Size Doesn’t Have to Be a Barrier: Direct Oral Anticoagulants in Extremes of Weight

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Disclosures

The planner(s) and speaker(s) have indicated that there are no relevant financial relationships with any ineligible companies to disclose.

Learning Objectives

At the end of this session, learners should be able to:

- Understand the proposed pharmacokinetic and pharmacodynamic changes in anticoagulation therapy in patients of weight extremes
- Identify current guideline recommendations for anticoagulation in patients who are underweight or obese
- Summarize available literature to assess the efficacy and safety of direct oral anticoagulant (DOACs) in underweight and obese patient populations
- Recognize appropriate anticoagulant therapy in patients of weight extremes

Outline

- Background
- Pharmacokinetic Considerations
- Available Literature
  - Current Guideline Recommendations
  - Additional Literature
- Bariatric Surgery Considerations
- DOAC Level Monitoring
- Limitations of Available Literature
- Summary

Abbreviation Key

- DOAC: direct oral anticoagulant
- BMI: body mass index
- AF: atrial fibrillation
  - Specifically, non-valvular atrial fibrillation
- VTE: venous thromboembolism
  - DVT: deep venous thrombosis
  - PE: pulmonary embolism
- PK: pharmacokinetics
- Vd: volume of distribution
- CrCl: creatinine clearance
- ISTH: International Society on Thrombosis and Haemostasis
- BID: twice daily
- MI: myocardial infarction
- GI: gastrointestinal
- SMD: standard mean difference

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Definitions

- DOAC: unless otherwise specified, include all the following:
  - Apixaban
  - Rivaroxaban
  - Edoxaban
  - Dabigatran

CDC BMI Category	BMI Range (kg/m^2)
Underweight	< 18.5
Healthy weight	18.5 to 25
Overweight	25 to < 30
Obesity	≥ 30
Class I Obesity	30 to < 35
Class II Obesity	35 to < 40
Class III Obesity	≥ 40

Centers for Disease Control and Prevention. Adult BMI Categories. Updated 2024.

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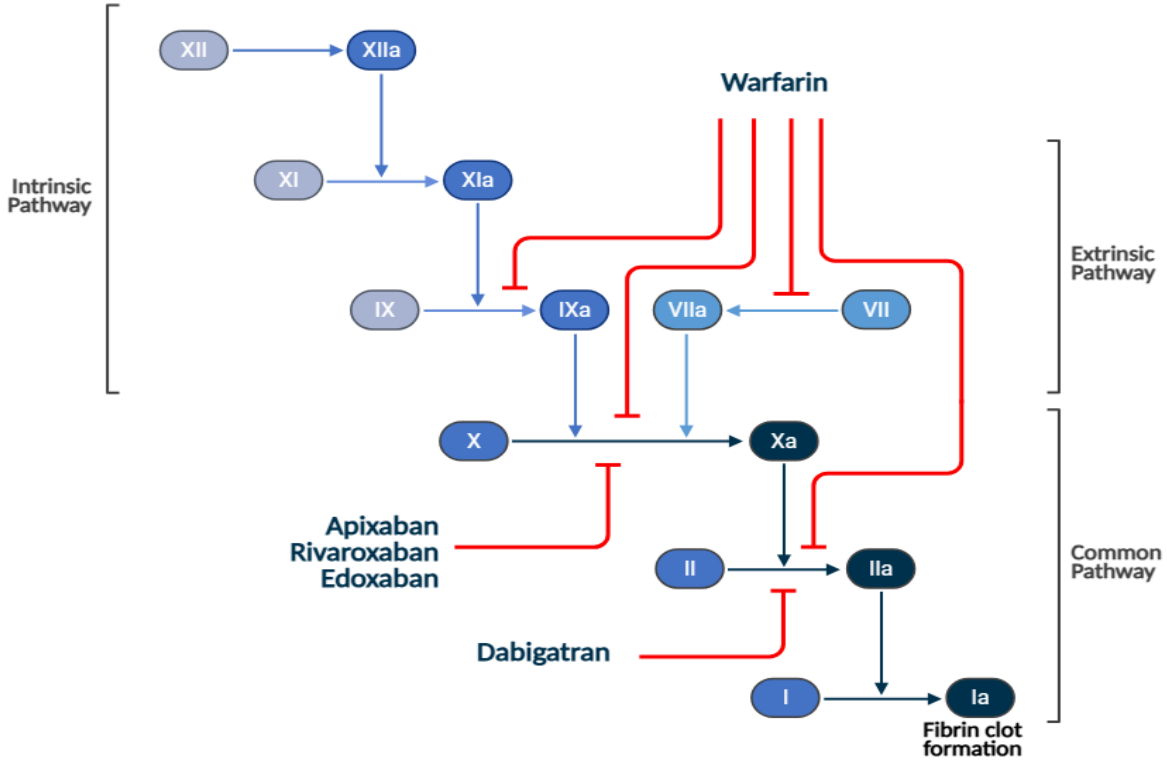
Background of DOACs

