

## Research Question

What is the rate of readmission related to bleed or thrombosis in patients on direct oral anticoagulants (DOACs) with a body mass index (BMI) greater than 40kg/m<sup>2</sup>

## Background

- 6.6% of patients in United States have a BMI > 40kg/m<sup>2</sup><sup>1</sup>
- Obesity increases risk of developing disease states requiring anticoagulation
  - 49% increased risk of atrial fibrillation (AF) in obese vs non-obese individuals<sup>2</sup>
  - Risk of venous thromboembolism (VTE) more than doubles in obese vs non-obese individuals<sup>3</sup>
- Product labeling does not identify limitations for use related to obesity
- However, International Society of Thrombosis and Haemostasis recommends against DOACs in patients with a BMI > 40kg/m<sup>2</sup> or weight > 120kg<sup>4</sup>
- Patients with a BMI > 40kg/m<sup>2</sup> were underrepresented in clinical studies<sup>4,5</sup>

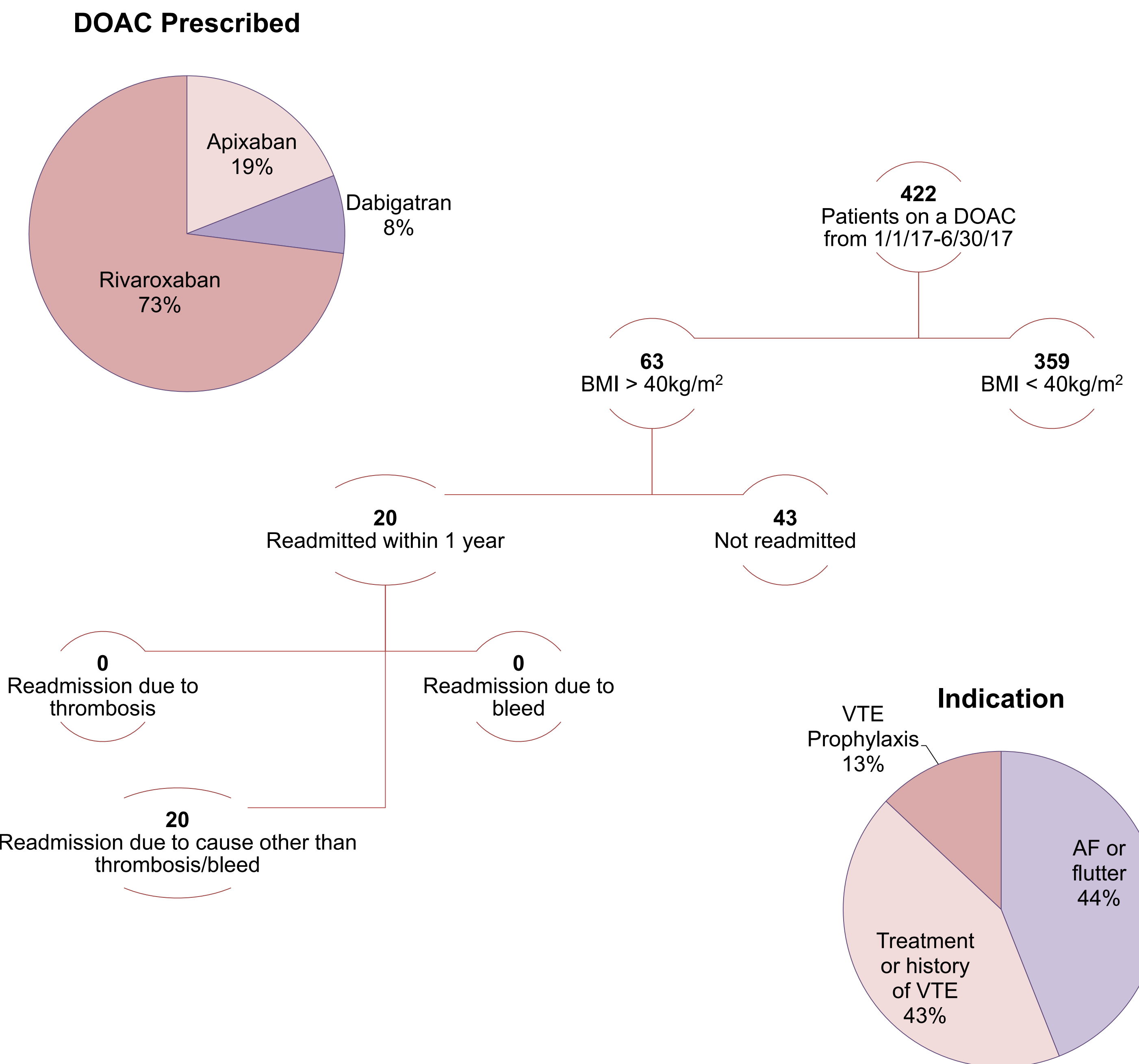
DOAC	Phase III Trials	Weight Category	N (%)
Dabigatran	RE-LY	Weight ≥ 100kg	3099 (17.1)
	RE-COVER I	BMI ≥ 35kg/m <sup>2</sup> Weight ≥ 100kg	306 (12) 502 (20)
	RE-COVER II	BMI > 35kg/m <sup>2</sup> Weight > 100kg	302 (23.6) 438 (34.2)
Rivaroxaban	ROCKET-AF	BMI 30 - <35 BMI ≥ 35	3308 (23.5) 1898 (13.5)
	EINSTEIN-DVT	Weight > 100kg	245 (14.2)
	EINSTEIN-PE	Weight > 100kg	345 (14.3)
Apixaban	ARISTOTLE	BMI 30 - <35 BMI 35 - <40 BMI ≥ 40	4379 (24.1) 1774 (9.8) 1006 (5.5)
	AMPLIFY	BMI > 35kg/m <sup>2</sup> Weight ≥ 100kg	349 (13.0) 522 (19.4)
Edoxaban	ENGAGE AF-TIMI 48	BMI 30 - <35 BMI 35 - <40 BMI ≥ 40	5209 (24.8) 2099 (10.0) 1149 (5.5)
	Hokusai-VTE	Weight > 100kg	611 (14.8)

