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SYLLABUS AND COURSE GUIDE

Weighing the Evidence: A Pharmacy Approach to Stroke Prevention in Obese Patients with Non-Valvular Atrial Fibrillation

Premiere Date: Sunday, December 6, 2020
6:30 PM - 8:00 PM ET (live)
Credit Expiration Date: Monday, December 6, 2021

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#NVAFbeat

LIVE FACULTY:
Kazuhiko Kido, PharmD, MS, BCCP, BCPS
Edith A. Nutescu, PharmD, MS CTS, FCCP

MODERATOR:
Deepak L. Bhatt, MD, MPH, FACC, FAHA, FSCAI, FESC

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INFORMATION FOR PARTICIPANTS

Statement of Need

Atrial fibrillation (AF) is estimated to affect over 5 million people in the United States and is associated with a five-fold increase in the relative risk of stroke. Obesity is an independent risk factor for cardiovascular disease (CVD) and is also associated with increased risk of developing non-valvular AF (NVAF). Patients with comorbid NVAF and obesity need appropriate management of their individual stroke risk. Guidelines for anticoagulant therapy in this patient population have been limited due to lack of available data.

Recent publications of subgroup analyses of randomized controlled trials (RCTs) and retrospective observational cohort studies have provided data on the efficacy and safety of direct oral anticoagulants (DOACs) versus warfarin in obese and extremely obese patients with NVAF. Because pharmacists are a trusted resource and have frequent access to patients, it is imperative that they are well-versed in the latest published data as well as existing guidelines and prescribing information for use of DOACs and warfarin to prevent stroke in patients with NVAF.

In this CME Outfitters virtual symposium, expert faculty will review key aspects of the prescribing information, guidelines, and recently published safety and efficacy data for DOACs and warfarin in order to enable pharmacists and other clinicians to support evidence-based therapeutic treatment decisions in obese patients with NVAF.

Learning Objectives

At the end of this CME/CE activity, participants should be able to:

- Assess existing guidelines and U.S. prescribing information for use of DOACs and warfarin to prevent stroke in obese patients with NVAF.
- Evaluate safety and efficacy data for DOACs and warfarin in obese patients with NVAF.
- Counsel obese patients with NVAF on risks and benefits of DOACs and warfarin to optimize adherence and health outcomes.

Target Audience

Health-system pharmacists and community pharmacists

Financial Support

Supported by an educational grant from the Bristol-Myers Squibb and Pfizer Alliance.

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FACULTY BIOS & DISCLOSURES

Deepak L. Bhatt, MD, MPH, FACC, FAHA, FSCAI, FESC (Moderator)

After graduating as valedictorian from Boston Latin School, Dr. Bhatt obtained his undergraduate science degree as a National Merit Scholar at MIT while also serving as a research associate at Harvard Medical School. He received his medical doctorate from Cornell University and a Master of Public Health with a concentration in clinical effectiveness from Harvard University. His internship and residency in internal medicine were at the Hospital of the University of Pennsylvania, and his cardiovascular training was at Cleveland Clinic. Dr. Bhatt completed fellowships in interventional cardiology and cerebral and peripheral vascular intervention and served as Chief Interventional Fellow at Cleveland Clinic, where he spent several years as an interventional cardiologist and an Associate Professor of Medicine. Most recently he received the AHA's Distinguished Scientist Award in 2019 in addition to numerous other honors. Dr. Bhatt has been listed in Best Doctors in America from 2005 to 2020.

Dr. Bhatt's research interests include acute coronary syndromes, preventive cardiology, and advanced techniques in cardiac, cerebral, and peripheral intervention. He has authored or co-authored over 1500 publications and has been listed by the Web of Science Group as a Highly Cited Researcher from 2014 to 2019. He was the international PI for the CHARISMA and CRESCENDO trials and co-PI of the three CHAMPION trials. He served as chair of COGENT and co-PI of STAMPEDE. Additionally, Dr. Bhatt serves as chair for REDUCE-IT and SCORED. In 2018, REDUCE-IT was listed and named the top cardiology trial by NEJM. In 2014, he was listed in the AHA/ASA top ten advances in heart disease and stroke research (for STAMPEDE and SYMPLICITY HTN-3).He serves as Senior Associate Editor for News and Clinical Trials for ACC.org, Editor of the peer-reviewed *Journal of Invasive Cardiology*, as well as Editor of *Cardiovascular Intervention: A Companion to Braunwald's Heart Disease and Atherothrombosis in Clinical Practice* published by Oxford University Press. He also serves as Editor-in-Chief of the *Harvard Heart Letter* for patients.

Kazuhiko Kido, PharmD, MS, BCCP, BCPS

Dr. Kido is currently a clinical assistant professor of clinical pharmacy at West Virginia University (WVU) School of Pharmacy. Dr. Kido graduated from University of Iowa College of Pharmacy and completed his PGY 1 pharmacy practice residency and PGY 2 cardiology pharmacy residency at University of Kentucky HealthCare. He also received his Master of Science Degree from Keio University and his Bachelor of Science Degree from Kyoritsu College of Pharmacy in Japan.

Dr. Kido is a cardiology clinical pharmacy specialist in the WVU outpatient heart failure clinic and on the WVU inpatient heart failure service. His areas of research interests include anticoagulation in morbidly obese populations and the optimization of sacubitril/valsartan in real-world settings. Dr. Kido has published multiple original research articles and review articles in peer-reviewed journals. Dr. Kido is an active member in the American College of Clinical Pharmacy and American Society of Health-System Pharmacists. He currently serves as a committee member for multiple national pharmacy associations.

Edith A. Nutescu, PharmD, MS CTS, FCCP

Dr. Nutescu is the Michael Reese Endowed Professor of Cardiovascular Pharmacotherapy and Head of the Department of Pharmacy Practice at University of Illinois at Chicago (UIC) College of Pharmacy. She also serves as the Co-Director of the Personalized Medicine Program at the University of Illinois Hospital and Health Sciences System (UI - Health) and is Affiliate Faculty in the Center for Pharmacoepidemiology and Pharmacoeconomic Research and Center for Dissemination and Implementation Science. Dr. Nutescu received her Doctor of Pharmacy from the UIC College of Pharmacy and her Master in Clinical and Translational Science from the UIC School of Public Health. She completed Pharmacy Practice and Specialty Residency (Primary Care with Cardiology Emphasis) training at Advocate Health Care, Lutheran General Hospital and UIC.

Dr. Nutescu's research interests focus on comparative effectiveness and safety of cardiovascular pharmacotherapy and thromboembolic diseases. She has authored over 180 scientific articles and her research has been continuously funded by the National Institutes of Health, National Heart Lung and Blood Institute, The Department of Health and Human Services, the Agency for Healthcare Research and Quality, and the National Center for Research Resources, among others. She is a recipient of the Ruth L. Kirchstein National Research Service Award and National Heart Lung and Blood Institute Clinical Research Career Development Award. She has lectured extensively, both nationally and internationally, on topics related to personalized medicine, thrombosis, cardiovascular diseases and stroke. Her book, "Anticoagulation Therapy: A Clinical Practice Guide," is used nationally and internationally to guide clinical practice guidelines and the bedside management of patients on anticoagulation therapy.

Dr. Nutescu serves as Scientific Editor for the journal *Pharmacotherapy* and has served on the editorial board for the *American Journal of Health-System Pharmacy,* and *Annals of Pharmacotherapy*. She is active in several professional organizations including the American College of Clinical Pharmacy, the American Heart Association, the International Society for Thrombosis and Haemostasis, Academy Health, the Anticoagulation Forum, and the National Blood Clot Alliance. She has served on the Board of Regents for the American College of Clinical Pharmacy, on the National Consumers League Senior Outpatient Medication Safety Coalition, and was the only pharmacist member to serve on the steering committee of the National Quality Forum and The Joint Commission that developed "National Consensus Standards for the Prevention and Care of Venous Thrombosis." Dr. Nutescu has been recognized as a Fellow of the American College of Clinical Pharmacy. She has received the American Society of Health System Pharmacists Foundation Award for Excellence in Medication-Use Safety, the American College of Clinical Pharmacy's Clinical Practice Award, the Russel R. Miller Award for her substantial contributions to the literature of clinical pharmacy, and the Therapeutics Frontiers Award for her outstanding contributions to pharmacotherapeutics in her field.