Direct Oral Anticoagulants

DOAC	Mechanism	Stroke Prevention in Non-Valvular AF	Treatment of VTE	Secondary VTE Prophylaxis
Apixaban (Eliquis®)	Factor Xa inhibitor	✓	✓	✓
Rivaroxaban (Xarelto®)	Factor Xa inhibitor	✓	✓	✓
Edoxaban (Savaysa®)	Factor Xa inhibitor	✓	✓	
Dabigatran (Pradaxa®)	Direct thrombin inhibitor (Factor IIa)	✓	✓	✓

Eliquis (apixaban). Bristol-Myers Squibb; Pfizer. 2021.
Xarelto (rivaroxaban). Janssen Pharmaceuticals Inc. 2026.
Savaysa (edoxaban). Daiichi Sankyo Inc. 2023.
Pradaxa (dabigatran). Boehringer Ingelheim. 2025.

Clotting Cascade



Joglar JA, Chung MK, Armbruster AL, et al. J Am Coll Cardiol. 2024;83(1):109-279.
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Recommended DOAC Dosing

DOAC	AF Dosing	VTE Treatment Dosing	Dosing Considerations
Apixaban (Eliquis®)	**Standard:** 5 mg twice daily **Reduced:** 2.5 mg twice daily If ≥ 2: age ≥ 80 years, **weight ≤ 60 kg**, SCr ≥ 1.5 mg/dL	**Acute:** 10 mg twice daily × 7 days, then 5 mg twice daily **Extended**: 2.5 mg twice daily after initial therapy	• Dose reductions for AF based on age, renal function, and weight
Rivaroxaban (Xarelto®)	**Standard:** 20 mg once daily with evening meal **Reduced**: 15 mg once daily if CrCl 15-50 mL/min	**Acute:** 15 mg twice daily × 21 days, then 20 mg once daily **Extended**: 20 mg once daily	• Doses should be taken with food. • Dose reductions based on renal function
Edoxaban (Savaysa®)	**Standard:** 60 mg once daily if CrCl >50-95 mL/min **Reduced**: 30 mg once daily if CrCl 15-50 mL/min, **weight ≤ 60 kg**, or P-gp inhibitors	60 mg once daily after 5-10 days parenteral anticoagulation 30 mg once daily if CrCl 15-50 mL/min or **weight ≤ 60 kg**	• Dose reductions based on renal function and weight
Dabigatran (Pradaxa®)	**Standard:** 150 mg twice daily **Reduced**: 75 mg twice daily if CrCl 15-30 mL/min (US only)	150 mg twice daily after 5-10 days parenteral anticoagulation	• Dose reductions based on renal function

Eliquis (apixaban). Bristol-Myers Squibb; Pfizer. 2021.
Xarelto (rivaroxaban). Janssen Pharmaceuticals Inc. 2026.
Savaysa (edoxaban). Daiichi Sankyo Inc. 2023.
Pradaxa (dabigatran). Boehringer Ingelheim. 2025

Background Recap

Apixaban, rivaroxaban, and edoxaban are factor Xa inhibitors

- Dabigatran is direct thrombin inhibitor

All 4 major DOACs are approved for stroke prevention in non-valvular AF and VTE treatment

Apixaban and edoxaban have dose reductions based on weight and renal function

- Rivaroxaban and dabigatran have dose reductions for renal function alone

Pharmacokinetic Considerations

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DOAC Pharmacokinetics

DOAC	Absorption	Distribution	Metabolism	Excretion
Apixaban	Moderate bioavailability	Highly protein bound, small Vd	Mainly CYP3A4 metabolism	Primarily non-renal
Rivaroxaban	High bioavailability (with food)	Highly protein bound, intermediate Vd	CYP2A4 and 2J2 metabolism	Both renal and non-renal
Edoxaban	High bioavailability	Moderately protein bound, intermediate Vd	CYP3A4 metabolism	Both renal and non-renal
Dabigatran	Low bioavailability	Moderately protein bound, high Vd	Glucuronic acid conjugation	Primarily renal
All 4 DOACs are lipophilic				

Steffel J, Collins R, Antz M, et al. Europace. 2021;23(10):1612-1676.
Eliquis (apixaban). Bristol-Myers Squibb; Pfizer. 2021.
Xarelto (rivaroxaban). Janssen Pharmaceuticals Inc. 2026.
Savaysa (edoxaban). Daiichi Sankyo Inc. 2023.

