Supplementary Material

Supplemental Figure S1. Cohort creation flow diagram

Supplemental Table S1. Description of Individual Databases Held at ICES

Supplemental Table S2. RECORD statement

Supplemental Table S3.Administrative drug definitions for study drugs of interest

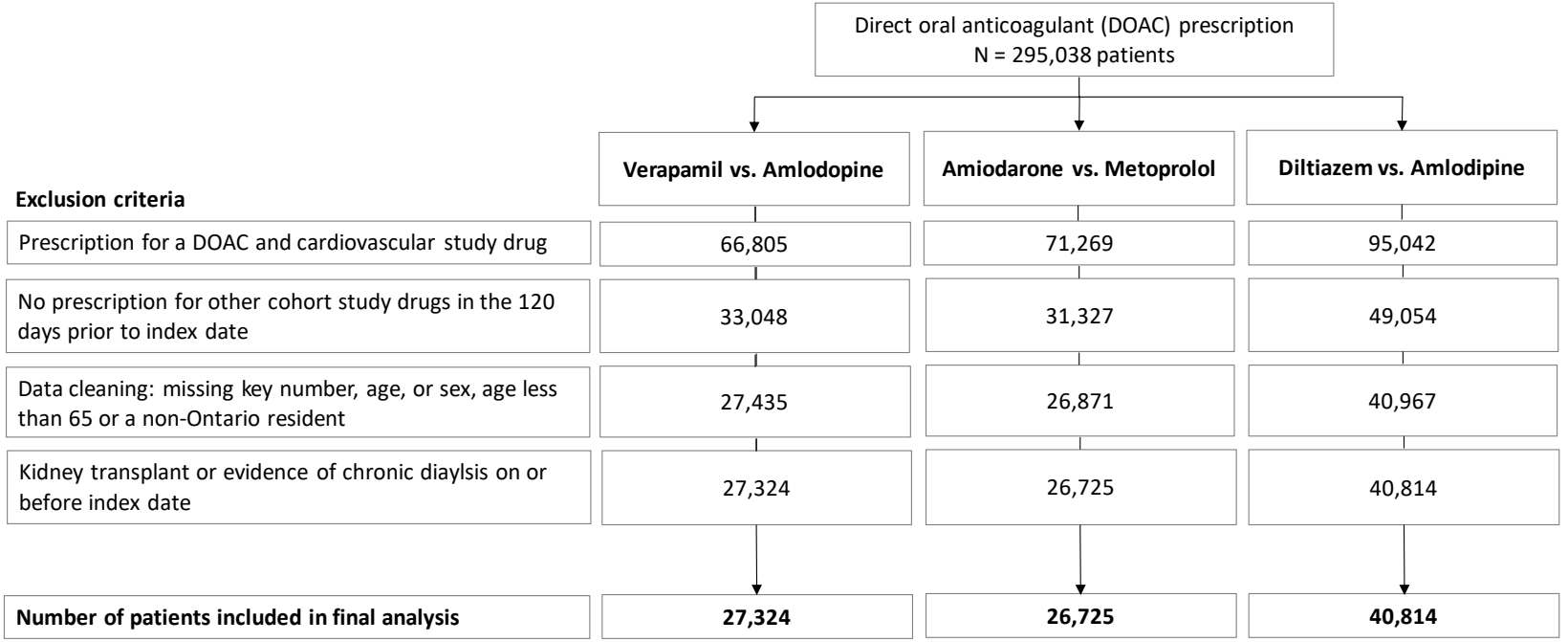
Supplemental Table S4. Ontario Drug Benefit Program Drug Identification Numbers Used to exclude strong CYP3A4/P-gp inhibitors 120 days prior to index date

Supplemental Table S5.Study outcome data definitions

Supplemental Table S6. Pre- and post-weighted standardized differences for baseline characteristics comparing initiation of amiodarone/metoprolol, verapamil/amlodipine, and diltiazem/amlodipine among direct oral anticoagulation (DOAC) users.

