Antithrombotic strategies after bioprosthetic aortic valve replacement

HSRD Cyberseminar

May 21, 2018

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Disclosure

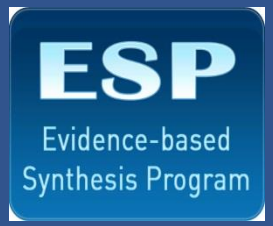
- This report is based on research conducted by the Evidence-based Synthesis Program (ESP) Center located at the Portland VA Medical Center, Portland, OR, funded by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Quality Enhancement Research Initiative. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (*eg*, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

Presentation Overview

- Clinical context
- Review of existing evidence
- Practice patterns and outcomes in VA
- Discussion:
  - Clinical considerations and implications

VA Evidence-based Synthesis Program Overview

- Sponsored by VA Office of Research and Development and the Quality Enhancement Research Initiative (QUERI)
- Established to provide timely and accurate syntheses/reviews of healthcare topics identified by VA clinicians, managers, and policy-makers, as they work to improve the health and healthcare of Veterans



VA Evidence-based Synthesis Program:

Provides evidence syntheses on important clinical practice topics relevant to Veterans, and these reports help:

- develop clinical policies informed by evidence the implementation of effective services
- support VA clinical practice guidelines and performance measures
- guide future research to address clinical knowledge gaps

Has a broad topic nomination process – e.g. VACO, VISNs, field – facilitated by ESP Coordinating Center (Portland) through an online submission process available at:

http://www.hsrd.research.va.gov/publications/esp/TopicNomination.cfm

ESP
Evidence-based Synthesis Program

Portland VA Evidence-based Synthesis Program: Current Report

Full Report (Papak, et al.) and VA data analysis (Bravata et al) available at the VA ESP website:

http://www.hsrd.research.va.gov/publications/esp/reports.cfm

ESP
Evidence-based Synthesis Program

Poll Question

For bAVR patients without any comorbidity that would drive antithrombotic medication choice, what is your preferred antithrombotic medication strategy?

(please choose single best answer)

1. Warfarin alone
2. Aspirin alone
3. Aspirin plus warfarin
4. Aspirin + warfarin first, then aspirin
5. Other strategy

Bioprosthetic Surgical Aortic Valve Replacement: Clinical Aspects

Jacquelyn Quin MD, Marco Zenati MD

Division Cardiac Surgery; VA Boston Healthcare System

Overview

- Rising incidence of aortic valve disease
- Aortic valve experience at VABHS
- Valve options
- Literature on anticoagulation
- Why study this with an ESP topic submission?

Trends in Aortic Valve Replacement for Elderly Patients in the United States, 1999-2011

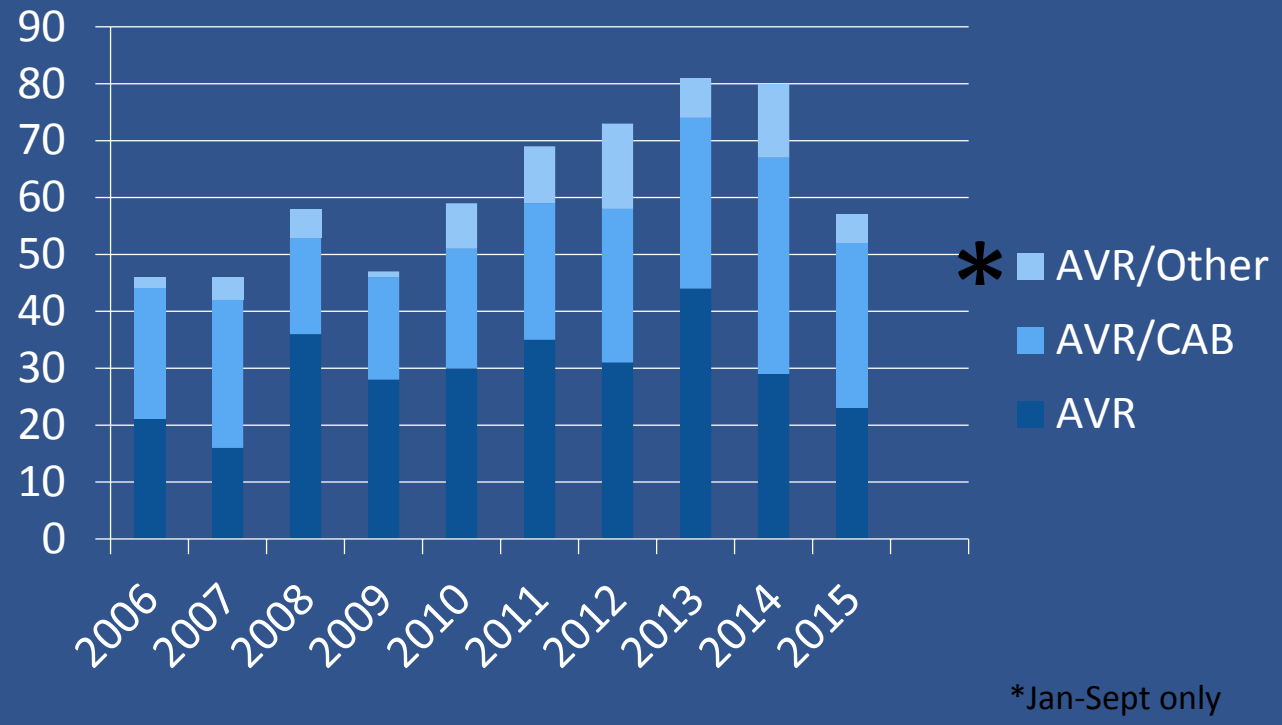
JA Barreto-Filho, JAMA Cardiology 2013

- Medicare fee-for-service beneficiaries age 65 or older
- Study dates 1999-2001

The incidence of Aortic Valve Replacements is increasing

- *19 procedures/100,000 person-years*
- *Main increases seen among patients age >75 years*

VABHS AVR cases 2006-2015



*Jan-Sept only

Average Age


Years
80
70
60
50
40
30
20
10
0
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015

Aortic valve implantation: Prosthetic Options

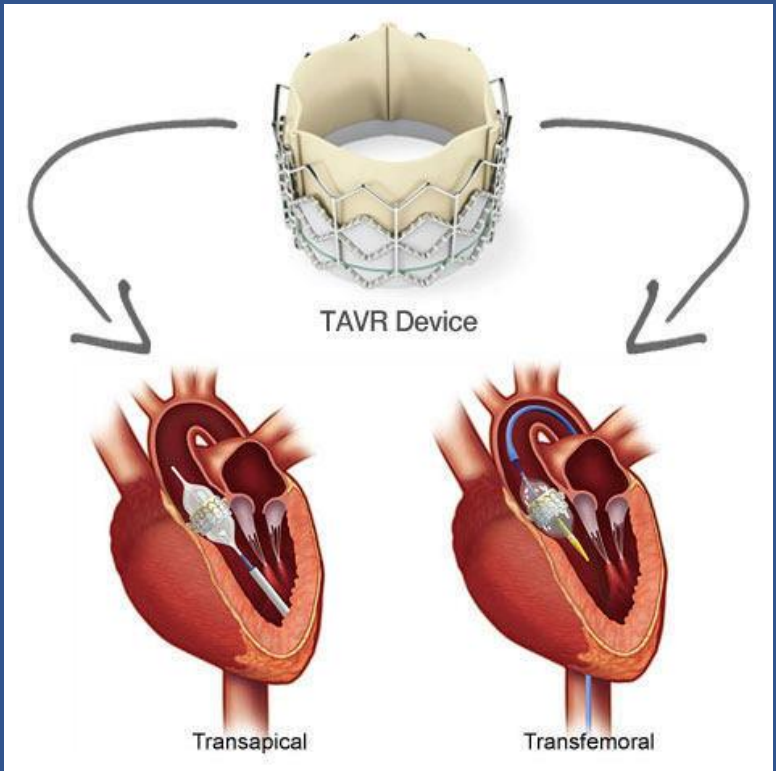
Mechanical Valves

- Favored in younger patients (except women of childbearing age)
- Extremely low valve deterioration rates
- Valve thrombogenic; lifelong anticoagulation needed
- Most commonly strategy: warfarin
  - Most common target INR 2.0 3.0 range
  - Certain valves acceptable target INR 1.5 2.0

Bioprosthetic Valves

- Commonly bovine or porcine based
- Possible technical advantages for implantation
- Lower thrombogenic potential; long term anticoagulation unnecessary
- Subject to structural deterioration
- Age threshold for implantation evolving (70 years →→ 60 years)

Transcatheter aortic valve replacement (TAVR):



- Intravascular implantation
- Initially reserved for high risk patients -> -> intermediate/low risk
- Avoids sternotomy / CPB
- Various access options
- Potential complications parallel SAVR
  - Stroke
  - Paravalvular leak
  - Heart block – need for pacemaker

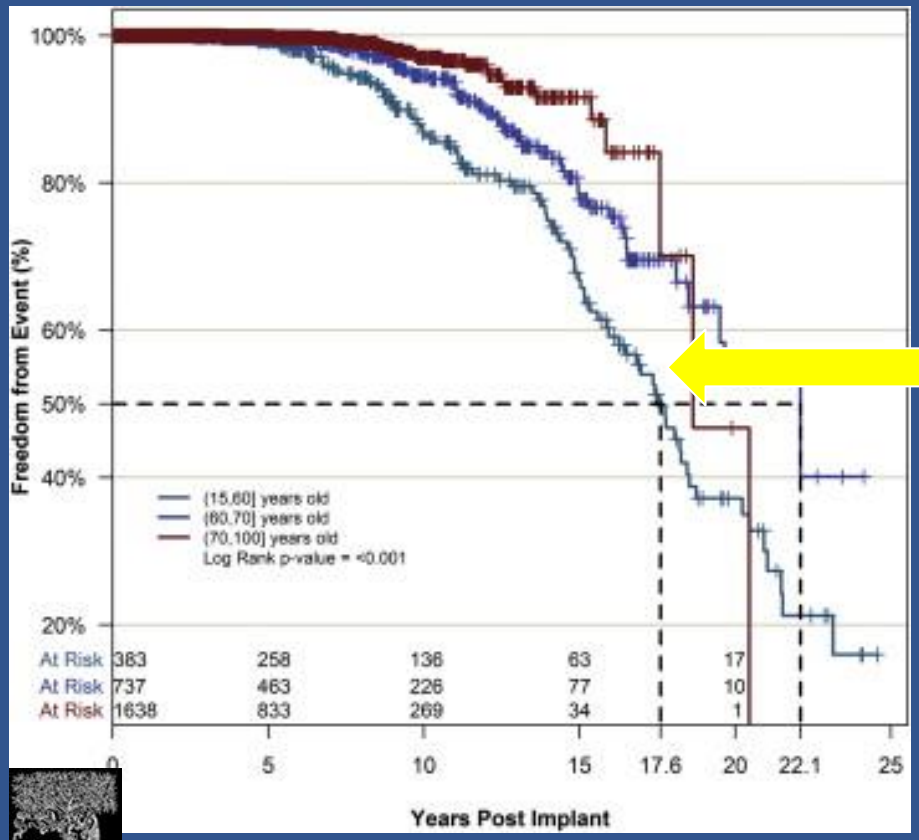
Very Long-Term Outcomes of the Carpentier-Edwards Perimount Valve in Aortic Position

