

# Retrospective Review of Anticoagulant Prescribing Patterns in Postoperative Atrial Fibrillation

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## Background

- Postoperative atrial fibrillation (POAF) is defined as the development of new-onset atrial fibrillation in the immediate postoperative period and is a common complication of cardiac surgery. (1-7)
- POAF is associated with an increased risk of thromboembolic stroke and led several international guidelines to recommend treatment with anticoagulation. (1,4,5,7-15)
- Currently, there is no consensus regarding the initiation, duration, choice, and long-term management of anticoagulation. (4,6,8,9,13,14)
- Anticoagulation treatment preferences may vary and it is currently unknown what the practice patterns in Alberta are regarding initiation, choice of anticoagulation and long-term management for patients who develop POAF after cardiac surgery.

## Methods

- Design:**
- Retrospective cohort
  - Patients who underwent cardiac surgery + developed POAF and were discharged from either the Foothills Medical Centre or the Mazankowski Alberta Health Institute from January 1, 2015 to December 31, 2020.

- Patient Identification:**
- Identified using the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPOACH) database
  - POAF: defined as those without pre-existing AF who developed AF during index admission after cardiac surgery as documented in APPOACH database.

Inclusion Criteria	Exclusion Criteria
Age ≥ 18	Pre-existing AF
Underwent cardiac surgery	Underwent one of the following procedures: mechanical valve replacement, insertion of a left ventricular assist device, heart transplantation, congenital surgery or repairs, maze procedure, or left atrial appendage excision procedure
Alberta resident with a valid Alberta healthcare number	In-hospital death or prolonged hospitalization (≥ 28 days)
Developed new-onset POAF after cardiac surgery during the index admission	Filled an anticoagulant in the 6 months prior to index admission
	Prescribed a low molecular weight heparin (tinzaparin, enoxaparin, or dalteparin) on discharge

- Primary outcome:**
- Proportion of patients (%) with POAF who were prescribed an oral anticoagulant (OAC) at discharge

- Secondary outcomes:**
- Proportion of patients (%) who were initiated on warfarin or a direct oral anticoagulant (DOAC) (apixaban, dabigatran, edoxaban, rivaroxaban) at discharge.
  - Proportion (%) of patients who have an anticoagulant either stopped, continued, switched, or initiated at 3 months and 6 months after discharge.
  - Indicators of outpatient follow-up care within 6 months post-discharge
  - Occurrence of complications within 30 days post-discharge in those initiated on anticoagulants vs. those not on anticoagulants.

- Data sources:**
- APPOACH database: Patient identification, demographics, co-morbidities, surgery parameters and complications, discharge medications
  - Pharmaceutical Information Network (PIN): OAC use pre/post surgery
  - Discharge Abstract Database (DAD): Outcomes using ICD codes for bleeding, thrombosis, atrial arrhythmias
  - National Ambulatory Care Reporting System (NACRS): Outcomes using ICD codes for bleeding, thrombosis, atrial arrhythmias
  - Practitioner Claims Database: follow-up care parameters; outcomes using ICD code for atrial arrhythmias