Low Body Weight PK Considerations

BMI ≤ 18.5 kg/m^2	
Absorption	• Decreased absorption possible depending on underlying cause
Distribution	• Decreased adipose tissue and lean body weight • Decreased Vd of lipophilic compounds • Increased tissue perfusion
Metabolism	• Suppression of CYP450 enzymes • Phase I reactions more affected than Phase II reactions
Excretion	• Renal function may be overestimated by CrCl
All effects:	Higher drug concentration, enhanced drug effects

Gigante B, Tamargo J, Agewall S, et al. Eur Heart J Cardiovasc Pharmacother. 2024;10(7):614-645.

High Body Weight PK Considerations

BMI ≥ 35 kg/m^2	
Absorption	• Altered gastric emptying
Distribution	• Higher adipose tissue, lean body mass • Increased Vd of lipophilic compounds • Decreased tissue perfusion
Metabolism	• Reduced hepatic blood flow • Increased Phase II metabolism
Excretion	• Renal blood flow increased • Increased CrCl
All effects:	Lower drug concentration, reduce drug effect

Gigante B, Tamargo J, Agewall S, et al. Eur Heart J Cardiovasc Pharmacother. 2024;10(7):614-645.

Question #1

Given apixaban's small Vd, what implications does a patient's Vd have for its pharmacokinetics and clinical use?

A. Apixaban is less likely to be affected by Vd changes
B. Apixaban is more likely to be affected by Vd changes
C. Apixaban is contraindicated in patients with an increased Vd
D. Apixaban is not distributed in patients with a decreased Vd

Pharmacokinetics Recap

PK changes in low body weight may cause increased drug effects

- Concern for increased risk of **bleeding** with DOACs

PK changes in high body weight may cause reduced drug effects

- Concern for increased risk of **embolism** with DOACs

Apixaban is least likely to be affected by body weight changes

Dabigatran is most likely to be affected by body weight changes

Available Literature - Guidelines

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Atrial Fibrillation

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2023 ACC/AHA/ACCP/HRS

Obesity is a strong risk factor for AF

Need for anticoagulation to prevent VTE determined by risk scores

- Preferred: CHA2DS2-VASc
- Anticoagulation indicated if CHA2DS2-VASc $\geq$ 2 (men) or $\geq$ 3 (women)

Selection of anticoagulation:

- DOAC preferred over warfarin
  - Except in moderate to severe mitral stenosis or mechanical heart valve recipients
- Based on 4 major trials: ARISTOTLE, ROCKET-AF, ENGAGE-TIMI, & RE-LY

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Joglar JA, Chung MK, Armbruster AL, et al. J Am Coll Cardiol. 2024;83(1):109-279.

2023 ACC/AHA/ACCP/HRS

Anticoagulation Considerations in Underweight

- Follow drug-specific monograph for dosing

Anticoagulation Considerations in Obesity

- In class III obesity (BMI $\geq$ 40 kg/m^2), DOACs are reasonable to choose over warfarin
- Patients with class III obesity are underrepresented in major DOAC clinical trials
- Post hoc analyses and large observational studies have shown comparable efficacy and safety of DOACs compared to warfarin

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Joglar JA, Chung MK, Armbruster AL, et al. J Am Coll Cardiol. 2024;83(1):109-279.

AF Landmark Trials

ARISTOTLE Post Hoc: Efficacy and Safety of Apixaban Versus Warfarin in Patients With Atrial Fibrillation and Extremes in Body Weight		
Dose Studied	**Outcome Studied**	**Weight-Stratified Patient Numbers**
5 mg BID or 2.5 mg BID if ≥2 criteria (age ≥ 80 years, weight ≤60 kg, SCr ≥ 1.5 mg/dL)	Efficacy: stroke or systemic embolism, death, MI at 2 years Safety: ISTH major or clinically relevant bleeding, intracranial, GI, or any bleeding at 2 years	**Total: 18,139** ≤60 kg: 1,985 (10.9%) 60-120 kg: 15,172 (83.6%) ≥120 kg: 982 (5.4%) 121 kg-140 kg: 725 ≥ 140 kg: 258

Key Findings:

Efficacy: The treatment effect of apixaban vs warfarin was consistent across all weight spectrums ($p > 0.05$)
Safety: Apixaban demonstrated better safety profile than warfarin in all weight categories and showed a greater relative risk reduction in patients in low and midrange groups

Granger CB, Alexander JH, McMurray JJV, et al. N Engl J Med. 2011;365:981-992.
Hohnloser SH, Fudim M, Alexander JH, et al. Circulation. 2019;139:2292-2300.