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Dr. Kido has no disclosures to report.

Dr. Nutesco has no disclosures to report.

Mae Ochoa, RPh (peer reviewer) has no disclosures to report.

Rachel Speer, PhD (planning committee) has no disclosures to report.

Evan Luberger (planning committee) has no disclosures to report.

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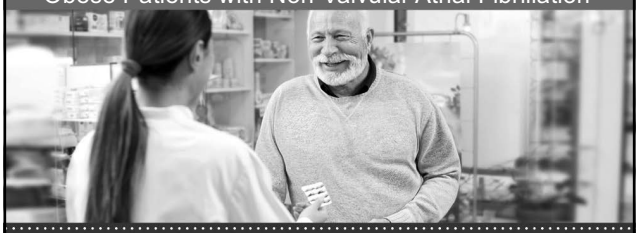
Weighing the Evidence

A Pharmacy Approach to Stroke Prevention in Obese Patients with Non-Valvular Atrial Fibrillation



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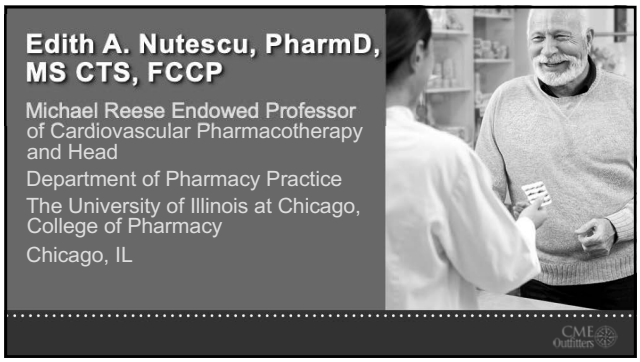
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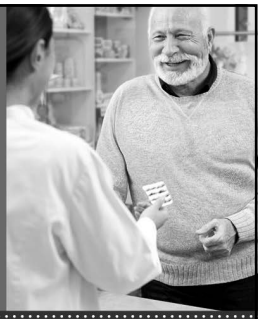
Learning Objective 1

Assess existing guidelines and U.S. prescribing information for use of NOACs and warfarin to prevent stroke in obese patients with NVAF.



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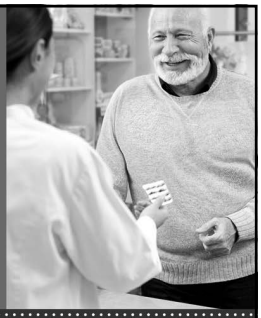
Learning Objective 2

Evaluate safety and efficacy data for NOACs and warfarin in obese patients with NVAF.



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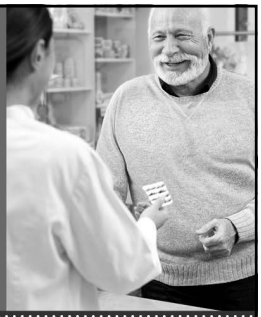
Learning Objective 3

Counsel obese patients with NVAF on risks and benefits of NOACs and warfarin to optimize adherence and health outcomes.



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Case Study

- 63-year-old female presented to the hospital for new onset atrial fibrillation
- **PMH**: hypertension, diabetes
- **Weight** 130 kg, body mass index (**BMI**) 45 kg/m^2
- **Vitals**: BP 130/85, P 90, RR 22, T 36.5 °C
- **Medications**: aspirin 81 mg once daily, lisinopril 10 mg once daily, metformin 500 mg twice daily
- **Allergy**: NKA
- **Labs**: all within normal range

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Obesity and AF

- 35%-40% of adults in the US are living with obesity
- Obesity is an independent risk factor for AF, and frequently coexists with other AF risk factors including hypertension, T2DM, and chronic kidney disease.
- Obesity accounts for 1 in 5 of all AF cases
- AF risk increased by 3%-7% per incremental BMI unit
- Obesity results in atrial remodeling, increased atrial size, interstitial fibrosis, pericardial fat, fat infiltration into atrial myocardium, and heterogeneous and slowed conduction.

AF = atrial fibrillation; BMI = body mass index; T2DM = type 2 diabetes mellitus.
Calkins H, et al. *Heart Rhythm*. 2017;14(10):e275-e444.

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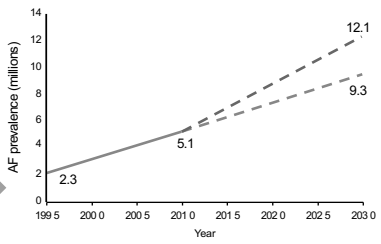
Epidemiology of AF in the US: Rising Prevalence

- As of 2010, prevalence estimates for AF in the US ranged from ~2.7 million to 6.1 million[1]
- **AF prevalence is predicted to increase by up to two-fold by 2030 to 12.1 million[1,2]**

Projections assume no increase (red dashed line) or logarithmic growth (blue dashed line) in incidence of AF from 2007.



1. Benjamin EJ, et al. *Circulation*. 2018;137:e67-e492. 2. Colilla S, et al. *Am J Cardiol*. 2013;112:1142:1147.

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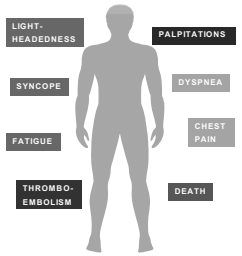
Clinical Presentation of AF



- AF *presents* with a wide range of symptoms[1]
  - May also be asymptomatic
- Impact of asymptomatic AF[2]
  - Potential for underlying electrical and structural damage to atrial myocardium
- While AF symptoms alone may not always be severe, untreated disease can result in significant morbidity and mortality[3]

1. Fuster V, et al. *Circulation*. 2006;114:e257-e354. 2. Page RL, et al. *Circulation*. 2003;107:1141-1145.
3. Stewart S, et al. *Am J Med*. 2002;113:359-364.

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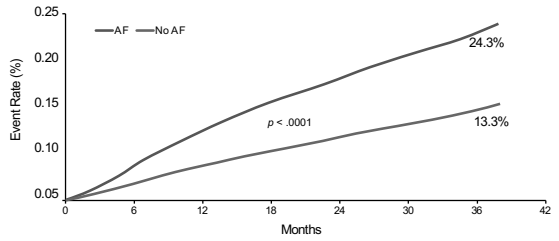
Cumulative Incidence of CV Death, MI, or Stroke After AF Diagnosis



Ruff CT, Bhatt DL, et al. *Int J Cardiol*. 2014;170(3):413-418.

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How Much AF is Enough to Increase Risk of Stroke?

Year	Study	n	AF Burden Measure	HR for stroke
2003	MOST	312	5 min	6.7 $p = 0.02$
2005	Capucci	725	> 24 hrs	3.1 $p = 0.04$
2009	Botto	568	CHADS + AF burden	6.2 (5 vs. 0.8%)
2012	Home monitor CRT	560	3.8 hrs	9.4 $p = 0.006$
2012	TRENDS	2486	5.5 hrs	2.4 $p = 0.06$
2012	ASSERT	2580	6 min	2.5 $p = 0.008$

CRT = cardiac resynchronization therapy

Camm AJ, et al. *Am J Cardiol*. 2012;110(2):270-276.; Glotzer T. Presentation at Transcatheter Cardiovascular Therapeutics (TCT). 2013.