## Results

Figure 1: Cohort Identification

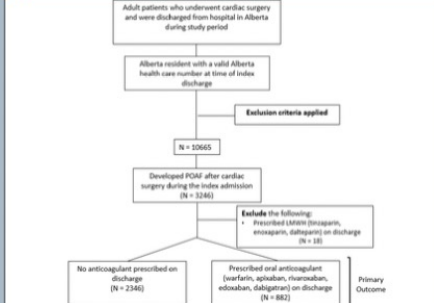


Table 1: Baseline Characteristics

Data point	Overall (N= 3228)	OAC prescribed (N= 882)	No OAC prescribed (N= 2346)
Age, years, mean (SD)	68.5 (9.53)	69.12 (8.93)	68.3 (9.73)
Male, N (%)	2463 (76.30%)	642 (72.79%)	1821 (77.62%)
Pre-operative comorbidities, N (%)			
Hypertension	2518 (78%)	664 (75.28%)	1854 (79.03%)
Heart failure	396 (12.27%)	127 (14.40%)	269 (11.47%)
Diabetes	1027 (31.82%)	222 (25.17%)	805 (34.31%)
Prior myocardial infarction	793 (24.50%)	131 (14.85%)	660 (28.13%)
Prior PCI	502 (15.55%)	125 (14.17%)	377 (16.07%)
Prior CABG	33 (1.02%)	7 (0.79%)	26 (1.11%)
Type of surgery, N (%)			
CABG	1896 (58.74%)	404 (45.80%)	1492 (63.60%)
Aortic valve replacement	1031 (31.94%)	303 (34.5%)	728 (31.03%)
Mitral valve replacement	140 (4.34%)	104 (11.79%)	36 (1.53%)
Mitral valve repair	217 (6.72%)	153 (17.35%)	64 (2.73%)
Combined CABG/valve	377 (11.68%)	143 (16.21%)	234 (9.97%)
Peri-operative STEM/PCI	544 (16.85%)	105 (11.90%)	439 (18.73%)
Peri-operative STEM/PCI	143 (4.43%)	25 (2.83%)	118 (5.03%)
CHADS <sub>2</sub> risk score			
CHADS <sub>2</sub> risk score, mean (SD)	1.55 (1.01)	1.46 (0.95)	1.59 (1.04)
CHADS <sub>2</sub> = 0, N (%)	460 (14.25%)	127 (14.40%)	333 (14.19%)
CHADS <sub>2</sub> = ≥1, N (%)	2768 (85.75%)	755 (85.60%)	2013 (85.81%)
Concomitant therapy at discharge, N (%)			
Acetylsalicylic acid	1356 (42.01%)	439 (49.77%)	917 (39.09%)
Ticagrelor	282 (8.74%)	7 (0.79%)	275 (11.72%)
Clopidogrel	208 (6.44%)	32 (3.63%)	176 (7.50%)
Beta-blocker	2329 (72.15%)	735 (83.33%)	1594 (67.95%)
Antiarrhythmic therapy	1077 (33.36%)	393 (44.56%)	684 (29.16%)
Digoxin	9 (0.28%)	5 (0.57%)	4 (0.17%)
Proton pump inhibitor	1888 (58.49%)	680 (77.10%)	1208 (51.49%)

Figure 2: Patients Prescribed OAC at Discharge (n=3228)

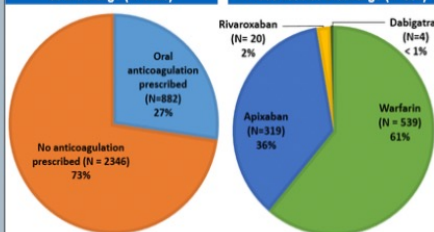


Figure 3: Classification of OAC Prescribed at Discharge (n=882)

Figure 4: Anticoagulation management at 3 and 6 months

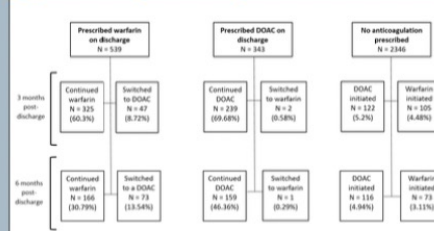
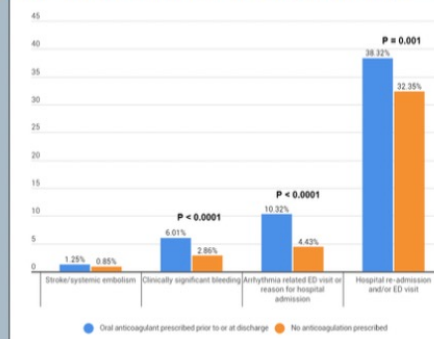


