

Taking the High-Weigh: Assessing the Efficacy of DOACs in Obese Patients



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Statement of Disclosure

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- Potential conflicts of interest: none
- Sponsorship: none
- Proprietary information or results of ongoing research may be subject to different interpretations
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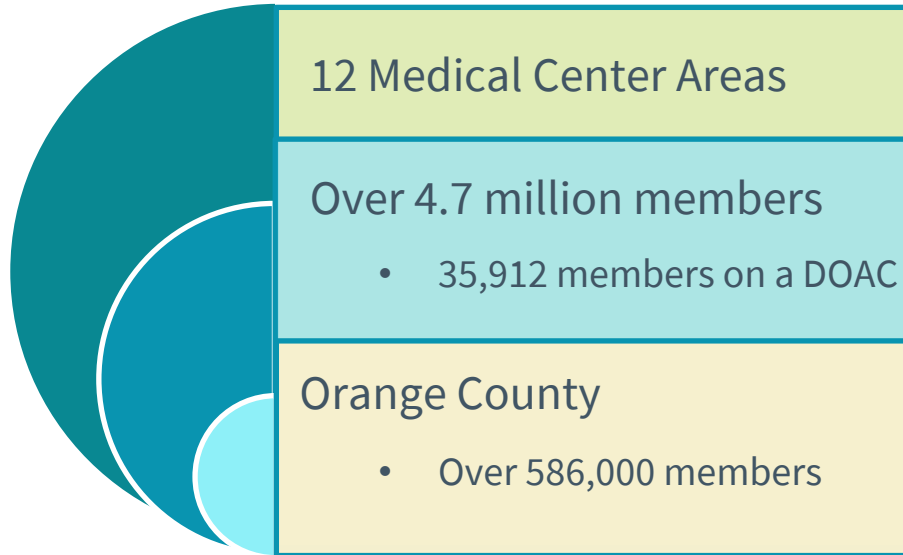


Learning Objective

Explain if obese patients taking a direct oral anticoagulant (DOAC) have similar or different thromboembolic incidences than non-obese patients



Kaiser Permanente Southern California (KP SCAL)



Pre-Test Assessment Questions

#1: According to the World Health Organization (WHO), obesity is classified with what BMI?

- A. BMI ≥ 30 kg/m²
- B. BMI ≥ 29 kg/m²
- C. BMI ≥ 25 kg/m²

#2: Which DOAC has a specified dose for use in obese patients?

- A. Dabigatran
- B. Edoxaban
- C. Betrixaban
- D. None

#3: Obese patients had significantly more thromboembolic events vs. non-obese patients?

- A. True
- B. False



Direct Oral Anticoagulants (DOACs)



- Common FDA-indications:
 - Venous thromboembolism (VTE)
 - Non-valvular atrial fibrillation (NV-AF)
- Fixed, standard doses
- Rapid onset of action
- Therapeutic lab monitoring not necessary