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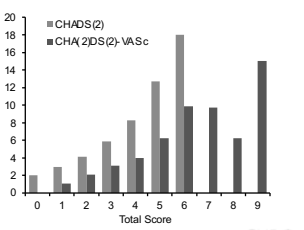
Stroke Risk Stratification in AF

$CHADS_2$	
Risk Factor	**Score**
Cardiac failure	1
Hypertension	1
Age ≥ 75 years	1
Diabetes	1
Stroke	2

CHA_2DS_2-VASc	
Risk Factor	**Score**
Cardiac failure	1
Hypertension	1
Age ≥ 75 years	2
Diabetes	1
Stroke	2
Vascular disease (MI, peripheral arterial disease, aortic atherosclerosis)	1
Age 65-74 years	1
Sex category (female)	1



Lip GY, et al. *Am J Med*. 2010;123(6):484-488.; Camm AJ, et al. *Eur Heart J*. 2010;31(19):2369-2429.

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Bleeding Risk Stratification in AF

HAS-BLED	
Risk Factor	**Points**
Hypertension	1
Abnormal liver or renal function	1 or 2
Stroke	1
Bleeding	1
Labile INR	1
Elderly (age > 65)	1
Drugs or alcohol	1 or 2
Maximum score	**9**

Score of 0 indicates low risk; 2-3, moderate; ≥ 4, high.

- Major bleeding risk is 3-*fold* higher in patients with HAS-BLED scores ≥ 3 vs < 3 (OR = 3.00, CI = 1.21-7.43)
- Patients classified as low- and moderate-risk by HAS-BLED have reduced bleeding risk vs those classified as low- and moderate-risk by other models (HEMORR2HAGES, ATRIA, or ORBIT)

Zeng J, et al. *Medicine (Baltimore)*. 2020;99(25):e20782.

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2019 ACC/AHA/HRS Guidelines for AF

Summary of Class I Recommendations	COR	LOE
For patients with AF and the CHA_2DS_2-VASc score of ≥ 2 in men or ≥ 3 in women, oral anticoagulants are recommended. Options include warfarin (LOE: A), dabigatran (LOE: B), rivaroxaban (LOE: B), apixaban (LOE: B), or edoxaban (LOE: B-R).	I	A, B, B-R
NOACs (dabigatran, rivaroxaban, apixaban, and edoxaban) are recommended over warfarin in NOAC-eligible patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve).	I	A
Among patients treated with warfarin, the international normalized ratio (INR) should be determined at least weekly during initiation of anticoagulant therapy and at least monthly when anticoagulation (INR in range) is stable	I	A
In patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve), the CHA_2DS_2-VASc score is recommended for assessment of stroke risk.	I	B
For patients with AF who have mechanical heart valves, warfarin is recommended.	I	B
Selection of anticoagulant therapy should be based on the risk of thromboembolism, irrespective of whether the AF pattern is paroxysmal, persistent, or permanent.	I	B
Renal function and hepatic function should be evaluated before initiation of a NOAC and should be reevaluated at least annually.	I	B-NR

COE = class of recommendation; LOE = level of evidence;
NOAC = Non-vitamin K oral anticoagulant, also called direct-acting oral anticoagulant (DOAC)

January CT, et al. *J Am Coll Cardiol*. 2019;74(1):104-132.

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NOAC Overview

	Dabigatran[1]	Rivaroxaban[2]	Apixaban[3]	Edoxaban[4]
MOA	DTI	Factor Xa Inhibitor	Factor Xa Inhibitor	Factor Xa Inhibitor
Administration	BID	QD	BID	QD
Peak Effect (hr)	2-3	2-4	1-3	1-2
Half-life	14-17 hours	5-9 hours	8-15 hours	10-15 hours
Renal Clearance	80%	33%	27%	50%
Drug-drug interactions	P-gp	P-gp and CYP3A4	P-gp and CYP3A4	P-gp
Food	No effect	Take with evening meal	No effect	No effect
Reversal Agent	Idarucizumab	Andexanet-alpha	Andexanet-alpha	N/A

MOA = Mechanism of action; QD = once daily; BID = twice daily; CYP3A4 = Cytochrome P450; P-gp = P-glycoprotein; hr = hour(s)

1. PI for Dabigatran. Drugs@FDA.com Website. July, 2020. 2. PI for Rivaroxaban. Drugs@FDA.com Website. March 2020.
3. PI for Apixaban. Drugs@FDA.com Website. November 2019. 4. PI for Edoxaban. Drugs@FDA.com Website. April 2020.

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Renal Dosing Adjustments in NVAF

eCrCl, mL/min*	Dabigatran[1]	Rivaroxaban[2]	Apixaban[3]	Edoxaban[4]
> 95	150 mg BID	20 mg QD with evening meal	No adjustment based on CrCl.	Not recommended
51-95				60 mg QD
31-50		15 mg QD with evening meal	2.5 mg BID for patients with ≥ 2 of the following: • age ≥ 80 years • body weight ≤ 60 kg • serum creatinine ≥ 1.5 mg/dL	30 mg QD
15-30	75 mg BID			
<15, not on dialysis	Not recommended	Not recommended		Not recommended
On dialysis	Not recommended	Not recommended	5 mg BID otherwise	Not recommended

*eCrCl measured with the Cockcroft-Gault method.
NVAF = nonvalvular atrial fibrillation.

1. PI for Dabigatran. Drugs@FDA.com Website. July, 2020. 2. PI for Rivaroxaban. Drugs@FDA.com Website. March 2020.
3. PI for Apixaban. Drugs@FDA.com Website. November 2019. 4. PI for Edoxaban. Drugs@FDA.com Website. April 2020.

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Hepatic Disease Considerations

Child-Pugh Class	Dabigatran[1]	Rivaroxaban[2]	Apixaban[3]	Edoxaban[4]
Class A	No dose adjustment required	No dose adjustment required	No dose adjustment required	No dose adjustment required
Class B	Large inter-subject variability, but no evidence of a consistent change in exposure of pharmacodynamics	Not recommended	Use with caution; dosing recommendations not provided	Not recommended
Class C	No dose adjustment required	Not recommended	Not recommended	Not recommended

1. PI for Dabigatran. Drugs@FDA.com Website. July, 2020. 2. PI for Rivaroxaban. Drugs@FDA.com Website. March 2020.
3. PI for Apixaban. Drugs@FDA.com Website. November 2019. 4. PI for Edoxaban. Drugs@FDA.com Website. April 2020.

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Drug Interactions

Concomitant medication	Dabigatran[1]	Rivaroxaban[2]	Apixaban[3]	Edoxaban[4]
P-gp inducers (eg, rifampin)	Avoid	Avoid	Avoid	Avoid
Combined P-gp and strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, St. John's wort)		Avoid	Avoid	
P-gp inhibitors (dronedarone, systemic ketoconazole)	CrCl 30-50 mL/min: Reduce dose CrCl <30 mL/min: Not recommended			No dose reduction for treatment of NVAF
Combined P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir)		Avoid	Reduce dose by 50% for pts receiving 5 or 10 mg BID. In patients already taking 2.5 mg BID, avoid apixaban	
Combined P-gp and moderate CYP3A inhibitors (e.g., erythromycin)		Do not use in patients with CrCl 15 to <80 ml/min unless potential benefit justifies potential risk		
Increased risk of bleeding with coadministration of anticoagulants (eg, heparin, enoxaparin, warfarin), antiplatelet agents (eg, aspirin, clopidogrel, prasugrel, ticagrelor, cangrelor), fibrinolytics, thrombolytics, SSRIs, SNRIs, and chronic NSAID use.				

NSAIDs = Nonsteroidal anti-inflammatory drugs; SNRIs = serotonin–norepinephrine reuptake inhibitor; SSRIs = elective serotonin reuptake inhibitor

1. PI for Dabigatran. Drugs@FDA.com Website. July 2020. 2. PI for Rivaroxaban. Drugs@FDA.com Website. March 2020.
3. PI for Apixaban. Drugs@FDA.com Website. November 2019. 4. PI for Edoxaban. Drugs@FDA.com Website. April 2020.

