NEW/NON-VITAMIN K ORAL ANTICOAGULANTS (NOAC) VS. WARFARIN: ANALYSIS OF ADHERENCE AND ADVERSE OUTCOMES

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ABBREVIATIONS

- AF-Atrial Fibrillation
- ACC-American College of Cardiology
- AHA-American Heart Association
- CHA_2DS_2-VASc-Congestive heart failure, Hypertension, Age (> 75 = 2 points), Diabetes, and Stroke/TIA (2 points)-Vascular disease, Age (65-74), Sex category (female gender 1 point)
- DVT-Deep Vein Thrombosis
- HRS- Heart Rhythm Society
- INR-International Normalized Ratio
- MOA-Mechanism of Action
- NOAC-New/Non Vitamin K Oral Anticoagulants
- PE-Pulmonary Embolism
- TIA-Transient Ischemic Attack
- WWH-Cherokee Nation W.W. Hastings Hospital

BACKGROUND

- DVT and PE are preventable blood clots
- AF is the most common type of heart arrhythmia
- Anticoagulant medications are used to prevent blood clot extension, prevent acute PE, to reduce stroke risk due to AF, and to reduce risk of recurrent thrombosis are first line therapies.

BACKGROUND

- Medication adherence has not been thoroughly measured within the NOAC patient population
- This study assesses differences in adherence, reasons for discontinuation, and adverse outcomes between NOAC and warfarin.

BACKGROUND

- Warfarin
  - MOA: Hepatic synthesis of coagulation factors II, VII, IX, and X, as well as proteins C and S, requires the presence of vitamin K.
  - Approved: 6/8/1954

BACKGROUND

- Dabigatran
  - MOA: Inhibits coagulation by preventing thrombin-mediated effects, including cleavage of fibrinogen to fibrin monomers, activation of factors V, VIII, XI, and XIII, and inhibition of thrombin-induced platelet aggregation.
  - Approved: 10/19/2010

BACKGROUND

- Rivaroxaban
  - MOA: Inhibits platelet activation and fibrin clot formation via direct, selective and reversible inhibition of factor Xa (FXa) in both the intrinsic and extrinsic coagulation pathways. FXa, as part of the prothrombinase complex consisting also of factor Va, calcium ions, factor II and phospholipid, catalyzes the conversion of prothrombin to thrombin. Thrombin both activates platelets and catalyzes the conversion of fibrinogen to fibrin.
  - Approved: 7/1/2011

BACKGROUND

- Other NOAC not on formulary at WWH
  - Apixaban
  - Edoxaban

GUIDELINES

- AF
  - 2012 CHEST
    - For patients with AF, including those with paroxysmal AF, for recommendations in favor of oral anticoagulation, we suggest dabigatran 150 mg twice daily rather than adjusted-dose vitamin K antagonist therapy (target INR range, 2.0-3.0) (2B)
  - 2014 AHA/ACC/HRS
    - With prior stroke, TIA, or CHA_2DS_2-VASc score ≥2, oral anticoagulants recommended: warfarin (1A), dabigatran, rivaroxaban, or apixaban (1B) and/or if unable to maintain therapeutic INR (1C)

GUIDELINES

- AF
  - 2016 European Society of Cardiology
    - Oral anticoagulation initiated in patient with AF eligible for NOAC, a NOAC is recommended in preference to vitamin K antagonist (1A); may consider NOAC in patient already stable on vitamin K antagonist if TTR not well controlled or patient preference without contraindications (IIb A)

GUIDELINES

- VTE
  - 2016 CHEST
    - NOACs are suggested over warfarin for initial and long-term treatment of VTE in patients without cancer (2B)

