MCRB™

An Analysis of the Latest Treatments, Economic Value, and Benefit Designs for Oral Anticoagulation Therapy

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The Managed Care Review Board™

- The first curriculum of its kind, The Managed Care Review Board™ is specifically designed and developed for managed care professionals
- It uses a multidisciplinary, evidence-based process for decision-making that contributes to the optimization of patient outcomes to enhance managed care stakeholders' ability to compare the effects of various treatment options on clinical outcomes, perceived value, and economic implications for the entire health care system
- www.ManagedCareReviewBoard.com is a website devoted to delivering these CE activities

Agenda

6:15 AM	Assessing the Clinical Benefits of Oral Anticoagulation Therapies in a Managed Care Setting *James Groce III, PharmD, CACP*
6:35 AM	Current Practice Guidelines Review *Neil Minkoff, MD*
6:50 AM	Faculty Idea Exchange
6:55 AM	Analyzing the Available Data to Assess the Value of Oral Anticoagulation Treatment Options *Fadia T. Shaya, PhD, MPH*
7:15 AM	Plan Benefit Designs: Maximizing Value for Current and Emerging Oral Anticoagulation Therapies *James Kenney, Jr., RPh, MBA*
7:30 AM	Faculty Idea Exchange
7:40 AM	Closing Comments, Post-survey, and Evaluations

Educational Objectives

After completing this activity, the participant should be better able to:

- Identify the risk of thromboembolic events associated with atrial fibrillation (AF) and venous thromboembolism (VTE)
- Utilize recent updates to the anticoagulation treatment guidelines
- Apply measures used to drive quality improvements in anticoagulation care
- Employ the benefit design methodologies for managed care organizations (MCOs) to improve the overall value of anticoagulant therapies
- Provide accurate and appropriate counsel as part of the managed care treatment team

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Assessing the Clinical Benefits of Oral Anticoagulation Therapies in a Managed Care Setting

James Groce III, PharmD, CACP
Professor of Pharmacy Practice
Campbell University School of Pharmacy
Clinical Assistant Professor of Medicine
University of North Carolina School of Medicine
Clinical Pharmacy Specialist-Anticoagulation
Moses H. Cone Memorial Hospital

Faculty Disclosure

- The ***faculty*** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

James Groce III, PharmD, CACP

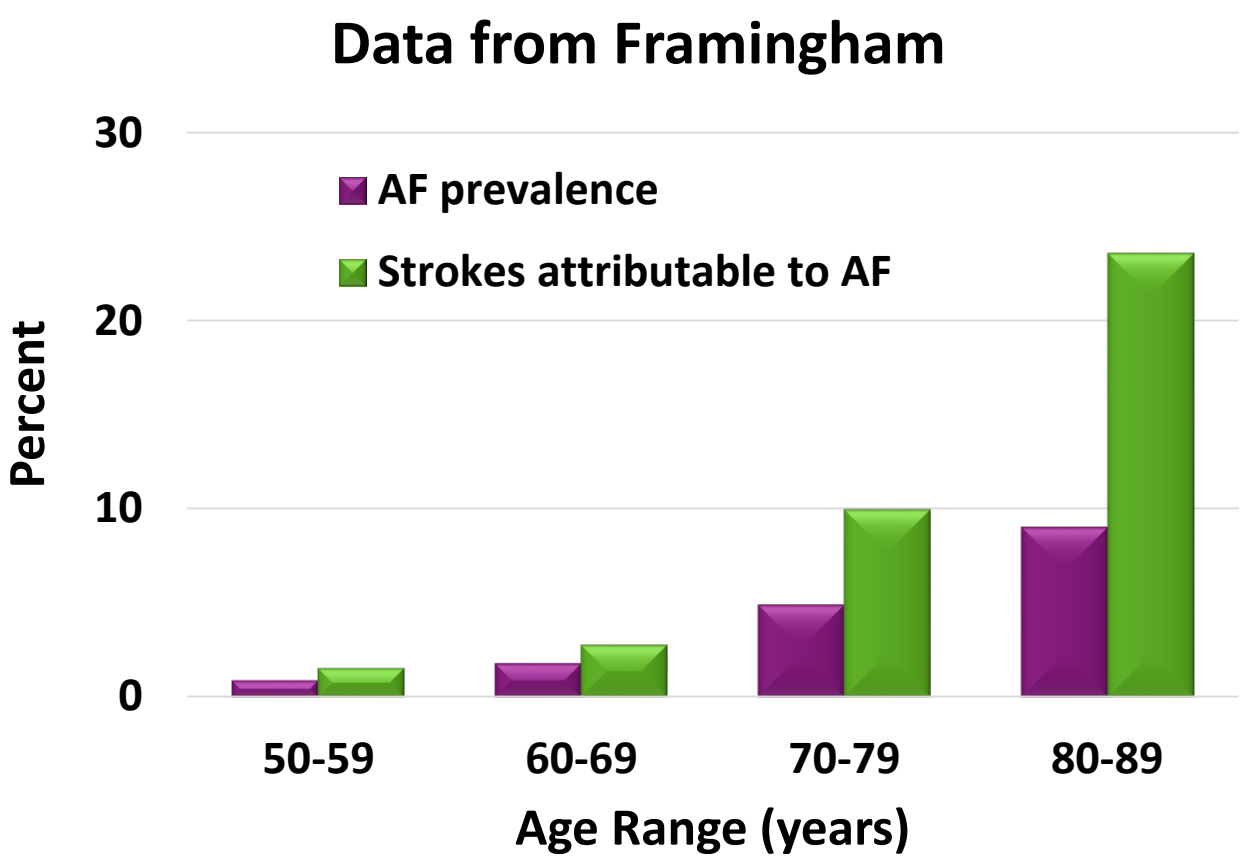
- *Consulting Fees:* Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, Inc., Janssen Pharmaceuticals, Inc., Pfizer, Inc.
- *Fees for Non-CME/CE Services Received Directly from a Commercial Interest or their Agents (e.g., speakers' bureaus):* Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, Inc., Janssen Pharmaceuticals, Inc., Pfizer, Inc.
- *Contracted Research:* Diagnostica Stago, Inc.

Agenda

- Background
  - Atrial fibrillation and stroke
  - Venous thromboembolism
- Novel oral anticoagulants
- Novel oral anticoagulants vs vitamin K antagonists
- Recent clinical trial data of the newer agents
  - RE-LY
  - ROCKET-AF
  - ARISTOTLE
  - ENGAGE-AF

ARISTOTLE=Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation; ENGAGE-AF=Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation; RE-LY=Randomized Evaluation of Long-Term Anticoagulation Therapy; ROCKET-AF=Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation.

Prevalence and Burden of Stroke in Atrial Fibrillation (AF)



AF and Stroke Risk

- Stroke risk in AF increased ~5-fold
- ~15% of all strokes are caused by AF
- Leading cause of mortality in AF
- Risk increases with age
- Associated with AF have worse outcomes
- Health care costs exceed ~$16 billion

Fuster V, et al. *Circulation*. 2006;114:e257-354.
Wolf PA, et al. *Stroke*. 1996;22:983-988.

Risk Stratification in Atrial Fibrillation

High Risk Factors	Moderate Risk Factors	Less Validated Risk Factors
Mitral stenosis	Age >75 years	Age 65-75 years
Prosthetic heart valve	Hypertension	Coronary artery disease
History of stroke or transient ischemic attack (TIA)	Diabetes	Female gender
	Heart failure of decreased left ventricular (LV) function	Thyrotoxicosis

Singer DE, et al. *Chest*. 2004;126:429S-456S.
Fang MC, et al. *Circulation*. 2005;112:1687-1691.

Prevalence and Burden of Venous Thromboembolism (VTE)

Prevalence and Burden of VTE	
US prevalence	~900,000 (1-2 per 1000)
Mortality	Up to 100,000/year • 10% to 30% die within one month of diagnosis • 25% die from sudden death
Complications	Occurs in 50% • Deep vein thrombosis (DVT): Post-thrombotic syndrome • Pulmonary embolism (PE): pulmonary hypertension
Recurrence within 10 years	Occurs in ~33% of patients
Genetic predisposition	Occurs in 5% to 8% of patients

Centers for Disease Control. http://www.cdc.gov/ncbddd/dvt/data.html. Accessed September 22, 2015.

Risk Factors for Venous Thromboembolism

Strong (odds ratio >10%)

- Fracture (hip or leg)
- Hip or knee replacement
- Major general surgery
- Major trauma
- Spinal cord trauma

Moderate (odds ratio 2 to 9%)

- Arthroscopic surgery
- Central venous lines
- Chemotherapy
- CHF/respiratory failure
- HRT
- Malignancy
- Oral contraceptives
- Paralytic stroke
- Pregnancy/postpartum
- Previous VTE
- Thrombophilia

Weak (odds ratio <2%)

- Bed rest 3 days
- Immobility due to sitting
- Increasing age
- Laparoscopic surgery
- Obesity
- Pregnancy
- Varicose veins

Anderson FA, Spencer FA. *Circulation*. 2003;107:I9-I16.

Anticoagulation Therapy for Patients with AF and VTE

Oral anticoagulation therapies have been used to prevent or treat thromboembolism, particularly VTE, in patients with AF[1,2]

For >50 years, vitamin K antagonists were the only oral anticoagulation therapies proven to reduce risk in AF and VTE patients[1]

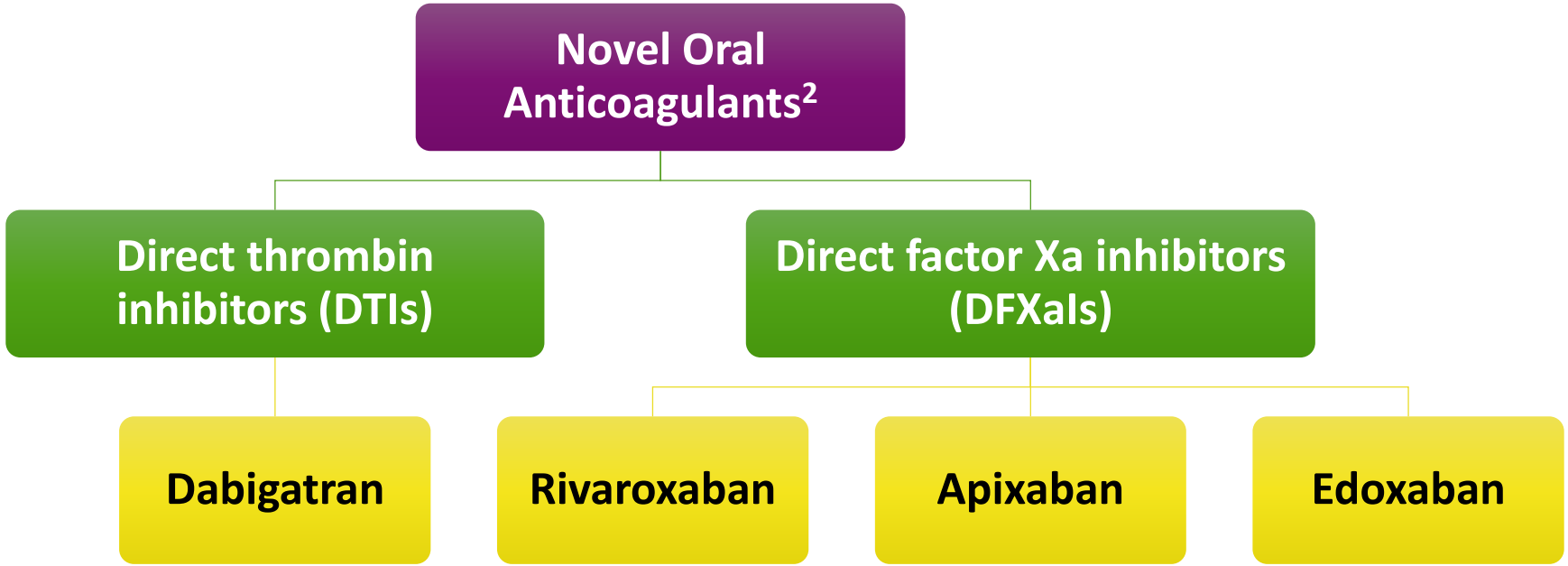
Several novel oral anticoagulants are now available as alternatives to warfarin[3]

AF=atrial fibrillation; VTE=venous thromboembolism.

1. Ebright J, Mousa SA. *Clin Appl Thromb Hemost.* 2015;21:105-114.
2. Kasmeridis C, et al. *Pharmacoeconomics.* 2013;31:971-980.
3. Eby C. *Int J Lab Hematol.* 2013;35:262-268.