Supplemental Table S7. Additional analyses

Supplemental Figure S1. Cohort creation flow diagram



Supplemental Table S1: Description of ICES databases used in this study

Database	Description
Ontario Drug Benefit (ODB) Database	The ODB formulary includes a wide range of routine outpatient medications, including oral preparations of the prescription drugs of interest to this study. The error rate in this database for drug and dose dispensed is minimal (~0.7%, 95% CI 0.5% to 0.9%). We will use the ODB database to determine exposure to the interfering drugs and to NOAC. The interfering drugs by type of NOAC are as follows: Dabigatran (verapamil, amiodarone, clarithromycin, atorvastatin, naproxen), Apixaban (verapamil, diltiazem, clarithromycin, atorvastatin, naproxen), Rivaroxaban (verapamil, diltiazem, clarithromycin, atorvastatin, naproxen). The date of first interfering drug prescription will considered as start of the exposure period. The date of first NOAC prescription will be designated as the index date. We will obtain information on each drug of interest including the drug identification number, trade name, therapeutic class, pill strength, quantity dispensed, days supplied, and formulations.
Canadian Institute of Health Information Discharge Abstract Database (CIHI-DAD)	The CIHI-DAD collects diagnostic, and procedural variables for each admission to a hospital in Ontario. Coding of primary and secondary diagnoses and inpatient procedures uses the 9th version of the Canadian Modified International Classification of Disease system (ICD-9 CA) prior to 2002 and the 10th version (ICD-10 CA) for all diagnoses after 2002. We will use the CIHI-DAD to assess hospital admissions with the primary outcome of major hemorrhage. In addition, we will use the CIHI-DAD to obtain demographics, assess hospitalizations prior to the index date and co-morbid conditions for each patient in the five years prior to the index date. These characteristics act as study inclusion or exclusion criteria, or confounders in the multivariable models.
Ontario Health Insurance Plan (OHIP) Claims History Database	Most physicians in Ontario submit billing claims using fee and diagnosis codes outlined in the OHIP Schedule of Benefits. These codes capture information on inpatient, outpatient, and laboratory services rendered to a patient. In addition, OHIP includes information on the nature of the service and diagnostic information. Similar to the CIHI-DAD, these variables will be used as covariates for propensity score matching for the exposure (interfering) drugs of interest. In chart re-abstraction studies, agreement between abstracted OHIP codes compared to the actual code recorded on the chart by the physician for the “most responsible” diagnosis was over 90% while percent agreement for procedural

	codes was over 88%.
Registered Persons Database (RPDB)	The RPDB captures information regarding Ontarians' gender, date of birth, postal code, and vital status.
National Ambulatory Care Reporting System (NACRS)	The NACRS is compiled by the Canadian Institute for Health Information (CIHI) and contains administrative, clinical (diagnoses and procedures), demographic, and administrative information for all patient visits made to hospital- and community-based ambulatory care centers (emergency departments, day surgery units, hemodialysis units, and cancer care clinics) in Ontario. At ICES, NACRS records are linked with other data sources (DAD, Ontario Mental Health Reporting System [OMHRS]) to identify transitions to other care settings, such as inpatient acute care or psychiatric care. Prior to April 1, 2002, diagnoses (up to 6 on a given NACRS record) are captured using the ICD-9 coding system and procedures (up to 10 on a given NACRS record) are captured using the CCP coding system. Following April 1, 2002, diagnoses (up to 10 on a given NACRS record) are captured using the ICD-10-CA coding system and interventions (up to 10 on a given NACRS record) are captured using the CCI coding system. NACRS emergency department diagnosis codes have been extensively validated.
Ontario Laboratory Information System (OLIS)	The Ontario Laboratory Information System (OLIS) is an electronic system that contains laboratory tests conducted for patients in Ontario. Data is available from 2007 to 2016 with serum creatinine values cleaned and at ICES Central. In the database the number of individuals older than 66 years having at least one serum creatinine is greater than 3 million. This database will allow us to establish a subset of patients with chronic kidney disease defined by serum creatinine laboratory values and estimated glomerular filtration rates.