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AF Landmark Trials

ROCKET-AF Post Hoc:
Relation of Risk of Stroke in Patients With Atrial Fibrillation to Body Mass Index

Dose Studied	Outcome Studied	Weight-Stratified Patient Numbers
20 mg daily or 15 mg daily if CrCl 30-49 mL/min	Efficacy: composite of stroke or systemic embolism Safety: major and nonmajor clinically relevant bleeding events	**Total: 14,030** BMI 18.5-24.99 g/m²: 3289 (23.4%) BMI 25-29.99 kg/m²: 5535 (39.5%) BMI ≥30 kg/m²: 5206 (37.1%)

Key Findings:

Efficacy: A significantly lower percentage of patients in overweight or obese group experienced primary endpoint compared to normal weight group, across DOAC and warfarin group
Safety: Bleeding event rates were similar across weight and treatment groups and no statistically significant associations observed

Patel MR, Mahaffey KW, Garg J, et al. N Engl J Med. 2011;365:883-891.
Balla SR, Cyr DD, Lokhnygina Y, et al. Am J Cardiol. 2017;119:1989-1996.

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AF Landmark Trials

ENGAGE-TIMI Post Hoc: Edoxaban versus Warfarin in Patients with Atrial Fibrillation at the Extremes of Body Weight		
Dose Studied	**Outcome Studied**	**Weight-Stratified Patient Numbers**
60 mg daily or 30 mg daily if CrCl 30-50 mL/min, weight ≤ 60 kg, or concomitant verapamil or quinidine	Efficacy: stroke or systemic embolism, death, net clinic outcomes of systemic embolic event Safety: major bleeding	**Total: 21,105** ≤ 55 kg: 1,082 (5.1%) 79.8-84 kg: 2,153 (10.2%) ≥120 kg: 1,093 (5.2%) BMI ≤ 18.5 kg/m²: 168 (0.8%) BMI 18.5-25 kg/m²: 4,501 (21.4%) BMI 25-30 kg/m²: 7,907 (37.6%) BMI 30-35 kg/m²: 2,103 (10.0%) BMI 35-40 kg/m²: 5,214 (24.8%) BMI > 40 kg/m²: 1,157 (5.5%)

Key Findings:

Edoxaban showed consistent pharmacokinetics across weight groups, and similar efficacy compared with warfarin.

Giugliano RP, Ruff CT, Braunwald E, et al. N Engl J Med. 2013;369:2093-2104.
Boriani G, Ruff CT, Kuder JF, et al. Thromb Haemost. 2021;121:140-149.

AF Landmark Trials

Trial	Total (n)	Dose Studied	Weight-Stratified Patient Numbers	Key Findings
RE-LY (Dabigatran)	18,113	110 mg BID or 150 mg BID (randomized)	No formal weight stratification published	No published analysis for weight extremes.

Connolly SJ, Ezekowitz MD, Yusuf S, et al. N Engl J Med. 2009;361:1139-1151.

Venous Thromboembolism

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ISTH Guidelines

2016 ISTH SSC Guidelines:

- Recommend against DOACs if BMI $\geq$ 40 kg/m^2 or weight $\geq$120 kg
  - If DOACs are used, recommend obtaining peak and trough concentrations

2021 ISTH Consensus Update:

- DOACs recommended over warfarin for treatment of VTE
  - Except in antiphospholipid syndrome
- BMI $\geq$ 40 kg/m^2 or weight $\geq$120 kg
  - Recommend usual dose of apixaban or rivaroxaban
  - NOT recommended: dabigatran or edoxaban
- Based on 4 major trials: AMPLIFY, EINSTEIN DVT/PE, Hokusai-VTE, RE-COVER/RE-COVER II

Kearon C, Akl EA, Ornelas J, et al. Chest. 2016;149(2):315-352.
Stevens SM, Woller SC, Kreuziger LB, et al. Chest. 2021;160(6):e545-e608.

2026 ACC/AHA Joint Committee: Evaluation & Management of Acute PE

DOACs recommended over warfarin, unless contraindicated

Underweight Considerations:

- No specific considerations, standard dose DOAC recommended

Obese Considerations:

- BMI > 30 kg/m^2: treatment with a DOAC is reasonable over warfarin
- Apixaban and rivaroxaban may be superior in efficacy and safety compared to warfarin

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Creager MA, Barnes GD, Giri J, et al. Circulation. 2026;153:e26-e30.