Novel Oral Anticoagulants

- Novel oral anticoagulants have similar or enhanced efficacy and safety compared with vitamin K antagonists for the prevention and treatment of thromboembolism[1]



1. Eby C. *Int J Lab Hematol.* 2013;35:262-268. 2. Mekaj YH, et al. *Ther Clin Risk Manag*. 2015;11:967-977.

Overview of Currently Approved Novel Oral Anticoagulants

Agent	Dabigatran[1]	Rivaroxaban[2]	Apixaban[3]	Edoxaban[4]
Brand name	Pradaxa®	Xarelto®	Eliquis®	Savaysa®
FDA approval date	2010	2011	2012	2015
Mechanism of action	DTI	DFXai	DFXai	DFXai
Indications				
To reduce the risk of SSE in patients with NVAF	✓	✓	✓	✓
For the treatment of DVT and PE	✓	✓	✓	✓
For the reduction in the risk of recurrence of DVT and of PE	✓	✓	✓	
For the prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery		✓	✓	

DFXaI=direct factor Xa inhibitor; DTI=direct thrombin inhibitor; DVT=deep venous thrombosis; NOAC=novel oral anticoagulant; NVAF=nonvalvular atrial fibrillation; PE=pulmonary embolism; SSE=stroke and systemic embolism.

1. Pradaxa® [PI]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2010. Revised January 2015. 2. Xarelto® [PI]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2011. Revised September 2015. 3. Eliquis® [PI]. Princeton, NJ: Bristol-Myers Squibb Company; 2012. Revised June 2015. 4. Savaysa® [PI]. Parsippany, NJ: Daiichi Sankyo, Inc. 2015. Revised January 2015.

Novel Oral Anticoagulants vs Vitamin K Antagonists

Vitamin K Antagonists[1,2]

Benefits

- Established efficacy
- Long track record
- Well-developed anticoagulation clinic infrastructure
- Multiple antidotes available
- INR to assess anticoagulant level
- Lower cost

Limitations

- Delayed onset/offset
- Greater drug-drug and food-drug interactions
- Unpredictable dose/response
- Narrow therapeutic window
- Requires frequent monitoring
- High incidence of bleeding
- Slow reversibility

Novel Oral Anticoagulants[1,2]

Benefits

- Rapid onset/offset
- Short half-life
- Minimal drug-drug and food-drug interactions
- Predictable anticoagulant effects
- Wide therapeutic window
- Once-daily or twice-daily oral dosing
- Equal or greater efficacy vs warfarin in preventing stroke in AF

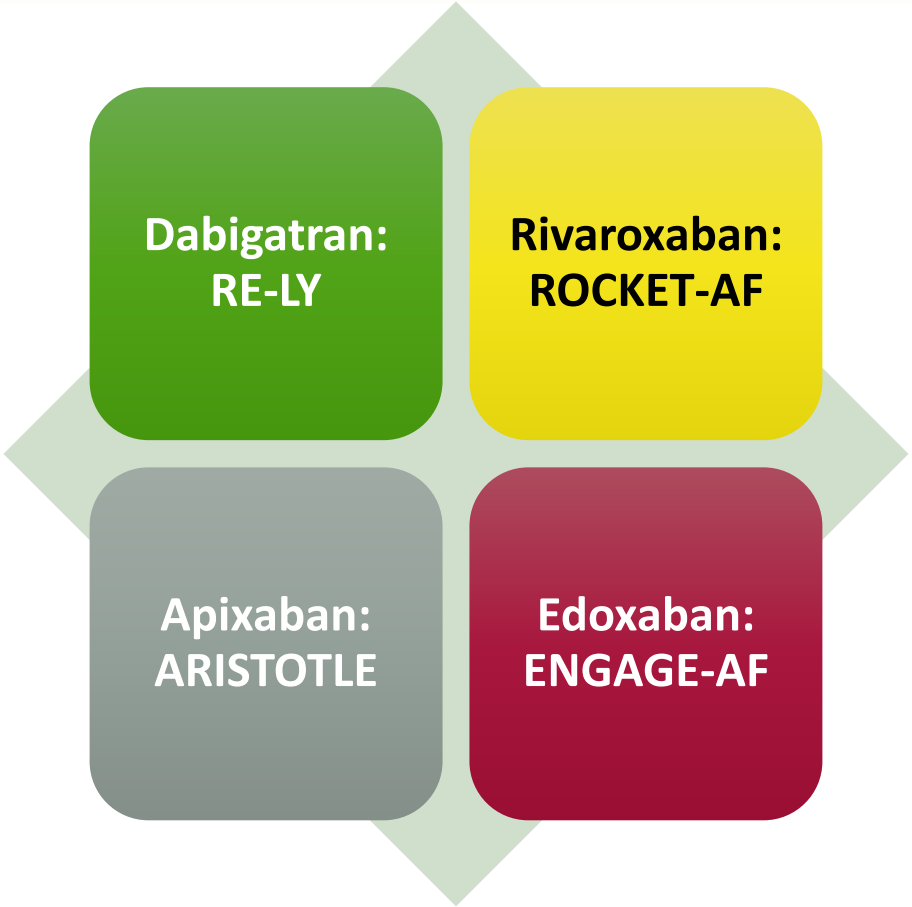
Limitations

- Important differences in the PK/PD between agents
- Careful monitoring of renal function may be required
- Only dabigatran currently has a reversal agent
- Higher cost

AF=atrial fibrillation; INR=international normalized ratio; PD=pharmacodynamics; PK=pharmacokinetics.

1. Bauer KA. *Hematology Am Soc Hematol Educ Program.* 2013:464-470. 2. Mekaj YH, et al. *Ther Clin Risk Manag*. 2015;11:967-977.

Clinical Benefits of the Newer Agents: Recent Clinical Trial Data and Analyses



ARISTOTLE=Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation; ENGAGE-AF=Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation; RE-LY=Randomized Evaluation of Long-Term Anticoagulation Therapy; ROCKET-AF=Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation.

Dabigatran: RE-LY Trial

Randomized Evaluation of Long-Term Anticoagulation Therapy	
Drug	Dabigatran
Doses investigated	150 mg, 110 mg
Dose frequency	Twice daily
Subjects (n)	18,113
Trial design	Randomized, open-label, blinded
Primary efficacy endpoint	SSE
Dose adjustment for drug clearance	No
Noninferiority hazard ratio margin	1.46

Conclusions

- **Both doses of dabigatran were noninferior to warfarin with respect to the primary efficacy outcome of stroke or systemic embolism (SSE)**
- **Both doses markedly reduced intracerebral, life-threatening and total bleeding**
- **Dabigatran had no major toxicity, but did increase dyspepsia and GI bleeding**

Connolly SJ, et al. *N Engl J Med.* 2009;3611139-1151.

Rivaroxaban: ROCKET-AF Trial

Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation	
Drug	Rivaroxaban
Dose investigated	20 mg with ability to reduce to 15 mg
Dose frequency	Once daily
Subjects (n)	14,266
Trial design	Multicenter, randomized, double-blind, double-dummy
Primary efficacy endpoint	SSE
Dose adjustment for drug clearance	Yes; 20 mg → 15 mg
Noninferiority hazard ratio margin	1.46

Conclusions

- **Rivaroxaban was noninferior to warfarin for preventing SSE in patients with NVAF at high risk for TE**
- **No significant difference between rivaroxaban and warfarin with respect to rates of major or clinically relevant non-major bleeding**
- **Rivaroxaban is a proven alternative to warfarin for moderate- or high-risk patients with AF**

AF=atrial fibrillation; NVAF=nonvalvular atrial fibrillation; SSE=stroke or systemic embolism; TE=thromboembolism.

Patel MR, et al. *N Engl J Med.* 2011;365:883-891.

Apixaban: ARISTOTLE Trial

Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation	
Drug	Apixaban
Dose investigated	5 mg with ability to decrease to 2.5 mg
Dose frequency	Twice daily
Subjects (n)	18,201
Trial design	Randomized, double-blind, double-dummy
Primary efficacy endpoint	SSE
Dose adjustment for drug clearance	Yes; 5 mg → 2.5 mg
Noninferiority hazard ratio margin	1.38

Conclusions

- Apixaban was superior to warfarin in preventing SSE, caused less bleeding, and resulted in lower mortality
- Apixaban was associated with a lower risk of stroke and bleeding; similar rates of bleeding were seen with rivaroxaban and dabigatran 150 mg

SSE=stroke or systemic embolism.

Granger CB, et al. *N Engl J Med.* 2011;365:981-992.

Edoxaban: ENGAGE-AF Trial

Effective Anticoagulation With Factor Xa Next Generation in Atrial Fibrillation	
Drug	Edoxaban
Doses investigated	60 mg, 30 mg
Dose frequency	Once daily
Subjects (n)	21,105
Trial design	Randomized, double-blind, double-dummy
Primary efficacy endpoint	SSE
Dose adjustment for drug clearance (mg)	Yes; 60 mg → 30 mg; 30 mg → 15 mg
Noninferiority hazard ratio margin	1.38

Conclusions

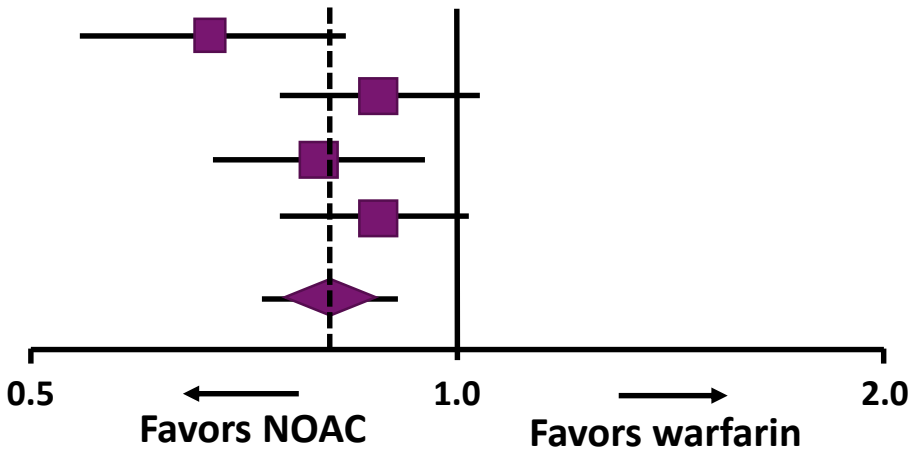
- Both doses of edoxaban were noninferior to warfarin with respect to the prevention of SSE and were associated with significantly lower rates of bleeding and death from CV causes
- Both doses of edoxaban appear to have a safety profile similar to that of warfarin

CV=cardiovascular; SSE=stroke or systemic embolism.

Giugliano RP, et al. *N Engl J Med.* 2013;369:2093-2104.

Efficacy and Safety of Novel Oral Anticoagulants vs Warfarin in Patients With AF: A Meta-analysis of Randomized Trials

	NOAC (events)	Warfarin (events)	RR (95% CI)	*P*
RE-LY*	134/6076	199/6022	0.66 (0.53-0.82)	0.0001
ROCKET AF†	269/7081	306/7090	0.88 0.75-1.03)	0.12
ARISTOTLE‡	212/9120	265/9081	0.80 (0.67-0.95)	0.012
ENGAGE AF-TIMI 48**	296/7035	337/7036	0.88 (0.75-1.02)	0.10
Combined (random)	911/29312	1107/29229	0.81 (0.73-0.91)	<0.0001

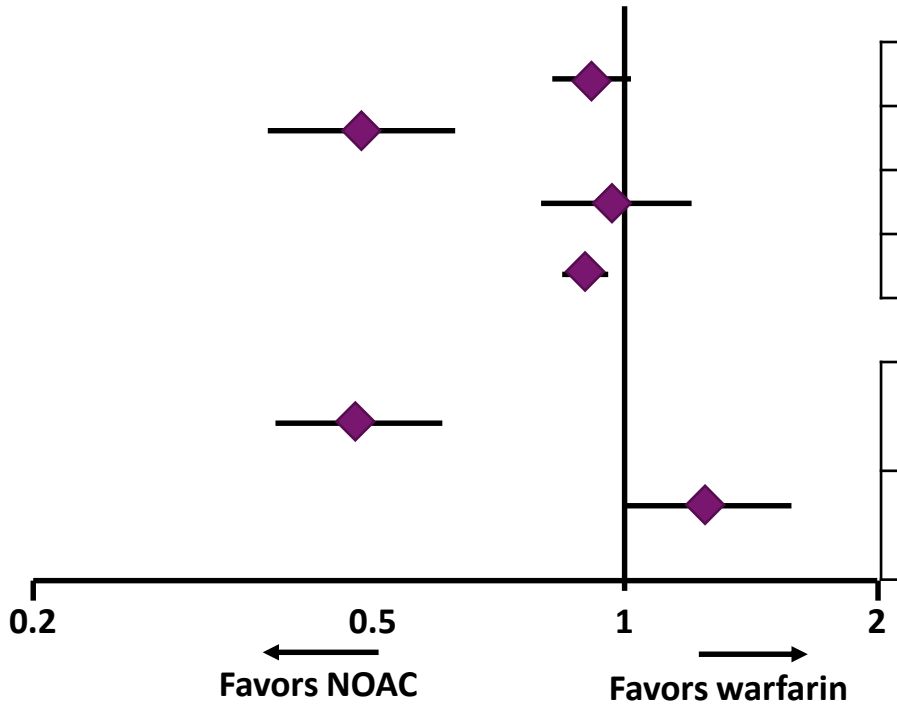


Data are n/N, unless otherwise indicated. Heterogeneity, p=0.13.
*Dabigatran 150 mg twice daily. †Rivaroxaban 20 mg once daily. ‡Apixaban 5 mg twice daily. **Edoxaban 60 mg once daily.
NOAC=novel oral anticoagulant; RR=risk ratio.