Supplemental Table S2. Reporting of studies Conducted using Observational Routinely collected health Data (RECORD) statement checklist

	Item No	STROBE items	RECORD items	Reported
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract. (b) Provide in the abstract an informative and balanced summary of what was done and what was found.	(1.1) The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. (1.2) If applicable, the geographic region and time frame within which the study took place should be reported in the title or abstract. (1.3) If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Title page and abstract
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported.		Introduction
Objectives	3	State specific objectives, including any pre-specified hypotheses.		Introduction
Methods				
Study design	4	Present key elements of study design early in the paper.		Methods
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection.		Methods
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. (b) For matched studies, give matching criteria and number of exposed and unexposed.	(6.1) The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. (6.2) Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. (6.3) If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at	Methods

			each stage.	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	(7.1) A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Methods
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group.		Methods
Bias	9	Describe any efforts to address potential sources of bias.		Methods
Study size	10	Explain how the study size was arrived at.		Results
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why.		Methods
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding. (b) Describe any methods used to examine subgroups and interactions. (c) Explain how missing data were addressed. (d) If applicable, explain how loss to follow-up was addressed. (e) Describe any sensitivity analyses.		Methods
Data access and cleaning methods		N/A	(12.1) Authors should describe the extent to which the investigators had access to the database population used to create the study population. (12.2) Authors should provide information on the data cleaning methods used in the study.	Methods
Linkage		N/A	(12.3) State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	Methods

Results				
Participants	13	(a) Report numbers of individuals at each stage of study- e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed. (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram.	(13.1) Describe in detail the selection of the persons included in the study (i.e., study population selection), including filtering based on data quality, data availability, and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Results, Supplemental Figure
Descriptive data	14	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders. (b) Indicate number of participants with missing data for each variable of interest. (c) Summarize follow-up time (e.g., average and total amount).		Results
Outcome data	15	Report numbers of outcome events or summary measures over time.		Results
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included. (b) Report category boundaries when continuous variables were categorized. (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period.		Results
Other analyses	17	Report other analyses done (e.g., analyses of subgroups and interactions, and sensitivity analyses).		Results, Supplemental Appendices
Key results	18	Summarize key results with reference to study objectives.		Discussion
Limitations	19	Discuss limitations of the study, considering sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	(19.1) Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they	Discussion

			pertain to the study being reported.	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.		Discussion
Generalizability	21	Discuss the generalizability (external validity) of the study results.		Discussion
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based.		Acknowledgements
Accessibility of protocol, raw data, and programming code		N/A	(22.1) Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	

Supplemental Table S3. Administrative data definitions for study drugs of interest

Drug name	Drug Identification Number (DIN)
Study drug	
DOAC	02312441, 02358808, 02316986, 02378604, 02378612, 02377233, 02397714, 09857463
Exposure drugs	
Amiodarone	00705934, 02036282, 02239835, 02240071, 02240604, 02242472, 02243836, 02245781, 02246194, 02364336
Verapamil	00554316, 00554324, 00812331, 00812358, 00867365, 00867373, 00886033, 00886041, 01934317, 02100487, 02100495, 02210347, 00742554, 00782483, 00782491, 02210355, 02210363, 02211920, 02231676, 02231677, 02237791, 02237921, 02237922, 02246894, 02246895, 02450488, 02450296
Diltiazem	00587753, 00587761, 00728314, 00728322, 00728330, 00771376, 00771384, 00862924, 00862932, 00886068, 00886076, 00888524, 00888532, 01917064, 01917072, 02009315, 02009323, 02048620, 02097214, 02097222, 02097249, 02097257, 02097265, 02097273, 02097370, 02097389, 02146916, 02146924, 02222957, 02222965, 02222973, 02229406, 02229407, 02229408, 02229526, 02229781, 02229782, 02229783, 02229784, 02230031, 02230032, 02230997, 02230998, 02230999, 02231052, 02231053, 02231054, 02231150, 02231151, 02231152, 02231154, 02231155, 02231743, 02231744, 02231745, 02242538, 02242539, 02242540, 02242541, 02243338, 02243339, 02243340, 02243341, 02245918, 02245919, 02245920, 02245921, 02245922, 02254808, 02254816, 02254824, 02254832, 02256738, 02256746, 02256754, 02256762, 02256770, 02271605, 02271613, 02271621, 02271648, 02271656, 02291037, 02291045, 02291053, 02291061, 02291088, 02355752, 02355760, 02355779, 02355787, 02370441, 02370492, 02370506, 02370514, 02370522, 02370611, 02370638, 02370646, 02370654
Active comparator drugs	
Amlodipine	00878901, 00878928, 00878936, 00903749, 02250497, 02250500,02259605, 02259613, 02272113, 02272121, 02273373, 02273381, 02280124, 02280132, 02280140, 02284065, 02284073, 02284383, 02284391, 02295148, 02297477, 02297485, 02297493, 02321858, 02321866, 02326760, 02326779, 02326787,

