



**HKU Discovers that  
Traditional Blood Thinner Drug is associated with  
a Higher Risk of Osteoporotic Fracture  
compared to Newer Drug**

**Press Conference**

*April 11, 2017*



# Speakers

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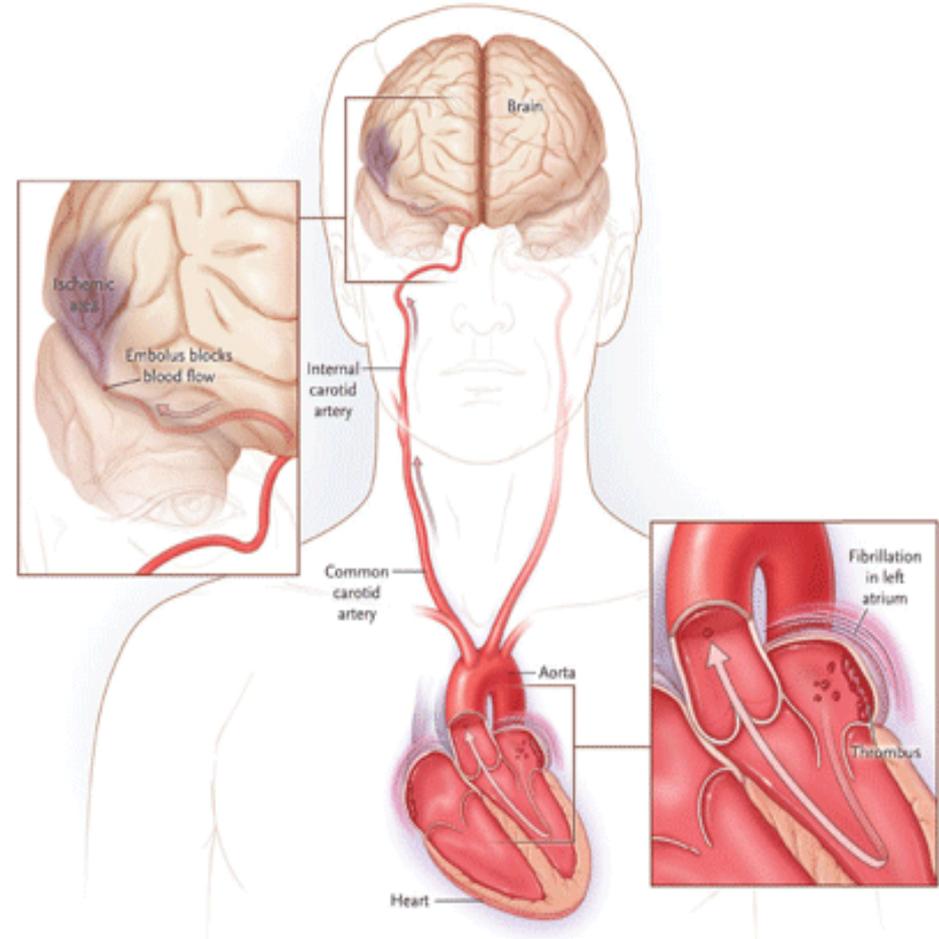
Department of Pharmacology and Pharmacy

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# AF and Ischemic Stroke in HK