VTE Landmark Trials

AMPLIFY Post Hoc: Efficacy, Safety, and Exposure of Apixaban in Patients with High Body Weight or Obesity and Venous Thromboembolism			
Dose Studied	**Outcome Studied**	**Weight-Stratified Patient Numbers**	
10 mg BID x 7 days, then 5 mg BID for 6 months	Efficacy: composite incidence of recurrent VTE or VTE-related death Safety: major bleeding, composite of major and non-major bleeding	**Total: 5,384** ≤60 kg: 476 (8.8%) >60 to <100 kg: 3868 (71.8%) ≥100 to <120 kg: 750 (13.9%) ≥120 kg: 290 (5.4%)	BMI ≤ 25 kg/m²: 1442 (26.8%) BMI 25-30 kg/m²: 2045 (34%) BMI 30-35 kg/m²: 1167 (21.7%) BMI > 35 kg/m²: 705 (13.1%)

Key Findings:

Efficacy: Rates of primary endpoint were similar between groups across all body weights, and the ≥ 120 kg group had the lowest relative risk
Safety: Bleeding rates (major and non-major) were lower with apixaban group across all weight groups.

Agnelli G, Büller HR, Cohen A, et al. N Engl J Med. 2013;369:799-808.
Cohen AT, Pan S, Byon W, et al. Adv Ther. 2021;38:3003-3018.

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VTE Landmark Trials

EINSTEIN DVT/PE Sub-Analysis:
Treatment of Venous Thromboembolism With Rivaroxaban in Relation to Body Weight

Dose Studied	Outcome Studied	Weight-Stratified Patient Numbers	
15 mg BID x 21 days, then 20 mg daily	Efficacy: symptomatic recurrent VTE Safety: bleeding, major or clinically relevant	**Total: 8,271** ≤ 50 kg: 167 (2%) 50-100 kg: 6711 (81%) ≥ 100 kg: 1393 (16.8%)	BMI ≤ 25 kg/m²: 2481 (33.1%) BMI 25-30 kg/m²: 3258 (37.9%) BMI 30-35 kg/m²: 1630 (19%) BMI > 35 kg/m²: 861 (10%)

Key Findings:

Efficacy: There was no shown association between body weight or BMI and risk of recurrent VTE
Safety: No association demonstrated in major or clinically relevant bleeding in rivaroxaban group across low or high weight or BMI groups

EINSTEIN Investigators, Bauersachs R, Berkowitz SD, et al. N Engl J Med. 2010;363:2499-2510.
Di Nisio M, Vedovati MC, Riera-Mestre A, et al. Thromb Haemost. 2016;116:739-746.

VTE Landmark Trials

Trial	Total (n)	Dose Studied	Weight-Stratified Patient Numbers	Key Findings
Hokusai-VTE (Edoxaban)	8,292	60 mg daily or 30 mg daily if CrCl 30-50 mL/min, weight ≤ 60 kg, or concomitant verapamil or quinidine	Patients meeting dose reduction criteria (including weight ≤60 kg): 733 (8.8%) Specific weight ≤60 kg subgroup: not separately reported	No published analysis for weight outcomes specifically. Efficacy: Rates of VTE were comparable between the 30 mg and 60 mg groups, and were lower than the warfarin group Safety: Lower incidence of bleeding in 30 mg compared to standard dose
RE-COVER/RE-COVER II (Dabigatran)	5,107	150 mg BID	No formal weight stratification published. However, subgroups defined in supplementary appendix: < 50 kg: 57 (1.1%) BMI < 25 kg/m²: 1369 (26.8%) BMI 25-30 kg/m²: 2078 (40.1%) BMI 30-35 kg/m²: 1071 (21%) BMI > 35 kg/m²: 579 (11.3%)	No specific weight-stratified outcomes reported.

Hokusai-VTE Investigators, Büller HR, Décousus H, et al. N Engl J Med. 2013;369:1406-1415.Verhamme P, Wells PS, Segers A, et al. Thromb Haemost. 2016;116:747-753.Schulman S, Kakkar AK, Goldhaber SZ, et al. Circulation. 2014;129:764-772.

Guideline Summary

Trial with Weight-Stratified Outcomes?		
DOAC	**AF**	**VTE**
Apixaban	✓	✓
Rivaroxaban	✓	✓
Edoxaban	✓	No weight-specific analysis
Dabigatran	No weight-specific analysis	No weight-specific analysis

Question #2

LN is a 82-year-old female with a 10-year history of AF and CHA2DS2-VASc of 5. She has been on apixaban 5 mg BID since her diagnosis and has no concerns or complaints with the medication.

- Weight 52 kg
- BMI 18.5 kg/m^2
- SCr 0.9 mg/dL, CrCl 39 mL/min
- No pertinent drug-drug interactions

What changes should be made based on current AF guidelines and available literature?