Table 2: Outpatient follow-up within 6 months of discharge

	OAC prescribed (N=882)	No OAC prescribed (N=2346)	P value	Overall (N=3228)
<b>Proportion of patients who received follow-up with:</b>				
General practitioner, N (%)	868 (98.4%)	2121 (90.4%)	<0.0001	2989 (92.6%)
Cardiologist, N (%)	744 (84.4%)	1775 (75.7%)	<0.0001	2519 (78%)
Cardiovascular surgeon, N (%)	387 (43.9%)	1051 (44.8%)	0.64	1438 (44.6%)
<b>Mean time in days (SD) to first follow-up with:</b>				
General practitioner	7 (10.6)	11.1 (16.7)	<0.0001	
Cardiologist	57.4 (34)	63.2 (36.80)	0.0002	
Cardiovascular surgeon	74.8 (74.8)	78.8 (38)	0.07	
<b>Those discharged on warfarin (N= 539)</b>				
Median time in days (IQR) to first INR	1.85 (0.97-3.72)			

Figure 5: Clinical Outcomes within 30 days of Discharge



- 239 (27.1%) of those prescribed an OAC on discharge versus 132 (5.6%) not prescribed an OAC on discharge (p<0.0001) had arrhythmia documented as outpatient within 6 months of discharge.

## Discussion

- A minority of patients who developed POAF were prescribed an OAC on discharge.**
- Results are comparable to other studies
  - Those prescribed OAC on discharge had a lower proportion of:
    - Perioperative NSTEMI/STEMI
    - Underwent CABG surgery
    - Concomitant ticagrelor or clopidogrel prescription
  - Significantly higher proportion of bleeding within 30 days of discharge in those prescribed anticoagulation
  - Careful assessment of risk of stroke in comparison to risk of bleeding associated with anticoagulation use is warranted (particularly in those with an inherently high risk of bleeding post-operatively)

- Of those prescribed an OAC, majority were prescribed warfarin.**
- Lack of evidence to support the safety of DOACs in the post-operative period
  - Perhaps extrapolated harm from studies those with mechanical valves

- Despite similar baseline CHADS2 score, anticoagulation appeared to be prescribed in patients who were at an increased risk of experiencing complications of AF.**
- Those prescribed an OAC on discharge had a higher occurrence of:
    - Arrhythmia-related ED visit or reason for hospital admission
    - Any ED visit/hospital admission
    - Documented AF an outpatient within 6 months of discharge
    - Concomitant prescription for antiarrhythmic therapy on discharge
  - No difference noted in occurrence of stroke between the two groups.

## Limitations

- Retrospective collection of patient data from administrative databases relying on accuracy of diagnostic coding
- Duration of POAF not determined
- Prescription fill history used as a measure of ongoing outpatient anticoagulation management
- Unable to comprehensively capture non-prescription use of acetylsalicylic acid which could impact interpretation of bleeding outcomes

## Conclusion

- OAC is prescribed in the minority of patients with POAF, with the majority of patient prescribed warfarin
- OAC initiation was associated with an increased occurrence of bleeding. Special consideration must be taken when assessing a patient's risk of AF complications against the increased risk of bleeding, particularly in the post-operative period.
- Further research warranted to:
  - Identify which patients would derive the greatest benefit from OAC initiation
  - Establish the safety and efficacy of anticoagulants, including DOACs, for those with POAF after cardiac surgery

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## Background

- Postoperative atrial fibrillation (POAF) is defined as the development of new-onset atrial fibrillation in the immediate postoperative period and is a common complication of cardiac surgery (1-7)
- Patients who develop POAF are at increased risk of: (1,4,5,7-15)
  - Thromboembolic stroke
  - Mortality
  - Prolonged hospital stay and readmissions
  - Developing persistent atrial fibrillation (AF)

## Background

- Currently, there is no consensus regarding the initiation, duration, choice, and long-term management of anticoagulation. (4,6,8,9,13,14)
- Anticoagulation treatment preferences may vary and it is currently unknown what the practice patterns in Alberta are regarding initiation, choice of anticoagulation and long-term management for patients who develop POAF after cardiac surgery.