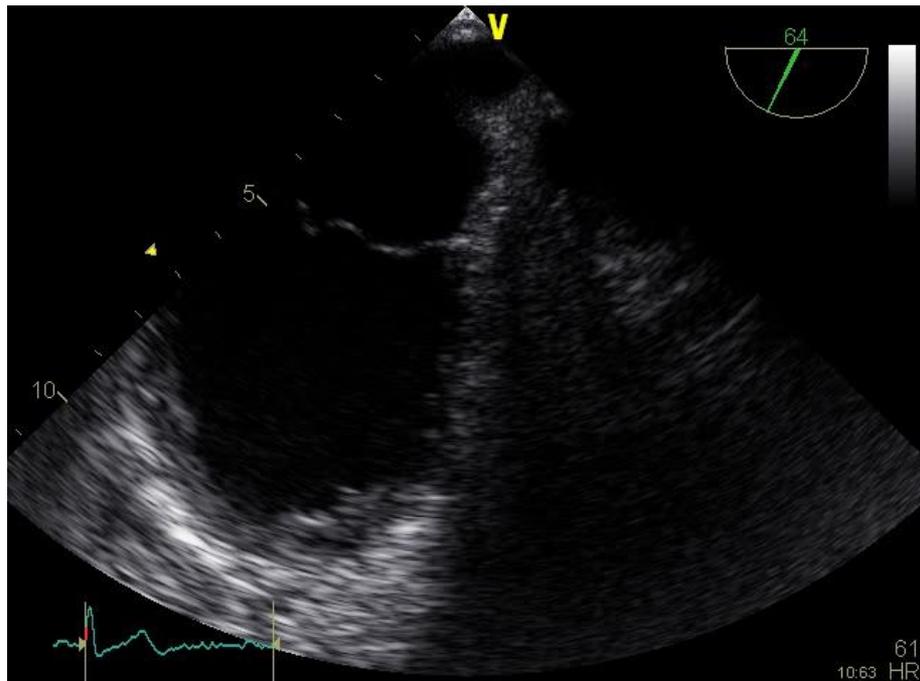
- **7,314,000 residents**
- **~55,000 - 70,000 AF patients** (1% population)
- **12,136 acute strokes in 2013-2014 (HA only)** (0.16%/year)
- **~2,500-3,000 AF related stroke/year** (0.04%/year)
- **~1,800-2,000 AF related stroke can be prevented if identified early**



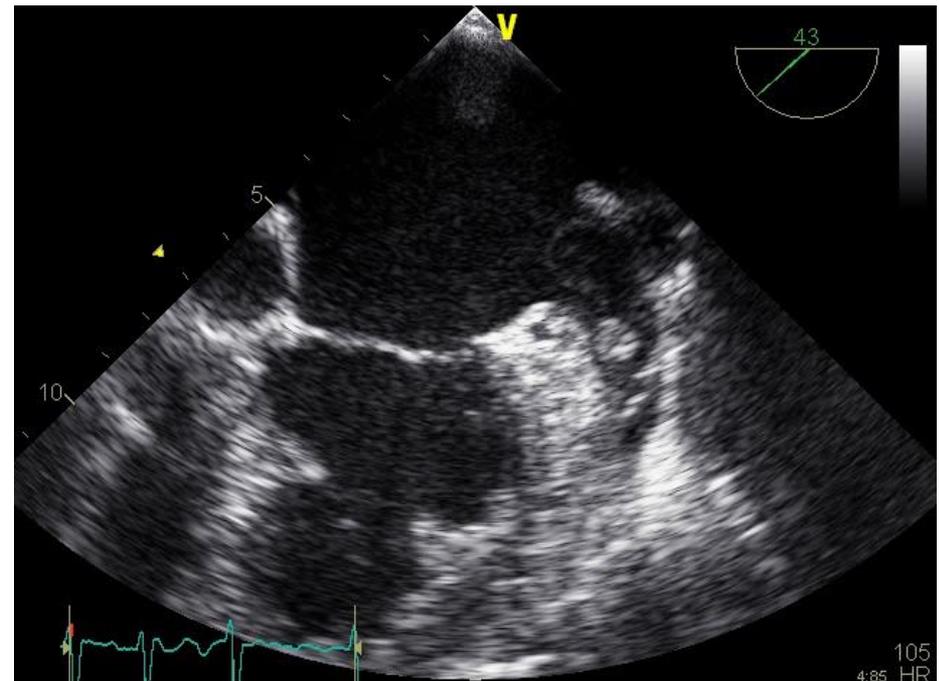


# AF and Ischemic Stroke

## Normal Sinus Rhythm



## Atrial Fibrillation





# Warfarin

- Warfarin reduces ischemic stroke in AF by 64%.
- It works by reducing several vitamin K-dependent reactions that are needed for blood clotting.
- As these reactions also play a role in bone mineralization, there is concern that warfarin use may adversely affect bone health.
- Despite the concerns for fracture risk, warfarin remained the only effective treatment > 50 years.