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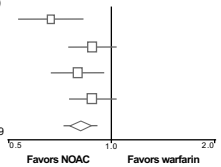
Efficacy of Novel OACs vs. Warfarin in Clinical Trials

Meta-analysis of four phase III trials: stroke/SE events

	NOAC (Events/N)	Warfarin (Events/N)	RR (95% CI)	*p*-value
RE-LY Dabigatran 150 mg bid	134/6076	199/6022	0.66 (0.53–0.82)	.0001
ROCKET AF Rivaroxaban 20 mg qd	269/7081	306/7090	0.88 (0.75–1.03)	.12
ARISTOTLE Apixaban 5 mg bid	212/9120	265/9081	0.80 (0.67–0.95)	.012
ENGAGE AF-TIMI 48 Edoxaban 60 mg qd	296/7035	337/7036	0.88 (0.75–1.02)	.10
Combined (random)	911/29,312	1107/29,229	0.81 (0.73–0.91)	<.0001



Heterogeneity: I^2 = 83%; p = .001

CI = confidence interval; RR = relative risk
Ruff CT, et al. *Lancet*. 2014;383(9921):955–962.

CME Outfitters

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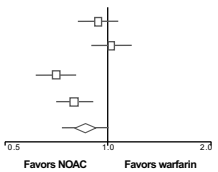
Safety of Novel OACs vs. Warfarin in Clinical Trials

Meta-analysis of four phase III trials: major bleeding events

	NOAC (Events/N)	Warfarin (Events/N)	RR (95% CI)	*p*-value
RE-LY Dabigatran 150 mg bid	375/6076	397/6022	0.94 (0.82–1.07)	.34
ROCKET AF Rivaroxaban 20 mg qd	395/7111	386/7125	1.03 (0.90–1.18)	.72
ARISTOTLE Apixaban 5 mg bid	327/9088	462/9052	0.71 (0.61–0.81)	<.0001
ENGAGE AF-TIMI 48 Edoxaban 60 mg qd	444/7012	557/7012	0.80 (0.71–0.90)	.0002
Combined (random)	1541/29,287	1802/29,211	0.86 (0.73–1.00)	.06



Heterogeneity: I^2 = 83%; p = .001

Ruff CT, et al. *Lancet*. 2014;383(9921):955–962.

CME Outfitters

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Under-Dosing of NOACs in NVAF: Prevalence and Clinical Consequences

- In a sample of 13,392 patients in the US with no renal indication for dose reduction, 13.3% received reduced doses of NOACs.[1]
  - Under-dosing was most common in patients with age ≥ 80 years, with CHA_2DS_2-VASc ≥ 4, or HAS-BLED ≥ 3.
- Among 8,425 patients in Israel newly diagnosed with NVAF and initiating NOAC therapy, 39% received off-label dose-reduced treatment.[2]
  - Underdosing was associated with poorer outcomes

	Reduced dose Events/N (%)	Std. dose Events/N (%)	OR (95% CI)	*P* value
Effectiveness: composite outcome of all-cause death, stroke, or MI	749/3285 (22.8)	447/5140 (8.7)	1.57 (1.34 - 1.83)	< .001
Safety: bleeding events requiring hospitalization	101/3274 (3.1)	80/5144 (1.6)	1.63 (1.14 - 2.34)	.008

1. Yao X, et al. *J Am Coll Cardiol.* 2017;69(23):2779-2790. 2. Arbel R, et al. *Am J Med.* 2019;132(7):847-855.

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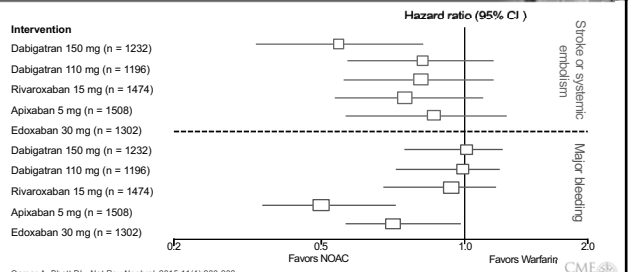
Efficacy and Safety of NOACs vs. Warfarin in Patients with Moderate CKD



Qamar A, Bhatt DL. *Nat Rev Nephrol.* 2015;11(4):200-202.

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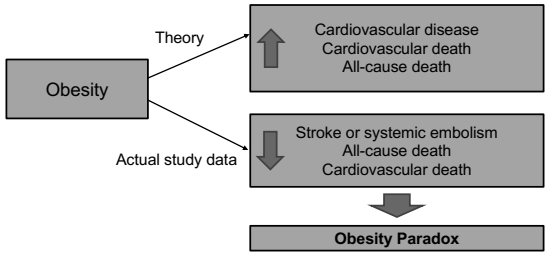
Obesity Paradox



Proietti M et al. *Stroke.* 2017;48:857-866.

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Obesity Paradox: Meta-analysis of ARISTOTLE, ROCKET-AF, and RELY trial outcomes

Stroke/SE*	Obese Events	Normal Weight Events	Odds Ratio M-H, Fixed, 95% CI
ARISTOTLE	152/7159	142/4052	0.60 [0.47, 0.75]
RE-LY	145/6279	182/4697	0.59 [0.47, 0.73]
ROCKET AF	179/5194	167/3314	0.67 [0.54, 0.83]
Total (95% CI)	**476/18632**	**491/12063**	**0.62 [0.54, 0.70]**

Major Bleeding **	Obese Events	Normal Weight Events	Odds Ratio M-H, Fixed, 95% CI
ARISTOTLE	258/7134	219/4035	0.73 [0.61, 0.87]
RE-LY	394/6279	344/4697	0.85 [0.73, 0.98]
ROCKET AF	279/5214	183/3327	0.97 [0.80, 1.18]
Total (95% CI)	**958/18627**	**746/12059**	**0.84 [0.72, 0.98]**

BMI was categorized as normal (18.5 to < 25 kg/m^2), overweight (25 to < 30 kg/m^2), and obese (≥ 30 kg/m^2).
*Heterogeneity. Chi2 = 0.89, df = 2 (p = 0.64; I2 = 0%. Test for overall effect: Z = 7.31 (p < 0.00001).
**Heterogeneity. Chi2 = 0.96, df = 2 (p = 0.62); I2 = 0%. Test for overall effect: Z = 0.06 (p = 0.95).
Proietti M et al. *Stroke*. 2017;48:857-866.

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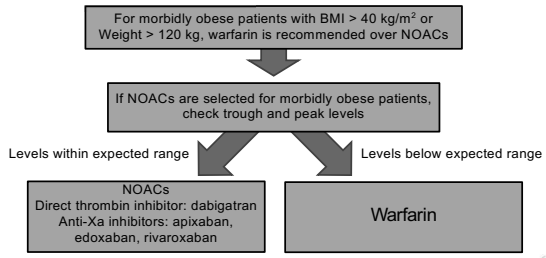
ISTH Statement



Martin K, et al. *J Thromb Haemost*. 2016;14(6):1308-13.

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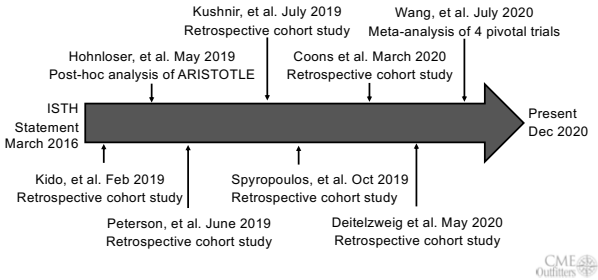
Timeline of NOAC Literature in Morbid Obesity



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NOAC Pharmacokinetic Studies in Morbidly Obese Subjects

	Kubitza et al.	Upreti et al.
NOAC	Rivaroxaban 10 mg, single dose	Apixaban 10 mg, single dose
Cohort	48 healthy subjects weighing ≤ 50 kg (n = 12), 70 to 80 kg (n = 12), or > 120 kg (n = 12)	54 healthy subjects weighing ≤ 50 kg (n = 18), 65 to 85 kg (n = 18), or ≥ 120 kg (n = 18)
Main results	• The >120 kg and 70 to 80 kg groups had similar C_{max} values (LS-means ratio 1.04, CI, 0.90-1.20) and AUC values (LS-means ratio, 1.12, 90% CI 0.98-1.28) • Rivaroxaban inhibited FXa activity to a similar extent in all 3 weight groups	• Compared with reference group (65 to 85 kg), subjects ≥ 120 kg had 31% lower C_{max} and 23% lower $AUC_{(0,\infty)}$ • Plasma anti-factor Xa activity showed a direct, linear relationship with apixaban plasma concentration, regardless of body weight

Kubitza D, et al. *J Clin Pharmacol*. 2007;47(2):218-226.; Upreti VV, et al. *Br J Clin Pharmacol*. 2013;76(6):908-916.

