 510	112 187
Age, year, mean	73.2	67.9	69.4	72.4	71.6
Charlson comorbidity index, mean	3.0	2.1	2.2	2.7	2.7
CHA ₂ DS ₂ -VASc, mean	4.3	3.4	3.5	4.1	4.0
HAS-BLED, mean	2.8	2.3	2.4	2.7	2.7
Female, %	43.5	37.2	40.1	46.8	42.7
Non-Hispanic white, %	79.7	80.8	78.9	77.0	79.1
≥ Bachelor degree, %	8.9	15.1	15.0	13.8	12.0
Household net worth ≥ \$500,000, %	19.1	25.8	25.8	24.5	22.5
Cardiologist, %	28.2	53.0	46.9	45.3	38.9
Antiplatelets, %	13.4	12.6	12.6	14.7	13.4
NSAIDs, %	18.3	22.0	22.1	21.3	20.2

Quarterly trends in oral anticoagulant choice for atrial fibrillation, from 2010Q4 to 2017Q1



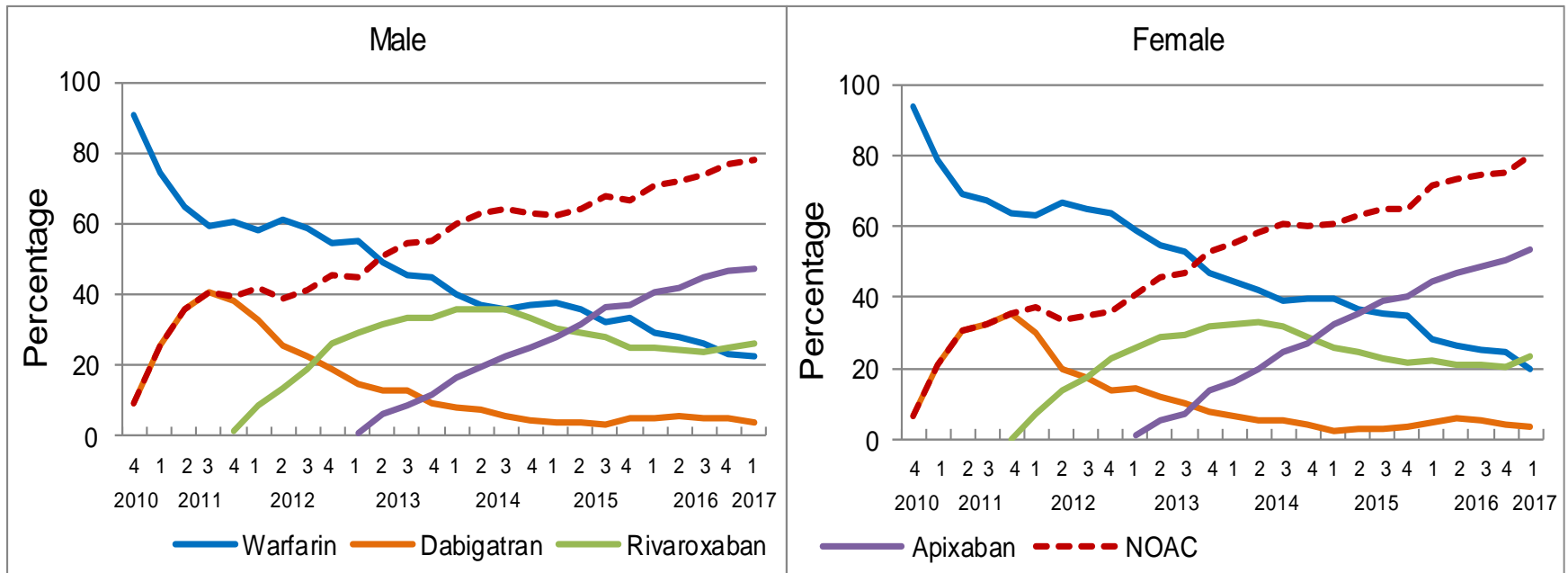
Y-axis refers to the percentage of incident OAC users prescribed a specific OAC

Quarterly trends in oral anticoagulant choice for atrial fibrillation by age, from 2010Q4 to 2017Q1



Y-axis refers to the percentage of incident OAC users prescribed a specific OAC

Quarterly trends in oral anticoagulant choice for atrial fibrillation by sex, from 2010Q4 to 2017Q1