Apixaban

Betrixaban

Dabigatran

Edoxaban

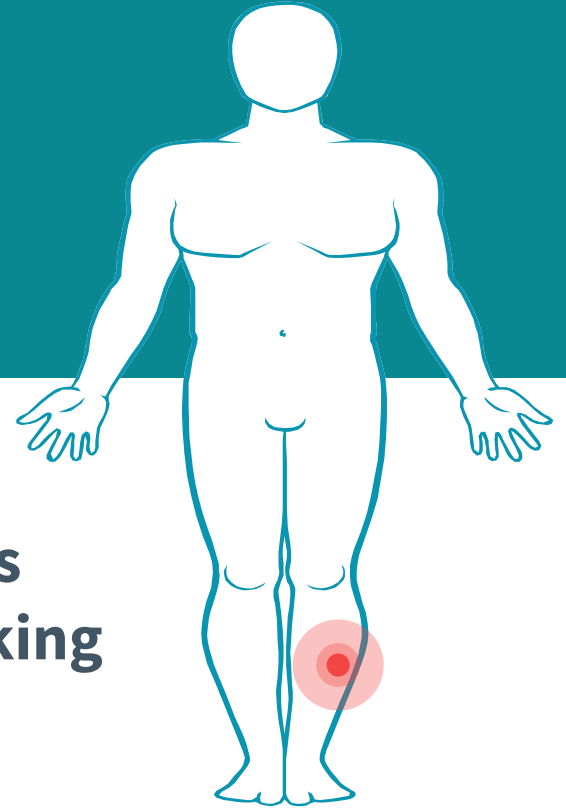
Rivaroxaban

DOAC Dosing Recommendations

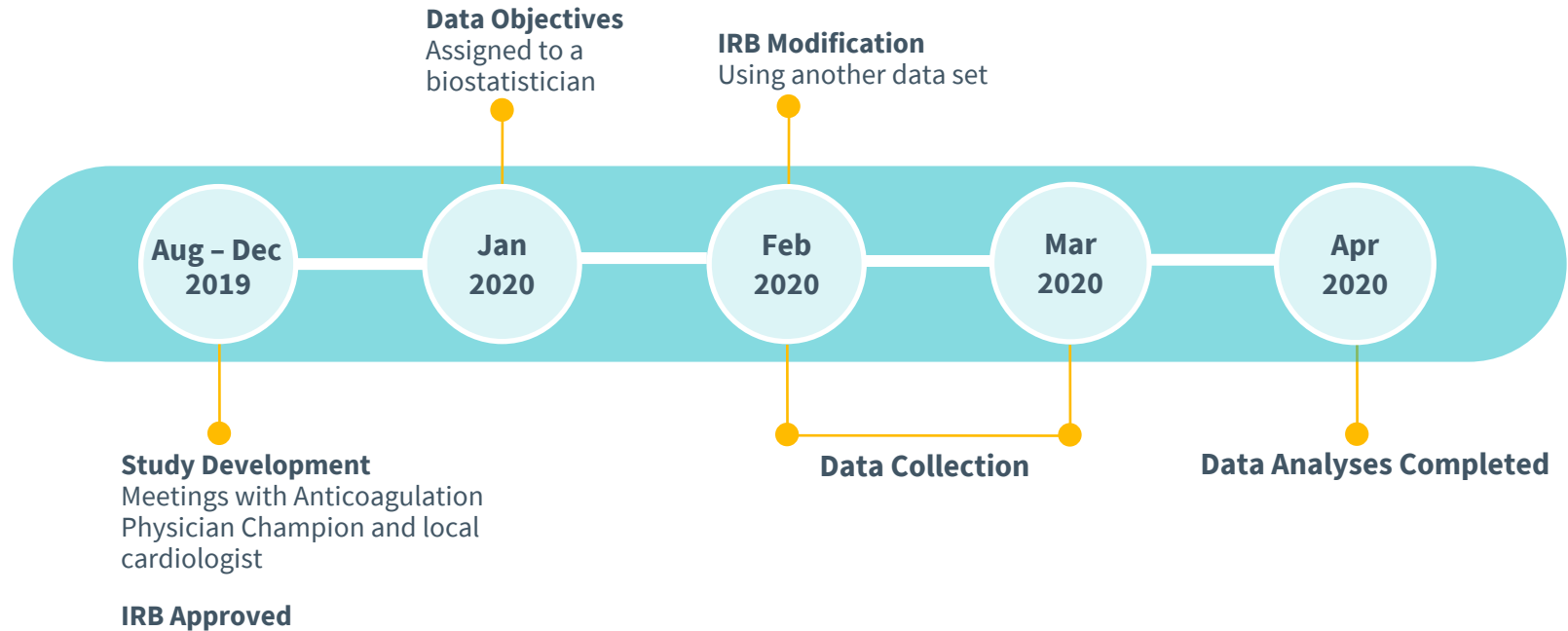
Source	Recommendation
The International Society on Thrombosis and Hemostasis (ISTH) (2016)	Do not recommend use of DOACs in BMI \geq 40 kg/m ²
Kaiser Permanente SCAL DOAC Guidelines (2019)	No dose recommendations in obese patients; clinical judgement necessary
DOAC Package Inserts	No dose recommendations in obese patients

Study Goal

Is there a difference in the incidence of thromboembolic and/or bleeding events among obese vs. non-obese patients taking a DOAC?