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NOAC Intensity and Levels

NOAC	Intensity (qualitative assessment)	Levels (quantitative assessment)
Dabigatran	aPTT, TT	Estimation: Diluted TT, ECT, ECA LC-MS/MS: level below 50 ng/mL
Apixaban	PT? (not recommended)	Chromogenic anti-Xa assays LC-MS/MS: quantification of lower levels (e.g., rivaroxaban level < 30 ng/mL, apixaban level < 50 ng/mL)
Rivaroxaban	PT	
Edoxaban	PT	

ECA: = ecarin chromogenic assay; ECT = ecarin clotting time; PT = prothrombin time;
LC-MS = liquid chromatography-mass spectrometry; TT = thrombin time; aPTT = activated partial thromboplastin time

Eikelboom JW, et al. *JAMA Cardiology*. 2017;2(5):566-574.

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NOAC Levels: Expected Steady-State Levels

NOAC	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Dose	150 mg BID	20 mg QD	5 mg BID	60 mg QD
Peak (ng/mL)	64-443	189-419	91-321	120-250
Trough (ng/mL)	31-225	6-87	41-230	10-40

Samuelson BT, et al. *CHEST*. 2017;151(1):127-138.

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NOAC PK Studies in Obese Patients in Real World Settings

	Prospective observational study by Martin et al.	Population pharmacokinetic study by Speed et al.
NOAC	Apixaban 5 mg twice daily or rivaroxaban 20 mg daily for AF or VTE	Rivaroxaban for AF or VTE
Cohort	116 samples (apixaban peak n = 19, apixaban trough n = 18, rivaroxaban peak n = 58, rivaroxaban trough n = 21). Mean body weight 139 kg, mean BMI 45 kg/m^2, 84% morbidly obese	913 patients ranging from weight 39 to 172 kg (n = 86: > 120 kg; n = 30: < 50 kg) Opportunistic sampling NONMEM software for population pharmacokinetic model estimation
Main results	No linear relationship between trough or peak anti-Xa levels and body weight or BMI	Significant covariate in the final model: • CL/F: Creatinine clearance with lean BW • Vd/F: lean body weight Total body weight and BMI had minimal influence on rivaroxaban PK parameters

CL = clearance; F = bioavailability; Vd = volume of distribution; VTE = venous thromboembolism

Martin AC, et al. *Thromb Haemost.* 2020 August 30. [Epub ahead of print].; Speed V, et al. *J Thromb Haemost.* 2020 June 8. [Epub ahead of print]

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Conclusions

- Reducing stroke risk in patients with AF is essential, regardless of whether a patient is symptomatic
- NOACs are generally recommended as first-line therapy for stroke prevention in NVAF
- Obesity paradox theory may support the use of NOACs in morbidly obese patients, but more data are needed
- Measuring NOAC levels is suggested in patients with BMI > 40 kg/m^2 or weight > 120 kg
  - Diluted thrombin time: dabigatran level
  - Chromogenic anti-Xa levels: apixaban, edoxaban, rivaroxaban

January CT, et al. *J Am Coll Cardiol.* 2019;74(1):104-132.; Martin K, et al. *J Thromb Haemost.* 2016;14(6):1308-13.; Proietti M, et al. *Stroke.* 2017;48:857-866.

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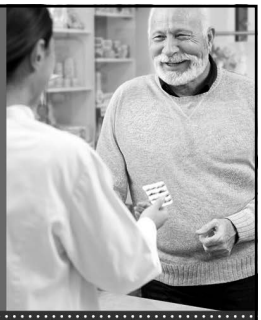
Learning Objective 2

Evaluate safety and efficacy data for NOACs and warfarin in obese patients with NVAF.



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Clinical Evidence in Morbidly Obese Patients Phase III Trials

	ARISTOTLE post-hoc analysis 5 BMI categories	ARISTOTLE post-hoc analysis 3 weight categories
Patients	18.5 to < 25 kg/m² (n = 4052) 25 to < 30 kg/m² (n = 6702) 30 to < 35 kg/m² (n = 4379) 35 to < 40 kg/m² (n = 1774) ≥ 40 kg/m² (n = 1006)	< 60 kg (n = 1985) 60-120 kg (n = 15,172) > 120 kg (n = 982)
Intervention	Apixaban vs Warfarin	
Outcomes	Primary efficacy: stroke or systemic embolism Primary safety: ISTH major bleeding	
Results	• No significant interaction between intervention and BMI in the primary efficacy outcome • No significant difference in major bleeding rate between BMI ≥ 40 and other BMIs	• Nonsignificant interaction between the three weight cohorts for the composite event of stroke or SE

Hohnloser S, et al. *Circulation*. 2019;139(20):2292-2300.; Sandhu R, et al. *Eur Heart J*. 2016;37(38):2869-2878.

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Phase III Trials: Efficacy by BMI Category

BMI (kg/m²)	Trial	HR (95% CI) of SSE for NOAC vs warfarin
30 – 34.99	RE-LY	.71 (0.47, 1.08)
	ROCKET-AF	1.02 (0.76, 1.36)
	ARISTOTLE	0.91 (0.62, 1.34)
	ENGAGE AF-TIMI 48	0.70 (0.50, 0.97)
35 – 39.99	ARISTOTLE	0.31 (0.13, 0.74)
	ENGAGE AF-TIMI 48	1.43 (0.76, 2.70)
≥ 40	ARISTOTLE	0.88 (0.35, 2.18)
	ENGAGE AF-TIMI 48	1.37 (0.37, 5.05)
18.5 to ≥ 40	meta-analysis of RE-LY, ROCKET-AF, ARISTOTLE, and ENGAGE AF-TIMI 48	0.82 (0.75, 0.89)

P value for interaction of BMI category and efficacy outcome:

- RE-LY < .001
- ROCKET-AF = .40
- ARISTOTLE = .11
- ENGAGE AF-TIMI 48 = .16

Wang SY, Giugliano RP. *Am J Cardiol*. 2020;127:176-183.

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Phase III Trials: Safety by BMI Category

BMI (kg/m²)	Trial	HR (95% CI) of Major Bleeding for NOAC vs warfarin
30 – 34.99	RE-LY	1.14 (0.89, 1.45)
	ROCKET-AF	1.15 (0.91, 1.45)
	ARISTOTLE	0.82 (0.62, 1.09)
	ENGAGE AF-TIMI 48	0.88 (0.69, 1.13)
35 – 39.99	ARISTOTLE	0.92 (0.57, 1.48)
	ENGAGE AF-TIMI 48	0.69 (0.45, 1.07)
≥ 40	ARISTOTLE	0.74 (0.35, 1.57)
	ENGAGE AF-TIMI 48	0.92 (0.54, 1.57)
18.5 to ≥ 40	meta-analysis of RE-LY, ROCKET-AF, ARISTOTLE, and ENGAGE AF-TIMI 48	0.86 (0.80, 0.92)

P value for interaction of BMI category and safety outcome:

- RE-LY = .95
- ROCKET-AF = .54
- ARISTOTLE = .039
- ENGAGE AF-TIMI 48 = .81

Wang SY, Giugliano RP. *Am J Cardiol*. 2020;127:176-183.