# Dabigatran

- Dabigatran is the first non-VKA oral anticoagulant (NOAC) approved for use in nonvalvular AF.
- According to a recent animal study<sup>1</sup>, dabigatran is associated with better bone safety compared to warfarin in rats.
- However, the actual risk of osteoporotic fracture with dabigatran vs warfarin in human is unclear.

<sup>1</sup>Fusaro M, Dalle Carbonare L, Dusso A, et al. Differential Effects of Dabigatran and Warfarin on Bone Volume and Structure in Rats with Normal Renal Function. PLoS One 2015;10:e0133847.



# Osteoporotic Fracture





Research

JAMA | **Original Investigation**

# Association Between Dabigatran vs Warfarin and Risk of Osteoporotic Fractures Among Patients With Nonvalvular Atrial Fibrillation

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# Research Objective

- To compare the risk of osteoporotic fractures with dabigatran vs. warfarin in AF patients.



# Research Method

- Study design: Observational cohort study.
- Subjects: Patients newly diagnosed with AF and prescribed dabigatran or warfarin in Hospital Authority.
- Outcomes: Osteoporotic hip fractures and vertebrae fractures.

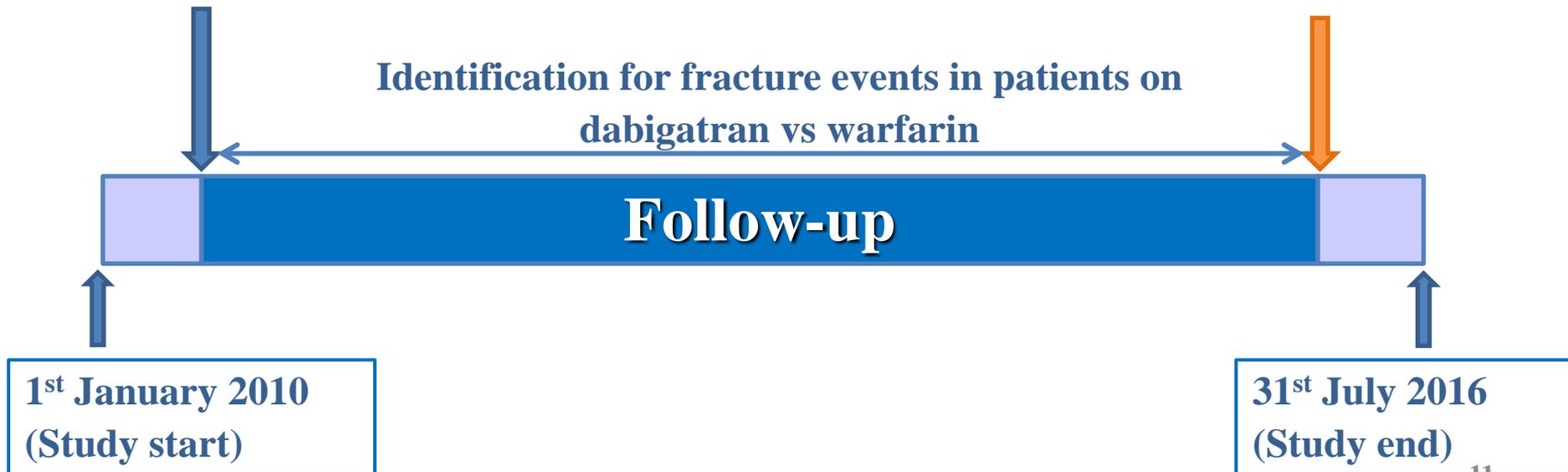


# Research Method

Start of follow-up  
(1<sup>st</sup> dabigatran or warfarin  
prescription)