PERFORMANCE IMPROVEMENT PROJECT

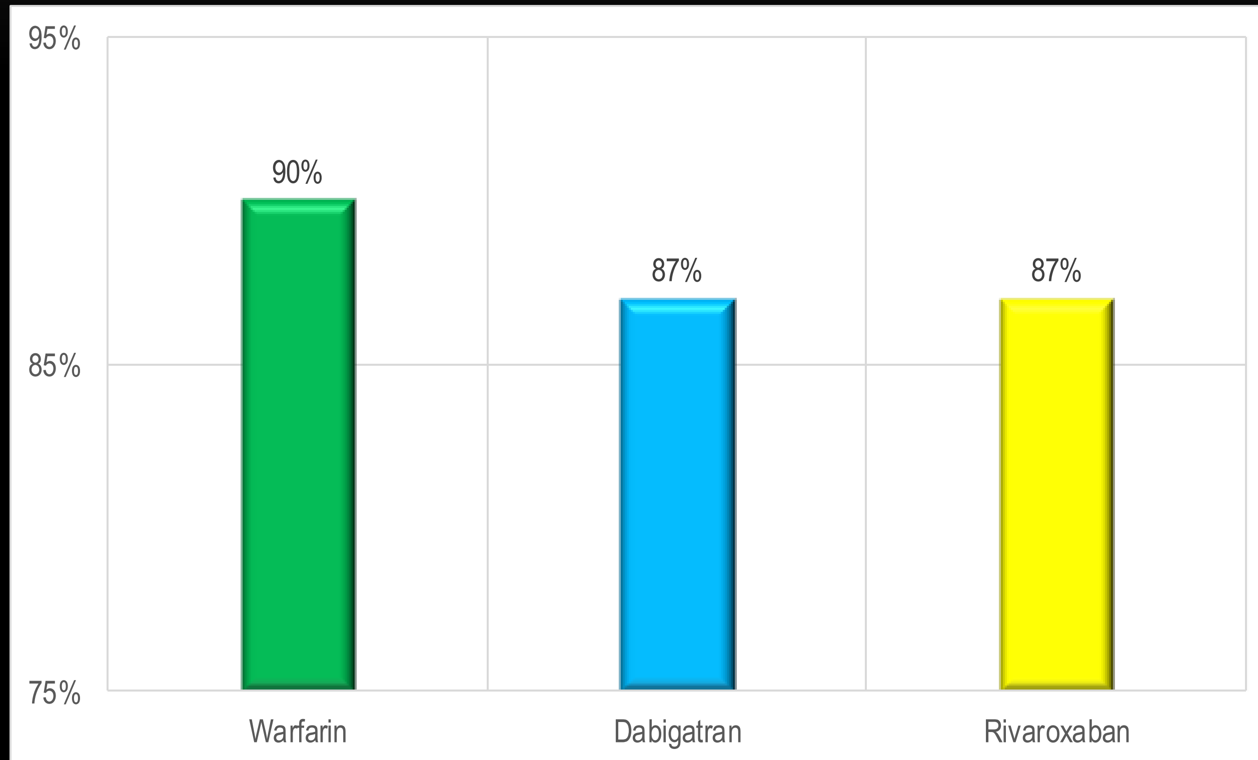
- Retrospective chart review from 03/01/2015 to 02/29/2016
- Inclusion criteria: diagnosis of nonvalvular AF, DVT, or PE
- Exclusion criteria: did not receive >1 prescription (initial or refill) of medication, or unclear start or stop date of therapy
- Reasons for discontinuation recorded
- 308 patients met inclusion criteria and were evaluated (warfarin—152; dabigatran—35; rivaroxaban—121)