A. Patient should not be on any anticoagulation
B. Current apixaban dose is appropriate
C. Apixaban should be lowered to 2.5 mg BID
D. Apixaban should be switched to warfarin

Guideline Summary

DOACs are preferred over warfarin in AF and VTE

DOACs are reasonable to choose over warfarin in patients with BMI $\geq$ 30-40 kg/m^2

In AF and low body weight, follow manufacturer's dosing guidance for apixaban and edoxaban

In VTE and BMI > 40 kg/m^2, apixaban and rivaroxaban are recommended

Additional Literature

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Evaluation of Safety and Efficacy Outcomes of Direct Oral Anticoagulants Versus Warfarin in Normal and Extreme Body Weights for the Treatment of Atrial Fibrillation or Venous Thromboembolism

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Novak, et al

Retrospective cohort study

- Multi-center, from Sept 2011 to Sept 2020

Objective:

- Evaluate thrombotic and bleeding outcomes in patients of weight extremes on DOAC or warfarin for AF or VTE treatment

Primary outcome:

- Composite safety outcome (new or recurrent thromboembolic event or severe or life-threatening bleeding event)

Pertinent secondary outcomes:

- Risk assessment stratified by BMI (failure and/or bleeding)

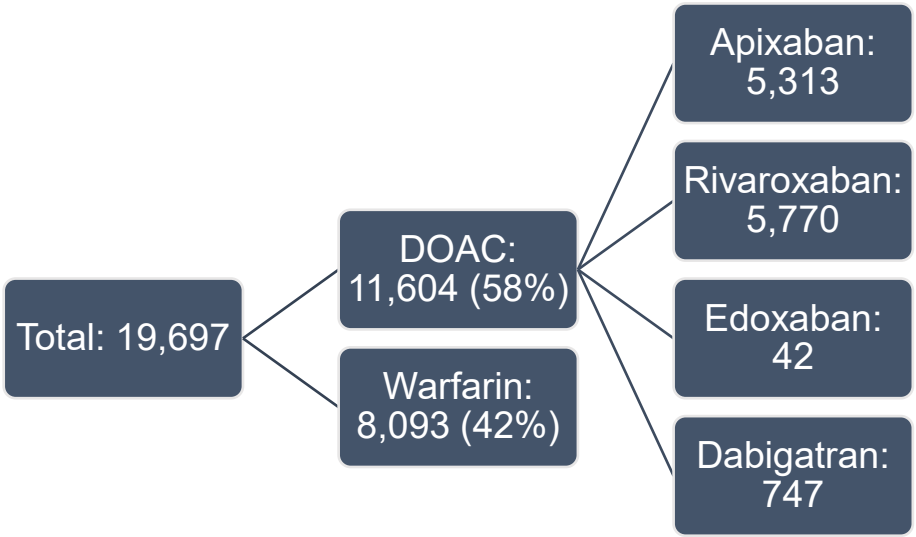
Subgroup analysis:

- Body weight > 150 kg

ADVOCATE HEALTH

Novak AR, Shakowski C, Trujillo TC, et al. J Thromb Thrombolysis. 2022;54:276-286.

Novak, et al



Baseline Characteristics (weight):

Weight Category	DOAC	Warfarin	P-value
BMI (median)	28 (24-33)	28 (24-33)	0.54
Underweight (BMI < 18.5 kg/m^2)	136 (1.2%)	159 (1.96%)	0.06
Pre-Obese (BMI 25-29.9 kg/m^2)	2179 (18.8%)	2044 (25.3%)	--
Obese class I (BMI 30-34.9 kg/m^2)	1332 (11.5%)	1279 (15.8%)	--
Obese class II (BMI 35-39.9 kg/m^2)	669 (5.8%)	606 (7.5%)	--
Obese class III (BMI > 40 kg/m^2)	453 (3.9%)	549 (6.8%)	--

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Novak AR, Shakowski C, Trujillo TC, et al. J Thromb Thrombolysis. 2022;54:276-286.

Novak, et al

Results:

Outcome	Adjusted OR (95% CI)	P-value
Primary outcome, adjusted for covariates, warfarin vs DOAC	1.337 (1.212 to 1.475)	< 0.001
BMI: obese vs normal	1.246 (1.113 to 1.395)	0.002
BMI: underweight vs normal	0.877 (0.622 to 1.234)	0.155

Composite Component	DOAC	Warfarin	P-value
Stroke and/or systemic embolism, n (%)	1135 (9.8%)	1348 (16.7%)	< 0.001
Bleed diagnosis, n (%)	901 (7.8%)	990 (12.2%)	< 0.001

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Novak AR, Shakowski C, Trujillo TC, et al. J Thromb Thrombolysis. 2022;54:276-286.

