

Comparison of Acute Major Bleeding Events of Dabigatran and Warfarin in Atrial Fibrillation

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Background

- Dabigatran: Direct thrombin inhibitor indicated for prevention of stroke in nonvalvular atrial fibrillation
- RE-LY trial compared its efficacy and safety to warfarin¹
- Issues: No reversal agent, no proven method for determining the extent of anticoagulation or treating major bleeding
- Anecdotal reports of more major bleeding with dabigatran than with warfarin
- Risks for major bleeding need to be compared between dabigatran and warfarin under real world conditions

Objectives

- **Primary:**
 - To estimate the proportions of major bleeds that are due to dabigatran and warfarin in atrial fibrillation patients
 - To determine if the relative rates of major bleeding events at Fraser Health (FH) hospitals match the expected values from current evidence and usage patterns
- **Secondary:**
 - To describe the treatment modalities used to manage major bleeding associated with dabigatran and its outcomes

Methods

- **Design:** Retrospective chart review
- **Sites:** Burnaby Hospital (BH), Delta Hospital (DH), Mission Memorial Hospital (MMH), Surrey Memorial Hospital (SMH)
- **Time Period:** 1 year from May 23, 2012 to May 23, 2013
- **Inclusion Criteria:** All >18 yr old, nonvalvular atrial fibrillation, received dabigatran or warfarin within 14 days of major bleed
- **Exclusion Criteria:** Heart-valve disorder, prosthetic heart valve, hemorrhagic disorder, bleeding diathesis, received other anticoagulant or thrombolytic within 14 days of major bleed

Limitations

- No access to patient-specific Pharmanet data
- Missing subjects who were not restarted on anticoagulation in hospital
- No information on anticoagulated subjects who did not bleed