Project Timeline



Study Methods

- Retrospective data analysis (N=19,398)
- KP Southern California Region
- Obese (BMI ≥ 30) vs. non-obese
- **Patient identification period:** January 2012 – November 2018
 - **Study end date:** December 2018



Inclusions

- ≥ 18 years old
- KP member for at least 365 days
- On a DOAC for NV-AF
- Minimum 30-day follow up

Exclusions

- Skilled nursing facility/hospice patient
- Pregnancy
- Mechanical valve, mitral valve stenosis, severe liver disease
- Missing BMI

Study Outcomes

Primary Outcome

- Incidence of thromboembolic events (TE)
 - CVA, arterial embolisms, renal infarctions

Secondary Outcome

- Combined incidence of thromboembolic/bleeding events (BE)
 - Intracranial bleeds, GI bleeds, other major bleeds

Baseline Demographics

	Non-obese (n=11,438)	Obese (n=7,960)	P-value
Age (years), %			<0.01
18 - 37	0.4	0.8	
38 - 57	4.2	10.8	
58 - 74	41.3	58.5	
≥ 75	54.1	29.9	
Sex			0.01
Female	43.8	42	
Chronic Heart Failure	14.7	18.3	<0.01
Hypertension	59.6	65.0	<0.01
Diabetes	21.3	37.1	<0.01
Stroke or TIA	8.2	5.7	<0.01
Vascular Disease	2.5	1.8	<0.01

*P<0.05 is considered significant, analyzed with chi-squared test.

Primary Outcome: Incidence of Thromboembolic Events

	Non-obese (n=11,438)	Obese (n=7,960)	P-value
Primary Outcome, %			0.001
TE (n=459)	2.7	2.0	
No TE (n=18,939)	97.3	98.0	

*P<0.05 is considered significant, analyzed with chi-squared test. TE = thromboembolic event.

Incidence of Thromboembolic Events Stratified by BMI

	Non-obese	Obese		
Body Mass Index (kg/m ²)	< 30 (n=11,438)	30 – 34.9 (n=4,432)	35 – 39.9 (n=2,103)	≥ 40 (n=1,425)
Primary Outcome, %				
TE (n=459)	2.7	2.1	1.9	1.6
No TE (n=18,939)	97.3	97.9	98.1	98.4

TE = thromboembolic event.

Secondary Outcome: Combined Incidence of TE/BE

	Non-obese (n=11,438)	Obese (n=7,960)	P-value
Secondary Outcome, %			<0.01
TE/BE (n=816)	4.6	3.7	
No TE/BE (n=18,582)	95.4	96.3	

*P<0.05 is considered significant, analyzed with chi-squared test. TE = thromboembolic event, BE = bleeding event.

Combined Incidence of TE/BE Stratified by BMI

	Non-obese	Obese		
Body Mass Index (kg/m ²)	< 30 (n=11,438)	30 – 34.9 (n=4,432)	35 – 39.9 (n=2,103)	≥ 40 (n=1,425)
Secondary Outcome, %				
TE/BE (n=816)	4.6	3.8	2.9	4.1
No TE/BE (n=18,582)	95.4	96.2	97.1	95.9

TE = thromboembolic event, BE = bleeding event.