- Tours University Hospital, Switzerland
- 2, 659 patients from 1984-2008
- Mean age at implantation: 70.7 ± 10.4 year
- Mean follow-up 6.7 ± 4.8 years (0-24.6 years)

Bourguignon, Ann Thoracic Surg. 2015;99(3):81-837

Fig 3

Kaplan Meier Freedom from structural valve deterioration by age groups

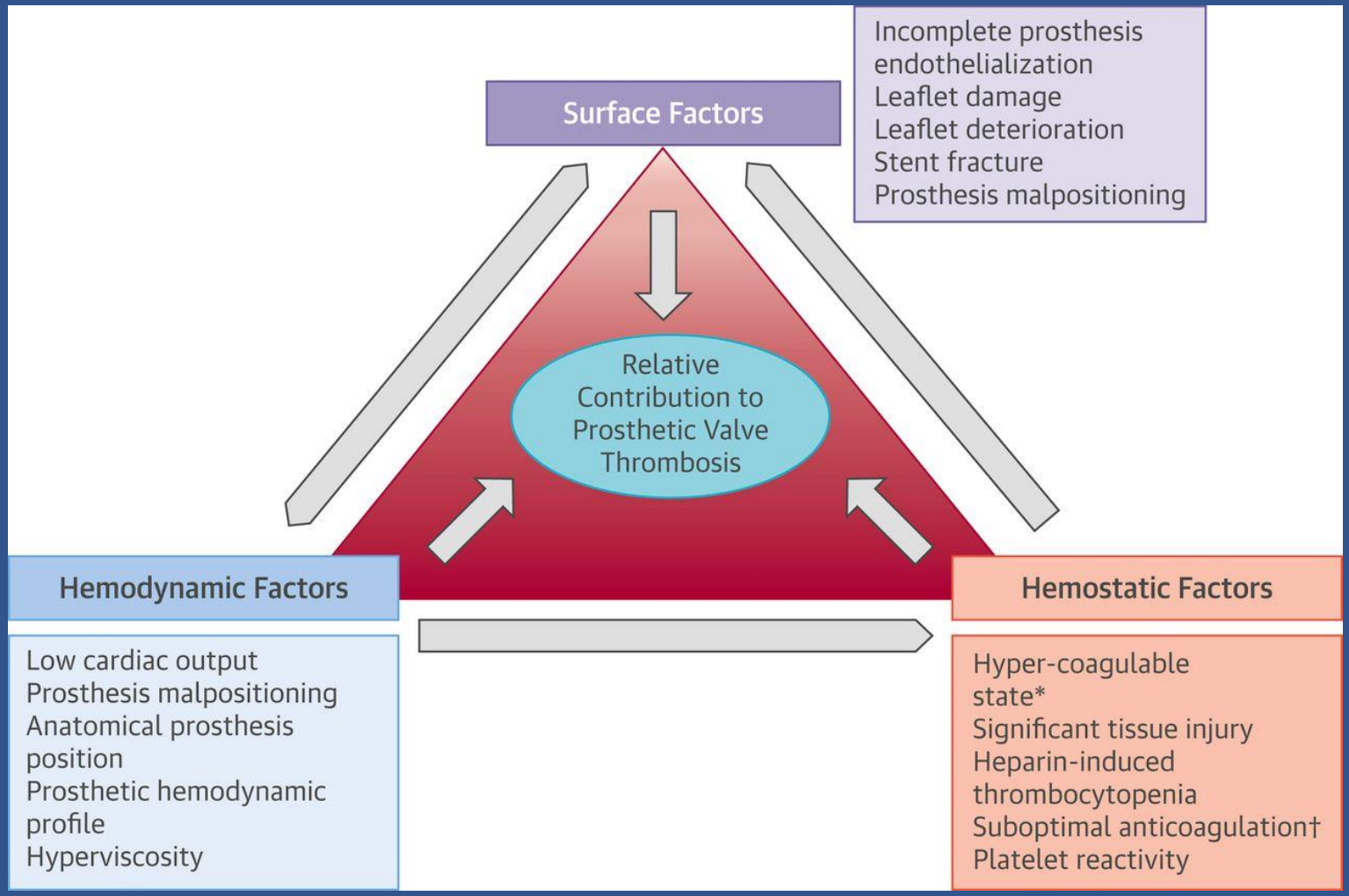


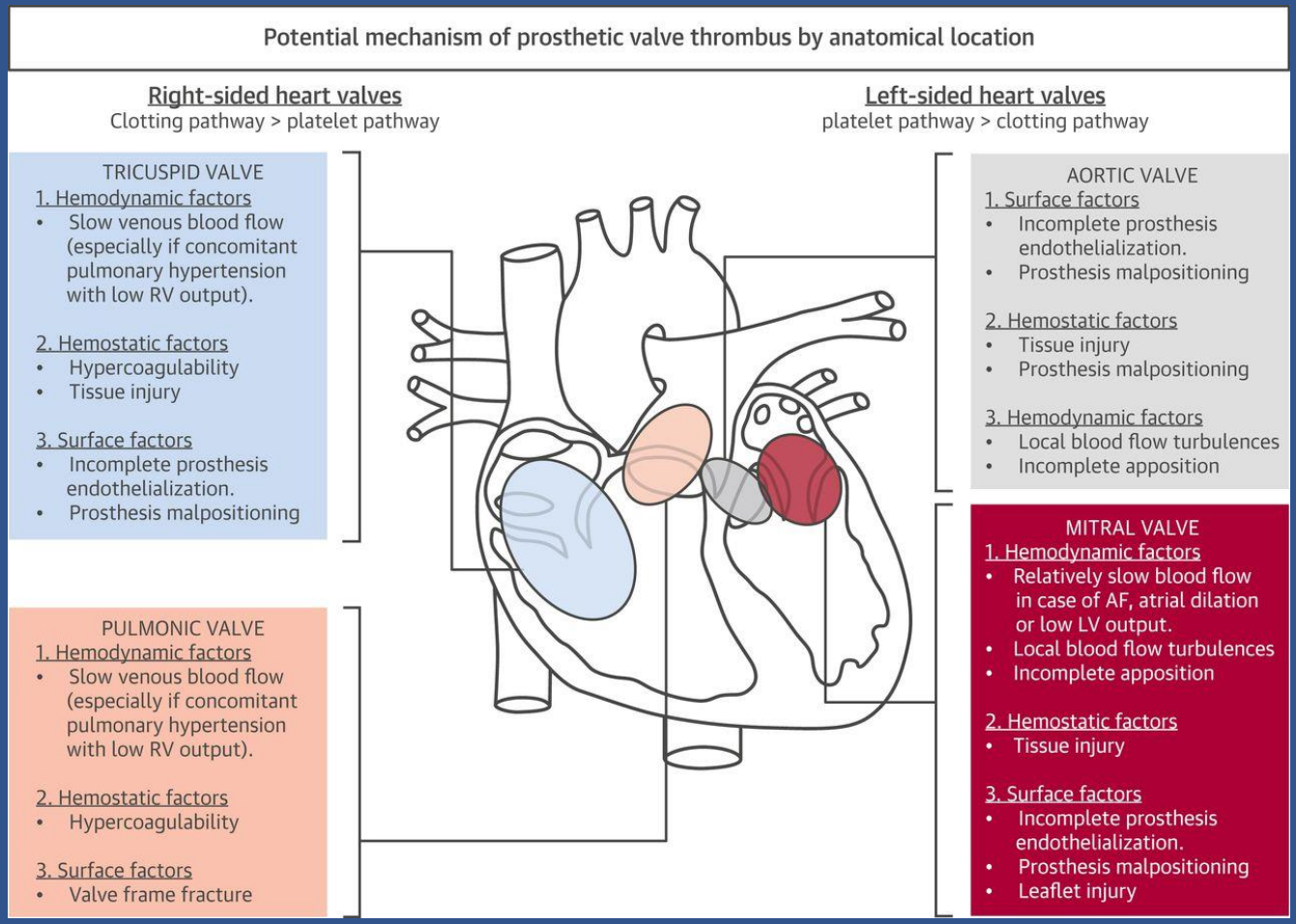
< 60 y/o age group:
Median longevity: 17.6 year /

The Annals of Thoracic Surgery 2015 99, 831 837DOI: (10.1016/j.athoracsur.2014.09.030)