- Limited PK/PD data suggest decreased exposure when some DOACs are used in patients with a BMI > 40kg/m<sup>4,5</sup>
  - Subgroup analysis of dabigatran demonstrated a lower trough with higher body weights, however weight was not a significant covariate for stroke
- Lower mean peak apixaban concentration, lower AUC, higher Vd, and shorter half-life in healthy overweight volunteers compared to reference group, however no differences were interpreted to likely be clinically significant
- Similar peak rivaroxaban concentration, AUC, and half-life in healthy overweight volunteers compared to reference group
- Potentially higher Vd of rivaroxaban in higher body weights in a PK modelling study

## Methods

- Single center retrospective cohort
- Inclusion criteria:
  - Hospitalization between January 1 to June 30, 2017
  - Active order for a DOAC during hospitalization
  - Age > 18
  - BMI > 40kg/m<sup>2</sup>
- Chart review:
  - Specific DOAC prescribed
  - Indication for anticoagulation
  - Readmissions within one year
  - Reasons for readmission (including bleed or thrombosis)

## Results



## Discussion/Conclusion

- Readmission rate related to bleed or thrombosis in patients with a BMI > 40kg/m<sup>2</sup> is lower than anticipated when compared to DOAC treatment failure rates published in the literature<sup>6-9</sup>
  - DOAC thrombotic failure rates: 1.1-2.7% in phase III trials
  - DOAC bleed failure rates: 0.6-5.6% in phase III trials
- Limitations:
  - Small study population
  - No comparator group
  - Low utilization of dabigatran and edoxaban
  - Treatment failure can occur outside hospital admission
  - No follow-up after discharge
- Results are supported by previous studies examining whether DOACs are safe and effective in obese patients<sup>10-13</sup>:

Trial	Study design	Weight Category	Clinically Relevant Results
Peterson et al.	Retrospective review of healthcare claims data	BMI > 40kg/m <sup>2</sup> or weight > 120kg	No difference in risk of bleed or thrombosis in 3563 matched pairs on rivaroxaban vs warfarin for AF
Kushnir et al	Retrospective, single-center chart review	BMI > 40kg/m <sup>2</sup>	No difference in bleed or thrombosis rates in patients on DOAC (apixaban and rivaroxaban) vs warfarin for VTE or AF
Kido and Ngorsuraches	Retrospective, single-center cohort	BMI > 40kg/m <sup>2</sup> or weight > 120kg	No difference in bleed or ischemic stroke/TIA rates in 64 matched pairs on DOAC (apixaban and rivaroxaban) vs warfarin for AF or flutter
Kalani et al	Retrospective, single-center chart review	BMI > 40kg/m <sup>2</sup> or weight > 120kg	No difference in bleed or thrombosis rates in patients on DOAC (apixaban, rivaroxaban, or dabigatran) vs warfarin for VTE, AF, or other indications

- Large-scale prospective data in this patient population is lacking; further research is warranted

**Main finding: Low readmission rate related to bleed or thrombosis in patients with BMI > 40kg/m<sup>2</sup>**

## References

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