	02326795, 02326809, 02326817, 02326825, 02326833, 02326841, 02330474, 02331071, 02331098, 02331284, 02331292, 02331489, 02331497, 02331500, 02331934, 02331942, 02333996, 02334003, 02334011, 02339374, 02339382, 02340178, 02340186, 02341093, 02341107, 02342782, 02342790, 02342804, 02343193, 02343207, 02343215, 02343274, 02343290, 02355582, 02355590, 02355604, 02357186, 02357194, 02357208, 02357704, 02357712, 02357720, 02362651, 02362678, 02364743, 02364751, 02367580, 02367599, 02369222, 02369230, 02369249, 02371022, 02371030, 02371049, 02371057, 02371332, 02371340, 02371359, 02371707, 02371715, 02371723, 02378744, 02378760, 02378779, 02385783, 02385791, 02385805, 02392127, 02392135, 02392143, 02397072, 02397080, 02398877, 02426986, 02426994, 02429217, 02429225, 02451530, 02451549, 02451557, 080878928
Metoprolol	00397423, 00397431, 00402540, 00402605, 00497827, 00534560, 00578444, 00590819, 00618632, 00618640, 00648019, 00648027, 00648035, 00648043, 00658855, 00719846, 00749354, 00751170, 00842648, 00842656, 00865605, 00865613, 00999104, 02028646, 02028654, 02028727, 02028735, 02028743, 02145413, 02145421, 02172550, 02172569, 02174545, 02174553, 02230045, 02230046, 02230448, 02230449, 02230664, 02230665, 02230803, 02230804, 02231121, 02231122, 02231546, 02231547, 02232546, 02232547, 02239771, 02239772, 02244642, 02244643, 02246010, 02247875, 02247876, 02248855, 02252252, 02253496, 02253518, 02253526, 02261898, 02267853, 02285169, 02285177, 02286599, 02286602, 02296713, 02302055, 02303396, 02303418, 02315106, 02315114, 02315122, 02315300, 02315319, 02315327, 02337320, 02337339, 02337347, 02337355, 02337363, 02337371, 02337398, 02347024, 02347032, 02347040, 02347059, 02350394, 02350408, 02350416, 02350424, 02351404, 02351412, 02354187, 02354195, 02356813, 02356821, 02356848, 02364824, 02364832, 02364840, 02364859, 02371367, 02371375, 02371383, 02442116, 02442124, 02442132, 09851453, 09991055, 22123250, 66124014, 66124015, 66124016, 80618632

Supplemental Table S4. Drug identification numbers in the Ontario Drug Benefit Program database used to exclude strong CYP3A4/P-gp inhibitors 120 days prior to index date