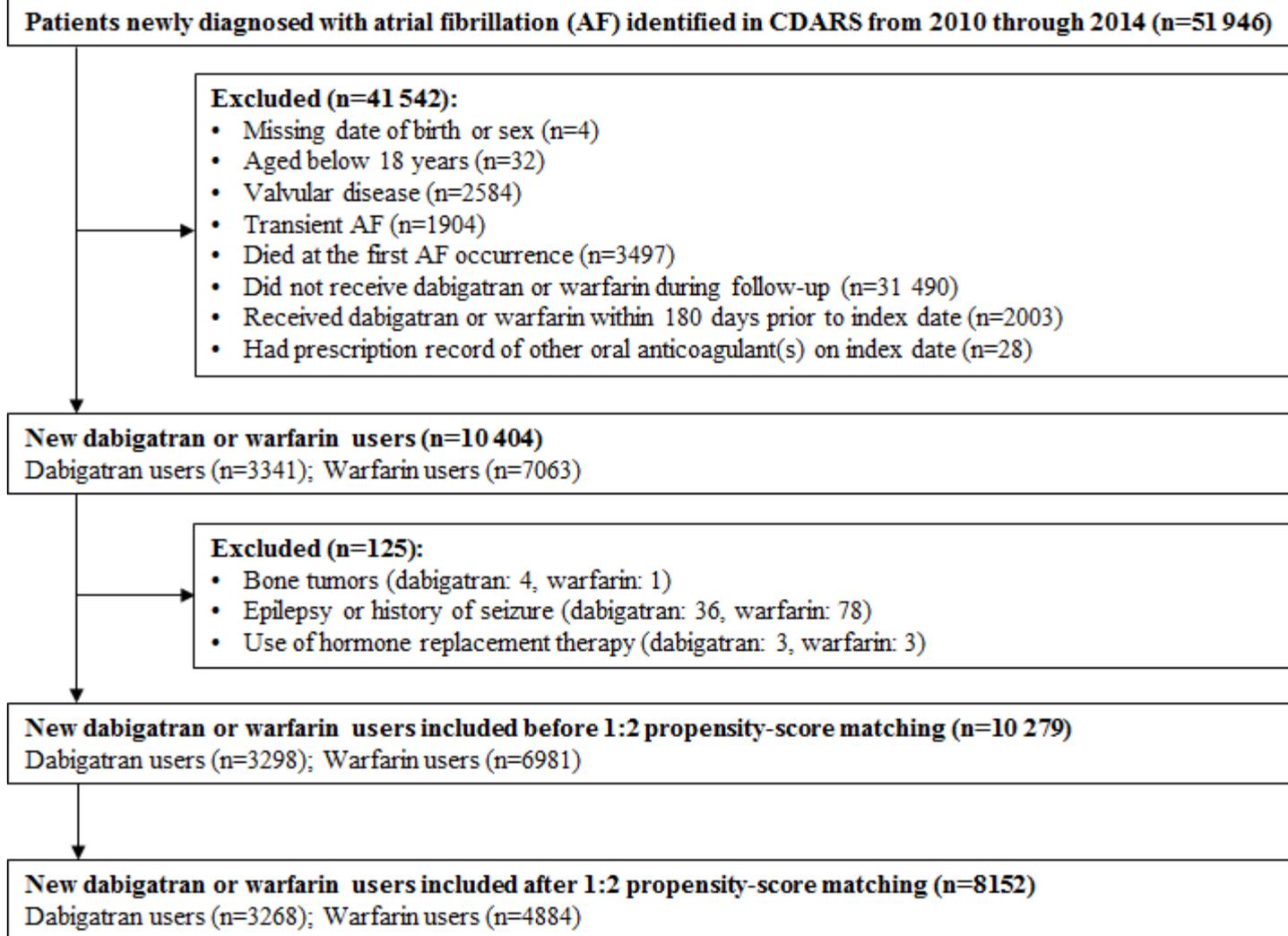
End of follow-up, the earliest of:

- Occurrence of osteoporotic fractures
- Discontinuation of treatment
- Switching to other oral anticoagulants
- Death
- Study end (31<sup>st</sup> July 2016)





# Flowchart for Cohort Selection





# Baseline Characteristics

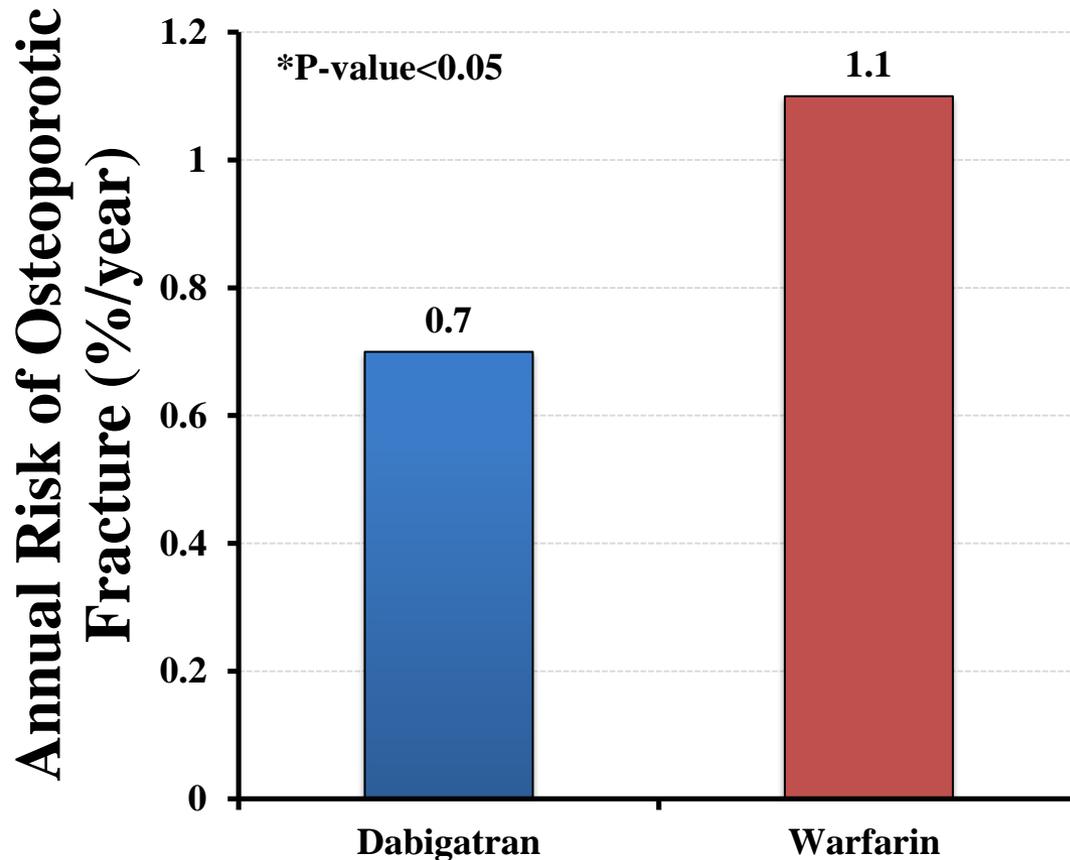
- Total: 3,268 dabigatran and 4,884 warfarin users.
- Mean age: 74 years; Gender: 50% Female.