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Retrospective Studies in Morbidly Obese Patients with Atrial Fibrillation

	Kido et al. Single center retrospective cohort study	**Peterson et al.** Retrospective cohort study using national insurance claim data	**Kushnir et al.** Single center, retrospective cohort study
Patients	Patients with atrial fibrillation (AF) and BMI > 40 or weight > 120 kg	Morbidly obese patients with AF based on diagnostic codes	Morbidly obese patients with BMI > 40 with AF or VTE
Intervention	NOAC (apixaban [n = 19], dabigatran [n = 20], or rivaroxaban [n = 25])	Rivaroxaban (n = 3563)	Apixaban (n = 103) or rivaroxaban (n = 174)
Comparison	Warfarin (n = 64)	Warfarin (n = 3563)	Warfarin (n = 152)
Outcomes	Primary efficacy : stroke or TIA Primary safety: major bleeding	Primary: ischemic stroke or SE Secondary: major bleeding	Efficacy: stroke Safety outcome: major bleeding
Results	NOAC vs warfarin: Stroke or TIA: • 1.75%/yr vs 2.07%/yr • RR 0.84, 95% CI 0.23–3.14 ISTH major bleeding • 2.18%/yr vs 4.97%/yr • RR 0.44, 95% CI 0.15–1.25	Rivaroxaban vs warfarin: Ischemic stroke or SE: • 1.5% vs 1.7% • HR 0.88, 95% CI 0.60–1.28 Major bleeding: • 2.2% vs 2.7% • HR 0.80, 95% CI 0.59–1.08	Stroke in AF cohort: • apixaban 1.0% • rivaroxaban 2.3% • warfarin 1.3% • (*p* = .71 between all cohorts) ISTH major bleeding in AF cohort: • apixaban 2.9% • rivaroxaban 2.9% • warfarin 7.9% • (*p* = .063 between all cohorts)

Kido K, et al. *Ann Pharmacother*. 2019; 53(2):165-170.; Peterson E, et al. *Am Heart J*. 2019;212:113-119.; Kushnir M, et al. *Lancet Haematol*. 2019;6:e359-e365.

CME Outfitters

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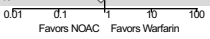
Meta-analysis of Retrospective Studies in Morbidly Obese Patients with AF: Efficacy

Stroke or SE event rate

Study or Subgroup	**NOAC Events**	**Warfarin Events**	**Weight**	**Odds Ratio M-H, Fixed, 95% CI**	**Odds Ratio M-H, Fixed, 95% CI**
Hohnloser 2019	4/480	11/502	8.7%		0.38 [0.12, 1.19]
Kido 2019	4/64	3/64	4.9%		1.36 [0.29, 6.32]
Kushnir 2019	5/277	2/153	4.2%		1.38 [0.26, 7.19]
Perales 2019	0/37	0/30			Not estimable
Peterson 2019	52/3563	59/3563	82.1%		0.88 [0.60, 1.28]
Total (95% CI)	**4421**	**4311**	**100.0%**		**.85 [0.60, 1.19]**
Total events	476	491			



Heterogeneity: Tau² = 0.00; Chi² = 2.66, df = 2 (*p* = 0.45); I² = 0%

Test for overall effect: Z = 0.94 (*p* = 0.35)

Kido K, et al. *Am J Cardiol*. 2020;126:23-28.

CME Outfitters

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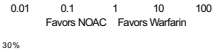
Meta-analysis of Retrospective Studies in Morbidly Obese Patients with AF: Safety

Major bleeding event rate

Study or Subgroup	**NOAC Events**	**Warfarin Events**	**Weight**	**Odds Ratio M-H, Fixed, 95% CI**	**Odds Ratio M-H, Fixed, 95% CI**
Hohnloser 2019	13/480	19/502	21.5%		0.71 [0.35, 1.45]
Kido 2019	5/64	12/64	10.7%		0.37 [0.12, 1.11]
Kushnir 2019	8/277	12/152	14.7%		0.35 [0.14, 0.87]
Peterson 2019	77/3563	96/3563	53.0%		0.80 [0.59, 1.08]
Total (95% CI)	**4384**	**4281**	**100.0%**		**0.63 [0.43, 0.94]**
Total events	103	139			



Heterogeneity. Tau² = 0.05; Chi² = 4.26, df = 3 (*p* = 0.23); I² = 30%

Test for overall effect: Z = 2.29 (*p* = 0.02)

Kido K, et al. *Am J Cardiol*. 2020;126:23-28.

CME Outfitters

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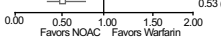
ARISTOPHANES Obesity Subgroup Analysis: Efficacy

	NOAC Incidence Rate (per 100 person-years)	Reference Incidence Rate (per 100 person-years)	Hazard Ratio (95% CI)	*P-value*
Apixaban vs. Warfarin (ref.)	**n = 18,181**	**n = 18,181**		
Stroke/SE	**1.3**	**1.8**	**0.63 (0.49-0.82)**	**0.001**
Ischemic	1.0	1.2	0.78 (0.63-0.96)	0.017
Hemorrhagic	0.2	0.6	0.37 (0.18-0.77)	0.007
Dabigatran vs. Warfarin (ref.)	**n = 6646**	**n = 6646**		
Stroke/SE	**1.6**	**1.3**	**1.23 (0.90-1.67)**	**0.194**
Ischemic	1.3	0.9	1.53 (1.03-2.26)	0.035
Hemorrhagic	0.2	0.4	0.47 (0.21-1.06)	0.070
Rivaroxaban vs. Warfarin (ref.)	**n = 22,053**	**n = 22,053**		
Stroke/SE	**1.4**	**1.6**	**0.84 (0.72-0.98)**	**0.029**
Ischemic	1.1	1.1	0.93 (0.78-1.11)	0.418
Hemorrhagic	0.2	0.5	0.53 (0.37-0.78)	0.001



Deitelzweig S, et al. *J Clin Med*. 2020;9(6):1633.

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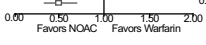
ARISTOPHANES Obesity Subgroup Analysis: Safety

	NOAC Incidence Rate (per 100 person-years)	Reference Incidence Rate (per 100 person-years)	Hazard Ratio (95% CI)	*P-value*
Apixaban vs. Warfarin (ref.)	**n = 18,181**	**n = 18,181**		
Major Bleeding	**4.1**	**6.8**	**0.54 (0.49-0.61)**	**<0.001**
GI Bleeding	2.0	3.2	0.54 (0.49-0.61)	<0.001
ICH	0.4	1.0	0.38 (0.25-0.56)	<0.001
Dabigatran vs. Warfarin (ref.)	**n = 6646**	**n = 6646**		
Major Bleeding	**4.2**	**5.5**	**0.75 (0.63-0.91)**	**0.003**
GI Bleeding	2.6	2.7	0.97 (0.76-1.25)	0.810
ICH	0.4	0.5	0.75 (0.40-1.41)	0.368
Rivaroxaban vs. Warfarin (ref.)	**n = 22,053**	**n = 22,053**		
Major Bleeding	**6.7**	**6.5**	**1.02 (0.90-1.17)**	**0.750**
GI Bleeding	3.9	3.1	1.25 (1.11-1.41)	<0.001
ICH	0.4	0.8	0.49 (0.34-0.70)	<0.001



Deitelzweig S, et al. *J Clin Med*. 2020;9(6):1633.

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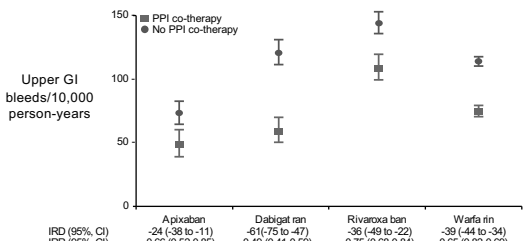
Upper GI Bleeding Risk with OACs With or Without PPI



IRD = incidence and risk difference; IRR = incidence rate ratios; PPI = proton-pump inhibitor
Ray WA, et al. *JAMA*. 2018;320(21):2221-2230.