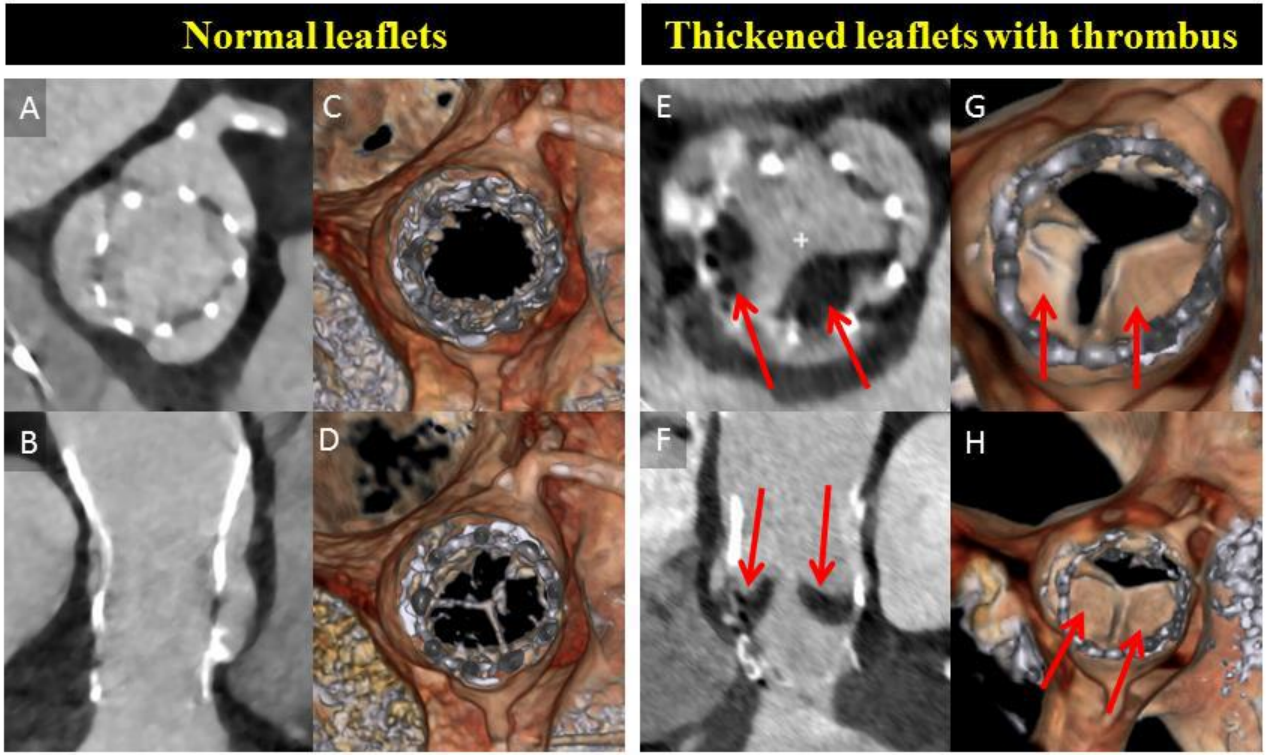
Prosthetic Heart Valve Thrombosis

G. Dangas, et. al; JACC 2016;68(24):2670-89

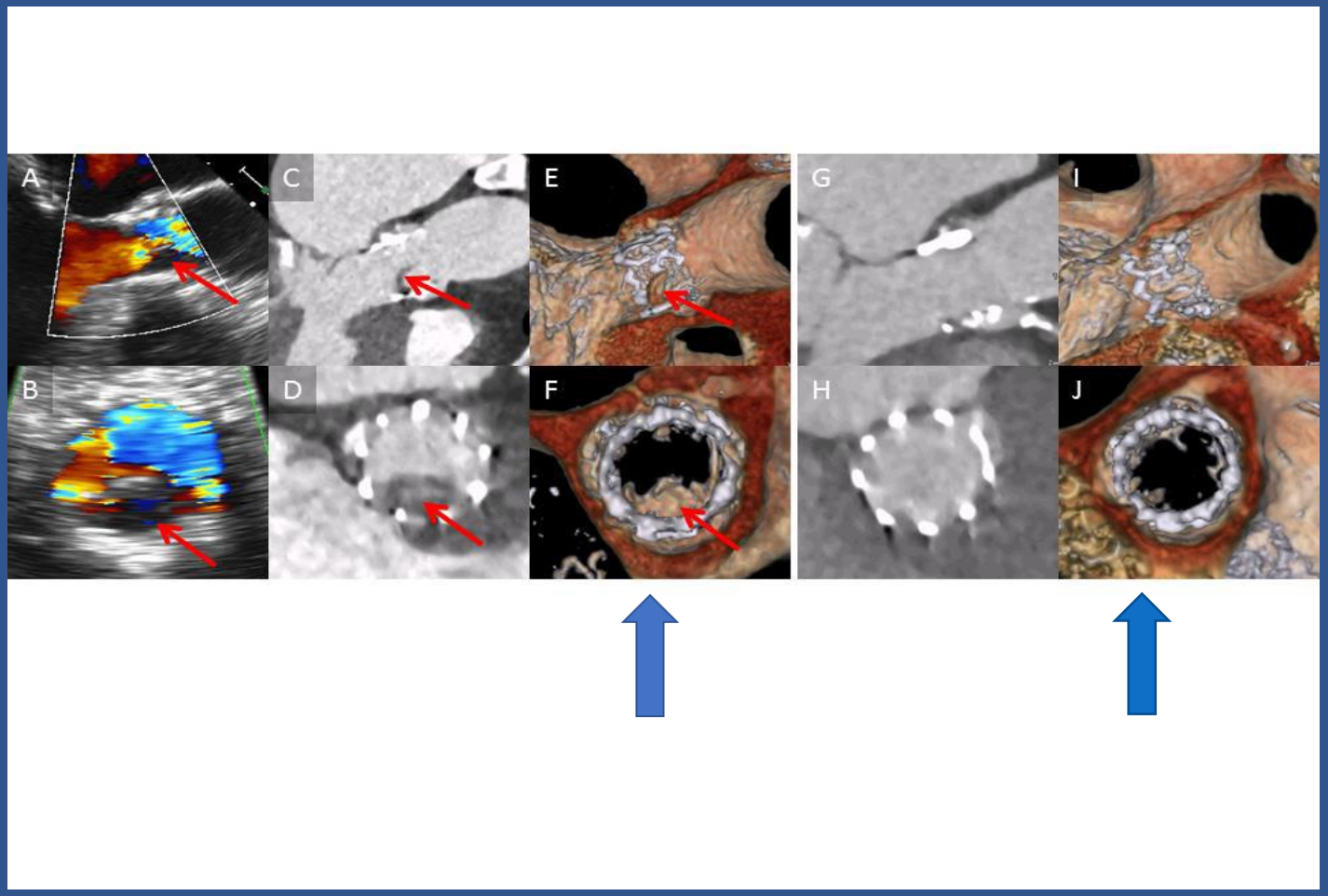




G. Dangas, et. al; JACC 2016;68(24):2670 89



Makkar et al NEJM 2015



Makkar et al NEJM 2015

Current bAVR guideline recommendations vary

- ACCP (2012): recommend aspirin (50-100 mg) over warfarin for first three months
- ACC/AHA (2017 update): VKA for 3-6 months in patients at low-risk for bleeding
- European Society of Cardiology (2012): oral anticoagulation may be considered for first three months

TAVR recommendations

- ACC/AHA: dual antiplatelet therapy for 6 months
  - Consider VKA for three months in patients at low risk for bleeding
- ACCF/AATS/SCAI/STS: dual antiplatelet therapy
- Canadian Cardiovascular Society: dual antiplatelet therapy 1-3 months

What is the optimal anti-thrombotic regimen post bAVR?

COMPARING ANTITHROMBOTIC STRATEGIES AFTER BIOPROSTHETIC AORTIC VALVE REPLACEMENT: A SYSTEMATIC REVIEW

Prepared for: Department of Veterans Affairs, Veterans Health Administration, Quality Enhancement Research Initiative, Health Services Research and Development Service

Prepared by: Evidence-based Synthesis Program (ESP) Center, VA Portland Health Care System; Devan Kansagara, MD, MCR, Director

Report authors: Joel Papak, MD; Joe Chiovaro, MD; North Noelck, MD; Laura Healy, PhD; Michele Freeman, MPH; Robin Paynter, MLIS; Allison Low, BA; Karli Kondo, PhD; Owen McCarty, PhD; Devan Kansagara, MD, MCR

Key questions and scope parameters

Key Question (KQ)	KQ1: What are the comparative benefits of antithrombotic strategies for patients who have had bAVR?	KQ2: What are the comparative harms of antithrombotic strategies for patients who have had bAVR?	KQ3: What are the comparative benefits and harms of antithrombotic strategies for patients who have had TAVR?
Population	Adult patients who have had bAVR. Exclude: bAVRs no longer used in practice; patients with valve replacements in positions other than the aorta (e.g., mitral valve, Ross procedure); pregnant women.		Adult patients who have had TAVR with stenting of aortic valves. Exclude: pregnant women
Intervention/ Comparators	• VKA • VKA plus ASA or other antiplatelet agents • ASA or other antiplatelet agents • Dual antiplatelet therapy • Non-vitamin K oral anticoagulants (NOACs) • No therapy	*Duration of antithrombotic therapy:* < 90 days ≥ 90 days	
Outcomes	• Mortality • Thromboembolic events • Stroke • Myocardial infarction • Heart failure • Readmission rates • Need for valve reoperation (e.g., valve thrombosis) • Length of stay • Need for change in antithrombotic strategy	• Major bleeding events - GI bleeds - Intracranial hemorrhage - Other (e.g., retroperitoneal) • Other/minor bleeding • Readmission rates • Pericardial or pleural effusion* *We will prioritize effusions requiring intervention.	Benefits and harms listed under KQs 1 and 2.
Timing	• Perioperative, defined as in-hospital or within 30 days. • Long-term, defined as >30 days to 1-year or longer.		
Study design	• Randomized controlled trials • Non-randomized controlled trials • Cohort studies (retrospective or prospective) or case-control studies that adequately control for important confounders		

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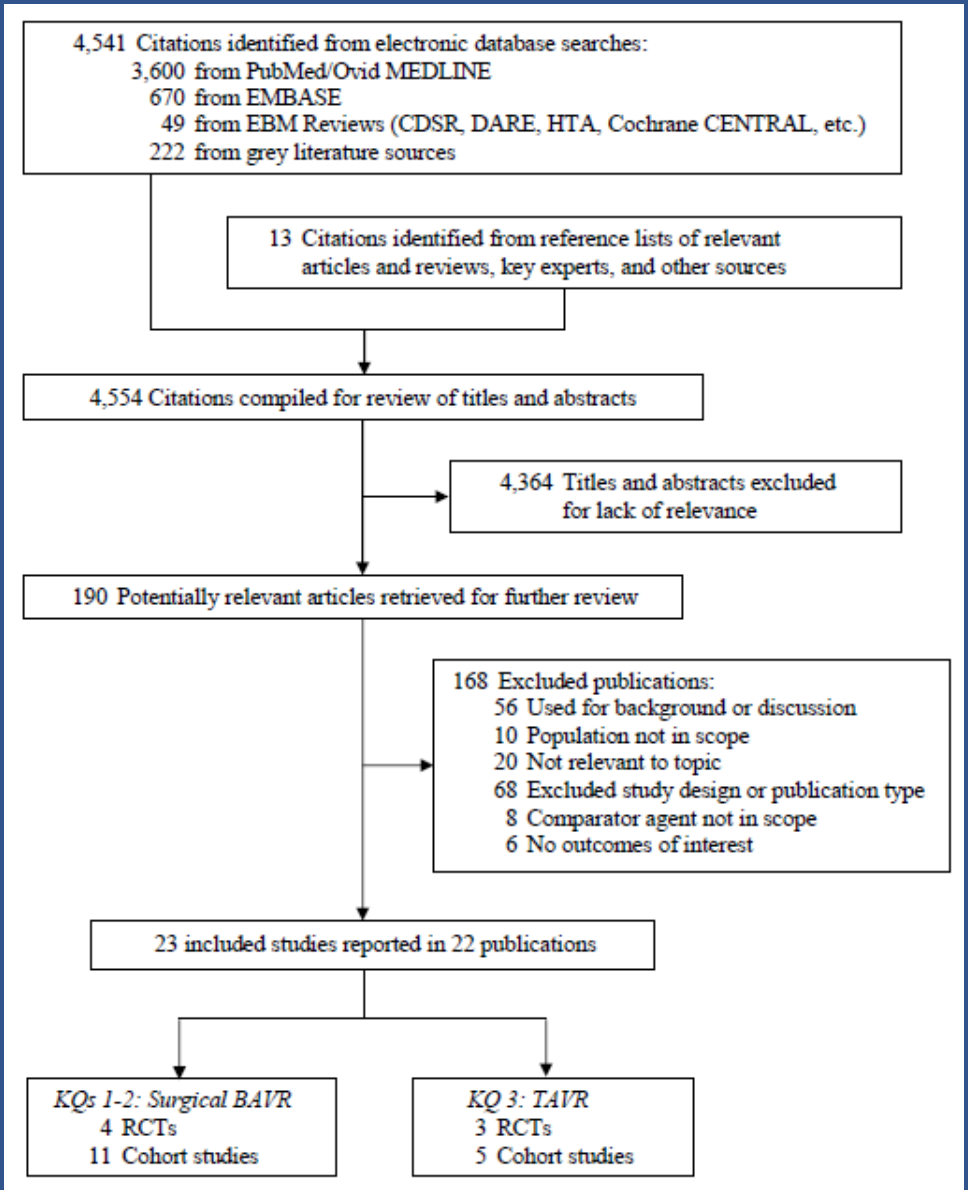
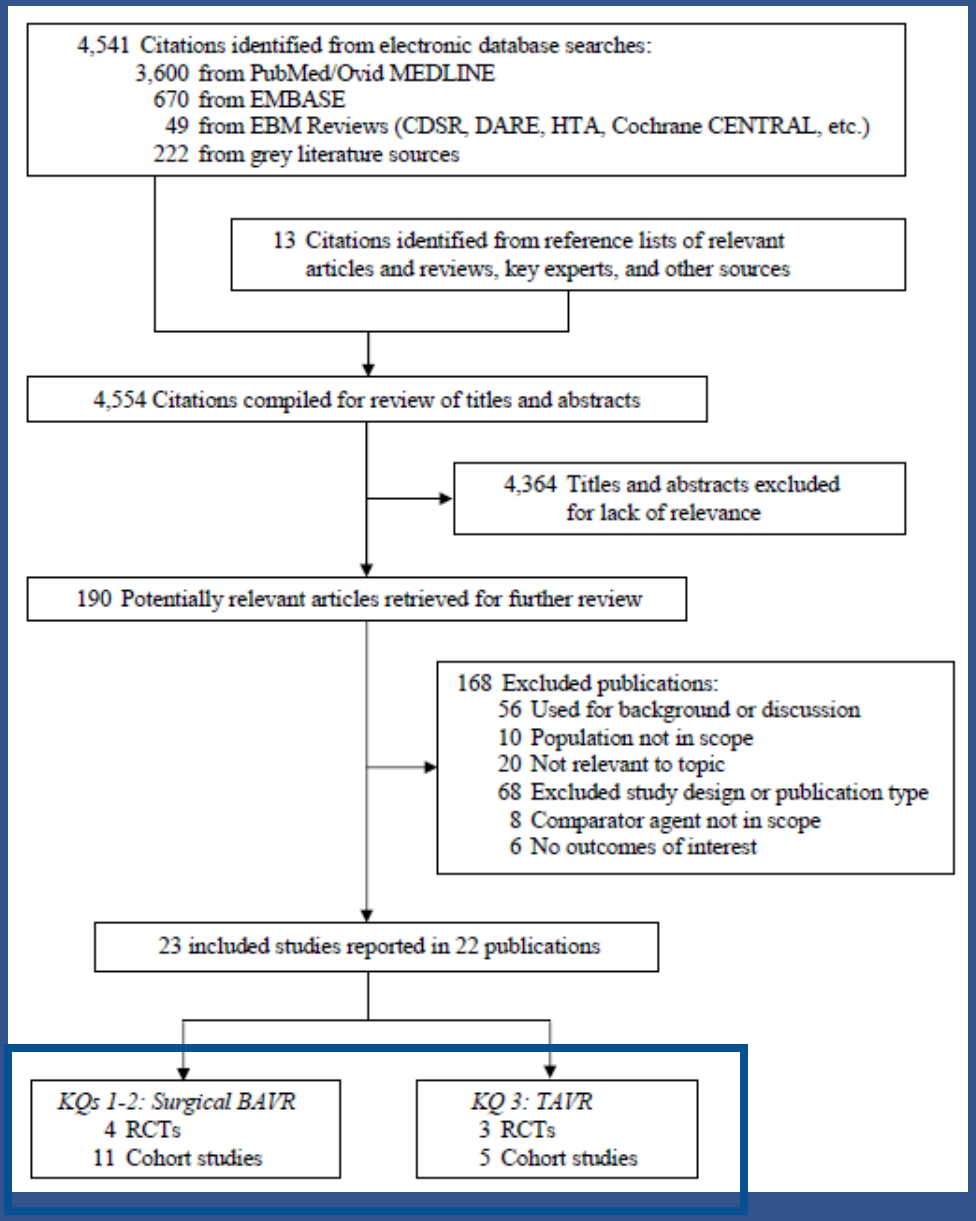
Summary of Findings