Ruff CT, et al. *Lancet.* 2014;383:955-62.

Efficacy and Safety of Novel Oral Anticoagulants vs Warfarin in Patients With AF: A Meta-analysis of Randomized Trials

	Pooled NOAC (events)	Pooled warfarin (events)	RR (95% CI)	*P*
Efficacy				
Ischemic stroke	665/29292	724/29221	0.92 (0.83-1.02)	0.10
Hemorrhagic stroke	130/29292	263/29221	0.49 (0.38-0.64)	<0.0001
Myocardial infarction	413/29292	2245/29221	0.97 (0.78-1.20)	0.77
All-cause mortality	2022/29292	2245/29221	0.90 (0.85-0.95)	0.0003
Safety				
Intracranial hemorrhage	204/29287	425/29211	0.48 (0.39-0.59)	<0.0001
Gastrointestinal bleeding	751/29287	591/29211	1.25 (1.01-1.55)	0.043

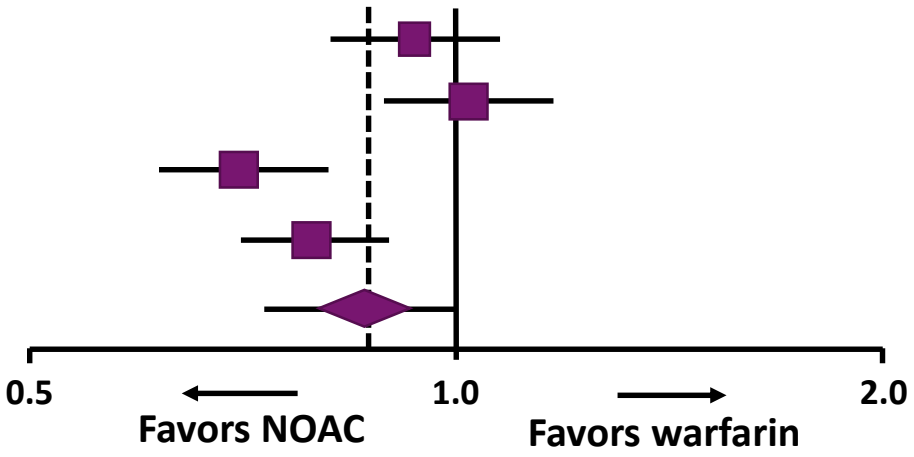


Data are n/N, unless otherwise indicated. Heterogeneity: ischemic stroke, *P*=0.22; hemorrhagic stroke, *P*=0.21; myocardial infarction, *P*=0.13; all-cause mortality, *P*=0.81; intracranial hemorrhage, *P*=0.22; gastrointestinal bleeding. *P*=0.009. NOAC=novel oral anticoagulant; RR=risk ratio.

Ruff CT, et al. *Lancet.* 2014;383:955-62.

Efficacy and Safety of Novel Oral Anticoagulants vs Warfarin in Patients With AF: A Meta-analysis of Randomized Trials

	NOAC (events)	Warfarin (events)	RR (95% CI)	*P*
RE-LY*	375/6076	397/6022	0.94 (0.82-1.07)	0.34
ROCKET AF†	395/7111	386/7125	1.03 (0.90-1.18)	0.72
ARISTOTLE‡	327/9088	462/9052	0.71 (0.91-0.81)	<0.001
ENGAGE AF-TIMI 48**	444/7012	557/7012	0.80 (0.71-0.90)	0.0002
Combined (random)	1541/29287	1802/29211	0.86 (0.73-1.00)	0.06



Data are n/N, unless otherwise indicated. Heterogeneity, *P*=0.001.
*Dabigatran 150 mg twice daily. †Rivaroxaban 20 mg once daily. ‡Apixaban 5 mg twice daily. **Edoxaban 60 mg once daily.
NOAC=novel oral anticoagulant; RR=risk ratio.

Ruff CT, et al. *Lancet.* 2014;383:955-62.

Efficacy and Safety of Novel Oral Anticoagulants vs Warfarin in Patients With AF: Summary

- First meta-analysis to include all four NOACs for stroke prevention in non-valvular atrial fibrillation
- NOACs had a favorable risk-benefit profile:
  - Significant reductions in stroke, ICH, and mortality
  - Similar major bleeding as seen with warfarin
  - Increased GI bleeding

"Our findings offer clinicians a more comprehensive picture of the NOACs as a therapeutic option to reduce the risk of stroke in the AF patient population"

Ruff CT, et al. *Lancet.* 2014;383:955-62.

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Current Practice Guidelines Review

Neil Minkoff, MD
Principal, FountainHead HealthCare
Chief Medical Officer, EmpiraMed, Inc.

Faculty Disclosure

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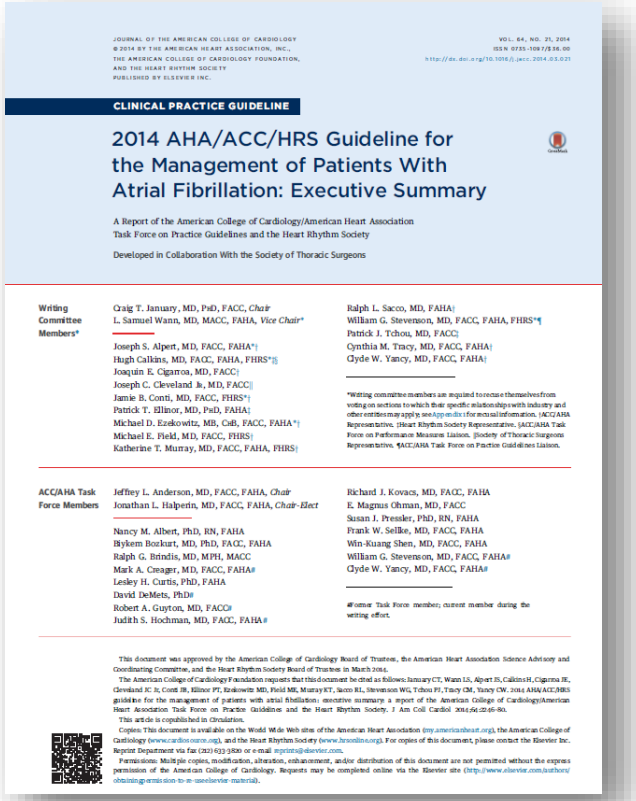
  Neil Minkoff, MD

  - *Consulting Fees:* Bayer, Boehringer Ingelheim, Novartis, Novo Nordisk, Inc., Salix, Sanofi, Serono, UCB, Vertex

Objective

- Review and discuss current guidelines for oral anticoagulation treatment in patients with atrial fibrillation (AF) and venous thromboembolism (VTE)

AF



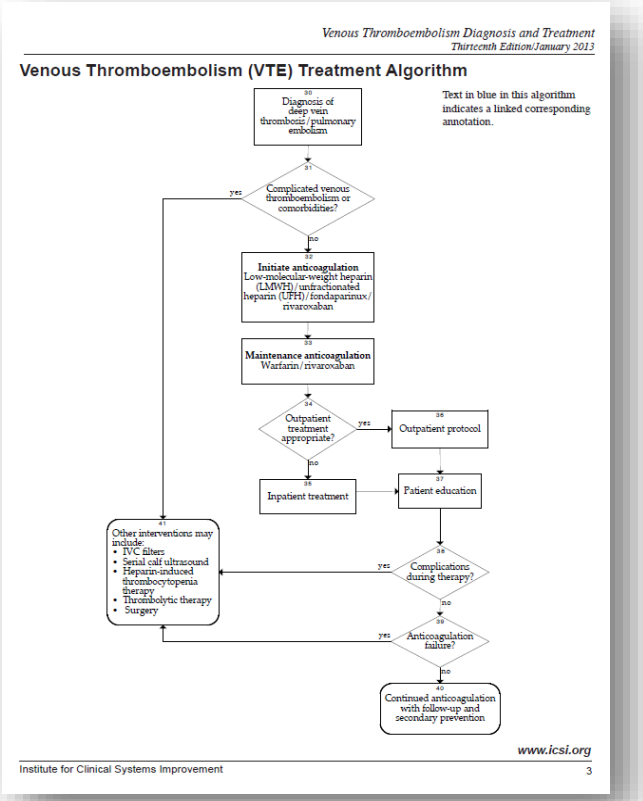
CLINICAL PRACTICE GUIDELINE

2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society

Developed in Collaboration With the Society of Thoracic Surgeons

VTE



Venous Thromboembolism Diagnosis and Treatment
Thirteenth Edition/January 2013

Venous Thromboembolism (VTE) Treatment Algorithm

Text in blue in this algorithm indicates a linked corresponding annotation.

Diagnosis of deep vein thrombosis / pulmonary embolism

Complicated venous thromboembolism or comorbidities?

Initiate anticoagulation
Low-molecular-weight heparin (LMWH) / unfractionated heparin (UFH) / fondaparinux / rivaroxaban

Maintenance anticoagulation
Warfarin / rivaroxaban

Outpatient treatment appropriate?

Outpatient protocol

Inpatient treatment

Patient education

Other interventions may include:
- IVC filters
- Serial calf ultrasound
- Heparin-induced thrombocytopenia therapy
- Thrombolytic therapy
- Surgery

Complications during therapy?

Anticoagulation failure?

Continued anticoagulation with follow-up and secondary prevention

www.icsi.org

Institute for Clinical Systems Improvement 3

January CT, et al. *J Am Coll Cardiol.* 2014;64:2246-2280.
Dupras D, et al. Institute for Clinical Systems Improvement. Venous Thromboembolism Diagnosis and Treatment. Updated January 2013. http://bit.ly/VTE0113. Accessed September 21, 2015.

AHA/ACC/HRS Guidance on the Use of Oral Anticoagulants in Atrial Fibrillation

Recommended primary prevention of thromboembolism with either aspirin or a vitamin K antagonist

Recommended adding clopidogrel to aspirin to reduce the risk of stroke in AF patients in whom warfarin is unsuitable

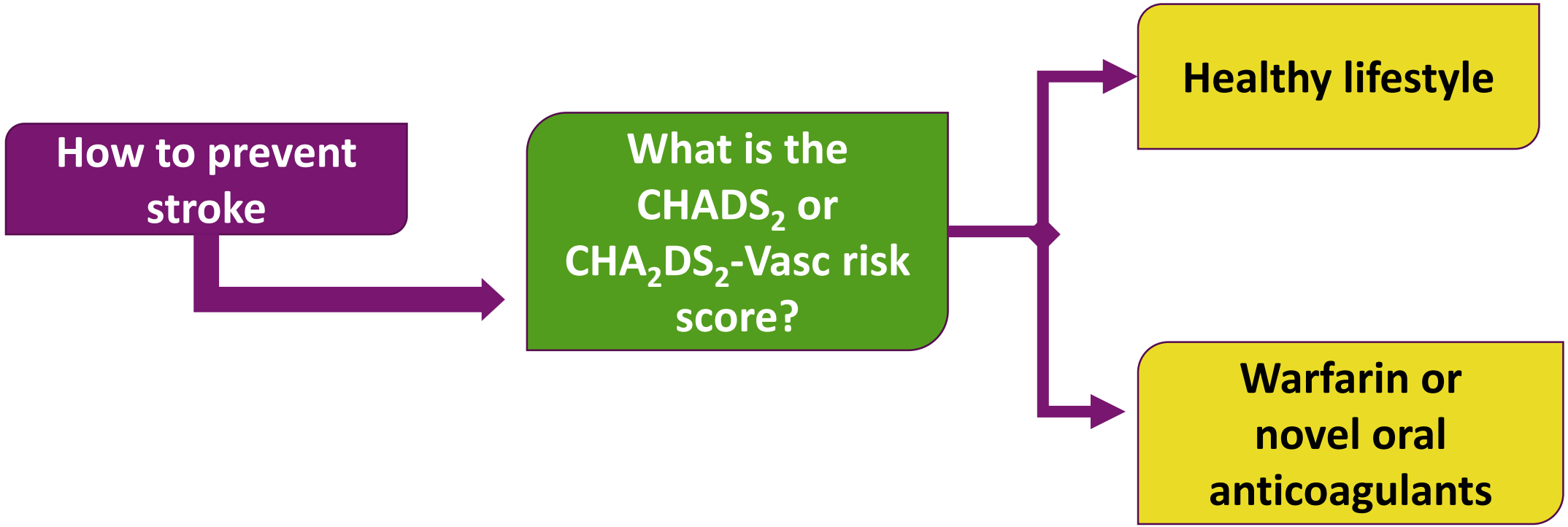
Recommend use of novel non-vitamin K anticoagulants including dabigatran, rivaroxaban, and apixaban*

***Edoxaban, a factor Xa inhibitor, was approved in January 2015, after release of the current guidelines**

ACC=American College of Cardiology; AHA=American Heart Association; HRS=Heart Rhythm Society.