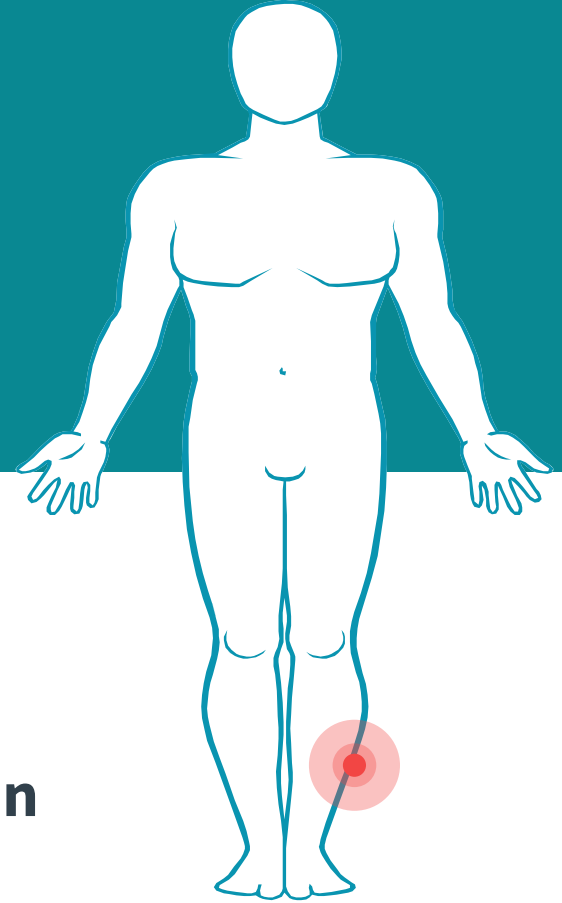
Association Between Study Outcomes and Body Mass Index

Study Outcomes	Hazard Ratio*	95% CI
Incidence of TE	0.84	0.69 – 1.03
Combined incidence of TE/BE	0.92	0.79 – 1.07

*Adjusted for age, sex, chronic heart failure, hypertension, diabetes, stroke/TIA, vascular disease. HR < 1 favors obese, HR > 1 favors non-obese. Analyzed using cox proportional hazard model.

Study Conclusion

Based on the adjusted hazard ratio, we found no significant difference between thromboembolic or bleeding incidences between obese vs. non-obese patients on a DOAC



Study Limitations

Revised data set did not include history of previous bleeds, race/ethnicity, other risk factors (e.g. hypercoagulable states, smoking)

Not a matched-cohort study

Did not include VTE indication

Minimum 30 day follow-up period

Learnings

Stepping into a leadership role

Project management

Time required for data analysis



Challenges

Time sensitivity

Data collection

IRB modification



Future Directions

- Presenting at various platforms
 - SCAL Anticoagulation peer group
 - OC Cardiology team meeting
- Disseminate results to Regional Anticoagulation Physician Champion



Post-Test Assessment Questions

#1: According to the World Health Organization (WHO), obesity is classified with what BMI?

- A. BMI ≥ 30 kg/m²
- B. BMI ≥ 29 kg/m²
- C. BMI ≥ 25 kg/m²

#2: Which DOAC has a specified dose for use in obese patients?

- A. Dabigatran
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- D. None

#3: Obese patients had significantly more thromboembolic events vs. non-obese patients?

- A. True
- B. False



Thank you!

Questions?

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APPENDIX

Incidence of Bleeding Events

	Non-obese (n=11,438)	Obese (n=7,960)	P-value
Bleeding Events, %			0.15
BE (n=402)	2.2	1.9	
No TE (n=18,996)	97.8	98.1	

*P<0.05 is considered significant, analyzed with chi-squared test. TE = thromboembolic event.

Adjusted Hazard Ratio – Bleeding Events

Study Outcomes	Hazard Ratio*	95% CI
Incidence of BE	1.01	0.82 – 1.26

*Adjusted for age, sex, chronic heart failure, hypertension, diabetes, stroke/TIA, vascular disease. HR < 1 favors obese, HR > 1 favors non-obese. Analyzed using cox proportional hazard model.

BMI Breakdown

BMI category	Number of patients	% (n=19,398)
< 18.5	235	1.2
18.5-24.9	4,581	23.6
25-29.9	6,622	34.1
30-34.9	4,432	22.9
35-39.9	2,103	10.8
≥ 40	1,425	7.4