Literature search yield



Literature search yield



Strength of evidence

The overall quality of evidence for each outcome is based on the consistency, coherence, and applicability of the body of evidence; as well as the internal validity (risk of bias) of individual studies.

The strength of evidence is classified as follows:

- High = Further research is very unlikely to change our confidence on the estimate of effect.
- Moderate = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- Low = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
- Insufficient = Any estimate of effect is very uncertain.

Berkman N, Lohr K, Ansari M, et al. *Grading the Strength of a Body of Evidence When Assessing Health Care Interventions for the Effective Health Care Program of the Agency for Healthcare Research and Quality: An Update.* Rockville, MD: Agency for Healthcare Research and Quality; Methods Guide for Comparative Effectiveness Reviews (AHRQ Publication No. 13(14) EHC130 EF);2013.

Antithrombotic strategies after surgical bAVR

Outcomes per treatment comparison	N studies per outcome (N=combined participants)	Summary of findings	Strength of Evidence	Comments
VKA vs ASA				
• Mortality	3 RCTs (N=355) 5 cohorts (N=17,331)	No difference. Best evidence from 2 studies, at 3 months: ▪ 1 low-ROB RCT (N=236): 3.8% vs 2.9%, P = .721 ▪ 1 large cohort study (N=15,456): 4.0% vs 3.0%, P > .05	Moderate	Small RCTs, likely underpowered, but results are consistent with one large, well-conducted cohort study
• TE events	3 RCTs (N=355) 8 cohorts (N=18,506)	No difference. Best evidence from 2 studies, at 3 months: ▪ 1 low-ROB RCT (N=236): 3.8% vs 2.9%, P = .721 ▪ 1 large cohort study (N=15,456): 1.0% vs 1.0%, P > .05	Moderate	
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(VKA + ASA) vs ASA				
• Mortality	1 RCT (N=119) 2 cohorts (N=18,485)	Best evidence from 1 large cohort RR (95% CI): 0.80 (0.66 to 0.96), NNT 153	Low	Findings are based mostly on one large, well-conducted cohort study, in which absolute benefits were small relative to risk of harm. Other cohort studies and 1 RCT showed no difference.
• TE events	1 RCT (N=119) 4 cohorts (N=19,551)	Best evidence from 1 large cohort RR (95% CI): 0.52 (0.35 to 0.76), NNT 212	Low	
• Major bleeding	1 RCT (N=135) 1 cohort (N=18,429)	Best evidence from 1 large cohort RR (95% CI): 2.80 (2.18 to 3.60), NNH 55	Low	
(VKA + ASA) vs VKA	0 studies	---	Insufficient	No evidence currently available.

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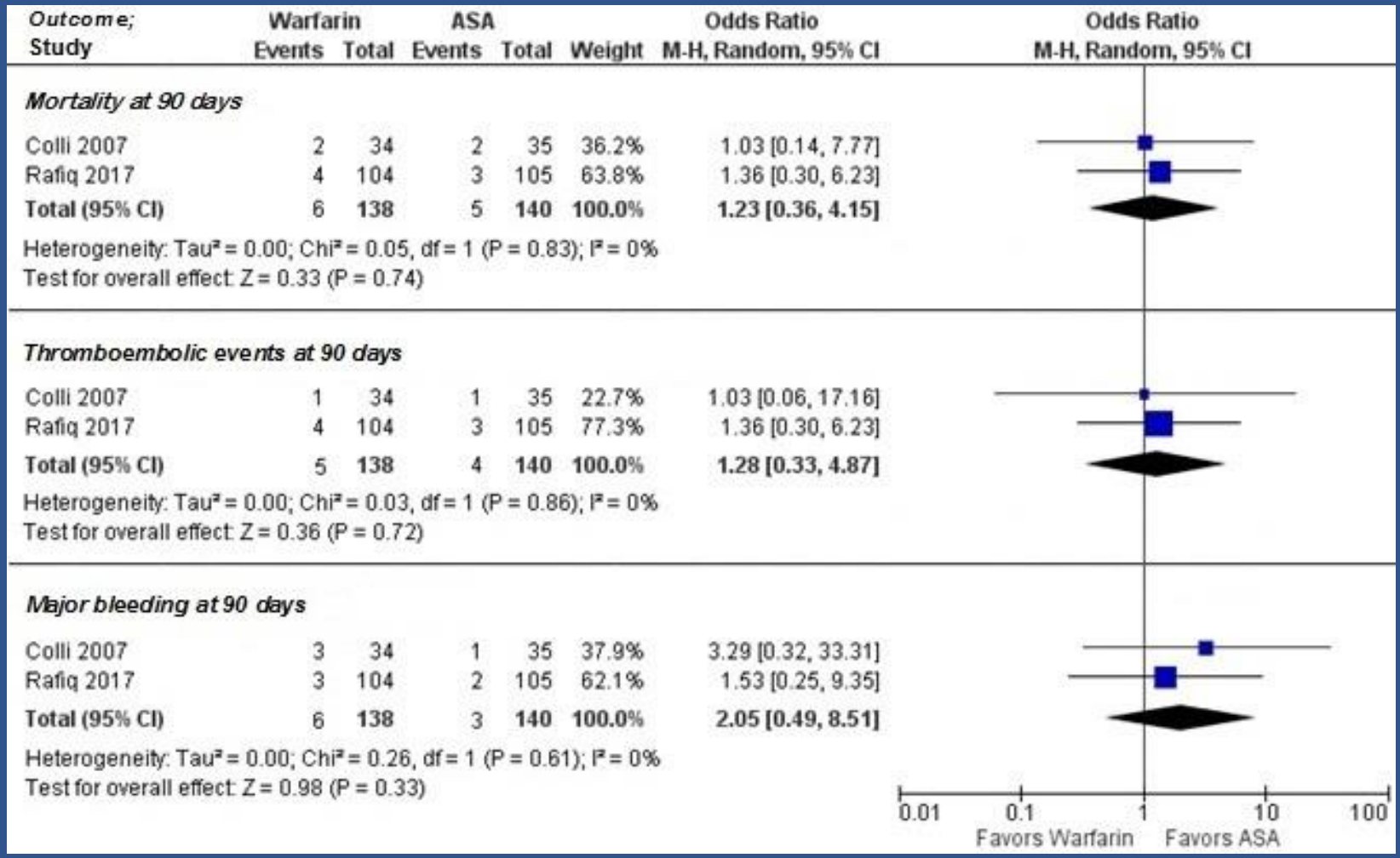
Outcomes at 90 days after bAVR (VKA vs ASA)



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Antithrombotic strategies after surgical bAVR, continued

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VKA vs no treatment				
• Mortality	2 cohorts (N=210)	Short-term: no differences at 3 months[1] Long-term: poorer survival with warfarin: 67.9% vs 76.1% at 8 years (P = .03)[2]	Insufficient	Evidence from smaller retrospective studies. INR generally not reported
• TE events	2 cohorts (N=347)	Elevated TE risk with warfarin in one study with 4.2 years followup.[3] Adjusted RR (95% CI): 3.0 (1.5 to 6.3), P = .0028; not specifed whether the referent group consisted of patients treated with ASA, no treatment, or a group combining patients treated with ASA and patients with no treatment.	Insufficient	
• Major bleeding	1 cohort (N=88)	No difference by treatment group in long-term freedom from hemorrhage.	Insufficient	
ASA vs no treatment				
• Mortality	1 cohort (N=360)	No difference.	Insufficient	ASA dose and duration were reported in only study
• TE events	3 cohorts (N=1983)	No difference.	Insufficient	
• Major bleeding	1 cohort (N=360)	No difference.	Insufficient	