Drug name	Drug Identification Number (DIN)
Cyclosporine	9857771,9857774, 755591,755605, 1907182, 2150662, 2150670, 2150689, 2150697, 2237671, 2242821, 2244324, 2247073, 2247074, 9850473, 9852182, 9857097, 9857129, 9857176, 9857184, 9857192, 9857206, 9857214, 9857613, 9857614, 9857770
Tacrolimus	2175983, 2175991, 2176009, 2243144, 2244148, 2244149, 2296462, 2296470, 2296489, 2331667, 2416816, 2416824, 2416832, 9851984, 9852069, 9852662, 9854786
Itraconazole	2047454, 2231347, 2462559, 9857756
Ketoconazole	633836, 703974, 788813, 2231061, 2237235, 2245662
Voriconazole	2256460, 2256479, 2256487, 2279991, 2396866, 2396874, 2399245, 2399253, 2409674, 2409682, 9854663
Posaconazole	2293404, 2424622, 9900020
Quinine	311731, 704644, 26131, 4782, 21733, 23868, 26883, 94412, 249580, 346837, 441740, 1913883
Rifampin	210463, 210471, 343617, 393444, 580376, 580384, 2024861, 2091887, 2092808, 9900056

Supplemental Table S5. Study outcome data definitions

Description	Code	Validation
Major hemorrhage		
Subarachnoid Hemorrhage	ICD10: I60, excluding I60.8	ICD9 codes were found to have a sensitivity: 94% (91-96), specificity: 83% (78-87), positive predictive value: 87% (83-90) and negative predictive value: 92% (88-95) in Arnason et al. (2006).[44]
Intracerebral Hemorrhage	ICD10: I61	
Other non-traumatic intracranial hemorrhage	ICD10: I62	
Upper Gastrointestinal	ICD10: I85.0, I98.20, I98.3, K22.10, K22.12, K22.14, K22.16, K22.6, K22.8, K25.0, K25.2, K25.4, K25.6, K26.0, K26.2, K26.4, K26.6, K27.0, K27.2, K27.4, K27.6, K28.0, K28.2, K28.4, K28.6, K29.0, K31.80, K63.80, K92.0, K92.1	
Lower Gastrointestinal	ICD10: K55.20, K62.5, K92.2	
Any hemorrhage (broad definition)	ICD10: I600, I601, I602, I603, I604, I605, I606, I607, I609, I61, I62, I850, I9820, I983, K2210, K2211, K2212, K2214, K2216, K226, K228, K250, K252, K254, K256, K260, K262, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K290, K3180, K6380, K920, K921, N923, N93.8, K29.71, N92.4, D69.9, R58, 430, 431, 432.0, 432.1, 432.9 I60, I61, I62.0, I62.1, I62.9, 531.0, 531.2, 531.4, 531.6, 532.0, 532.2, 532.4, 532.6, 533.0, 533.2, 533.4, 533.6, 534.0, 534.2, 534.4, 534.6, 578.0, 578.1, 578.9, K92.0, K92.1, I85.0, I98.20, I98.3, K22.10, K22.12, K22.14, K22.16, K25.0, K25.2, K25.4, K25.6, K26.0, K26.2, K26.4, K26.6, K27.0, K27.2, K27.4, K27.6, K28.0, K28.2, K28.4, K28.6, K29.0, K63.80, K31.80, 569.3, 578.1, 578.9 K55.20, K62.5, K92.2, 287.8, 287.9, 596.7, 784.8, 599.7, 627.1, 459.0, 719.1, 786.3, N02.0, N02.1, N02.2, N02.3, N02.4, N02.5, N02.6, N02.7, N02.8, N02.9, K66.1, N93.8, N93.9, N95.0, R04.1, R04.2, R04.8, R04.9, R31.0, R31.1, R31.8, R58, D68.3, H35.6, H43.1, H45.0, M25.0, Z513	

	OHIP fee: E025, G275
Negative outcomes	
Fracture	ICD10: S720, S721, S52, S422, S723, S321, S322, S324, S323, S325, S327, S328, S825, S826, S827, S828, S829, S820, S821, S822, S823, S824, S222, S223, S224, S228, S229, S421, S420 CCI: 1VA73, 1VC73, 1VA74, 1VA53, 1VC74, 1VA80, 1TV73, 1TV74, 1TV03, 1VC73, 1VC74, 1VC03, 1VC80 OHIP fee: F014, F022, F023, F025, F026, F028, F030, F032, F033, F046, F024, F027, F031, Z203, F095, F096, F097, Z211
Anxiety	ICD10: F40-F48
Depression	ICD10: F32

Abbreviations: ICD International Classification of Disease, OHIP Ontario Health Insurance Plan, CCI Canadian Classification of Health Interventions.