# Methods

## **Design:**

- Retrospective cohort
- Patients who underwent cardiac surgery + developed POAF and were discharged from either the Foothills Medical Centre or the Mazankowski Alberta Health Institute
- January 1, 2015 to December 31, 2020.

## **Patient Identification:**

- Identified using the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) database
- POAF: defined as those without pre-existing AF who developed AF during index admission after cardiac surgery as documented in APPROACH database.

# Methods

Inclusion Criteria	Exclusion Criteria
Age $\geq$ 18	Pre-existing AF
Underwent cardiac surgery	Underwent one of the following procedures: mechanical valve replacement, insertion of a left ventricular assist device, heart transplantation, congenital surgery or repairs, maze procedure, or left atrial appendage exclusion procedure
Alberta resident with a valid Alberta healthcare number	In-hospital death or prolonged hospitalization ( $\geq$ 28 days)
Developed new-onset POAF after cardiac surgery during the index admission	Filled an anticoagulant in the 6 months prior to index admission
	Prescribed a low molecular weight heparin (tinzaparin, enoxaparin, or dalteparin) on discharge



# Methods

## Primary outcome:

- Proportion of patients (%) with POAF who were prescribed an oral anticoagulant (OAC) at discharge

## Secondary outcomes:

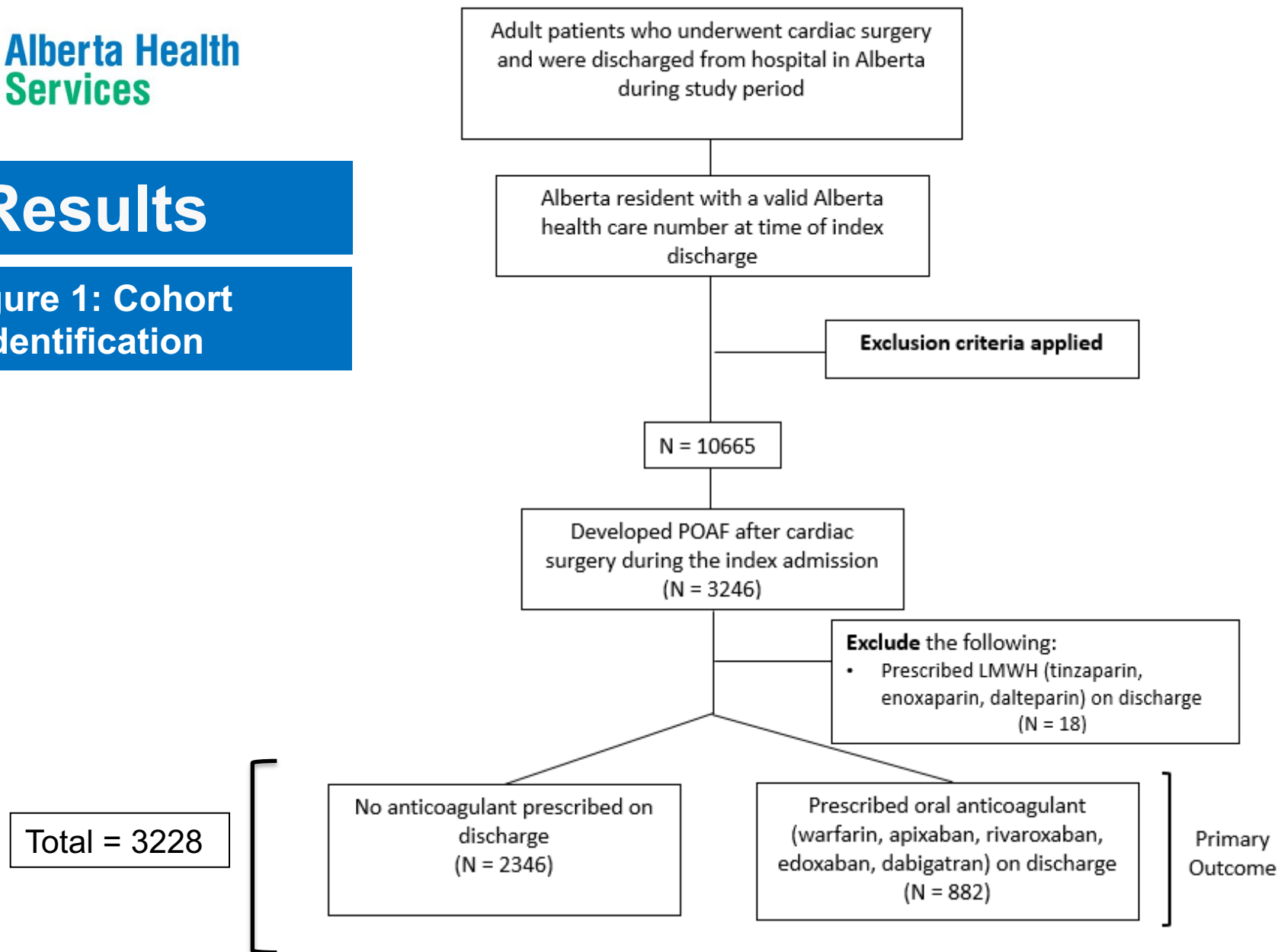
- Proportion of patients (%) who were initiated on warfarin or a direct oral anticoagulant (DOAC) (apixaban, dabigatran, edoxaban, rivaroxaban) at discharge.
- Proportion (%) of patients who have an anticoagulant either stopped, continued, switched, or initiated at 3 months and 6 months after discharge.
- Indicators of outpatient follow-up care within 6 months post-discharge
- Occurrence of complications within 30 days post-discharge in those initiated on anticoagulants vs. those not on anticoagulants.