PERFORMANCE IMPROVEMENT PROJECT

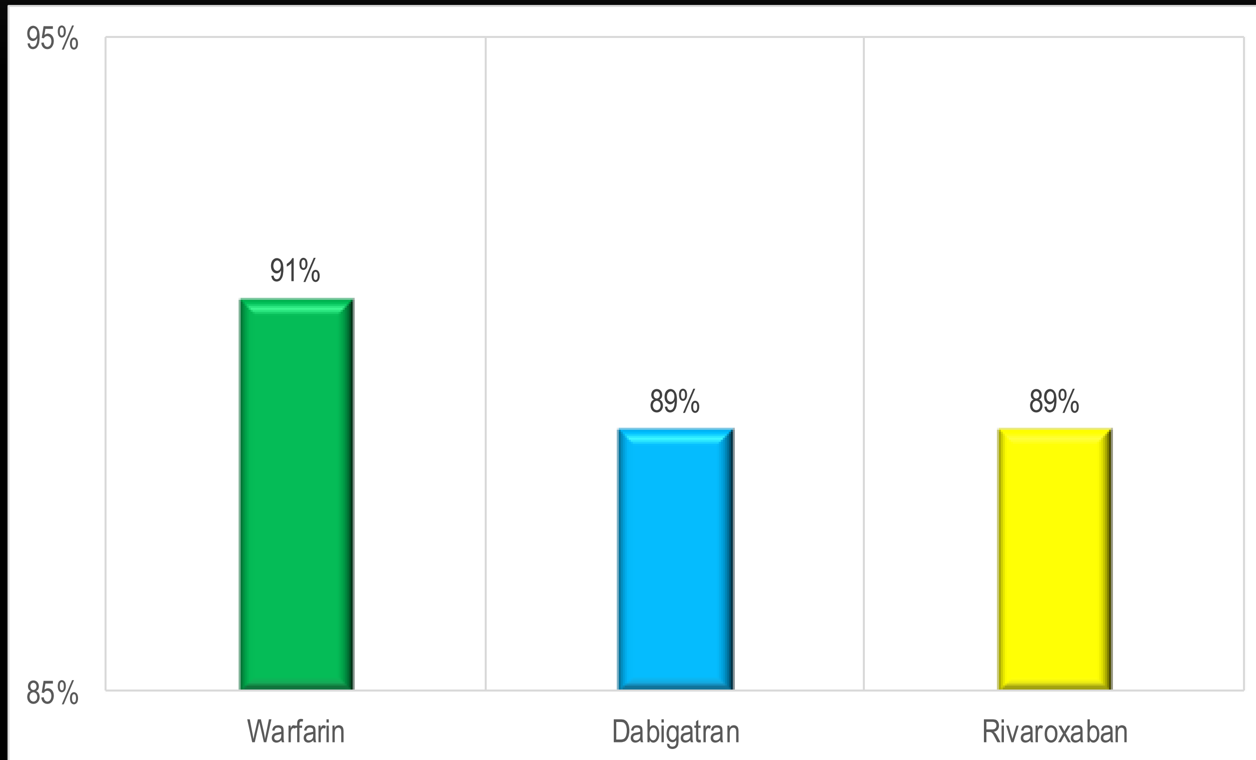
- Adherence recorded as a medication possession ratio
- Mean and median gap between refill prescriptions calculated
- Chart was reviewed for occurrence of a bleeding episode
  - Bleeding episode was recorded as mild (not requiring intervention), moderate (requiring intervention but not higher level of care such as hospitalization), or severe (requiring intervention and higher level of care)

RESULTS

Average Adherence Rates (p=0.34)