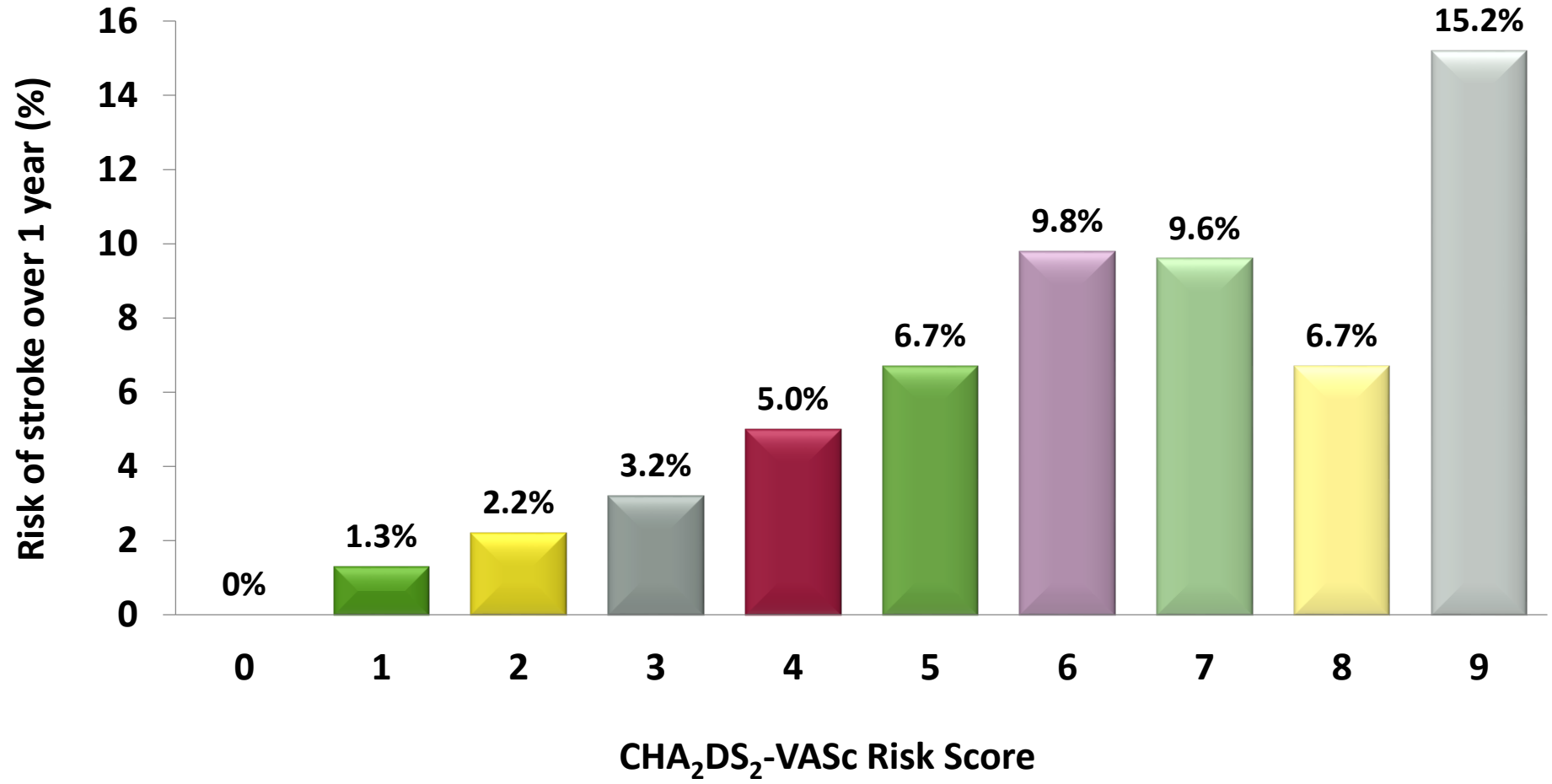
1. Fuster V, et al. *Circulation*. 2006;114:e257-e354.
2. Fuster V, et al. *J Am Coll Cardiol.* 2011;57:e101-e198.
3. January CT, et al. *J Am Coll Cardiol.* 2014;64:2246-2280.

2014 AHA/ACC/HRS Treatment Algorithm for Stroke Prevention in AF



January CT, et al. *J Am Coll Cardiol.* 2014;64:2246-2280.

Predicted Annual Stroke Rate vs CHA_2DS_2-VASc Risk Score



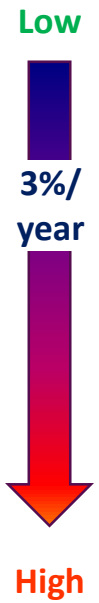
Olesen J, et al. *BMJ.* 2011;342:d124.

$CHADS_2$: Stroke Risk Score in Patients with AF

	Points
Congestive heart failure	1
Hypertension	1
Age >75 years	1
Diabetes	1
Stroke or TIA	2
Maximum score	**6**
Low risk	**0-1**
Moderate – High risk	**≥2**

Threshold for Anticoagulation

Score	Risk of Stroke (%/year)
0	1.9
1	2.8
2	4.0
3	5.9
4	8.5
5	12.5
6	18.2



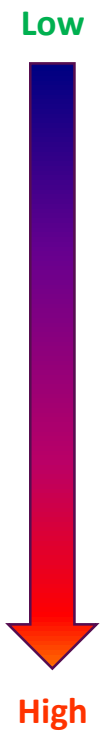
January CT, et al. *J Am Coll Cardiol.* 2014;64:2246-2280.

CHA_2DS_2-VASc: Stroke Risk Score in Patients with AF

	Score
Congestive heart failure or LVEF ≤35%	1
Hypertension	1
Age >75 years	2
Diabetes	1
Stroke or TIA or thromboembolism	2
Vascular disease (MI/PAD/Aortic plaque)	1
Age 65-75 years	1
Sex **C**ategory (female)	1
Maximum score	**9**
Low risk	**0-1**
Moderate – High risk	**≥2**

Threshold for Anticoagulation

Score	Risk of Stroke (%/year)
0	0
1	1.3
2	2.2
3	3.2
4	4.0
5	6.7
6	9.8
7	9.6
8	6.7
9	15.2



LVEF=left ventricular ejection fraction; MI=myocardial infarction; PAD=peripheral artery disease.

January CT, et al. *J Am Coll Cardiol.* 2014;64:2246-2280.

Antithrombotic Therapy Recommendations in AF

Antithrombotic therapy selected based on risk

Warfarin

- Recommended for mechanical heart valves and target INR intensity based on type and location of prosthesis
- With warfarin, determine INR at least weekly during initiation of therapy and monthly when stable

Novel Oral Anticoagulants

- Recommended for prior stroke, TIA, or in patients with CHA_2DS_2-VASc score ≥2

INR=international normalized ratio; TIA=transient ischemic attack.

January CT, et al. *J Am Coll Cardiol.* 2014;64:2246-2280.

Comparison of Oral Anticoagulants: Safety, Efficacy, and Pharmacology

	Warfarin[1]	Rivaroxaban[2]	Apixaban[3]	Dabigatran[4]	Edoxaban[5]
Indications	• AF • VTE (treatment; 2º prevention; prophylaxis)	• AF • VTE (treatment; 2º prevention; prophylaxis)	• AF • VTE (treatment; 2º prevention; prophylaxis)	• AF • VTE (treatment; 2º prevention)	• AF • VTE (treatment)
Target	Vitamin K inhibitor	Factor Xa	Factor Xa	Thrombin	Factor Xa
Prodrug	No	No	No	Yes	No
Bioavailability	100%	60% to 80%	60%	6%	62%
Time to peak	4-5 days	2-4 hours	1-2 hours	1-3 hours	1-2 hours
Half-life	40 hours	7-11 hours	12 hours	8-15 hours	10-14 hours
Renal clearance	None	33%	25%	80%	50%
Drug interactions	Multiple	3A4/P-gp	3A4/P-gp	P-gp	P-gp

1. COUMADEN®[PI]. Princeton, NJ: Bristol-Myers Squibb Company; September 2011. 2. Xarelto® [PI]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2011. Revised September 2015. 3. Pradaxa® [PI]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2010. Revised January 2015. 4. Eliquis® [PI]. Princeton, NJ: Bristol-Myers Squibb Company; 2012. Revised June 2015. 5. Savaysa® [PI]. Parsippany, NJ: Daiichi Sankyo, Inc. 2015. Revised January 2015.

Dosing Adjustments for Patients with Renal Impairment

Renal Function	Warfarin[1]	Dabigatran[2]	Rivaroxaban[3]	Apixaban[4]	Edoxaban[5]
Normal/mild impairment	Dose adjusted for INR	150 mg BID (CrCl >30 mL/min)	20 mg HS (CrCl >50 mL/min)	5.0 or 2.5 mg BID	60 mg QD *Do not use if CrCL >95 mL/min*
Moderate impairment	Dose adjusted for INR	150 or 75 mg BID (CrCl >30 mL/min)	15 mg HS (CrCl 30-50 mL/min)	5.0 or 2.5 mg BID	60 mg QD (CrCl 50-95 mL/min)
Severe	Dose adjusted for INR	75 mg BID (CrCl 15-30 mL/min)	15 mg HS (CrCl 15-30 mL/min)	No recommendation	30 mg QD (CrCL 15-50 mL/min)
End stage renal disease (ESRD) not on dialysis	Dose adjusted for INR	Not recommended (CrCl <15 mL/min)	Not recommended (CrCl <15 mL/min)	No recommendation	Not recommended (CrCl <15 mL/min)
ESRD on dialysis	Dose adjusted for INR	Not recommended (CrCl <15 mL/min)	Not recommended (CrCl <15 mL/min)	No recommendation	Not recommended (CrCl <15 mL/min)

1. COUMADEN®[PI]. Princeton, NJ: Bristol-Myers Squibb Company; September 2011. 2. Xarelto® [PI]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2011. Revised September 2015. 3. Pradaxa® [PI]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2010. Revised January 2015. 4. Eliquis® [PI]. Princeton, NJ: Bristol-Myers Squibb Company; 2012. Revised June 2015. 5. Savaysa® [PI]. Parsippany, NJ: Daiichi Sankyo, Inc. 2015. Revised January 2015.

Summary of the 2014 AHA/ACC/HRS Risk-Based Recommendations

- Antithrombotic therapy selection based on risk of thromboembolism[1]
- CHA_2DS_2-VASc score recommended to assess stroke risk[1]
- With prior stroke, TIA, or CHA_2DS_2-VASc score ≥2, oral anticoagulants recommended including warfarin, dabigatran, rivaroxaban, or apixaban[1]
  - Edoxaban, approved in 2015, may also be considered[2]
- With warfarin, determine INR at least weekly during initiation and monthly when stable[1]
- Direct thrombin or factor Xa inhibitor recommended, if unable to maintain therapeutic INR[1]
- Re-evaluate the need for anticoagulation at periodic intervals[1]

1. January CT, et al. *J Am Coll Cardiol.* 2014;64:2246-2280.
2. Savaysa® [PI]. Parsippany, NJ: Daiichi Sankyo, Inc. 2015. Revised January 2015.

Venous Thromboembolism: Patient Identification

- Treatment should be individualized for patients with complicated venous thromboembolism (VTE) or specific comorbidities
  - Massive pulmonary embolism (PE)
  - Known history of heparin-induced thrombocytopenia
  - Active severe hemorrhage or recent intracranial hemorrhage
  - Severe renal dysfunction
  - Extensive ilio-femoral thrombosis/phlegmasia
  - Pregnancy
  - Familial bleeding disorders

Dupras D, et al. Institute for Clinical Systems Improvement. Venous Thromboembolism Diagnosis and Treatment. Updated January 2013. http://bit.ly/VTE0113. Accessed September 21, 2015.