Figure 1: Inclusion and exclusion of subjects

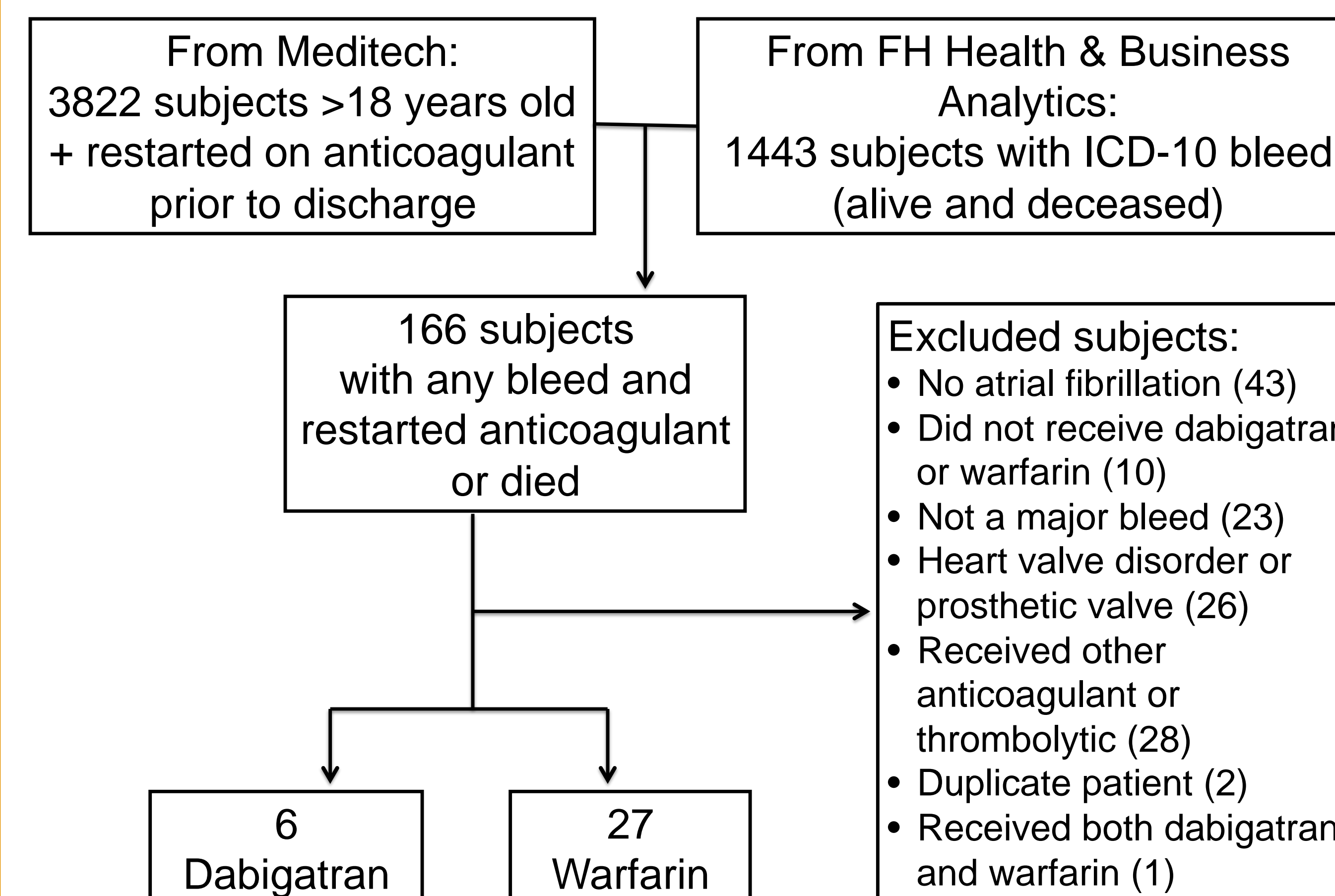


Table 1: Subject characteristics

Characteristic	Dabigatran (N=6)	Warfarin (N=27)
Age – mean yr ± SD	79.8 ± 8.7	82.1 ± 9.1
Male – no. (%)	2 (33.3)	13 (48.1)
CHADS ₂ – mean ± SD	2.7 ± 1.0	3.1 ± 1.3
CHA ₂ DS ₂ VASc – mean ± SD	4.7 ± 1.5	5.1 ± 1.4
HAS-BLED score – mean ± SD	3.2 ± 0.8	3.4 ± 1.3
Concurrent antiplatelet – no. (%)	2 (33.3)	7 (25.9)
Onset of bleeding – no. (%)		
Prior to admission	6 (100)	21 (77.8)
During hospital stay	0	6 (22.2)
Type of major bleed – no. (%)		
Reduction in Hgb level of at least 20 g/L	0	6 (22.2)
Transfusion of at least 2 units of pRBC	6 (100)	22 (81.5)
Symptomatic bleeding in critical area or organ	0	2 (7.4)
Area of major bleed – no. (%)		
Gastrointestinal	5 (83.3)	19 (70.4)
Epistaxis	1 (16.7)	1 (3.7)
Intracranial	0	1 (3.7)
Intraarticular	0	1 (3.7)
Other	0	5 (18.5)

Results

- **Ideal:** Case control study using patient-specific Pharmanet data
 - Would have provided data for control group who received anticoagulation without bleeding
 - Would have allowed comparison of FH bleed rates to RE-LY
- **Actual:** Aggregate numbers from BC Ministry of Health
 - Number of patients: dabigatran = 1048, warfarin = 2891
 - Allows illustration of relative bleed rates

	FH	RE-LY
Dabigatran	0.57%	5.8%
Warfarin	0.93%	6.6%
RR	0.61	0.87

Figure 2: Treatment modalities used to manage dabigatran-associated major bleeds

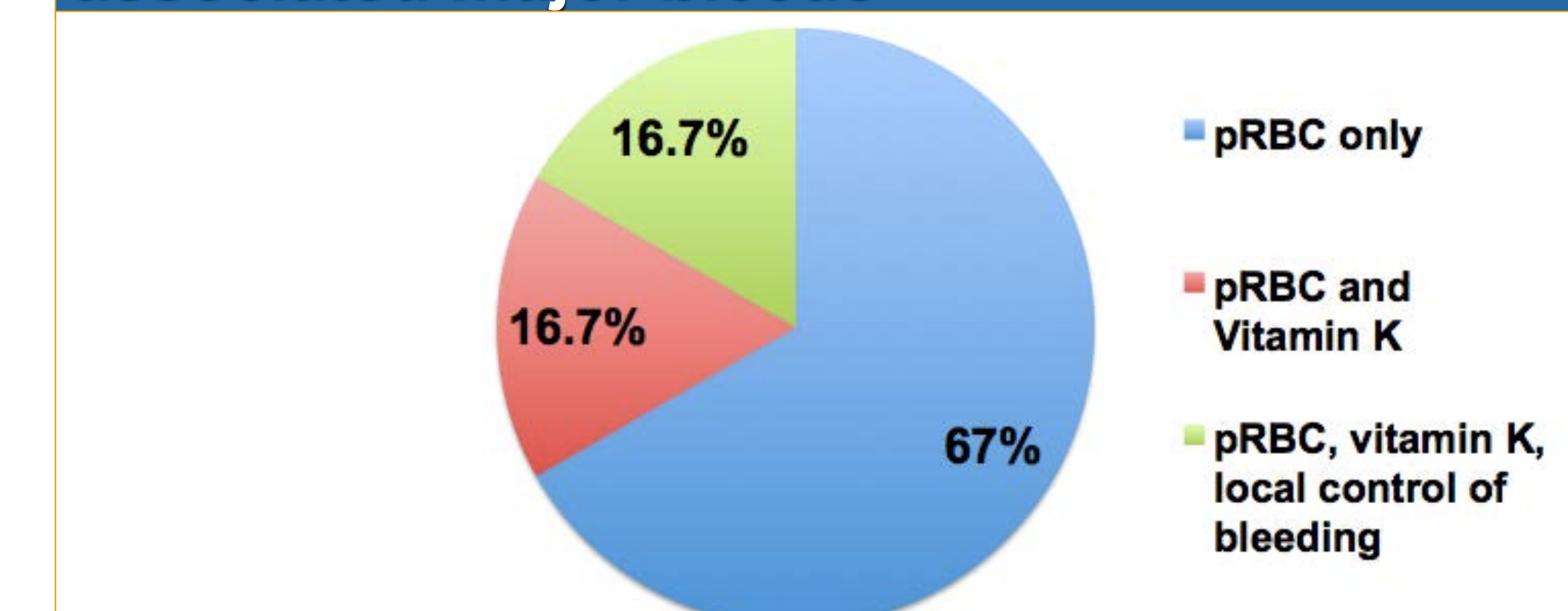


Table 2: Outcomes

Outcomes	Dabigatran (N=6)
Treatment modality – no. (%)	
pRBC 2 or 3 units	5 (83.3)
pRBC at least 4 units	1 (16.7)
Local control of bleeding	1 (16.7)
Vitamin K	2 (33.3)
Discharge disposition – no. (%)	
From home to home	5 (83.3)
From home to care facility	0
From care facility to care facility	1 (16.7)
Death	0
Anticoagulation restarted in hospital – no. (%)	
Dabigatran	6 (100)

Conclusions

- Insufficient information to rule out an increased or decreased risk of major bleed with dabigatran vs. warfarin
- Dabigatran-associated major bleeds appeared to be primarily managed with blood transfusions

References

1. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *New Engl J Med* 2009;361:1139-1151.