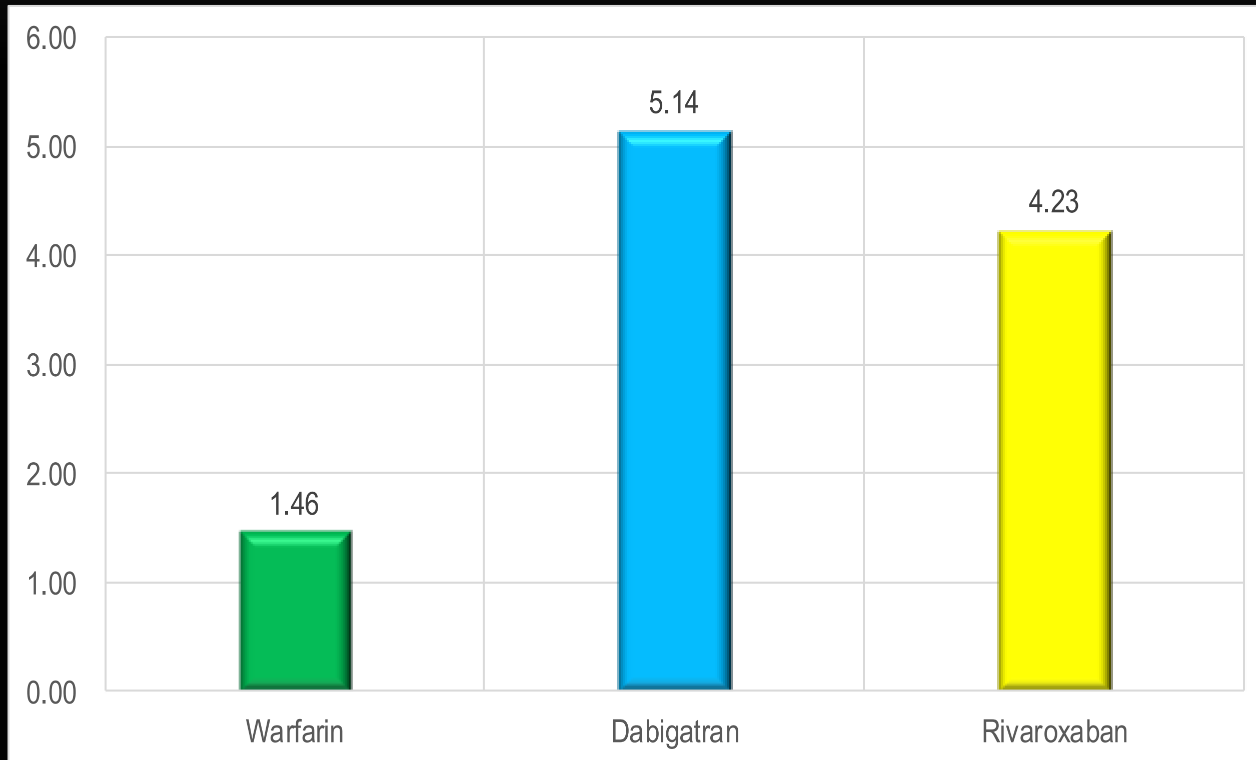


RESULTS

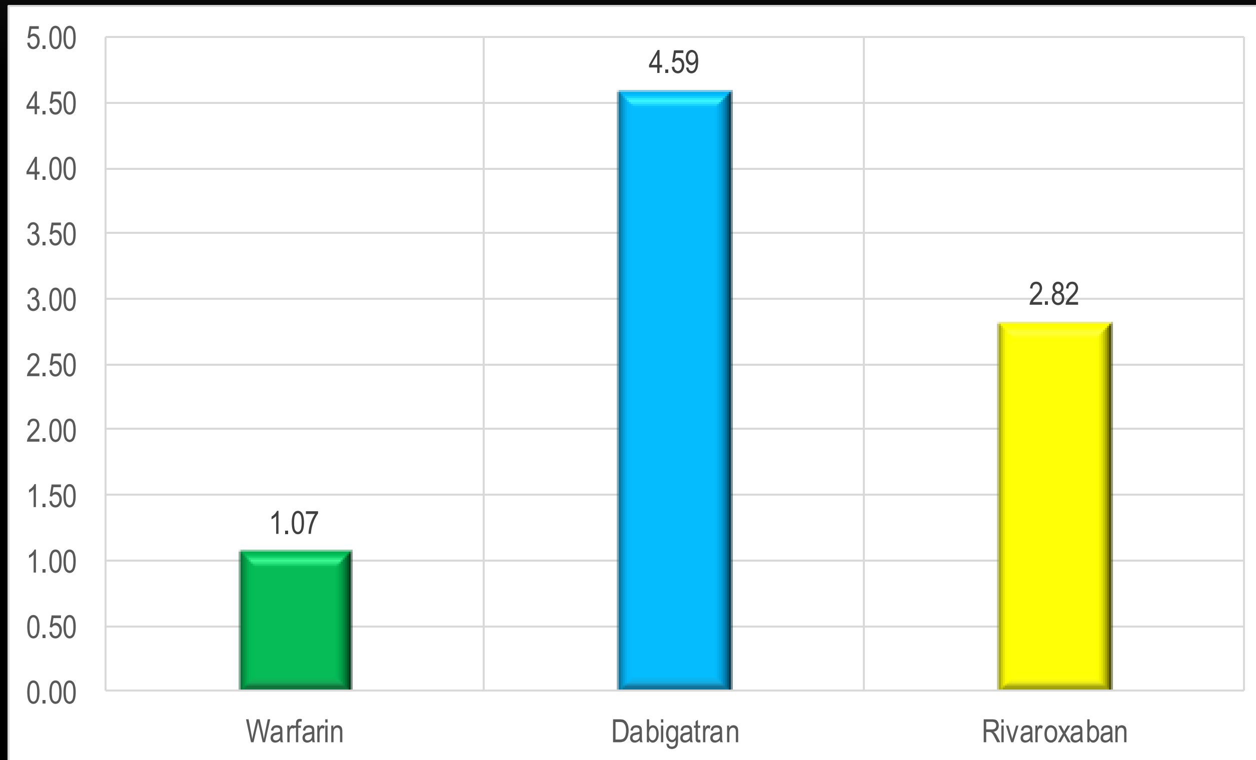


RESULTS

Average Days Gap in Therapy (p=0.0005)