CME Outfitters

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Conclusions

- Analysis of Phase III clinical trial data and retrospective cohort studies support the use of NOACs in morbidly obese patients with atrial fibrillation

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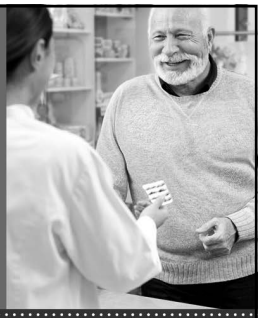
Learning Objective 3

Counsel obese patients with NVAF on risks and benefits of NOACs and warfarin to optimize adherence and health outcomes.



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Case Study

- 74-year-old male with PMH of atrial fibrillation comes to the cardiology multidisciplinary clinic for a regular follow-up
- As an ambulatory care pharmacist, you are reviewing his medication regimen prior to the physician's appointment
- Morbidly obese (BMI 50 kg/m^2, weight 150 kg)
- Dabigatran 150 mg twice daily
- Serum creatinine 1.5 mg/dl and eCrCl is about 30 ml/min
- He started taking St. John's Wort for depression, which was recommended by his primary care physician 2 months ago
- He does not know why he needs to stay on dabigatran and forgets to take it at least 1-2 times weekly

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Case Study

- 65-year-old African American woman
- HTN (uncontrolled 165/95), DM, CRI (CrCL 35mL/min) and HLD
- Presents to emergency room with dizziness and palpitations
- EKG: Atrial fibrillation, rate of 110bpm
- Exam: normal; Labs within normal limits; Cr 1.5, Wt = 124Kg, BMI 47.0
- Medications: lisinopril 40mg daily, atorvastatin 20 mg daily, aspirin 81 mg daily, diltiazem XR 120 mg daily, glipizide 20 mg daily
- SH: ETOH (+), 2-3 drinks/day
  - She is a widower who lives alone 30 miles from the nearest clinic. She has limited dexterity as well as trouble with transportation because she does not drive.
  - She has Medicare part D insurance coverage but is concerned about a high co-pay on her medications, which she can't afford.
  - She is forgetful and expresses a preference for medication that she can take once daily as all her current medications can be taken once daily.

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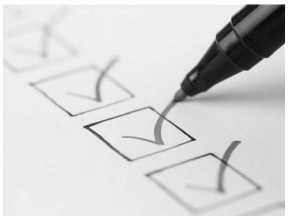
A Systematic Approach: Clinical Screening Checklist



- Valvular vs. non-valvular AF
- Stroke risk
- Bleeding risk
- Drug interactions
- Ongoing need for aspirin + clopidogrel
- Renal dysfunction
- Weight
- Older age
- Adverse effects
- Adherence
- Finances /Medication cost, co-pay
- Patient preferences

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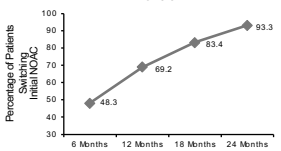
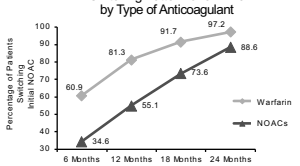
NOAC Switching Patterns: Time

	NOAC	Vitamin K Antagonist	Injectable
Time to First Switch (Days), median (IQR)*	309.5 (119.0-552.0)	118.0 (41.0-287.0)	166.5 (67.5-340.5)

Switching Pattern Over Time Overall



Switching Pattern Over Time by Type of Anticoagulant



* Denotes statistically significant difference ($p < .001$) between types of anticoagulants.

Manzoor BS, et al. *J Thromb Thrombolysis.* 2017;44(4):435-441.

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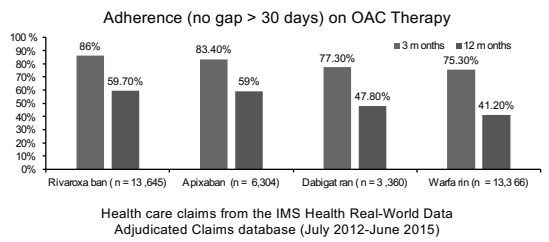
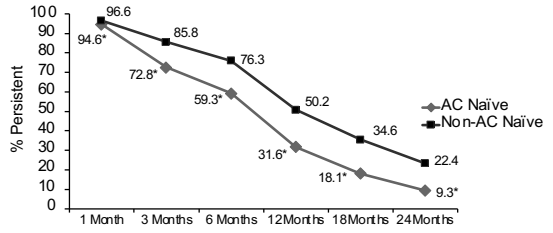
Treatment Persistence and Time to Discontinuation



McHorney CA, et al. *J Manag Care Spec Pharm*. 2017;23(9):980-988.

55

Treatment Persistence with Index NOAC



*Denotes a statistically significant difference between new and previous users ($p < 0.05$).
Manzoor B, et al. *Pharmacotherapy*. 2017;37(10):1221-1230.

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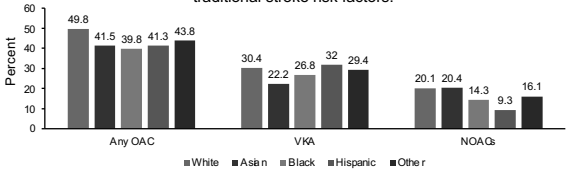
Disparities in OAC Prescribing

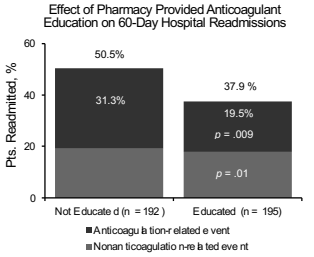
Minority AF patients were less likely to receive any OAC and NOACs compared to whites even after adjusting for demographic factors, income, insurance status, and traditional stroke risk factors.



Percent of anticoagulant prescriptions by race in patients with atrial fibrillation CHA_2DS_2-VASc score greater than or equal to 2.
P-value: * < 0.05, † < 0.01, ‡ < 0.001 (reference group: white race).
Other race includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, having 2 or more race, or indicated as other race.
VKA = vitamin K anticoagulant
Tedla YG, et al. *J Stroke Cerebrovasc Dis*. 2020;29(5):104718.

57

Pharmacists Play an Important Role in AF Care



Pharmacist involvement in anticoagulation management has been found to:

- Improve patient adherence
- Reduce AEs associated with anticoagulation
- Reduce the rates of anticoagulation-related emergency department (ED) visits and hospitalizations

Wilhelm SM, Petrovitch EA. *Am J Health Syst Pharm*. 2011;68(21):2086-2093.
Gebhart F. Drug Topics. 2019. https://www.drugtopics.com/view/pharmacists-want-more-time-patients.

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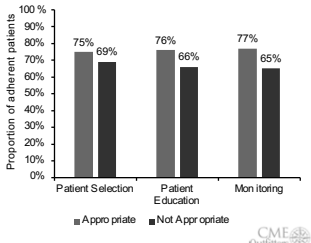
Specific Pharmacist Interventions Associated with Greater NOAC Patient Adherence

- Specific pharmacist-based interventions were associated with better dabigatran adherence!
- Longer duration of monitoring (> 12 months) and providing more intensive care to nonadherent patients improved adherence



Shore S, et al. *JAMA*. 2015;313(14):1443-1450.

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Factors Influencing Adherence

Category	Factors
Patient-centered Factors	• Demographics: age, sex, ethnicity, education, marital status, income • Psychosocial: beliefs, motivation, attitudes • Social: tobacco and alcohol use • Health literacy and numeracy • Patient knowledge • Cognitive decline • Physical limitations
Therapy-related Factors	• Medication: side effects, route of administration, taste and storage • Disease: symptoms and severity • Complexity of treatment • Duration of treatment • Behavior change required
Healthcare System Factors	• Barriers to accessibility • Long wait time • Difficulty in filling prescriptions • Unhappy office/clinic encounters
Social and Economic Factors	• Costs vs. Income • Inability to take time off • Social support

Amin A, Marrs JC. *Clin Appl Thromb Hemost*. 2016;22(7):605-616.