Venous Thromboembolism: Recommended Initial Therapy

- Pulmonary embolism (PE)
  - Unfractionated heparin (UFH), low-molecular-weight heparin (LMWH) or fondaparinux
  - May consider rivaroxaban for the initial treatment
- Deep vein thrombosis (DVT)
  - LMWH or fondaparinux
  - May consider rivaroxaban for the initial treatment

Dupras D, et al. Institute for Clinical Systems Improvement. Venous Thromboembolism Diagnosis and Treatment. Updated January 2013. http://bit.ly/VTE0113. Accessed September 21, 2015.

Venous Thromboembolism: Recommended Maintenance Therapy

- Goal INR of 2.5 (range 2.0-3.0) is recommended
- Clinicians should generally use warfarin for continued anticoagulation
  - LMWH is recommended in the setting of cancer
  - Clinicians may consider using rivaroxaban for continued anticoagulation
- Heparin/fondaparinux and warfarin should be started at the same time
- UFH or LMWH and/or fondaparinux should be given for a minimum of five days and continued until INR ≥2.0 for two consecutive days

Dupras D, et al. Institute for Clinical Systems Improvement. Venous Thromboembolism Diagnosis and Treatment. Updated January 2013. http://bit.ly/VTE0113. Accessed September 21, 2015.

Venous Thromboembolism: Summary

- Acute treatment of VTE generally require 3 months of anticoagulation
  - Treatment options include LMWH, vitamin K antagonists, or direct factor Xa or direct factor IIa inhibitors
- Maintenance treatment is based on balancing the risk of VTE recurrence against the risk of major hemorrhage from treatment
- Development of novel oral anticoagulants simplifies acute-phase treatment and may avoid the need for LMWH
- Patients with PE can also be treated in the acute phase as outpatients, a decision dependent on prognosis and severity of PEs

Wells PS, et al. *JAMA*. 2014. 311:717-728.

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An Analysis of the Latest Treatments, Economic Value, and Benefit Designs for Oral Anticoagulation Therapy

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Analyzing the Available Data to Assess the Value of Oral Anticoagulation Treatment Options

Fadia Tohme-Shaya, PhD, MPH
Professor and Vice Chair for Academic Affairs PHSR
University of Maryland School of Pharmacy

Faculty Disclosure

- The ***faculty*** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

Fadia Tohme-Shaya, PhD, MPH

- No financial interest/relationships relating to the topic of this activity

Stroke and Venous Thromboembolism

Atrial Fibrillation (AF)[1]

- Untreated AF increases risk of stroke 4- to 5-fold
- Warfarin historically has been used for stroke prophylaxis in AF
- Novel oral anticoagulants provide predictable anticoagulation with fixed, unmonitored dosing, improved outcomes, and lower cost

Venous Thromboembolism (VTE)[2,3]

- Burden of VTE
  - Second most common medical complication and cause of excess length of hospital stay
  - Third most common cause of excess mortality
- Estimated costs: $13.5-$27.2 billion/year
- Warfarin used to treat VTE
- Suboptimal use of warfarin can lead to potentially preventable poor patient outcomes and higher healthcare costs

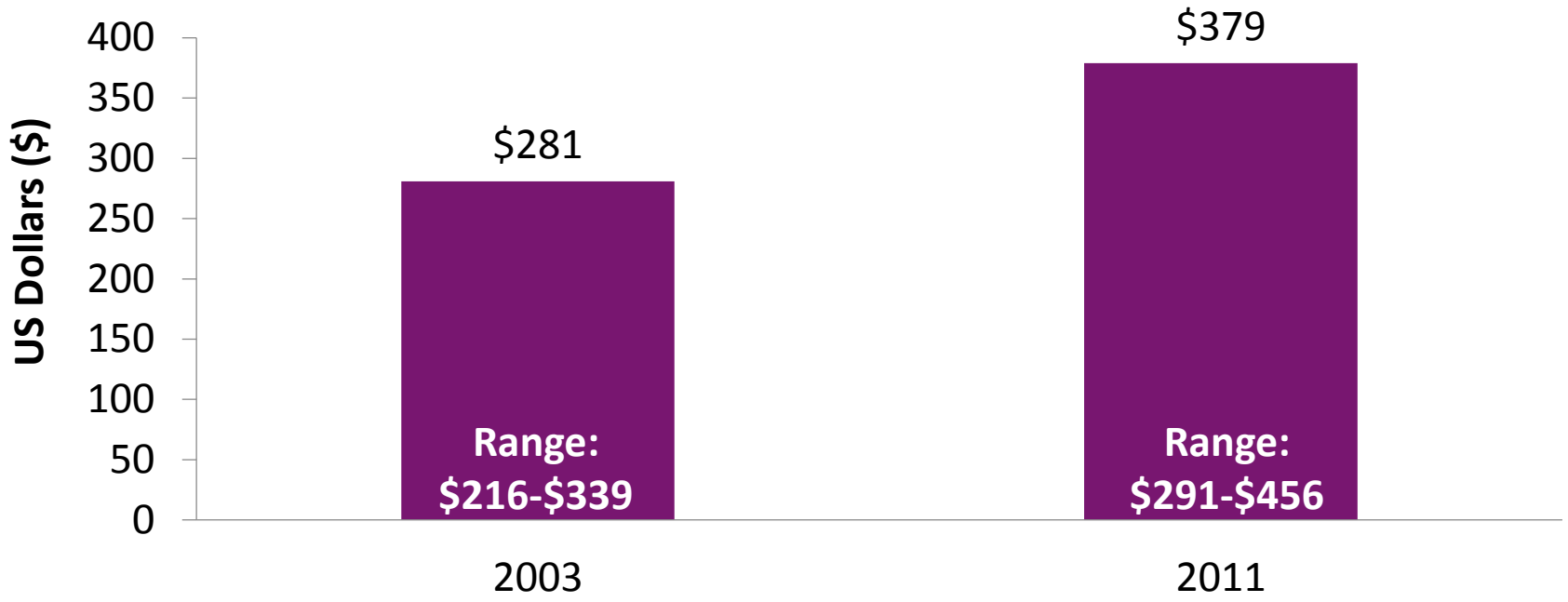
1. Biskupiak J, et al. *J Manag Care Pharm.* 2013;19:789-798.
2. Amin A, et al. *J Hematol Thrombo Dis*. 2015;3:3.
3. Gerts WH, et al. *Chest.* 2008;133:381S-453S.

Anticoagulation Therapy with Vitamin K Antagonists

- Oral vitamin K antagonists (VKA; eg, warfarin) have been the mainstay of treatment to reduce the risk of stroke in patients with nonvalvular AF and VTE[1,2]
- While effective in reducing the risk of stroke, VKAs are limited by[1,2]
  - Narrow therapeutic window
  - Multiple food and drug interactions
  - Need for regular laboratory monitoring
  - Risk of bleeding events
- As a result, considerable variability exists in the amount of time patients spend within the therapeutic range exposing them to increased stroke risk when they are below the range and bleeding when they are above the range[2]

1. Yang E. *Vasc Health Risk Manag*. 2014;10:507-522.
2. Biskupiak J, et al. *J Manag Care Pharm.* 2013;19:789-798.

Increasing Cost of Anticoagulation Monitoring



- Analysis of 600 adult patients US receiving warfarin at 3 anticoagulation clinics
- An average of 18 clinic contacts over a mean follow-up of 10.5 months
- Patients were within the recommended INR for 62% of the time; 25% of days below and 13% of days above range

Biskupiak J, et al. *J Manag Care Pharm.* 2013;19:789-798.

Annual Costs of Managing the Consequences of VKA Therapy

	Range ($)
Annual overall costs (per patient) for VKA therapy	$18,454 to $38,270
Annual inpatient costs	$7,841 to $22,582
1-year costs for intracranial hemorrhage and major gastrointestinal bleeding	$7,584 to $193,804

- Most serious consequence of uncontrolled over anticoagulation with VKAs is hemorrhage, particularly intracranial hemorrhage or gastrointestinal bleeding
- Although relatively rare, costs of managing and treating them are high

Biskupiak J, et al. *J Manag Care Pharm.* 2013;19:789-798.

Risk Reduction with Novel Oral Anticoagulants

- Several targeted oral anticoagulants (dabigatran,[1] rivaroxaban,[2] apixaban,[3] edoxaban[4]) are now approved for treatment of AF and VTE
- All have been shown to be efficacious for the treatment of AF and VTE in randomized phase III clinical trials
- In addition, these agents offer pharmacologic advantages over other therapies including
  - Oral administration
  - Rapid onset of action
  - Few drug-drug or drug-food interactions
  - Predictable pharmacokinetics
  - No need for regular monitoring

1. Pradaxa® [PI]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2010. Revised January 2015. 2. Xarelto® [PI]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2011. Revised September 2015. 3. Eliquis® [PI]. Princeton, NJ: Bristol-Myers Squibb Company; 2012. Revised June 2015. 4. Savaysa® [PI]. Parsippany, NJ: Daiichi Sankyo, Inc. 2015. Revised January 2015.

Why Calculate the Cost-Efficacy of Oral Anticoagulation?

- Clinical event rates differ between patients treated with VKAs vs novel oral anticoagulants[1]
- Several economic analyses have been completed on studies to describe the economic and clinical benefit of each agent[2-4]
- This information is necessary to guide and support decision making of healthcare providers, policy makers, and payers

1. Ruff CT, et al. *Lancet*. 2014;383:955-962.
2. Amin A, et al. *J Hematol Thrombo Dis*. 2015;3:3.
3. Canestaro WJ, et al. *Circ Cardiovasc Qual Outcomes*. 2013;6:724-731.
4. Krejczy M, et al. *BioMed Res Int*. 2015; http://dx.doi.org/10.1155/2015/876923.

Determining the Value of Oral Anticoagulation Therapy

- The relatively high cost and expanding use of the novel oral anticoagulants make them an important target for economic evaluation
- Economic evaluation tools include
  - Cost-effectiveness analysis (CEA) compares the cost and effectiveness of two or more treatments
  - Cost-utility analysis (CUA) is a subtype of CEA, applying quality-adjusted life-years (QALY) as a measure of effectiveness
    - Primary outcome measure in CUA is the incremental cost-effectiveness ratio (ICER)
    - ICER describes the ratio of the additional costs of a treatment (vs an alternative) to QALYs gained

Joensuu JT, et al. *PLoS ONE*. 10(3): e0119683. doi:10.1371/journal.

Modeling the Cost-Effectiveness of Novel Oral Anticoagulants vs VKAs for Stroke Prophylaxis in AF

- Developed a Markov model to compare the cost-effectiveness of stroke prevention in AF patients with apixiban, dabigatran, rivaroxaban, and warfarin
- Model constructed using data from clinical trials to evaluate lifetime costs and QALYs
- Modeled population: cohort of 70-year-old patients with
  - Nonvalvular AF at increased risk for stroke ($CHADS_2$ ≥1)
  - Creatinine clearance ≥50 mL/min
  - No previous contraindications to anticoagulation
- Willingness-to-pay threshold: $50,000/QALY gained

Harrington AR, et al. *Stroke.* 2013;44:1676-1681.