RESULTS

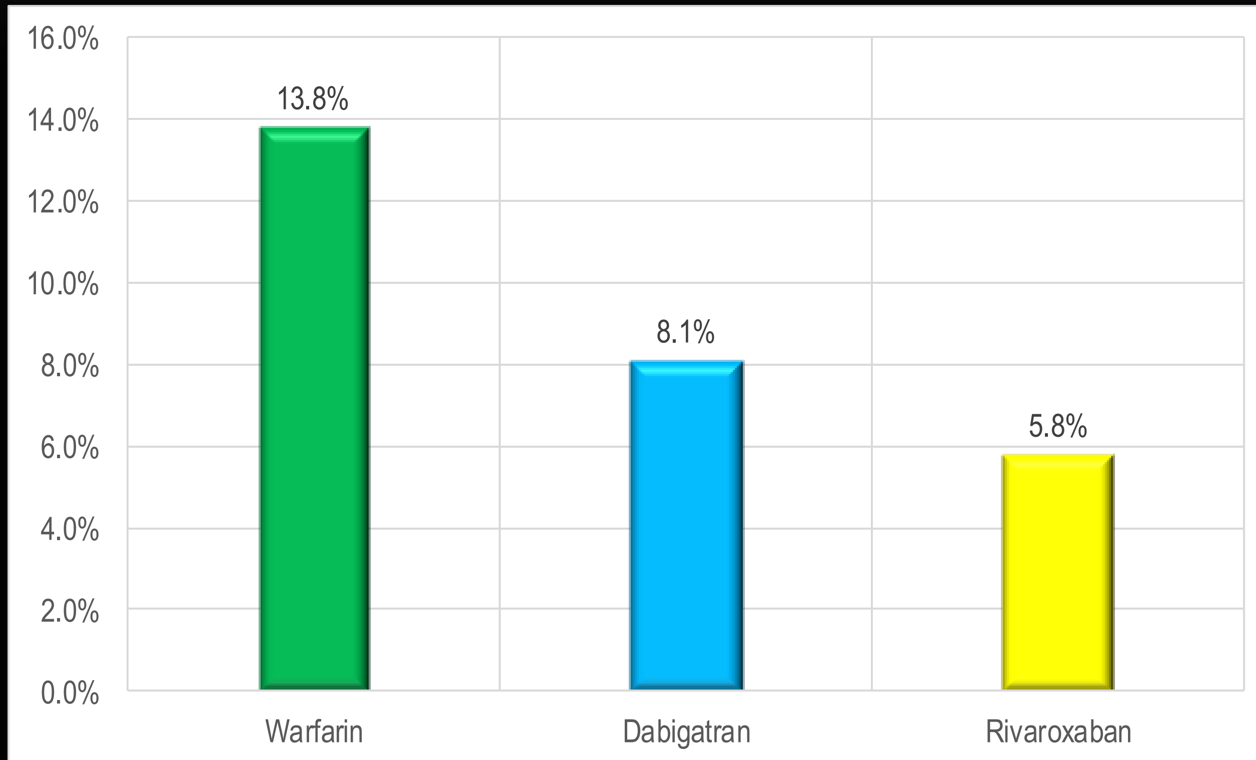


RESULTS

- Overall 46 bleeding episodes were recorded (warfarin—32, dabigatran—3, and rivaroxaban—11)
- Six interventions (warfarin—4, rivaroxaban—2) were classified as moderate requiring discontinuation of anticoagulation, and the remainder were mild events being seen by a provider but no changes in therapy
- The most common occurrence of bleeding among all groups was hematuria. Other bleeding events included epistaxis, rectal bleeding, gastritis, GI bleed, and uterine bleeding