Y-axis refers to the percentage of incident OAC users prescribed a specific OAC

Factors associated with choice of NOACs vs warfarin for incident OAC users

	2010Q4-2012	2013-2014	2015-2017Q1
Age (ref: 18-64 year)			
65-74 year	0.59 (0.56-0.63)	0.56 (0.52-0.59)	0.54 (0.50-0.57)
≥ 75 year	0.44 (0.41-0.47)	0.44 (0.41-0.47)	0.49 (0.46-0.52)
Sex (ref: male)			
Female	1.00 (0.95-1.06)	1.06 (1.01-1.11)	1.19 (1.14-1.25)
Charlson comorbidity index (ref: 0-1)			
2-3	0.79 (0.75-0.84)	0.81 (0.77-0.86)	0.87 (0.82-0.92)
≥ 4	0.56 (0.52-0.60)	0.58 (0.55-0.62)	0.65 (0.61-0.69)
CHA ₂ DS ₂ -VASc (ref: 0-1)			
2-3	0.66 (0.61-0.71)	0.61 (0.55-0.67)	0.54 (0.49-0.60)
≥ 4	0.41 (0.38-0.44)	0.41 (0.37-0.45)	0.39 (0.35-0.44)
HAS-BLED (ref: 0-1)			
2	0.67 (0.62-0.71)	0.69 (0.64-0.75)	0.66 (0.61-0.72)
≥ 3	0.55 (0.51-0.58)	0.54 (0.50-0.58)	0.55 (0.51-0.59)
Prescriber specialty (ref: cardiologist)			
Primary care physician	0.36 (0.34-0.38)	0.35 (0.33-0.37)	0.41 (0.39-0.44)

Factors associated with choice among NOACs for incident NOAC users

	Dabigatran vs Apixaban		Rivaroxaban vs Apixaban	
	2013-2014	2015-2017Q1	2013-2014	2015-2017Q1
Age (ref: 18-64 year)				
65-74 year	0.96 (0.84-1.09)	0.88 (0.78-1.00)	0.96 (0.87-1.06)	0.83 (0.78-0.89)
≥ 75 year	0.75 (0.65-0.85)	0.69 (0.61-0.78)	0.84 (0.76-0.92)	0.64 (0.60-0.69)
Sex (ref: male)				
Female	0.85 (0.76-0.94)	0.85 (0.77-0.94)	0.90 (0.84-0.98)	0.84 (0.80-0.89)
Charlson comorbidity index (ref: 0-1)				
2-3	0.94 (0.83-1.06)	0.98 (0.88-1.10)	0.91 (0.84-1.00)	0.91 (0.86-0.96)
≥ 4	0.83 (0.72-0.96)	0.77 (0.67-0.88)	0.87 (0.78-0.96)	0.75 (0.70-0.80)
CHA ₂ DS ₂ -VASc (ref: 0-1)				
2-3	0.75 (0.64-0.89)	1.04 (0.88-1.24)	0.82 (0.72-0.92)	0.84 (0.77-0.91)
≥ 4	0.64 (0.55-0.76)	0.77 (0.65-0.91)	0.67 (0.59-0.76)	0.62 (0.57-0.67)
HAS-BLED (ref: 0-1)				
2	0.88 (0.76-1.01)	0.90 (0.78-1.03)	0.91 (0.82-1.02)	0.85 (0.79-0.92)
≥ 3	0.78 (0.68-0.90)	0.80 (0.70-0.92)	0.86 (0.77-0.96)	0.69 (0.64-0.74)
Prescriber specialty (ref: cardiologist)				
Primary care physician	2.02 (1.78-2.29)	0.97 (0.86-1.10)	1.68 (1.53-1.85)	1.26 (1.19-1.34)

Strengths and Limitations

- Strengths
 - Large sample of incident OAC users with AF
 - Absence of lag time in data availability
- Limitations
 - Unable to examine how patient or physician preferences impact treatment choice from claims
 - No information on whether patients actually took the drugs
 - No information on the use of over-the-counter drugs

Conclusions

- The use of NOACs has increased substantially, predominantly driven by increased use of apixaban
- Clinical practice tended to respond rapidly to evidence of harm associated with dabigatran
- Warfarin and apixaban was generally preferred for elderly, patients with higher stroke or bleeding risk, and those with more comorbidities
- The association between female sex and choice of a NOAC vs warfarin changed over time, from no significant association in 2010Q4-2012 to a positive association in 2013-2017Q1

Next Steps

- “Personalized decision making for oral anticoagulant choice in atrial fibrillation”
 - Aim 2. Elicit preferences for multiple attributes of the oral anticoagulants among patients with AF and their physicians
 - Aim 3. Build on the existing literature and knowledge generated in Aim 2 to create and pilot test a personalized decision tool for patients with AF considering anticoagulant therapy
- Studies using OptumLabs data
 - Racial/ethnic and socioeconomic disparities in oral anticoagulant therapy adherence in atrial fibrillation
 - Oral anticoagulant switching in patients with atrial fibrillation

Thank you!
Questions?