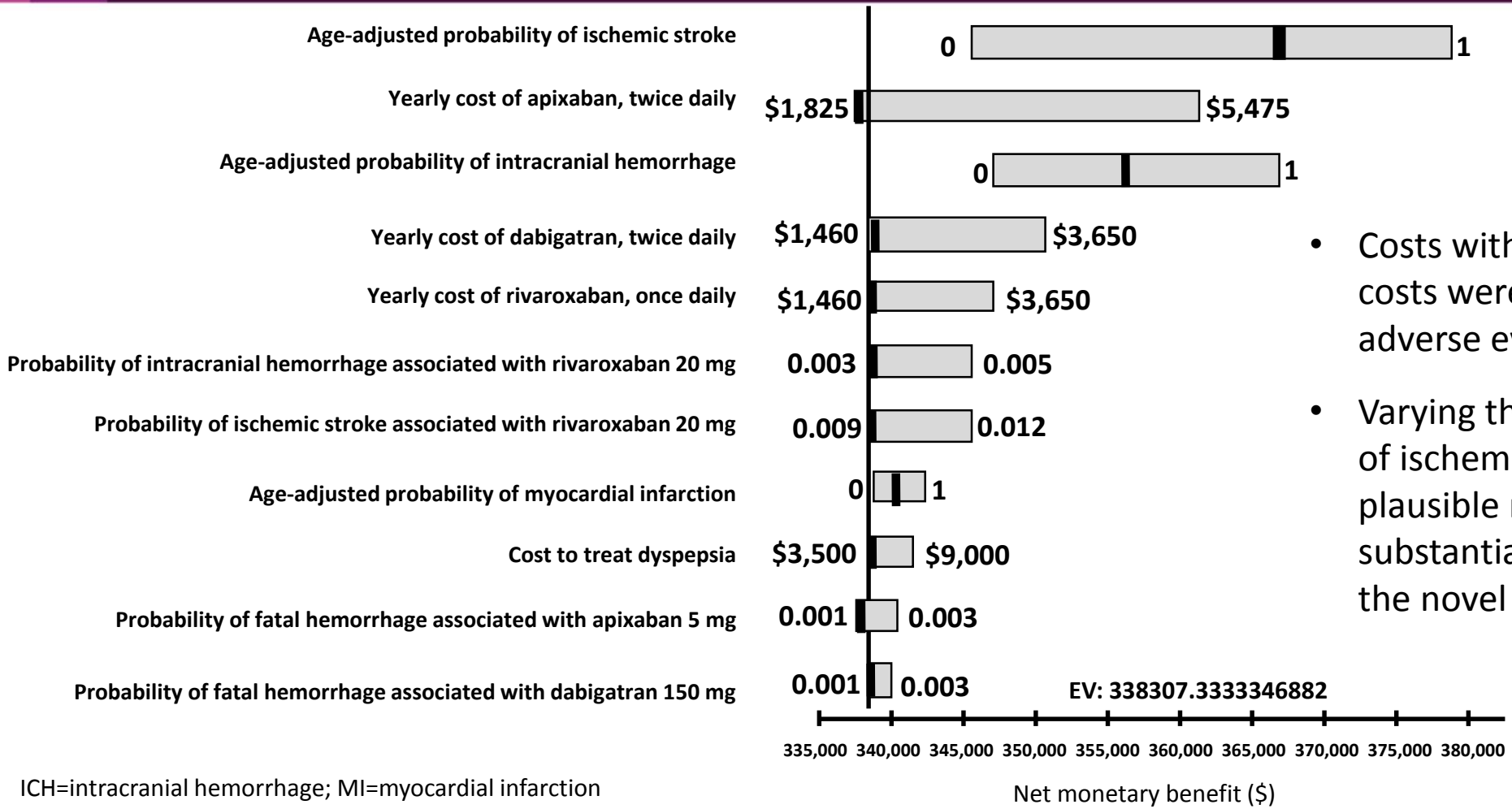
Projected Costs, QALYs, and ICER for Patients with Nonvalvular AF Receiving Anticoagulation Therapy

Strategy	Base Case			Probabilistic Sensitivity Analysis		
	Total Cost ($)	QALY	ICER ($/QALY)	Total Cost ($)	QALY	ICER ($/QALY)
Warfarin	77,813	7.97	---	77,772	7.97	---
Rivaroxaban (20mg)	78,738	8.26	3190/QALY	78,719	8.26	3266/QALY
Dabigatran (150mg)	82,719	8.41	11,150/QALY	82,705	8.41	11,211/QALY
Apixaban (5mg)	85,326	8.47	15,026/QALY	85,337	8.47	15,130/QALY

- In the base case, the estimated QALY for apixaban 5 mg was 8.47—the highest of all the agents included in the model
- Warfarin had the lowest QALY estimate (7.97)
- Compared with warfarin, apixaban 5 mg provided an additional 0.5 QALYs at a cost of $7,513, resulting in an ICER of $15,026 per QALY gained, well below the threshold of $50,000 per QALY gained

Harrington AR, et al. *Stroke.* 2013;44:1676-1681.

Sensitivity Analysis Indicates Adverse Events and Acquisition Costs Influence the Total Cost of Anticoagulation Therapy

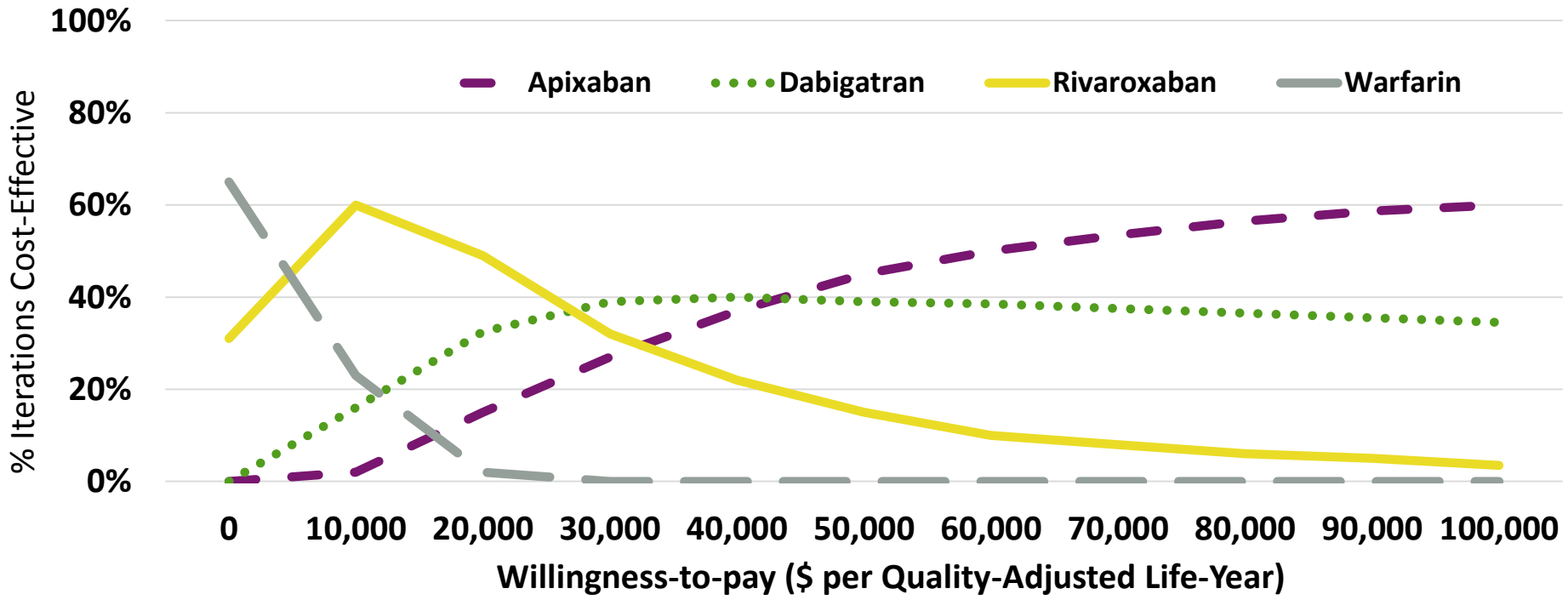


- Costs with the most influence on total costs were costs of therapy and cost of adverse events
- Varying the age-associated probabilities of ischemic stroke, ICH, and MI over plausible ranges simultaneously did not substantially influence the ICER values of the novel agents compared with warfarin

ICH=intracranial hemorrhage; MI=myocardial infarction

Harrington AR, et al. *Stroke.* 2013;44:1676-1681.

Results of this Model Suggest the Novel Agents are Cost-Effective Alternatives to Warfarin



- This curve illustrates the probability that a treatment will be cost-effective at varying willingness-to-pay thresholds
- This study suggests the novel oral anticoagulants are cost-effective alternatives to warfarin for the prevention of stroke in patients with nonvalvular AF at a threshold of $50,000 per quality-adjusted life-year

Harrington AR, et al. *Stroke.* 2013;44:1676-1681.

A Similar Analysis Found the Novel Agents May **Not** be Cost-Effective Compared to Warfarin

- Markov model designed to compare dabigatran 150 mg BID, apixaban 5 mg BID, rivaroxaban 20 mg QD, and warfarin therapy
- Modeled population: hypothetical cohort of 70-year-old warfarin-eligible patients with AF initiating treatment on an oral anticoagulant
- Model took a societal perspective and lifetime horizon to evaluate non-CNS embolism, MI, GI bleeds, non-GI bleeds, ICH, and ischemic stroke
- Used a cost-effectiveness threshold of $100,000 per quality-adjusted life-year

Canestaro WJ, et al. *Circ Cardiovasc Qual Outcomes.* 2013;6:724-731.

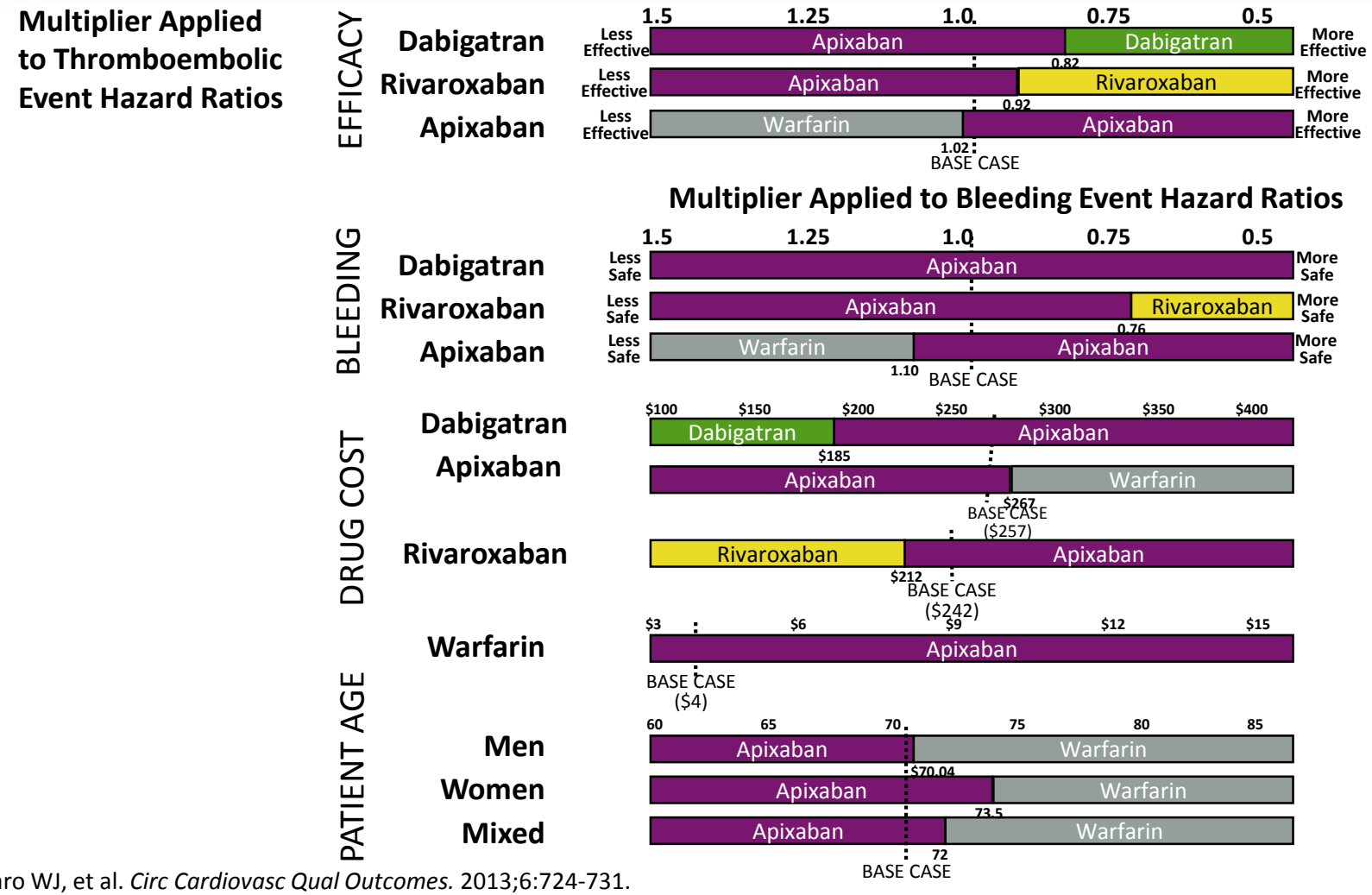
A Similar Analysis Found the Novel Agents May Not be Cost-Effective Compared to Warfarin

Strategy	Base Case				
	Total Cost ($)	QALY	ICER ($/QALY)	Cost-effectiveness Ratio to Warfarin D$/DQALY	Incremental Cost-effectiveness, D$/DQALY
Warfarin	49,638	5.87	8450	Reference	Reference
Rivaroxaban	84,192	6.18	13,618/QALY	111,465	Ruled out by extended dominance
Apixaban	87,794	6.28	13,989/QALY	93,063	93,063
Dabigatran	88,994	6.15	14,473/QALY	140,557	Ruled out by simple dominance

- All novel agents produced greater quality-adjusted life expectancy than warfarin but at a much greater cost
- Compared with warfarin, dabigatran, rivaroxaban, and apixaban cost $140,557, $111,465, and $93,062 per additional QALY gained, respectively
  - At a threshold of $100,000 per QALY, apixaban provided the greatest absolute benefit while still being marginally cost-effective vs warfarin

Canestaro WJ, et al. *Circ Cardiovasc Qual Outcomes.* 2013;6:724-731.