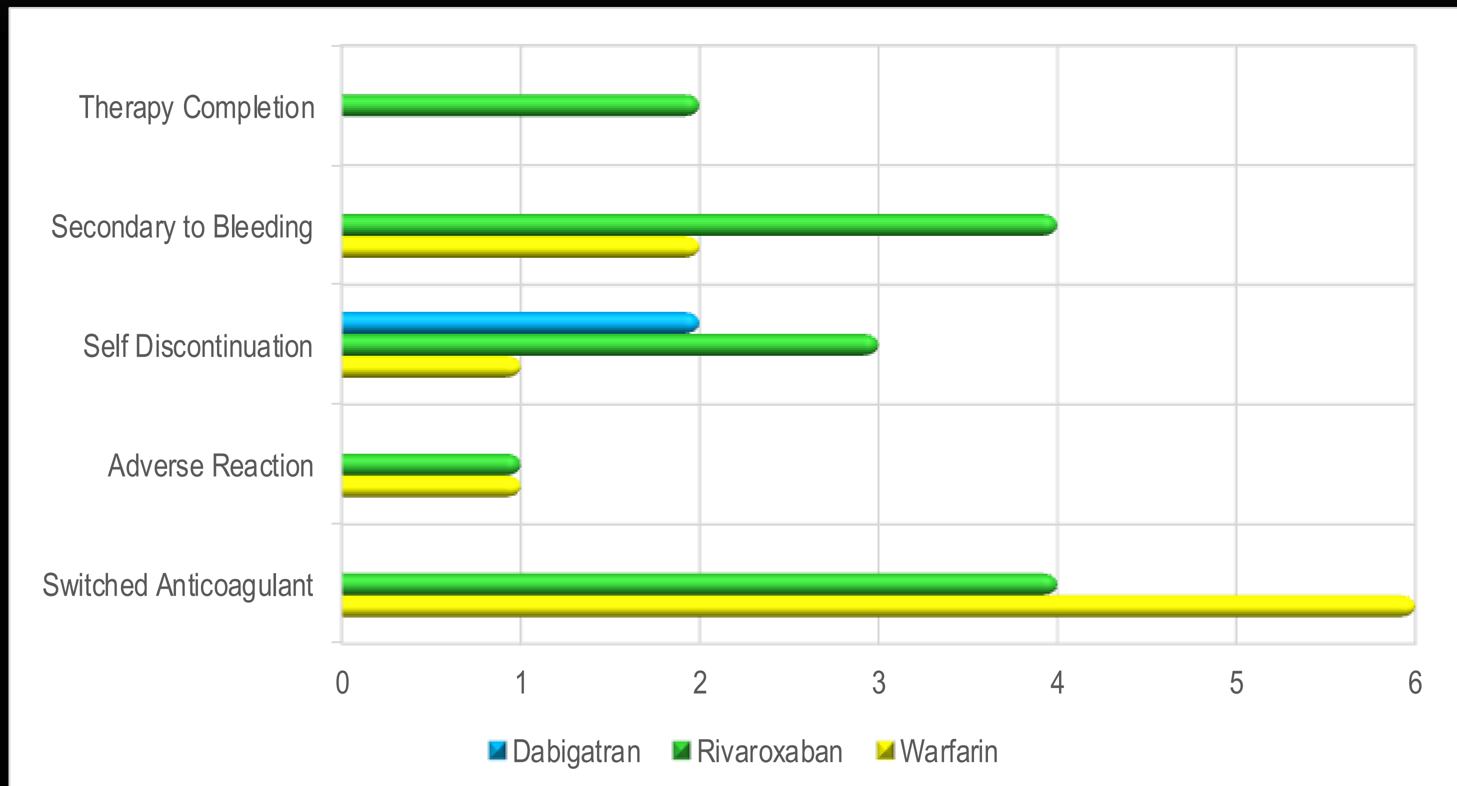
RESULTS

Average Bleeding Incidence ($p<0.05$)



RESULTS

Reasons for Discontinuation



Overall 27 patients discontinued anticoagulation

(warfarin—11, dabigatran—2, and rivaroxaban—14)

PROJECT DISCUSSION

- Similar adherence rates between warfarin, dabigatran, and rivaroxaban
- Limitations: conducted only with WWH data, short duration and converting electronic health records during study timeframe
- Average adherence with NOAC was greater than expected; improvements can still be made
- Adherence with NOAC may also wane with time as patient may become complacent if no event is experienced
- Bleeding was more frequent among warfarin patients, which may mean NOAC are a better option for patients at higher bleeding risk; however, more patients were discontinued off of rivaroxaban for bleeding

OTHER STUDIES

- Lai, et al. Study
  - Compared adherence and treatment persistence for warfarin vs rivaroxaban in Singapore.
  - 137 warfarin and 94 rivaroxaban
  - Medication Possession Ratio 10% lower with warfarin therapy (95% CI 6.4% to 13.6% p<0.0001)
  - Gaps in treatment persistence higher with warfarin therapy (95% CI 8.0% vs 1.1% p=0.03)
- Law, et al. Study
  - Pharmacoeconomic study comparing low-molecular-weight heparin and warfarin to direct oral anticoagulants
  - Total cost avoidance from hospital perspective $1488.04 per VTE event per patient
  - For patient would cost additional $204.10 to $349.04 over 6 months assuming no reimbursement

FUTURE PROJECT

- AWP Cost of each item
  - Coagucheck Strip $8.33 each
  - Capillary Tube $0.25
  - Warfarin $0.58/tablet
  - Rivaroxaban $15.52/tablet
- Reviewing to evaluate who meets criteria for conversion
  - 115 possible patients being reviewed
  - Exclusions/Cautions: valve replacement, cancer, antiphospholipid antibody syndrome, history of GI bleed

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