Novak, et al

Additional Results:

- Subgroup analysis of weight > 150 kg:
  - DOAC vs warfarin groups differed significantly, as more patients in the warfarin group experienced the primary outcome

Interpretation:

- **33.7% higher odds** for patients in the warfarin group to experience the composite outcome compared to DOAC group
- BMI was found to be a significant predictor of the composite outcome
  - Obese patients were 24.6% more likely to experience outcome compared to normal BMI patients
  - Underweight patients were not more likely to experience the outcome compared to normal BMI patients
- Subgroup analysis supports DOAC use in severely obese patients

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Novak AR, Shakowski C, Trujillo TC, et al. J Thromb Thrombolysis. 2022;54:276-286.

Novak, et al

Limitations:

- Apixaban and rivaroxaban were primary DOACs used
- Inability to assess medication adherence or quality of warfarin regimen
- Selection bias could confound choice of warfarin vs DOACs in more high risk patients
- This study does not provide data > 180 kg or BMI > 50 kg/m^2

Conclusion:

- Both underweight and overweight populations taking DOACs vs warfarin demonstrated a lower incidence of the composite outcome (recurrent embolism, stroke, or severe bleeding)

ADVOCATE HEALTH

Novak AR, Shakowski C, Trujillo TC, et al. J Thromb Thrombolysis. 2022;54:276-286.

Treatment of Atrial Fibrillation and Venous Thromboembolism with Factor Xa Inhibitors in Severely Obese Patients

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Dobry, et al

Retrospective, observational study

- Multi-center, from Jan 2012 to Dec 2022

Objective:

- Evaluate safety and efficacy of apixaban and rivaroxaban in patients with weight $\geq$ 150 or BMI $\geq$ 50 kg/m^2

Primary outcomes:

- Efficacy: composite of thromboses (stroke, systemic embolism, VTE) within 12 months
- Safety: major bleeding within 12 months

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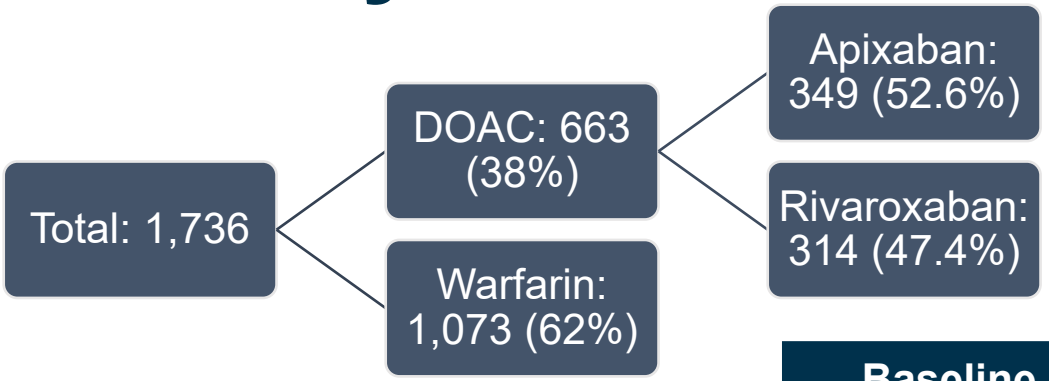
Dobry P, Edwin SB, Haymart B, et al. J Thromb Haemost. 2024;22:3500-3509.

Dobry, et al



Baseline Characteristic	DOAC	Warfarin	SMD
Weight (kg)	162.7 ± 27	163.2 ± 25.1	0.02
BMI (kg/m^2)	53.5 ± 8.6	54.2 ± 8.9	0.07
AF	450 (68.9%)	410 (62.8%)	0.07
VTE	176 (27%)	213 (32.6%)	
AF and VTE	27 (4.1%)	30 (4.6%)	

ADVOCATE HEALTH

Dobry P, Edwin SB, Haymart B, et al. J Thromb Haemost. 2024;22:3500-3509.

Dobry, et al

Results:

Outcome	DOAC	Warfarin	Adjusted OR (95% CI)	P-value
Stroke, systemic embolism, and/or VTE, n (%)	27 (4.1%)	58 (5.4%)	1.005 (0.6 to 1.68)	0.21
Bleeding events, major or nonmajor	2.7%	3%	0.9 (0.47 to 1.7)	0.75

Interpretation:

- No statistically significant difference in composite of stroke, systemic embolism, or VTE between DOAC and warfarin groups
- No significant difference in bleeding events between groups

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Dobry P, Edwin SB, Haymart B, et al. J Thromb Haemost. 2024;22:3500-3509.