Cost-Effectiveness of an Agent is Sensitive to Assumptions About its Efficacy and Safety



- Apixaban was minimally cost-effective at a threshold of $100,000 per QALY gained
- When assumptions about treatment efficacy, risks, patient demographics, and drug costs were varied, warfarin emerged as an optimal choice in an equal number of simulations
- Although all the novel oral anticoagulants produce greater quality-adjusted life expectancy than warfarin, they may not represent good value for money

Canestaro WJ, et al. *Circ Cardiovasc Qual Outcomes.* 2013;6:724-731.

Edoxaban: The Most Recently Approved Targeted Oral Anticoagulant

- Edoxaban is a factor Xa inhibitor approved in January 2015 and is indicated for
  - Reduction of risk of stroke and systemic embolism in patients with nonvalvular AF
  - Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) following 5-10 days of initial therapy with a parenteral anticoagulant
- Cost-effectiveness of edoxaban in the treatment of AF[1,2] and VTE[3] has been examined in a limited number of studies

1. Miller JD, et al. *Circ Cardiovasc Qual Outcomes.* 2015;8:A104. Abstract
2. Krejczy M, et al. *BioMed Res Int*. 2015; http://dx.doi.org/10.1155/2015/876923.
3. Amin A, et al. *J Hematol Thrombo Dis*. 2015;3:3.

Cost-Effectiveness of Edoxaban vs Rivaroxaban in Nonvalvular AF

- A Markov model was designed to asses the cost-effectiveness of once-daily edoxaban vs rivaroxaban for stroke prevention in AF patients from a US health plan perspective
  - Model simulated lifetime risk and treatment of stroke, systemic embolism, major bleeding, clinically relevant non-major bleeding, MI, and death in AF patients treated with edoxaban or rivaroxaban
- Incremental cost-effectiveness ratios of <$50,000, $50,000-$150,000, and >$150,000 per QALY gained used as thresholds for highly cost-effective, cost-effective, and not cost-effective

Miller JD, et al. *Circ Cardiovasc Qual Outcomes.* 2015;8:A104. Abstract.

Edoxaban was More Cost-Effective than Rivaroxaban in Nonvalvular AF

	Base Case	
	Edoxaban (60 mg/30 mg dose-reduced) once daily	Rivaroxaban (20 mg/q5 mg dose-reduced) once daily
Total healthcare cost per patient ($)	45,358	49,472
D cost vs rivaroxaban ($)	-4,114	---
Total QALYs per patient	7.29	7.24
D QALYs vs rivaroxaban	+0.061	---
Incremental healthcare cost per QALY gained	Edoxaban dominant	---

- Edoxaban was dominant relative to rivaroxaban
  - Edoxaban was associated with lower total healthcare cost and better effectiveness in terms of QALYs in the base case analysis
- Probabilistic sensitivity analyses showed edoxaban as either dominant or a cost-effective alternative (ICER<$50,000) to rivaroxaban 88.4% of the time

Miller JD, et al. *Circ Cardiovasc Qual Outcomes.* 2015;8:A104. Abstract.

Medical Cost May Be Avoided When the Novel Anticoagulants Are Used vs Warfarin

- Estimation of the medical cost differences for VTE patients treated with each of the novel anticoagulants vs warfarin in a hypothetical health plan population in the US with 1 million covered lives

	Cost Difference vs Warfarin ($)		
	2016	2017	2018
Dabigatran	(682,819)	(696,475)	(710,405)
Rivaroxaban	(2,256,767)	(2,301,902)	(2,347,940)
Apixaban	(4,298,261)	(4,384,226)	(4,471,911)
Edoxaban	(1,612,687)	(1,644,941)	(1,677,840)

- In this model, the reductions in medical costs associated with the use of the novel anticoagulants vs warfarin were projected to steadily increase through 2018

Amin A, et al. *J Med Econ*. 2015;18:399-409.
Amin A, et al. *J Hematol Thrombo Dis*. 2015;3:3.

Summary

- Warfarin therapy is often used to reduce risk of stroke in AF patients and treat VTE but can be challenging to use
- Novel anticoagulants may provide more consistent anticoagulation and do not require monitoring; however, the potential benefits of these novel anticoagulants come at an increased cost
- Cost-effectiveness analysis provides a means to assess the value of an anticoagulation regimen
- Results of these analyses are influenced by the multiple variables and assumptions included in the model
- Current data suggests the novel agents produce greater quality-adjusted life expectancy compared to warfarin, but their overall cost-effectiveness is influenced by the willingness-to-pay threshold factored into the model

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An Analysis of the Latest Treatments, Economic Value, and Benefit Designs for Oral Anticoagulation Therapy

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Plan Benefit Designs: Maximizing Value for Current and Emerging Oral Anticoagulation Therapies

James Kenney, Jr., RPh, MBA
Manager, Specialty and Pharmacy Contracts
Harvard Pilgrim Health Care

Faculty Disclosure

- The ***faculty*** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

James Kenney, Jr., RPh, MBA

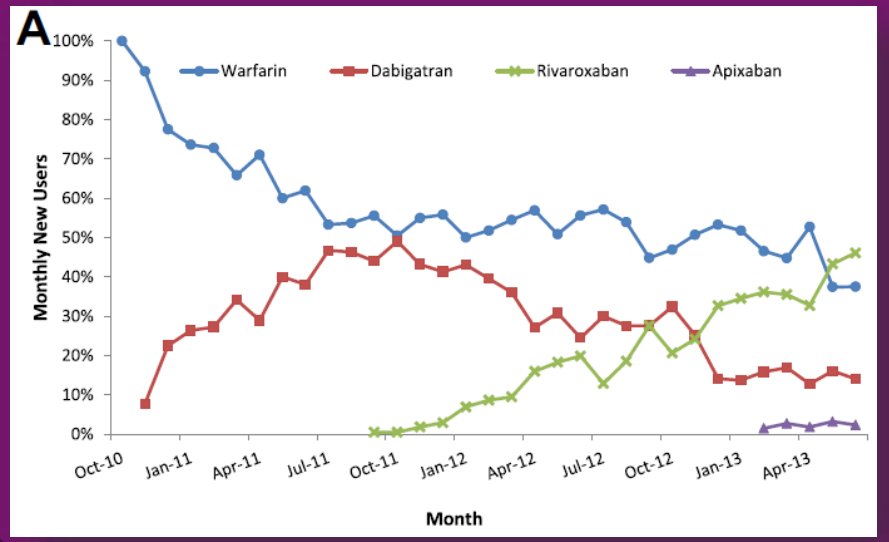
- No financial interest/relationships relating to the topic of this activity

Objective

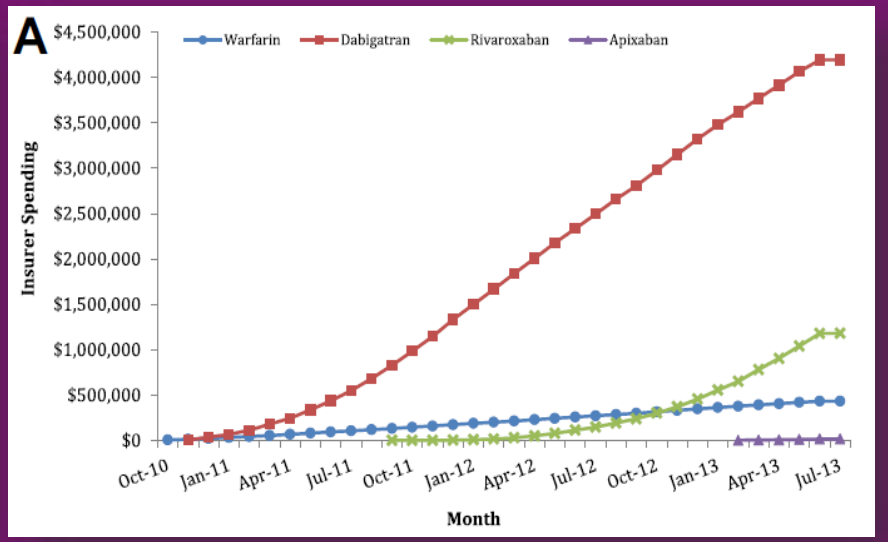
- Employ benefit design methodologies for managed care organizations to improve the overall value of anticoagulant care

Utilization and Costs Associated with Novel Oral Anticoagulants are Rapidly Increasing

Monthly New Users



Insurer Spending



- Analysis of a large insurer database to identify patients with atrial fibrillation (AF) prescribed oral anticoagulation between 2010-2013
  - 6,893 patients initiated anticoagulation
  - By end of the study period, non-vitamin K antagonist oral anticoagulants represented 62% of new prescriptions and 98% of prescription cost

Desai NR, et al. *Am J Med*. 2014;127:1075-82.

Plan Benefit Design is Structured to Manage Costs While Delivering Quality Care

Manage costs by restricting resource (eg, drug) utilization

Medical and pharmacy designs are usually independent

Cost sharing is used to influence patterns of utilization

Patient cost-share related to acquisition cost of the drug	**Assumes an inelastic demand or willingness to pay**

Willey VJ, et al. *Am J Manag Care*. 2008;14:S252-S263.

Utilization Management via Formulary Structure and Guideline-Directed Care

Formulary Design

Tiers

Most common approach is three-tiers:
1) generics, 2) preferred brands, 3) non-preferred brands

Application of Guidelines/Algorithms/Disease Management

Components of Formulary Management

More Formulary Control			
Need for data/ use of CER	Levels of evidence for prior authorization	Quantity limits	Start/stop rules

Contracts	
Work with manufacturers; outcomes-based contracts	Net effective pricing

Cost Shifting and Adherence

- As health care costs rise, pharmacy plan sponsors have traditionally shifted more of the cost to members, but increasing out-of-pocket expenses can negatively impact adherence

Member Decision Factors

- **Cost**
- **Adherence**
- **Efficacy & tolerability**

Benefit Design Factors

- **Medical vs pharmacy**
- **Copay vs coinsurance**
- **Specialty tiers**

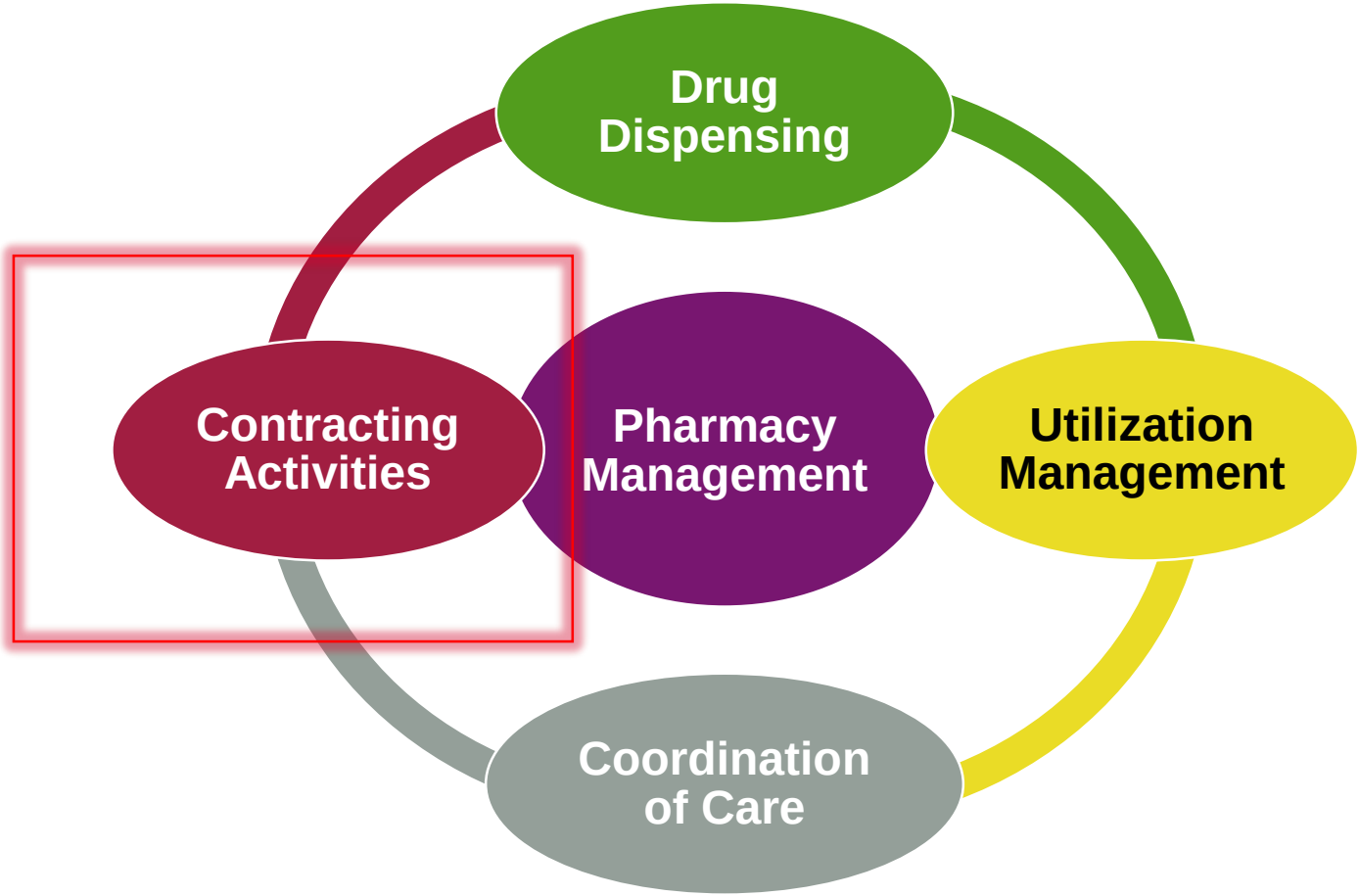
Pharmacy Benefit Institute. 2014-2015 Prescription Drug Benefit Cost and Plan Design Report. 2015.