Supplemental Table S6. Pre- and post-weighted standardized differences for baseline characteristics comparing initiation of amiodarone/metoprolol, verapamil/amlodipine, and diltiazem/amlodipine among direct oral anticoagulation (DOAC) users.

Characteristic	Pre-weighted Standardized Differences	Post-weighting Standardized Differences	Pre-weighted Standardized Differences	Post-weighting Standardized Differences	Pre-weighted Standardized Differences	Post-weighting Standardized Differences
CV medication vs. comparator	**Amiodarone vs Metoprolol**		**Verapamil vs Amlodipine**		**Diltiazem vs Amlodipine**	
Demographics						
Female	**0.12**	0.02	**0.13**	0.03	0.06	0.00
Age group						
66-75	0.09	0.01	**0.12**	0.05	0.01	0.00
76-85	0.01	0.02	0.04	0.01	0	0.00
86-95	**0.11**	0.00	**0.12**	0.06	0.02	0.00
Over 95	0.02	0.01	0.02	0.00	0.01	0.00
Income quintiles						
1 (low)	0.05	0.00	0.04	0.03	0.01	0.00
2	0.01	0.01	0.01	0.00	0	0.00
3	0.01	0.00	0.01	0.01	0.02	0.00
4	0.02	0.00	0.02	0.01	0	0.00
5 (high)	0.05	0.01	0.03	0.00	0.01	0.00
Rural residence	0.01	0.02	**0.17**	0.08	0.06	0.00
Index year						
2008	**0.12**	0.02	**0.11**		0.07	0.00
2009	**0.34**	0.02	**0.37**	0.05	0.04	0.01
2010	0.06	0.01	0.04	**0.12**	0.03	0.00
2011	0.06	0.00	0.05	0.01	0	0.01
2012	0.03	0.01	0.09	0.00	0.01	0.00
2013	**0.10**	0.01	0.08	0.01	0.02	0.00
2014	0.08	0.00	**0.15**	0.02	0.04	0.00
2015	**0.10**	0.00	**0.15**	0.06	0.08	0.01
2016	**0.16**	0.02	**0.17**	0.05	0.07	0.01
Co-morbid illness						

Major hemorrhage	0	0.01	0.08	0.05	0.02	0.00
Hypertension	0	0.04	**0.29**	**0.15**	**0.29**	0.03
Diabetes	0.07	0.02	**0.17**	0.06	**0.10**	0.01
Stroke/TIA	0.05	0.02	**0.13**	0.09	0.05	0.01
Atrial fibrillation/flutter	**0.30**	0.00	0.06	0.03	**0.59**	0.04
Myocardial infarction	0.02	0.02	0.05	0.03	0.02	0.00
Heart failure	**0.40**	0.01	**0.12**	0.05	**0.15**	0.01
Coronary artery disease	**0.19**	0.00	**0.14**	0.09	0.03	0.00
Coronary artery bypass grafting	0.03	0.01	0.02	0.02	0.05	0.00
Percutaneous cardiac intervention	0.07	0.00	0.08	0.04	0.05	0.00
Peripheral vascular disease	0.01	0.01	0.05	0.02	0.01	0.00
Venous thromboembolism	0.06	0.01	0.07	0.05	0.02	0.01
Healthcare utilization						
Hospitalizations	**0.20**	0.02	**0.28**	**0.14**	**0.14**	0.00
ED visits	**0.25**	0.02	**0.22**	0.08	**0.25**	0.01
Medications						
Beta blocker	-	-	**0.43**	**0.22**	**0.19**	0.00
NSAID	0.09	0.02	0.03	0.01	0.08	0.00
Proton pump inhibitor	**0.10**	0.01	0.09	0.04	0	0.00
Antiplatelet agent	0.03	0.01	**0.12**	0.08	0.06	0.01
SSRI	0.03	0.00	0.02	0.02	0.03	0.00
Lipid lowering agent	**0.15**	0.01	**0.15**	0.07	**0.11**	0.01
DOAC type						
Apixaban	0.06	0.00	0.06	0.01	0.08	0.09
Dabigatran	0.07	**0.10**	**0.15**	**0.13**	**0.18**	**0.16**
Rivaroxaban	**0.12**	0.09	0.07	**0.11**	**0.22**	**0.21**
Mean daily dose						