60

Pharmacist Role In Collaborative Therapeutic Decision-Making

- Estimate patients' stroke/systemic embolism and major bleeding risks
  - CHA_2DS_2-VASc score
  - HAS-BLED score
- Identify appropriate candidates for anticoagulation therapy in patients with AF
- Recommend the appropriate anticoagulant to multidisciplinary team based on:
  - Efficacy and safety results from pivotal trials
  - Comorbidities (e.g., obesity)
  - Organ function (kidney, liver)
  - Cost, insurance coverage
  - Drug-drug interactions
  - Patient preference
- Communicate the team's recommendation with patients
- Educate patients on the selected anticoagulant to enhance adherence and optimize therapy outcomes

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Patient-Centered Education

- According to the Joint Commission, patient education on anticoagulation therapy should include:
  - Necessity of follow-up monitoring
  - Importance of adherence
  - Drug-food and drug-drug interactions
  - Potential for side effects
- Counseling should be tailored to each patient based on their medication and literacy level

Hawes EM. *Pharmacy (Basel).* 2018;6(2):34.

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The Need for Shared Decision-Making (SDM) in AF Management

- Less than half of high-risk patients with AF receive anticoagulants[1]
- Of those who start anticoagulation, 30% - 50% stop treatment within 12 months[2,3]
- 2019 AHA/ACC/HRS guidelines note that SDM can improve adherence to anticoagulant therapy[4]

2019 AHA/ACC/HRS Recommendation[4]	Class	Level
In patients with AF, anticoagulant therapy should be individualized on the basis of shared decision-making after discussion of the absolute risk and relative risks of stroke and bleeding, as well as the patient's values and preferences.	I	C

1. Ogilvie IM, et al. *Am J Med.* 2010;123(7):638-645.e4.; 2. Hylek EM, et al. *Circulation.* 2007;115(21):2689-2696; 3. Gallagher AM, et al. *J Thromb Haemost.* 2008;6(9):1500-1506.; 4. January CT, et al. *J Am Coll Cardiol.* 2019;74(1):104-132.

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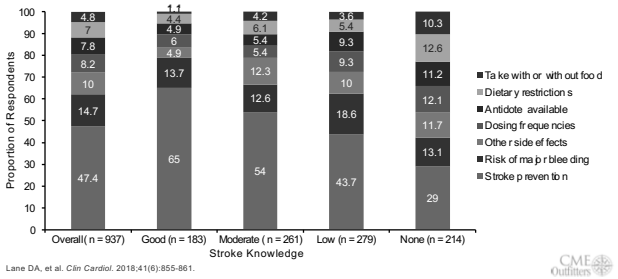
Patient Preferences for OAC Therapy



Lane DA, et al. *Clin Cardiol*. 2018;41(6):855-861.

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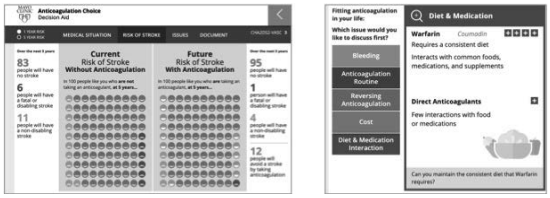
Anticoagulation Choice Tool for Shared Decision-Making

The Anticoagulation Choice tool was shown to improve patient involvement in decision-making, clinician satisfaction, and several measures of SDM quality, with no significant effect on treatment decisions or visit duration.



Kunneman M, et al. *JAMA Intern Med*. 2020;180(9):1215-1224.;
Mayo Clinic. Anticoagulation Choice Decision Aid. 2015. https://anticoagulationdecisionaid.mayoclinic.org/.

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Back to Our Patient

- Several patient-specific factors need to be considered when selecting oral anticoagulation for patients
  - Thrombosis and bleeding risks, weight, renal function, age, and concomitant drug therapy
  - Patient preferences and cost considerations are critical
- Use of clinical decision support tools can aid in treatment selection and patient education
- A systematic approach to screening and discussing drug selection is vital for selection of best agent

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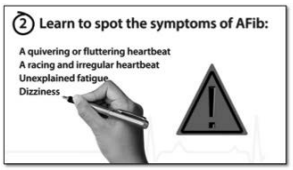
NVAF Whiteboard for Patient Education

~ 2-minute **free** animation educating patients on:

- Description of NVAF
- Risk factors for NVAF
- Symptoms of NVAF
- Treatment options
- Downloadable "Questions to Ask Your HCP"



Available at https://www.cmeoutfitters.com/cardiology

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SMART Goals

Specific, **M**easurable, **A**ttainable, **R**elevant, **T**imely

- Select appropriate anticoagulation at the appropriate dose
  - Utilize a systematic approach to screening
  - Individualize treatment selection
  - Don't underestimate the risk of undertreatment
- Consider measuring NOAC levels in morbidly obese patients where appropriate
  - Diluted thrombin time: dabigatran level
  - Chromogenic anti-Xa levels: apixaban, edoxaban, rivaroxaban
- Apply clinical study findings of NOACs and warfarin in obese patients with AF to appropriate patients in your practice
- Engage patients in SDM and reinforce the importance of adherence and persistence

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To Ask a Question

Please click on the *Ask Question* tab and type your question.
Please include the faculty member's name if the question is specifically for him/her.

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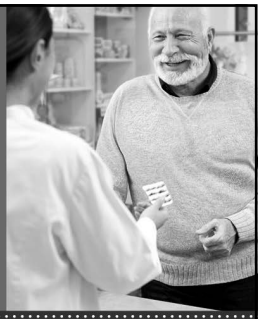
Questions & Answers



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Participants can print their certificate or statement of credit immediately.

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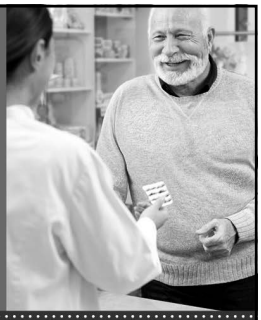
Visit the Cardiology Hub

Free resources for HCPs and patients on atrial fibrillation and other cardiology topics

www.cmeoutfitters.com/cardiology-education-hub/



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Live and On-Demand Activities for ACPE Credit

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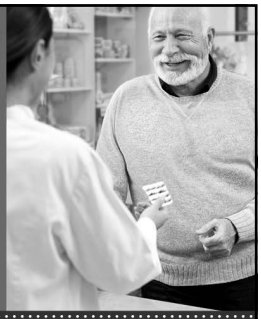

This continuing education activity is provided by CME Outfitters

MM-109-120620-90

Attendance Form for Groups

Please complete and FAX to **614.929.3600**

Activity Title and Faculty:

Weighing the Evidence: A Pharmacy Approach to Stroke Prevention in Obese Patients with Non-Valvular Atrial Fibrillation

with Deepak L. Bhatt, MD, MPH, FACC, FAHA, FSCAI, FESC (Moderator), Kazuhiko Kido, PharmD, MS, BCCP, BCPS, and Edith A. Nutescu, PharmD, MS CTS, FCCP

Site/Institution Name: ______________________________

Practice Setting: ❑ Office-based ❑ Hospital ❑ Clinic ❑ Managed Care ❑ Small Group Practice (less than 5) ❑ Large Group Practice (more than 5) ❑ Other: ______________________________

Address: ______________________________

City: ____________________ State: ________ ZIP: ____________

Site Coordinator: ____________________ Phone: ____________________

Fax: ____________________ Email: ____________________

Completion Date: ____________ We participated in: ____________________

Attendee Name (please print)	Please Circle Discipline						
____________________	MD	DO	PA	NP	RN	Pharm	Other: ____________
____________________	MD	DO	PA	NP	RN	Pharm	Other: ____________
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Please FAX completed form to 614.929.3600 and use additional sheets as necessary.
Questions? Call 877.CME.PROS. Thank you for participating in this continuing education activity!