Antithrombotic strategies after surgical bAVR, continued

Outcomes per treatment comparison	N studies per outcome (N=combined participants)	Summary of findings	Strength of Evidence	Comments
VKA vs no treatment				
• Mortality	2 cohorts (N=210)	Short-term: no differences at 3 months[1] Long-term: poorer survival with warfarin: 67.9% vs 76.1% at 8 years (P = .03)[2]	Insufficient	Evidence from smaller retrospective studies. INR generally not reported
• TE events	2 cohorts (N=347)	Elevated TE risk with warfarin in one study with 4.2 years followup.[3] Adjusted RR (95% CI): 3.0 (1.5 to 6.3), P = .0028; not specifed whether the referent group consisted of patients treated with ASA, no treatment, or a group combining patients treated with ASA and patients with no treatment.	Insufficient	
• Major bleeding	1 cohort (N=88)	No difference by treatment group in long-term freedom from hemorrhage.	Insufficient	
ASA vs no treatment				
• Mortality	1 cohort (N=360)	No difference.	Insufficient	ASA dose and duration were reported in only study
• TE events	3 cohorts (N=1983)	No difference.	Insufficient	
• Major bleeding	1 cohort (N=360)	No difference.	Insufficient	

Antithrombotic strategies after surgical bAVR, continued

Outcomes per treatment comparison	N studies per outcome (N=combined participants)	Summary of findings	Strength of Evidence	Comments
VKA vs no treatment				
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Antithrombotic strategies after TAVR

Outcomes per treatment comparison	N studies per outcome (N=combined participants)	Summary of findings	Strength of Evidence	Comments
ASA vs DAPT				
• Mortality	3 RCTs (N=421) 1 cohort (N=144)	No difference. Combined estimate (95% CI) at 3-6 months from meta-analysis of all 3 trials, ASA vs DAPT: 0.86 (0.38 to 1.95)	Moderate	Consistent findings of no difference among 3 low ROB trials. Sample sizes limit power to detect small differences in treatment effect.
• TE events	3 RCTs (N=421) 1 cohort (N=144)	No difference. Combined estimate (95% CI) at 3-6 months from meta-analysis of 2 trials, ASA vs DAPT: 0.46 (0.13 to 1.62)	Moderate	
• Major bleeding	3 RCTs (N=421) 1 cohort (N=144)	Marginally significant increased risk with DAPT vs ASA in one trial (N=222): 10.9% vs 3.6%, P = .038 Combined estimate (95% CI) at 3-6 months from meta-analysis of 2 trials, ASA vs DAPT: 0.43 (0.17 to 1.08)	Moderate	
APT vs (APT + OAC)				
• Mortality	2 cohorts (N=806)	No difference.	Insufficient	Treatment arms contain a mix of antithrombotic regimens.
• TE events	2 cohorts (N=806)	No difference.	Insufficient	
• Major bleeding	2 cohorts (N=806)	No difference at 1 year for DAPT (N=315) vs OAC (N=199, includes 188 VKA, 7 rivaroxaban, and 4 dabigatran) More bleeding complications at 30 days with DAPT (ASA+clopidogrel) vs SAPT (adding/maintaining ASA or maintaining clopidogrel), propensity score-matched (N=182): 30.8% vs 9.9%, P = .002.	Insufficient	

Antithrombotic strategies after TAVR

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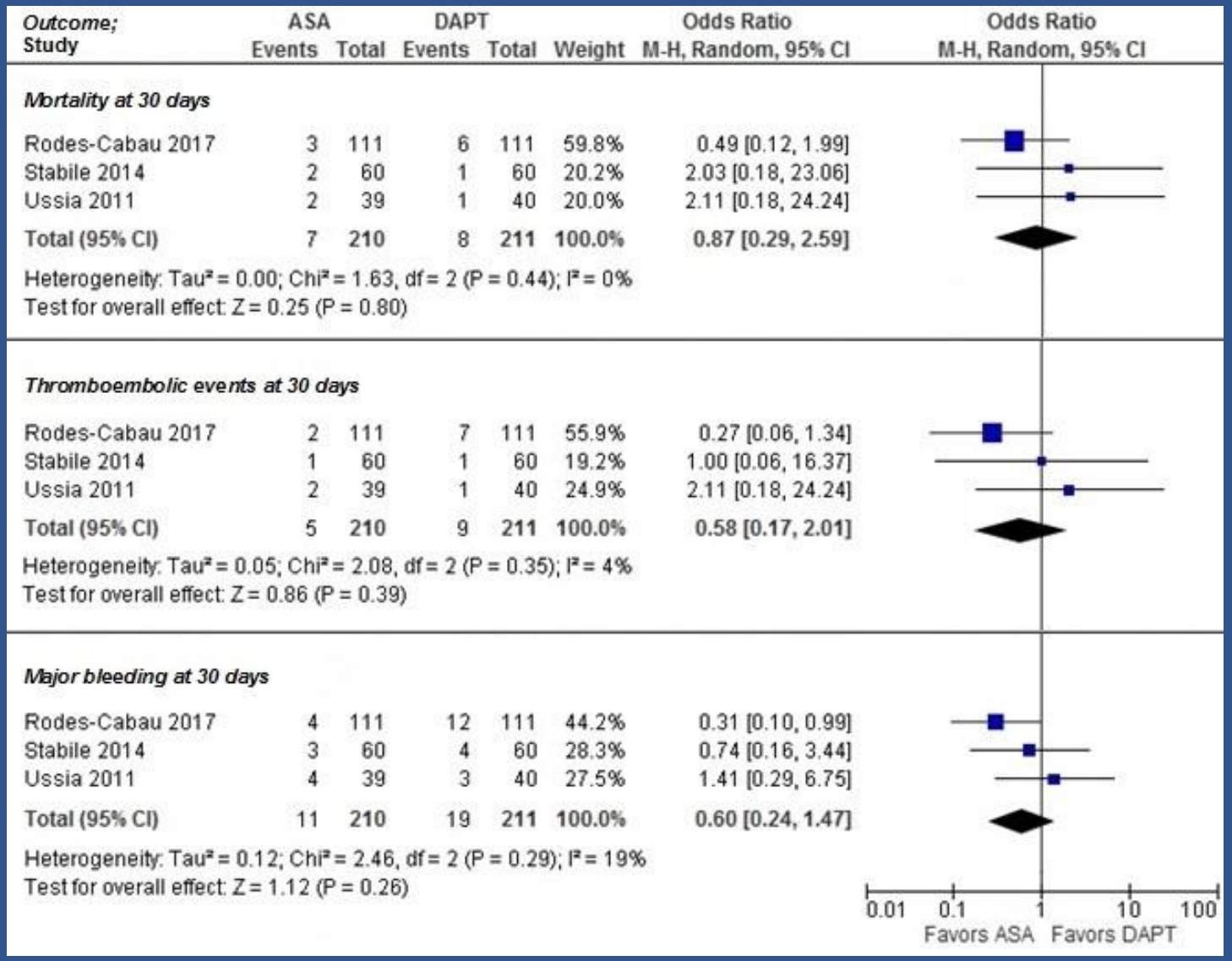
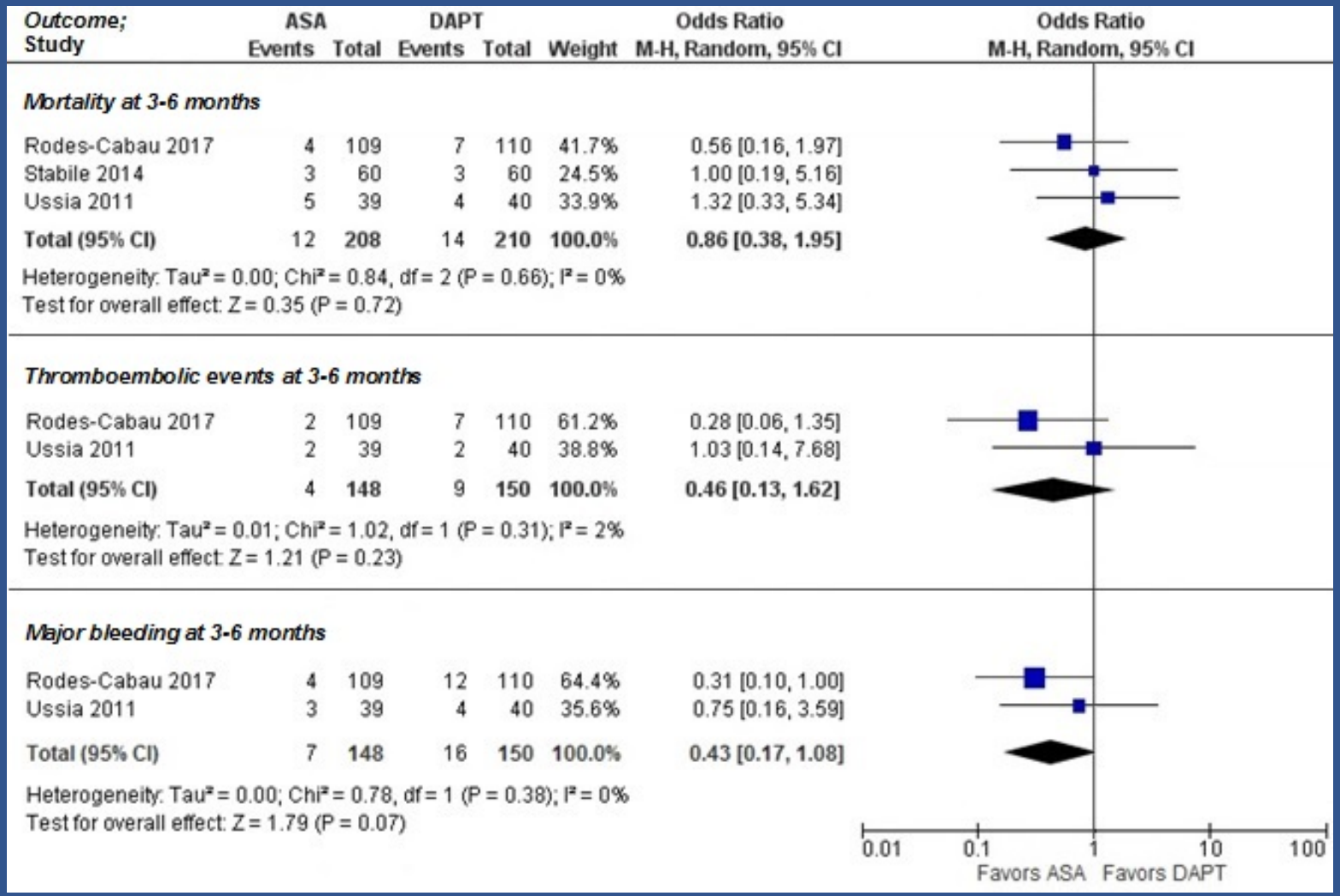
Outcomes at 30 days after TAVR (ASA vs DAPT)



Outcomes at 3-6 months after TAVR (ASA vs DAPT)



Antithrombotic strategies after TAVR

Outcomes per treatment comparison	N studies per outcome (N=combined participants)	Summary of findings	Strength of Evidence	Comments
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Antithrombotic strategies after TAVR, continued