Dobry, et al

Limitations:

- Inability to assess medication adherence
- More patients prescribed warfarin due to timing of study with ISTH guidance
- This study was not powered to detect differences between apixaban and rivaroxaban
- Doses of anticoagulants not reported

Conclusion:

- Apixaban and rivaroxaban showed no difference in the odds of thrombosis or major bleeding in severely obese patients (weight ≥ 150 kg or BMI ≥ 50 kg/m^2) with AF and/or VTE compared to warfarin

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Dobry P, Edwin SB, Haymart B, et al. J Thromb Haemost. 2024;22:3500-3509.

Question #3

CF is a 48 year-old male who presents with unprovoked DVT (first for CF). He was cleared for discharge on anticoagulation for outpatient management.

- Weight 162 kg
- BMI 48 kg/m^2
- CrCl 118 mL/min
- No interacting medications

What anticoagulation agent is most appropriate for CF based on available data and current VTE guidelines?

A. Rivaroxaban
B. Edoxaban
C. Warfarin
D. Dabigatran

Bariatric Surgery Considerations

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Bariatric Surgery

Restrictive methods:

- Sleeve gastrectomy
- Adjustable gastric banding

Malabsorptive methods:

- Roux-en-Y gastric bypass
- Duodenal switch

Gigante B, Tamargo J, Agewall S, et al. Eur Heart J Cardiovasc Pharmacother. 2024;10(7):614-645.

Bariatric Surgery PK Considerations

Post-Surgery	
Absorption	• Increased gastric emptying, slower small intestinal transit
Distribution	• Decreasing adipose tissue • Decreasing Vd of lipophilic compounds
Metabolism	• Normalization of metabolism pathways
Excretion	• Limited fluid intake post-surgery can impair renal function
All effects:	Inadequate or variable DOAC absorption, reduced drug effects

Gigante B, Tamargo J, Agewall S, et al. Eur Heart J Cardiovasc Pharmacother. 2024;10(7):614-645.

Anticoagulation Post-Bariatric Surgery

AF Guidelines

- Warfarin may be reasonable to choose over DOACs
- Patient population not well represented in any major AF trials
- If DOAC used, reasonable to monitor DOAC levels

VTE Guidelines

- Not discussed

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Joglar JA, Chung MK, Armbruster AL, et al. J Am Coll Cardiol. 2024;83(1):109-279.

DOAC Level Monitoring

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DOAC Monitoring

- Labs: Anti-Xa (assay or chromogenic), aPTT, PT/INR, TT
- Per AF and VTE guidelines
  - Routine monitoring of DOAC plasma levels is not indicated
- May be indicated to assess certain situations, but only suggests if patient is taking anticoagulation:
  - Potential nonadherence
  - Before emergency invasive procedures/surgeries
  - After bariatric surgery

Tomaselli GF, Mahaffey KW, Cuker A, et al. J Am Coll Cardiol. 2020;76(5):594-622.
Samuelson BT, Cuker A, Siegal DM, et al. Chest. 2017;151(1):127-138.

DOAC Monitoring

- Lack of well-established therapeutic ranges
  - Peak/trough Anti-Xa levels are considered acceptable at a wide range
  - Prolonged aPTT, PT, or TT do not discriminate between "on therapy" and elevated levels
  - The majority of patients are expected to have levels in the "on therapy" range at any time during treatment
  - No clear guidance on how providers should interpret DOAC levels

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Question #4

Which statement about DOAC monitoring in weight extremes is most accurate based on available data?

A. Anti-Xa levels should be routinely checked
B. There are different therapeutic ranges depending on patient weight
C. Routine monitoring is not recommended
D. DOAC monitoring is the same as warfarin monitoring

Limitations

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Limitations of Available Literature

- Underweight population is underrepresented in most major DOAC trials
- No randomized trials specifically evaluate alternative DOAC dosing strategies
- Less data available for edoxaban and dabigatran
- Variable pharmacokinetic data
- Post-bariatric surgery underrepresented in major trials

Summary

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Summary

- Weight-related PK changes can alter drug concentration and effects, leading to efficacy and safety concerns
- Current AF and VTE guidelines list DOACs as a reasonable choice over warfarin for patients with high body weight
- Manufacturer-recommended dose adjustments should be followed for patients with low body weight
- AF and VTE guidelines are informed by post hoc or sub-analyses of specific DOAC landmark trials
- Apixaban and rivaroxaban have the most available data supporting use in these patients
- DOAC level monitoring is generally not indicated to assess efficacy or safety of DOAC regimen

Summary Table

DOAC	Low Body Weight		High Body Weight	
	AF	VTE	AF	VTE
Apixaban	✓	✓	✓	✓
Rivaroxaban	✓	✓	✓	✓
Edoxaban	✓	Limited data	✓	Limited data
Dabigatran	Limited data	Limited data	Limited data	Limited data

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Questions?

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