Apixaban	0.03	0.03	0.01	0.01	0.04	0.02
Dabigatran	0	0.03	0.08	0.07	0.03	0.01
Rivaroxaban	**0.21**	**0.13**	0.09	**0.10**	**0.21**	**0.12**
High daily DOAC dose	0.03	0.01	0.05	0.03	**0.13**	0.01
DOAC duration prior to CV medications	**0.34**	0.03	**0.13**	0.06	0.04	0.01
eGFR (mL/min/1.73m^2)	**0.21**	**0.21**	**0.11**	0.06	0.07	0.02

*Std. Diff. Standardized differences ≥0.1 are statistically significant and bolded.

Abbreviations: mg milligram, ED emergency department, TIA transient ischemic attack, SSRI selective serotonin reuptake inhibitor, NSAID non-steroidal anti-inflammatory drug, eGFR estimated glomerular filtration rate, CV cardiovascular, DOAC direct oral anticoagulant

Supplemental Table S7. Additional analyses

Model[a]	Weighted HR (95%CI)
Additionally adjusted for kidney function (eGFR)	
Amiodarone (vs. metoprolol)	0.85 (0.66-1.11)
Verapamil (vs. amlodipine)	1.17 (0.63-2.21)
Diltiazem (vs. amlodipine)	1.04 (0.86-1.26)
Excluding individuals with a hospitalization 90 days prior to cardiac medication initiation	
Amiodarone (vs. metoprolol)	0.80 (0.59-1.09)
Verapamil (vs. amlodipine)	1.45 (0.95-2.22)
Diltiazem (vs. amlodipine)	0.99 (0.83-1.19)
Negative outcomes (major hemorrhage only)	
Amiodarone (vs. metoprolol)	0.81 (0.37-1.81)
Verapamil (vs. amlodipine)	1.09 (0.81-1.45)
Diltiazem (vs. amlodipine)	1.36 (0.80-2.33)
Any hemorrhage or receipt of packed red blood cells	
Amiodarone (vs. metoprolol)	0.97 (0.87-1.08)
Verapamil (vs. amlodipine)	1.02 (0.82-1.27)
Diltiazem (vs. amlodipine)	0.91 (0.85-0.98)
Limited to 90 days follow-up after CV medication initiation	
Amiodarone (vs. metoprolol)	1.10 (0.74-1.61)
Verapamil (vs. amlodipine)	1.30 (0.59-2.85)
Diltiazem (vs. amlodipine)	1.32 (1.01-1.73)
DOAC type (major hemorrhage)	**p-value[d]**
Amiodarone	0.211
Verapamil	0.494
Diltiazem	0.541
DOAC dose	
Amiodarone	0.268
Verapamil	0.723
Diltiazem	0.649
Additionally adjusted for previous warfarin use (180 days)	
Amiodarone (vs. metoprolol)	0.76 (0.60-0.96)
Verapamil (vs. amlodipine)	1.32 (0.88-1.98)
Diltiazem (vs. amlodipine)	0.99 (0.85-1.15)

[a] Models adjusted for weights calculated using all variables listed in Table 1.
[b] Composite of anxiety/depression used for amiodarone and diltiazem; fractures were used for verapamil and diltiazem due to no anxiety/depression events in the verapamil group. Models adjusted for weights calculated using all variables listed in Table 1
[c] DOAC type and DOAC dose models adjusted for weights calculated using all variables listed in Table 1. [d] P-values represent significance testing for interaction term.

Abbreviations HR hazard ratio, CI confidence intervals, eGFR estimated glomerular filtration rate CV cardiovascular DOAC direct oral anticoagulant