Outcomes per treatment comparison	N studies per outcome (N=combined participants)	Summary of findings	Strength of Evidence	Comments
VKA monotherapy vs multiple antithrombotic therapy (MAT)				
• Mortality	1 cohort (N=621)	No difference.	Insufficient	Evidence is from one study.
• TE events	1 cohort (N=621)	No difference.	Insufficient	
• Major bleeding	1 cohort (N=621)	Increased risk of hemorrhage with MAT vs VKA: Adjusted HR (95% CI) for VARC-2 major or life-threatening bleeding, median 13 months followup: 1.85 (1.05 to 3.28), P = .04	Insufficient	
VKA vs NOAC (apixaban)				
• Mortality	1 cohort (N=272)	No difference.	Insufficient	Evidence is from one study.
• TE events	1 cohort (N=272)	No difference.	Insufficient	
• Major bleeding	1 cohort (N=272)	No difference.	Insufficient	

Antithrombotic strategies after TAVR, continued

Outcomes per treatment comparison	N studies per outcome (N=combined participants)	Summary of findings	Strength of Evidence	Comments
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• Major bleeding	1 cohort (N=272)	No difference.	Insufficient	

Conclusions about the existing literature

- Aspirin and warfarin probably have similar effects on mortality, thromboembolic events, and bleeding (moderate SOE)
- The combination of warfarin plus aspirin does not provide a large advantage over aspirin alone and carries a substantially higher bleeding risk (low SOE)
- Aspirin may be similarly effective to dual antiplatelet therapy after TAVR (moderate SOE)

Caveats about the existing literature

- Event rates in many studies were low and there are few RCTs
- A very large trial would be required to detect small absolute differences
  - 6226 patients/arm to detect a 1% difference in thromboembolic events
- The TAVR studies are relatively small, and can't exclude small differences in treatment effect

Antithrombotic Use After Bioprosthetic Aortic Valve Replacement in the Veterans Health Administration System

May 21, 2018

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Barbara Homoya, RN; Anthony J. Perkins, MS; Kathy Snow, MS;
Jacquelyn A. Quin, MD; Zhang Ying, PhD;
and Laura Myers, PhD

HSR&D Health Services Research & Development Service
CHIC Center for Health Information and Communication
VA QUERI Quality Enhancement Research Initiative

Objectives

- Describe post-bAVR antithrombotic medication practices across the VHA
- Describe post-bAVR outcome rates
- Examine the relationship between antithrombotic medication strategies and post-bAVR outcomes

Methods: Cohort Construction
bAVR in FY2005-2015

- Any AVR based on CPT or ICD9 codes
  - During FY2005-15 period
  - At a VA facility
- Include bAVR and exclude mechanical AVR
  - Text mining of notes
  - Hierarchy of notes starting with Nurse Intraoperative Report
  - Identify implanted prosthesis item name, vendor, model, lot/series, size
  - "Carpentier Edwards Perimount, model 2700/2700TFX"
- Validated with targeted chart review: 100% specificity, approach may have excluded some patient who actually received bAVR but all patients in this cohort had bAVR (none had mAVR)

Methods: Antithrombotic Medications

- **Data Sources**: CDW data: outpatient VA pharmacy, non-VA pharmacy files, health factors
- **Validation**: targeted chart review

Classification	MEDICATIONS
Warfarin	Warfarin (Coumadin), Jantoven
Aspirin	Aspirin, ASA, Bufferin
	Aspirin/Dipyridamole (Aggrenox)
	Dipyridamole
Non aspirin Antiplatelet	Clopidogrel (Plavix)
	Ticlopidine (Ticlid)
	Prasugrel (Effient)
Direct oral anticoagulants (DOACs)	Dabigatran (Pradaxa)
	Apixaban (Eliquis)
	Rivaroxaban(Xarelto)
	Edoxaban (Savaysa)
	Betrixaban
	Eribaxaban
~~Full Dose Low Molecular Weight Heparins~~	~~Ardeparin~~
	~~Bemiparin~~
	~~Certoparin~~
	~~Dalteparin (Fragmin)~~
	~~Enoxaparin (Lovenox)~~
	~~Nadroparin (Fraxiparine)~~
	~~Parnaparin~~
	~~Reviparin~~
	~~Tinzaparin (Innohep)~~
Other	Danaparoid (Organon)
	Hirudin (Lepirudin) REFLUDAN
	Bivalirudin (Angiomax)
	Argatroban
	Eptifibatide
	Fondaparinux (Arixtra)
	Idraparinux
	Tirofiban
	Bciximab (ReoPro)

Final Medication Classification:

1. Aspirin alone
2. Warfarin alone
3. Aspirin plus Warfarin
4. Dual anti-platelets
5. No antithrombotic
6. Other

Risk Adjustment Methods

Compared outcomes among patients receiving three most common antithrombotic medication strategies:

- Aspirin + Warfarin
- Dual antiplatelets
- Aspirin only (reference)

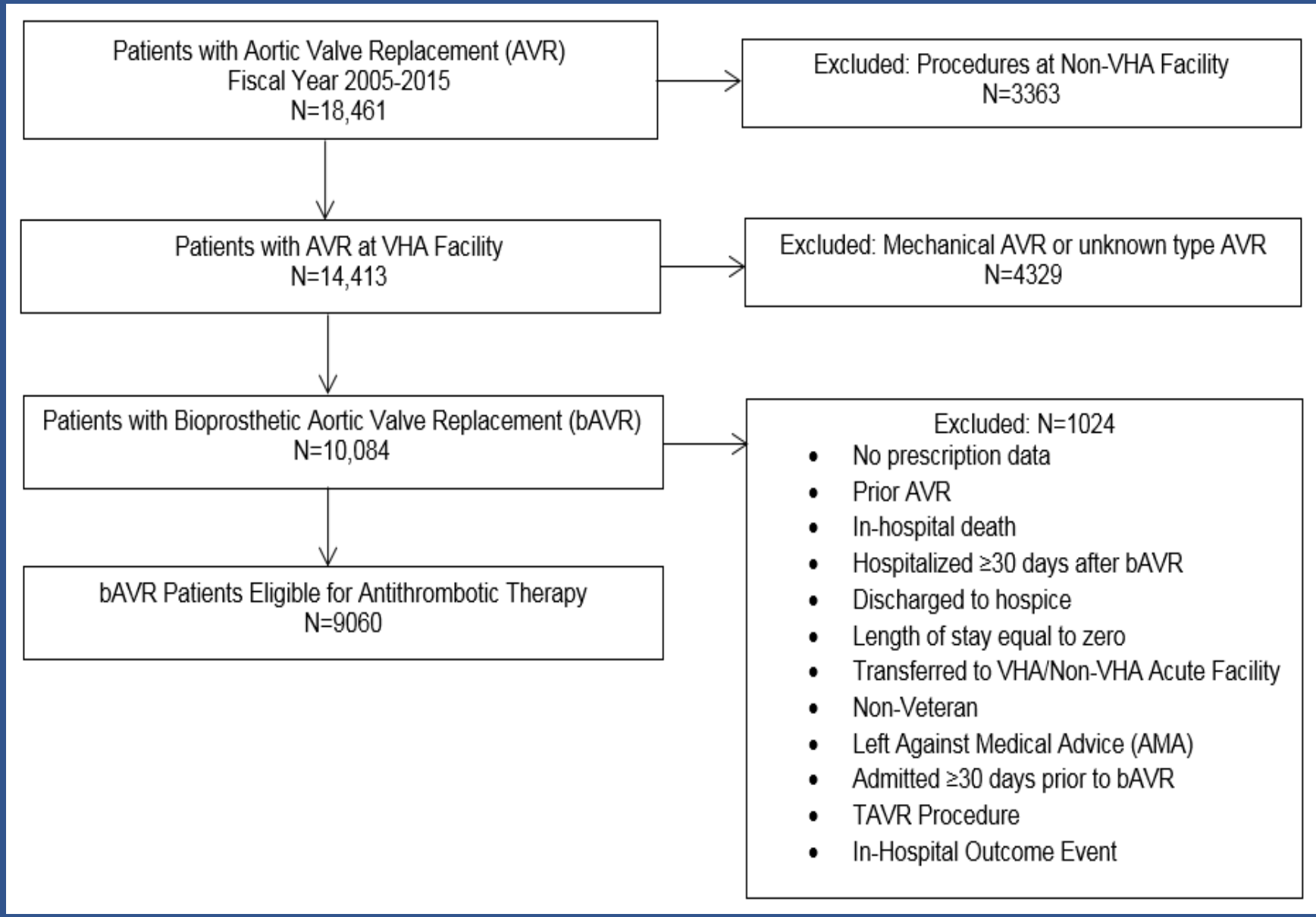
Propensity score:

- Multinomial logit model to predict antithrombotic medication group using baseline variables significantly associated with medication group
- Included random effect for surgical facility to account for similarities in medication use within a facility
- Predicted probabilities of each antithrombotic medication were used as covariates in final models

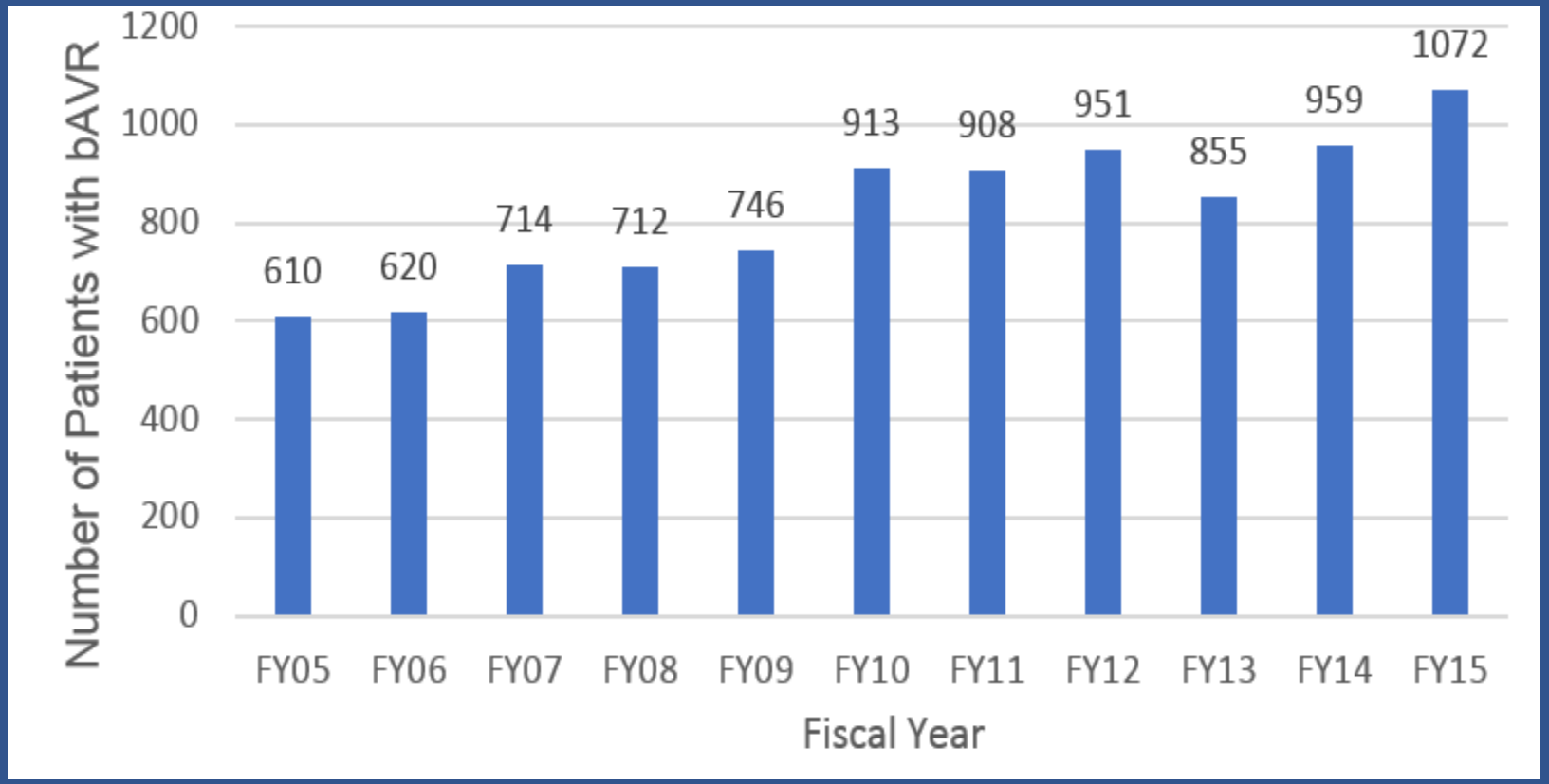
Risk adjusted modeling: mixed effects logistic regression