# Methods

Data Source	Information gathered
<b>APPROACH</b> (Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease) Database	Patient identification, demographics, co-morbidities, surgery parameters and complications, discharge medications
<b>Pharmaceutical Information Network (PIN)</b>	Anticoagulant use pre/post surgery
<b>Discharge Abstract Database (DAD)</b>	Outcomes using ICD codes for bleeding, thrombosis, atrial arrhythmias
<b>National Ambulatory Care Reporting System (NACRS)</b>	Outcomes using ICD codes for bleeding, thrombosis, atrial arrhythmias
<b>Practitioner Claims Database</b>	Follow-up care parameters; outcomes using ICD code for atrial arrhythmias
<b>Medical laboratory</b>	Laboratory data

# Results

Figure 1: Cohort Identification





# Results: Baseline Characteristics

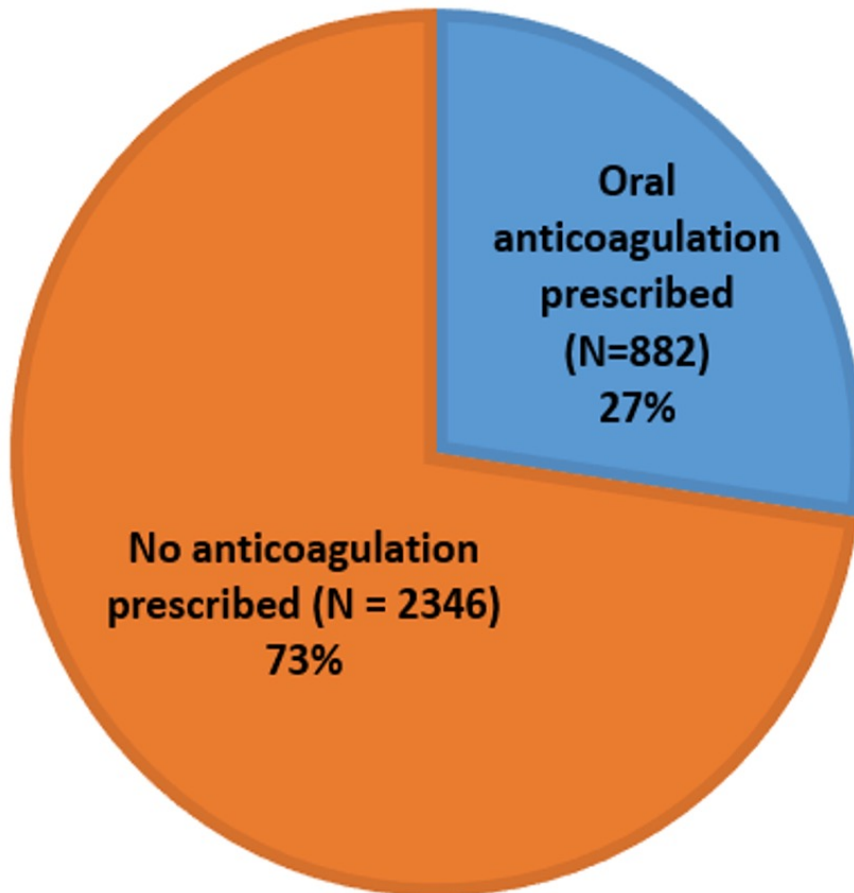
Data Point	Oral Anticoagulation Prescribed (N = 882)	No anticoagulation prescribed (N=2346)	Overall (N=3228)
Age, years, mean (SD)	69.12 (8.93)	68.3 (9.73)	68.5 (9.53)
Male, N (%)	642 (72.79%)	1821 (77.62%)	2463 (76.30%)
Hypertension	664 (75.28%)	1854 (79.03%)	2518 (78%)
Heart failure	127 (14.40%)	269 (11.47%)	396 (12.27%)
Prior MI	131 (14.85%)	660 (28.13%)	791 (24.50%)
Prior PCI	125 (14.17%)	377 (16.07%)	502 (15.55%)
Prior CABG	7 (0.79%)	26 (1.11%)	33 (1.02%)
CHADS <sub>2</sub> , risk score, mean (SD)	1.46 (0.95)	1.59 (1.04)	1.55 (1.01)
CABG	404 (45.80%)	1492 (63.60%)	1896 (58.74%)
Aortic valve replacement	303 (34.35%)	728 (31.03%)	1031 (31.94%)
Mitral valve replacement	104 (11.79%)	36 (1.53%)	140 (4.34%)
Mitral valve repair	153 (17.35%)	64 (2.73%)	217 (6.72%)
Combined CABG/valve	143 (16.21%)	234 (9.97%)	377 (11.68%)
Acetylsalicylic acid	439 (49.77%)	917 (39.09%)	1356 (42.01%)
Ticagrelor	7 (0.79%)	275 (11.72%)	282 (8.74%)
Clopidogrel	32 (3.63%)	176 (7.50%)	208 (6.44%)
Beta-blocker	735 (83.33%)	1594 (67.95%)	2329 (72.15%)
Antiarrhythmic therapy	393 (44.56%)	684 (29.16%)	1077 (33.36%)
Proton pump inhibitor	680 (77.10%)	1208 (51.49%)	1888 (58.49%)