Pharmacy Benefit Design is Evolving

- Pharmacy benefit design is slowly evolving from simply cost-shifting to more complex offerings and adoption of new management tools

Pharmacy Benefit Institute. 2014-2015 Prescription Drug Benefit Cost and Plan Design Report. 2015.

The Emerging Benefit Design Model



Contracting and Rebates

- Create "preferred" products within key therapeutic classes
  - Maximize rebate potential
  - Control utilization

EMD Serono Specialty Digest, 9th Edition. Managed care strategies for specialty pharmaceuticals http://www.amcp.org/EMDSeronoSpecialtyDigest9th.pdf. Accessed September 22, 2015.

The Emerging Benefit Design Model

Limited Networks

- Establishing pharmacy networks is a popular approach to cost management
- Widely distributed retail chain pharmacies (>55,000) makes the limited network approach possible

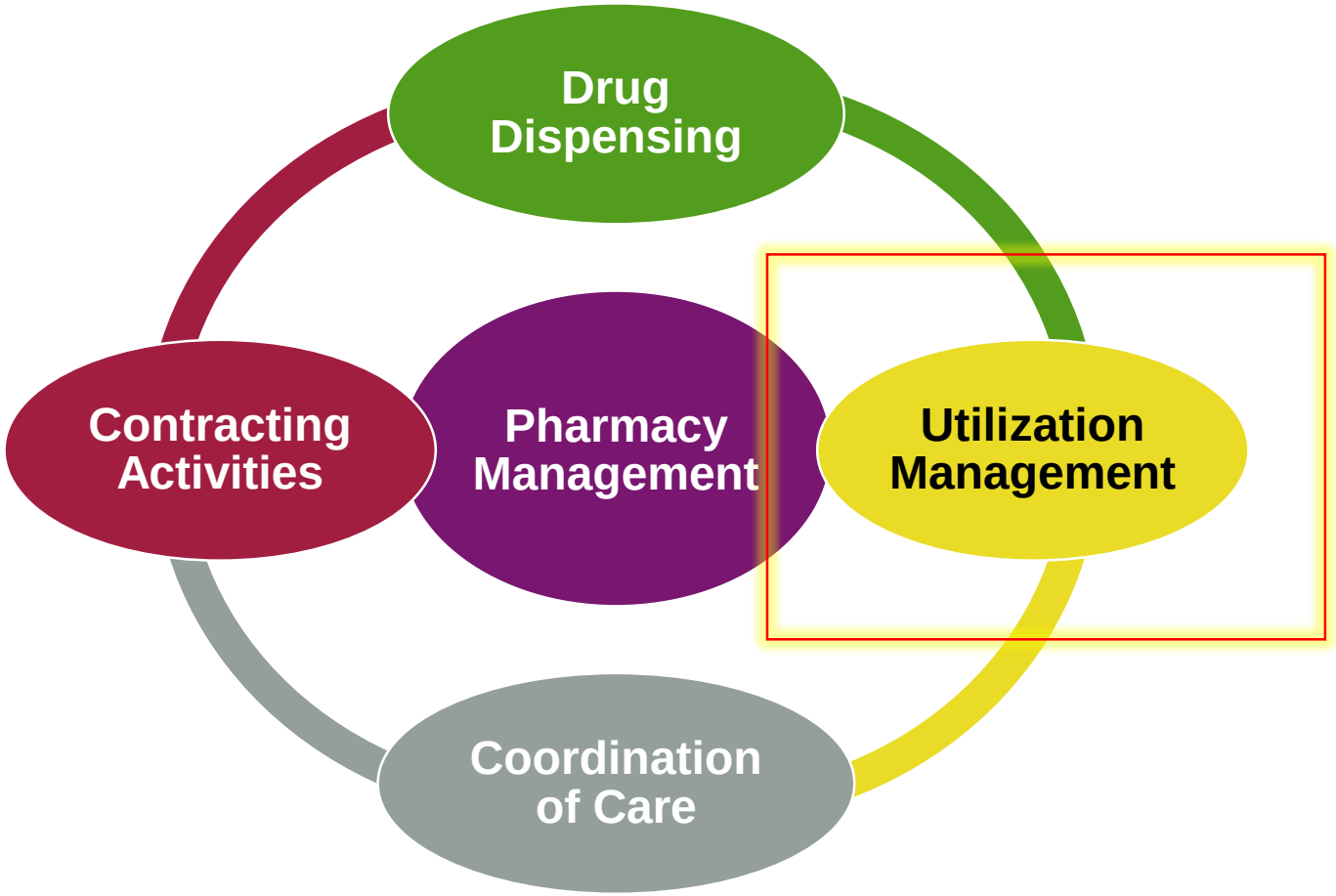
Carrey S. The Institute for Healthcare Consumerism. http://www.theihcc.com/en/communities/pharmacy_benefit_management/8-ways-pharmacy-benefit-design-may-evolve-in-2013_hfpq9mpi.html. Accessed September 23, 2015.

Drug Dispensing

- Channel management
  - The overall member cost share of a drug varies based on where the prescription is filled
  - Payers incentivize plan members to use certain distribution channels (eg, pharmacies) by reducing the patient out-of-pocket expenses
- A new trend is varying incentives within a channel
  - For example, incentivize the use of particular brick and mortar retail pharmacies over online or mail order facilities
  - This allows plan sponsors to keep the broad network while still managing costs as the preferred retailers typically offer better pricing

Carrey S. The Institute for Healthcare Consumerism. http://www.theihcc.com/en/communities/pharmacy_benefit_management/8-ways-pharmacy-benefit-design-may-evolve-in-2013_hfpq9mpi.html. Accessed September 23, 2015.

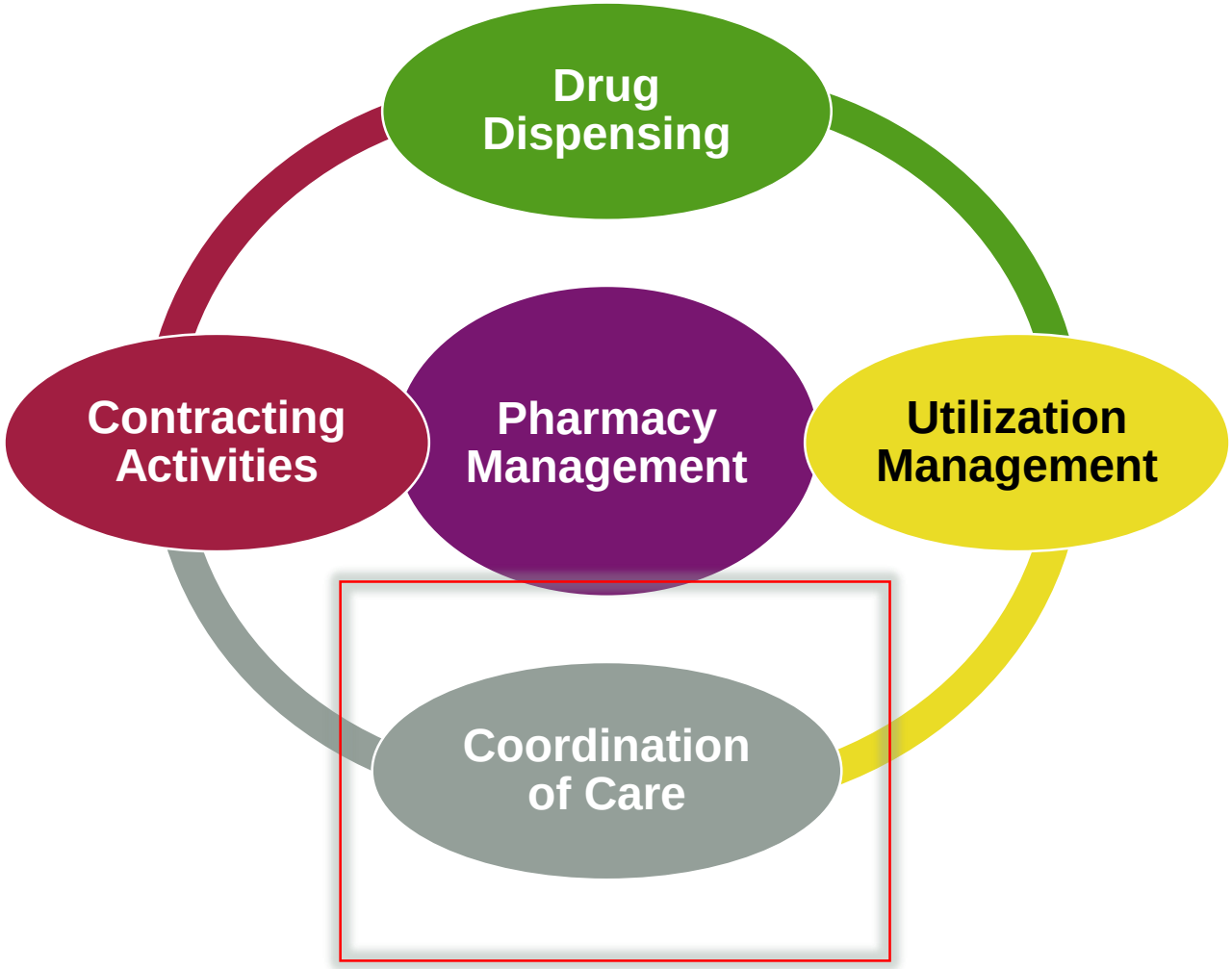
The Emerging Benefit Design Model



Utilization Management Tools

- Prior authorization
- Step therapy
- Quantity limits
- Drug utilization review

The Emerging Benefit Design Model



Health Care Reform is Driving the Emergence of Coordinated Care

Emphasis on Rewarding Value Not Volume

Value-based purchasing, shared savings, gain-sharing, bundled payments, capitation, etc.

Use of Incentives to Drive Coordination of Care

CMS 5-Star Rating System: Plans with >4 Stars receive bonuses and higher rebates

New Structures are Promoting Integration of Care

Accountable Care Organizations (ACOs), Medical Homes, home-based chronic care management, community health teams, health care innovation zones

Patient-Centered Models of Coordinated Care Delivery

Models and Tactics Used by Accountable Care Organizations to Drive Value	

• Patient-Centered Medical Homes (advance primary care)
  ○ An organizational structure that supports health promotion, patient-centered care, and clinical integration
	• Payment mechanisms focused on “fee-for-value” rather than “fee-for-volume”:
	  – Quality incentives for improved processes and outcomes
	  – Incremental roll out to improve probability of success
	  ▪ Fee-for-service: per case/at risk quality payment (bundled/capitated)

Integrating the Patient into the Care Model

Disease and Treatment Variables	Health Care Delivery Variables
Presence of asymptomatic disease	Patient education
Tolerability/drug interactions	Strengthening provider-patient relationship
Treatment efficacy	Patient empowerment
Patient adherence	Medication therapy management
Presence of comorbidities	Medication reminders
	Routine monitoring and adjustment of therapy
	Open and integrated communication channels between health care providers involved in the management of the patient

Integrating Medication Management into the Coordinated Care Model

Program	Actions
• Medication Therapy Management (MTM) – Integration with care management – Coordinate site of care – Ensure appropriate dosing – Adherence – Patient education – Expectation management	• Design workflow and integration with Care Management • Analyze drug utilization patterns to select targeted drugs/disease • Train personnel – Specialty diseases – Medications – Site-of-care logistics

Summary

- Utilization of novel oral anticoagulants continues to increase
- Payers are challenged to devise strategies to simultaneously encourage appropriate use and deliver high quality care
- Strategies include multi-tier formularies, contracting activities, channel management, utilization management, and care management
- New models of care are emerging that integrate medication therapy management into the overall coordination of care

MCRB™

An Analysis of the Latest Treatments, Economic Value, and Benefit Designs for Oral Anticoagulation Therapy

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