- With medication group and propensity score (fixed effects) and random effect for surgical facility
- Added baseline variables significantly associated with outcomes

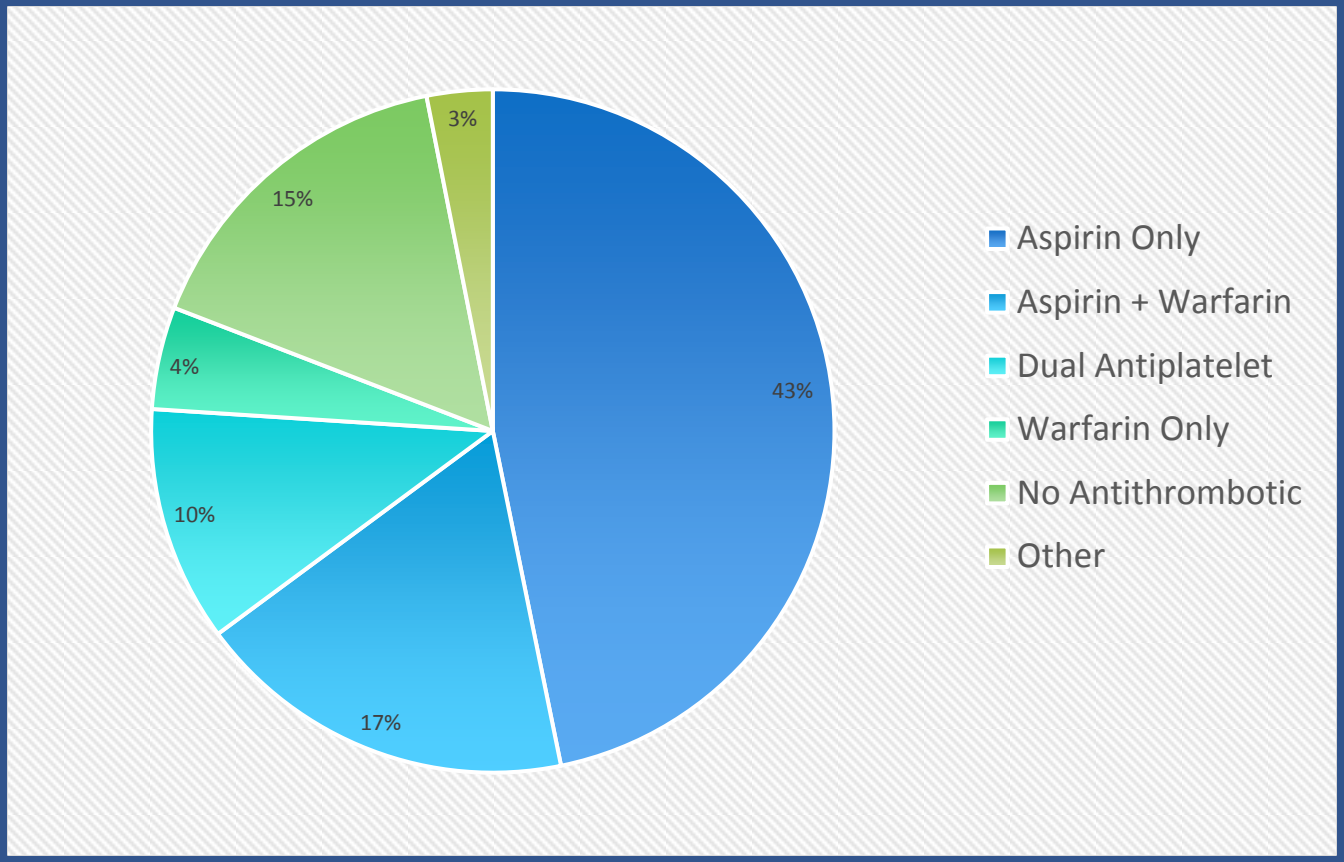
Cohort Construction



Number of Patients with bAVR by Year in VHA

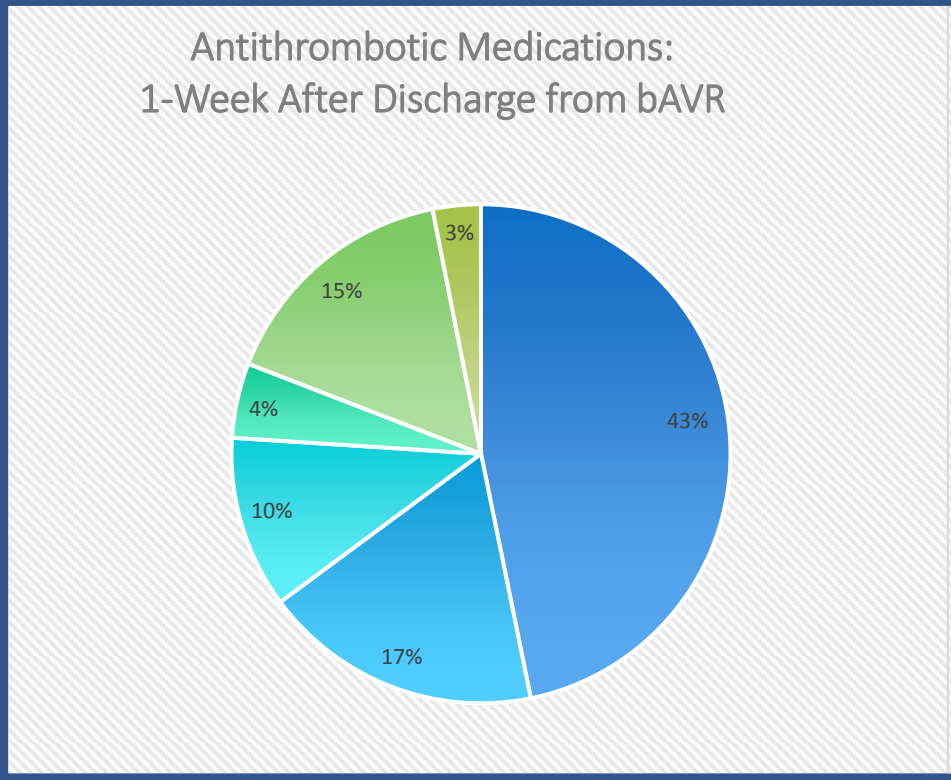


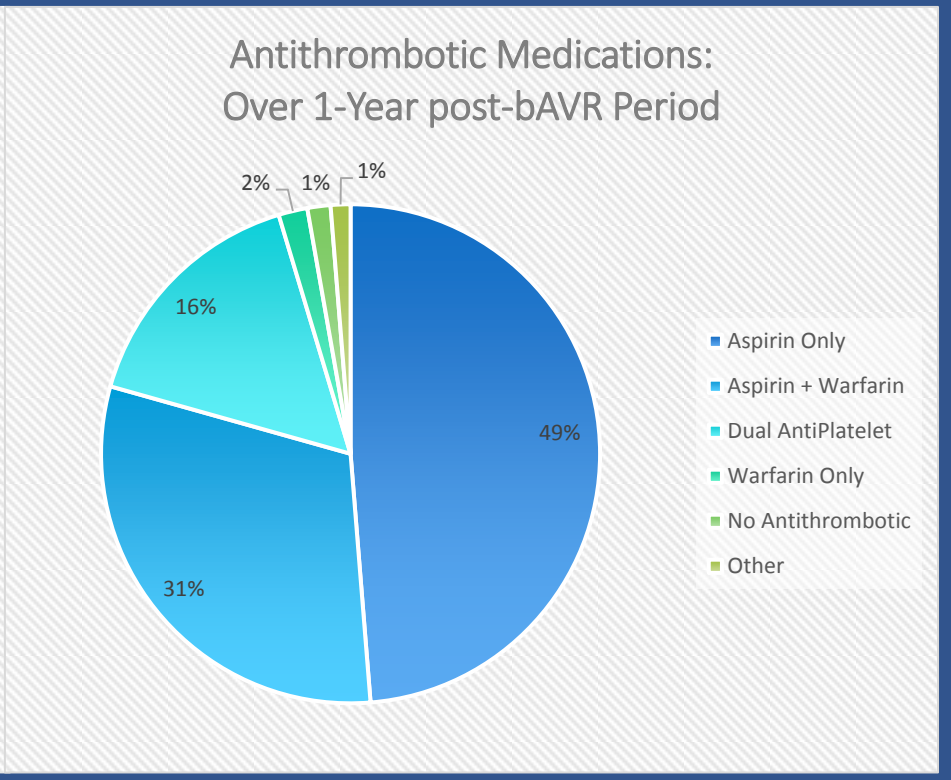
Antithrombotic Medication Use: within 1 Week of Discharge post-bAVR



Nearly half of all patients receive aspirin alone.