Type of surgery

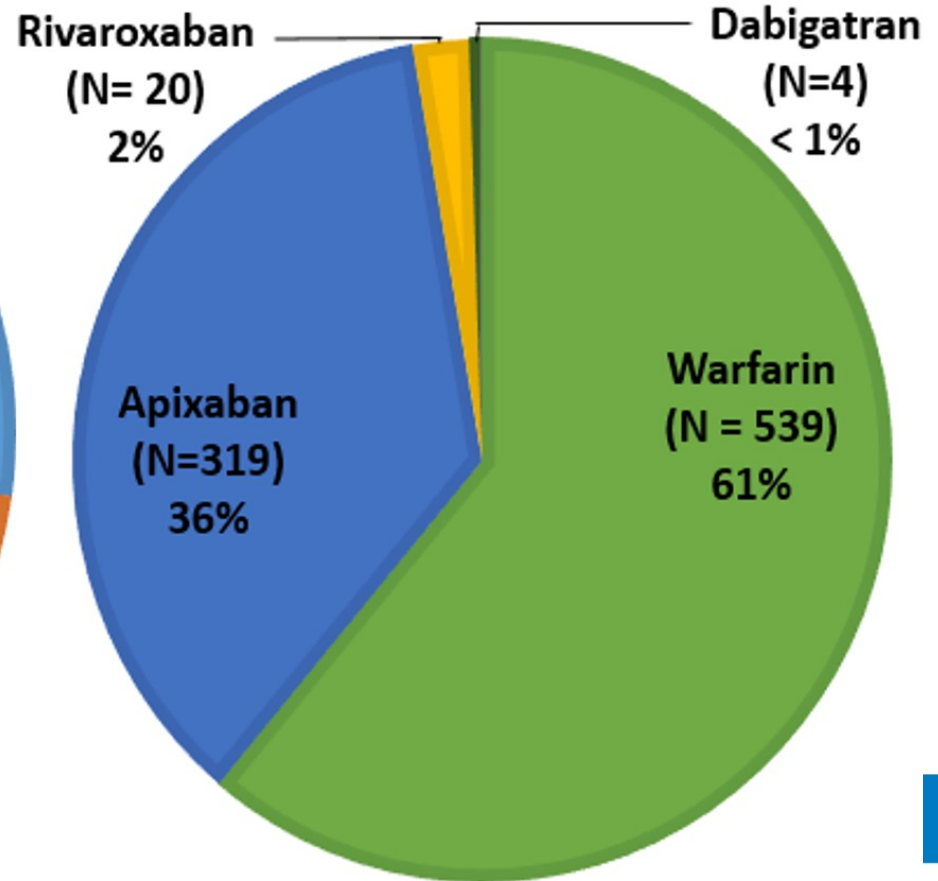
Concomitant therapy at discharge

# Results

**Figure 2: Patients Prescribed OAC at Discharge (n=3228)**

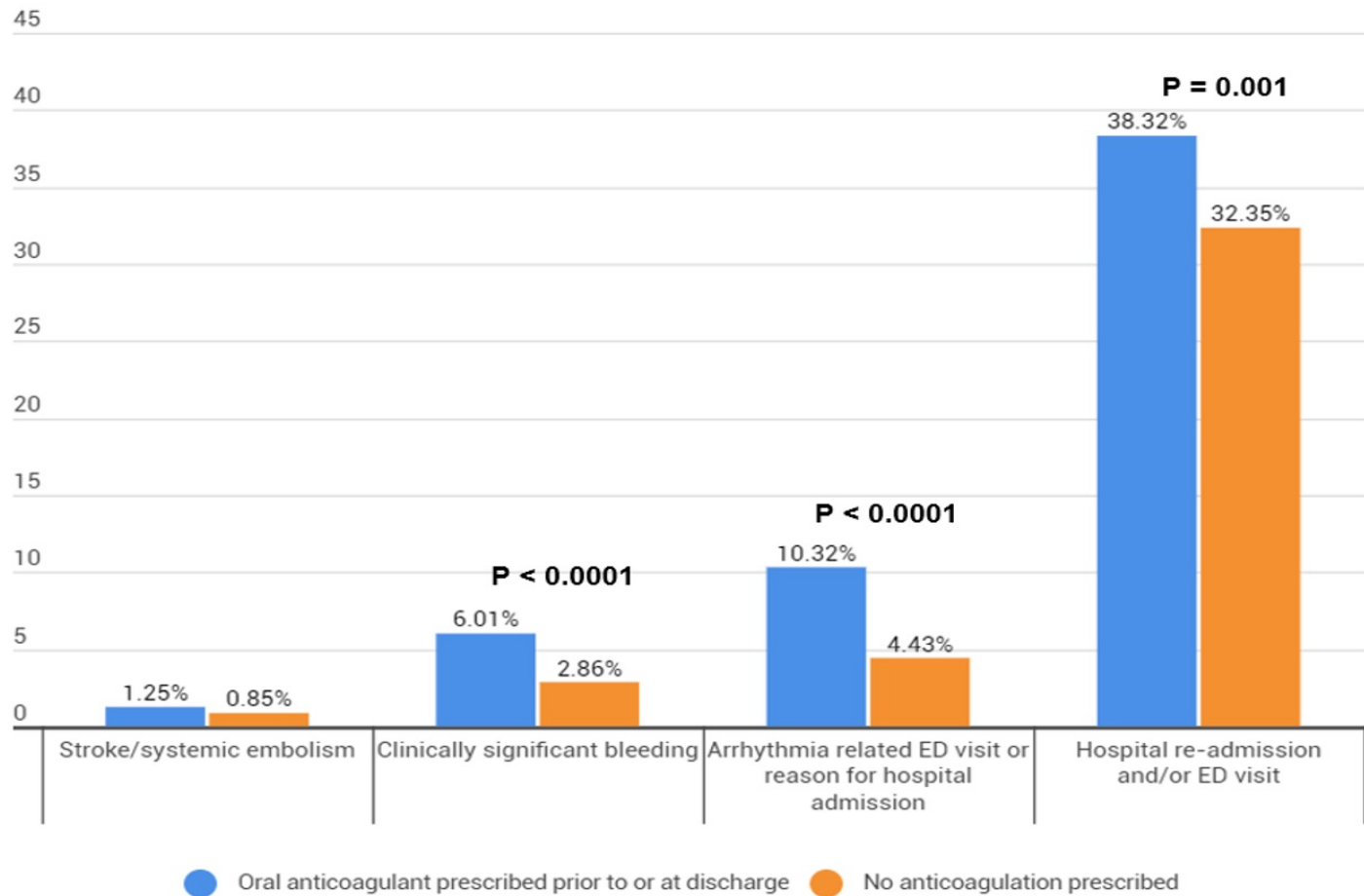


**Figure 3: Classification of OAC Prescribed at Discharge (n=882)**



# Results

Figure 5: Clinical Outcomes within 30 days of Discharge



- 239 (27.1%) of those prescribed an OAC on discharge versus 132 (5.6%) not prescribed an OAC on discharge ( $p < 0.0001$ ) had arrhythmia documented as outpatient within 6 months of discharge.

## Discussion

Overall, the **minority** of patients (27%) who developed POAF were prescribed an OAC on discharge.

- Consistent with previous literature<sup>(15)</sup>
- High risk of bleeding post-operatively → increased risk of bleeding with addition of anticoagulant (majority within first 30 days)
- Concomitant indications for antiplatelets
  - Prior MI
  - Underwent CABG

## Discussion

The **majority** prescribed warfarin (61%) over DOAC (39%)

- Overall lack of evidence for use of DOACs in this patient population
- Extrapolated harm from studies including those with a mechanical valve
- Proportion of patients with non-mechanical mitral valve replacement/repair surgery

## Discussion

Overall, those prescribed anticoagulation on discharge had a higher occurrence of :



Documented AF as an outpatient within 6 months of discharge



Arrhythmia related ED visit/reason for hospital admission



Any hospital readmission or ED visit



More likely to have concomitant prescription for antiarrhythmic or beta-blocker on discharge



# Limitations

- Retrospective study design
- Patient data gathered from administrative databases
  - Relies on accuracy and completeness of diagnostic coding
  - No chart review
- Duration of POAF not determined
- Prescription fill history used as a measure of ongoing outpatient anticoagulation management
- Unable to comprehensively capture non-prescription use of acetylsalicylic acid → could impact interpretation of bleeding outcomes

## Conclusion

- In patients who develop new-onset POAF after cardiac surgery, a minority are prescribed oral anticoagulation
  - Majority are prescribed warfarin versus DOACs
- Special consideration must be taken when assessing a patient's risk of AF complications against the increased risk of bleeding, particularly in the post-operative period.
- Further research warranted to:
  - Identify which patients would derive the greatest benefit from OAC initiation
  - Establish the safety and efficacy of anticoagulants, including DOACs, for those with POAF after cardiac surgery

# Questions?

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