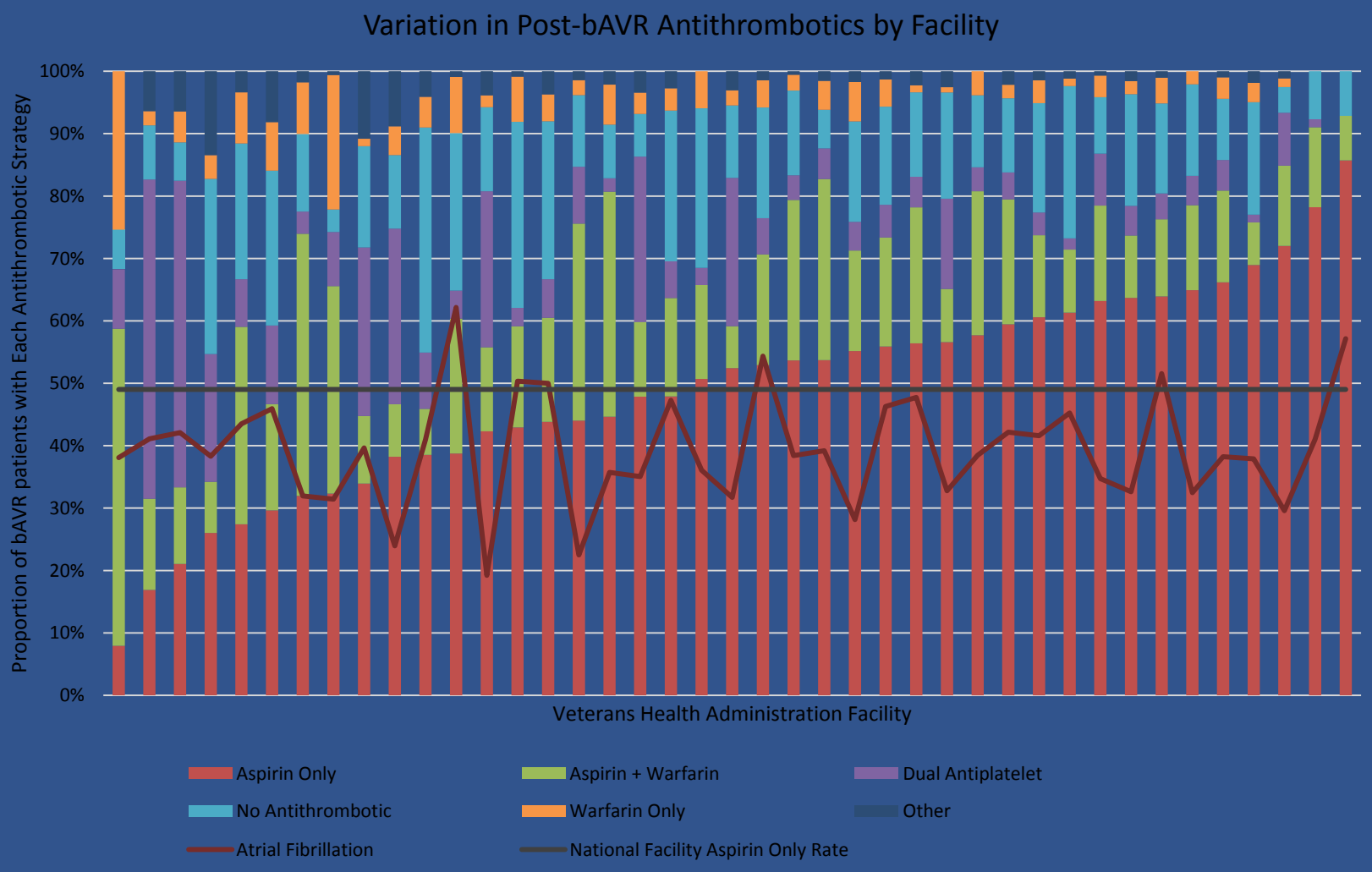
Change in Antithrombotic Medication Use: Within 7-days of Discharge to 1-Year After bAVR





- *Antithrombotic medications are commonly changed after discharge, many patients are switched to warfarin-based strategy*
- *Patients discharged on no medications commonly receive some medication over time*

Variation in Post-bAVR Antithrombotics by Facility



Includes VAMCs with ≥10 bAVR patients

Baseline Characteristics by Antithrombotic Strategy

Characteristic	Aspirin+ Warfarin (N=1638) 16.8%	Aspirin Only (N=4240) 43.42%	Dual Anti Platelet (N=1010) 10.3%	No Antithrombotic (N=1451) 14.9%	Other Only (N=282) 2.9%	Warfarin Only (N=439) 4.5%
bAVR with CABG procedure	47.9	44.2	67.5	44.6	69.9	43.3
History of Smoking	26.8	29.5	30.6	24.4	29.4	25.7
Hypertension	86.8	87.1	90.8	89.1	91.1	90.7
Hyperlipidemia	73.6	73.8	80.2	71.5	84.8	72.7
Diabetes mellitus	39.0	38.4	45.6	42.4	47.2	37.4
MI	10.3	10.0	19.3	9.1	19.2	7.5
Atrial fibrillation	66.6	30.2	28.1	37.7	28.4	70.2
Congestive heart failure	36.3	25.8	30.9	30.2	28.4	41.0
Stroke	4.4	3.0	4.6	4.6	5.7	3.6
Cirrhosis	1.2	1.4	0.9	2.4	1.8	1.1
Pulmonary embolism/deep vein thrombosis	0.8	0.1	0.2	0.1	0.0	0.7
Peripheral arterial disease	24.2	20.9	23.2	21.4	25.2	17.8
Carotid endarterectomy or stent	1.5	0.8	6.4	1.2	5.3	1.6
Coronary artery disease, CABG, or PCI	74.8	71.4	88.5	72.8	90.8	70.8
Valvular heart disease	30.1	23.9	20.1	25.0	23.8	27.8
Aspirin allergy	1.6	2.0	3.2	3.6	14.9	5.2
Aspirin before the bAVR	67.7	72.3	76.6	66.2	65.6	49.4
Warfarin before the bAVR	30.2	3.5	3.3	8.6	2.8	38.5
Clopidogrel before the bAVR	7.4	4.5	32.7	4.3	44.3	8.4

As expected, there are <u>many</u> differences in patients among the medication groups

Post-bAVR Outcomes

90-Day Outcomes	**Overall** (N=9060)
	% (N)
Composite outcome	4.4 (398)
Death	1.4 (127)
Bleeding	1.6 (149)
Thromboembolism	1.6 (142)
Myocardial infarction	0.6 (50)
Stroke	0.5 (45)
Pulmonary Embolism or deep vein thrombosis	0.6 (51)

Association Between Antithrombotic Strategy and Outcomes

90-Day Mortality	Unadjusted			Propensity Score Adjusted			Fully Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Aspirin + Warfarin	1.23	0.77-1.96	0.393	1.09	0.63-1.92	0.751	1.10	0.63-1.94	0.739
Dual Antiplatelet	0.91	0.49-1.72	0.781	0.85	0.39-1.85	0.678	0.92	0.43-1.96	0.827
Aspirin Only	1.00	-	-	1.00	-	-	1.00	-	-
Propensity for Aspirin + Warfarin				1.59	0.57-4.46	0.376	0.54	0.16-1.87	0.328
Propensity for Dual Antiplatelets				1.35	0.38-4.81	0.645	0.91	0.26-3.16	0.883
Hyperlipidemia							0.55	0.35-0.87	0.011
Mitral valve prolapse							2.14	1.07-4.27	0.032
Charlson Comorbidity Index							1.13	1.03-1.24	0.010
Age (years)							1.04	1.02-1.07	0.001
Number of prior admissions							1.21	1.06-1.39	0.006
History of atrial fibrillation							1.59	0.95-2.66	0.078
Average systolic blood pressure							1.02	1.00-1.03	0.031

No differences in 90-day mortality were observed across the three antithrombotic medication strategies

Association Between Antithrombotic Strategy and Outcomes

90-Day Thromboembolism	Unadjusted			Propensity Score Adjusted			Fully Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Aspirin + Warfarin	1.13	0.73-1.78	0.580	0.88	0.52-1.49	0.631	0.82	0.48-1.40	0.458
Dual Antiplatelet	1.25	0.75-2.10	0.396	1.21	0.63-2.34	0.564	1.20	0.62-2.32	0.589
Aspirin Only	1.00	-	-	1.00	-	-	1.00	-	-
Propensity for Aspirin + Warfarin				2.36	0.94-5.91	0.067	1.93	0.75-4.96	0.174
Propensity for Dual Antiplatelets				1.19	0.37-3.80	0.772	1.04	0.32-3.40	0.952
Charlson Comorbidity Index							0.85	0.76-0.95	0.005
History of coagulation defect							2.44	1.15-5.18	0.020
History of PE/DVT*							11.56	3.19-41.89	<0.0001
History of transient ischemic attack							2.88	1.11-7.46	0.029
History of stroke							2.26	1.13-4.51	0.021
CHADVASC score							1.22	1.04-1.41	0.012

*PE refers to pulmonary embolism and DVT refers to deep vein thrombosis.

No differences in 90-day thromboembolic events were observed across the three medication groups

Association Between Antithrombotic Strategy and Outcomes

90-Day Bleeding	Unadjusted			Propensity Score Adjusted			Fully Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Aspirin + Warfarin	2.58	1.71-3.89	<0.0001	1.89	1.16-3.08	0.011	1.92	1.17-3.14	0.010
Dual Antiplatelet	1.71	1.00-2.93	0.050	1.85	0.94-3.64	0.075	1.86	0.95-3.63	0.070
Aspirin Only	1.00	-	-	1.00	-	-	1.00	-	-
Propensity for Aspirin + Warfarin				2.77	1.18-6.53	0.020	2.17	0.91-5.16	0.080
Propensity for Dual Antiplatelets				0.89	0.26-3.05	0.849	0.99	0.29-3.34	0.986
Age (years)							1.05	1.02-1.07	<0.0001
History of coagulation defect							2.42	1.21-4.87	0.013
History of bleeding							6.86	3.87-12.16	0.000
History of liver disease							2.93	1.57-5.44	0.001

Aspirin plus warfarin was associated with higher odds of bleeding compared with aspirin alone even after risk adjustment

Association Between Antithrombotic Strategy and Outcomes

90-Day Any Adverse Event (Death, Thromboembolism, or Bleeding)	Unadjusted			Propensity Score Adjusted			Fully Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Aspirin + Warfarin	1.60	1.23-2.09	<0.0001	1.29	0.94-1.76	0.112	1.29	0.94-1.77	0.113
Dual Antiplatelet	1.31	0.94-1.83	0.108	1.37	0.90-2.09	0.140	1.37	0.90-2.07	0.141
Aspirin Only	1.00	-	-	1.00	-	-	1.00	-	-
Propensity for Aspirin + Warfarin				2.14	1.21-3.78	0.009	1.65	0.93-2.93	0.084
Propensity for Dual Antiplatelets				0.96	0.45-2.05	0.916	0.97	0.46-2.04	0.943
Hyperlipidemia							0.70	0.54-0.90	0.006
Age (years)							1.03	1.02-1.05	<0.0001
Number prior admissions							1.11	1.02-1.21	0.016
History coagulation defect							1.68	0.99-2.86	0.057
History of PE/DVT*							3.68	1.12-12.12	0.032
History of bleeding							2.87	1.73-4.76	<0.0001

*PE refers to pulmonary embolism and DVT refers to deep vein thrombosis.

No differences in the odds of the 90-day combined endpoint were observed after risk adjustment

Limitations

- One facility excluded because no access to TIU notes
- Focus on first bAVR: may include some patients with distant prior AVR
- Extensive, detailed chart review would be required to understand clinical reasoning for medication choices and extent to which patient preferences drive medication practices
- Focus on post-discharge period: medications and outcomes during in-hospital period were not included
- Although non-VHA medication data included: there may be under-reporting of non-VHA medications
- Focused on first antithrombotic strategy post-bAVR: did not examine patterns in anthrombotics (e.g., warfarin for three months followed by aspirin)

Conclusions

- bAVR is increasing across the VHA
- Three most common antithrombotic strategies post-bAVR:
  1. Aspirin alone
  2. Aspirin plus warfarin
  3. Dual anti-platelets
- Considerable facility variation in antithrombotic strategies
- Clinically reasonable differences in patient characteristics across medication strategies
- Overall, adverse events were uncommon
- Patients in the aspirin plus warfarin group did not realize improved rates of mortality or thromboembolism, but were at higher risk of bleeding

QUESTIONS? Comments?

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