	Dabigatran (N=3268)	Warfarin (N=4884)	Standardized Difference*
Age, mean $\pm$ SD	74.2 $\pm$ 10.1	73.3 $\pm$ 11.0	0.08
Female	1,657 (50.7)	2,395 (49.0)	0.03
Prior ischemic stroke/transient ischemic attack	1,094 (33.5)	1,515 (31.0)	0.05
Diabetes mellitus	984 (30.1)	1,402 (28.7)	0.03
Congestive heart failure	689 (21.1)	1,271 (26.0)	-0.12
History of falls	505 (15.5)	723 (14.8)	0.02
Chronic Obstructive Pulmonary Disease	270 (8.3)	406 (8.3)	<0.001

\*Propensity-score matching technique was used to assemble two groups of similar patients for a fair comparison. Small standardized differences indicate a negligible difference in covariates between treatment groups



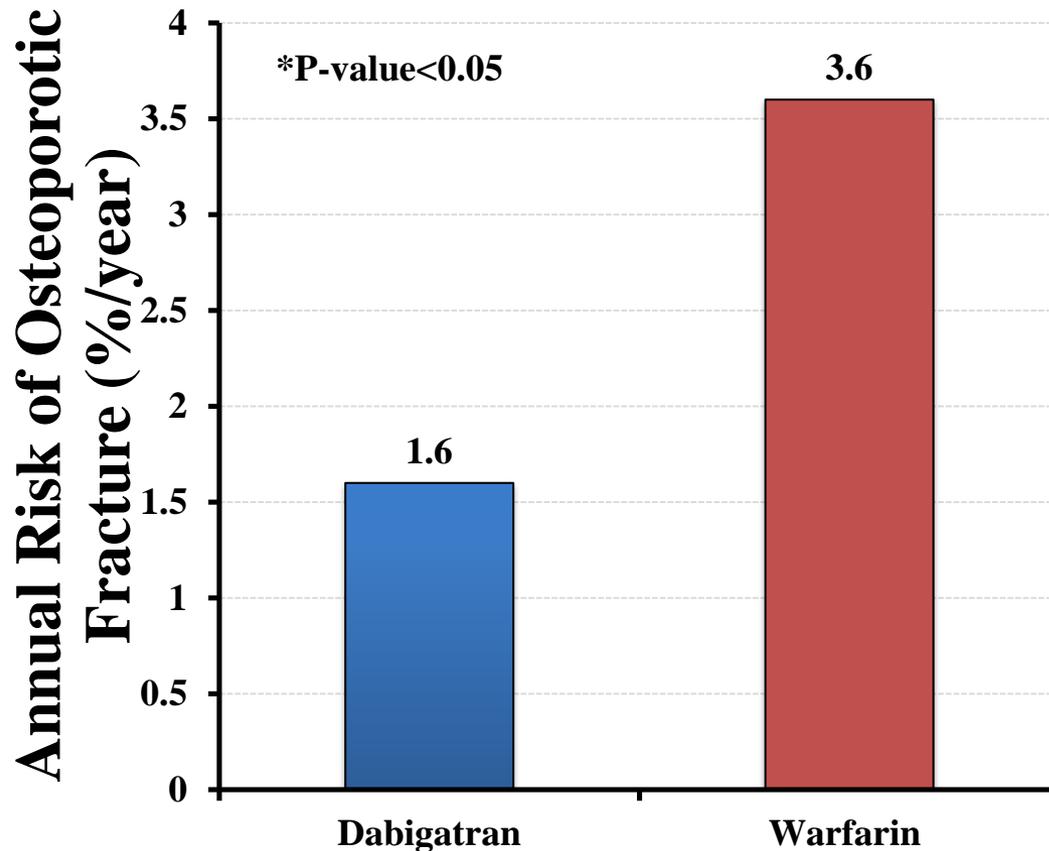
# Risk of Osteoporotic Fracture



After a mean follow-up of 500 days, the incidences of osteoporotic fracture for dabigatran was 0.7%/year compared with warfarin 1.1%/year (36% relative risk reduction).



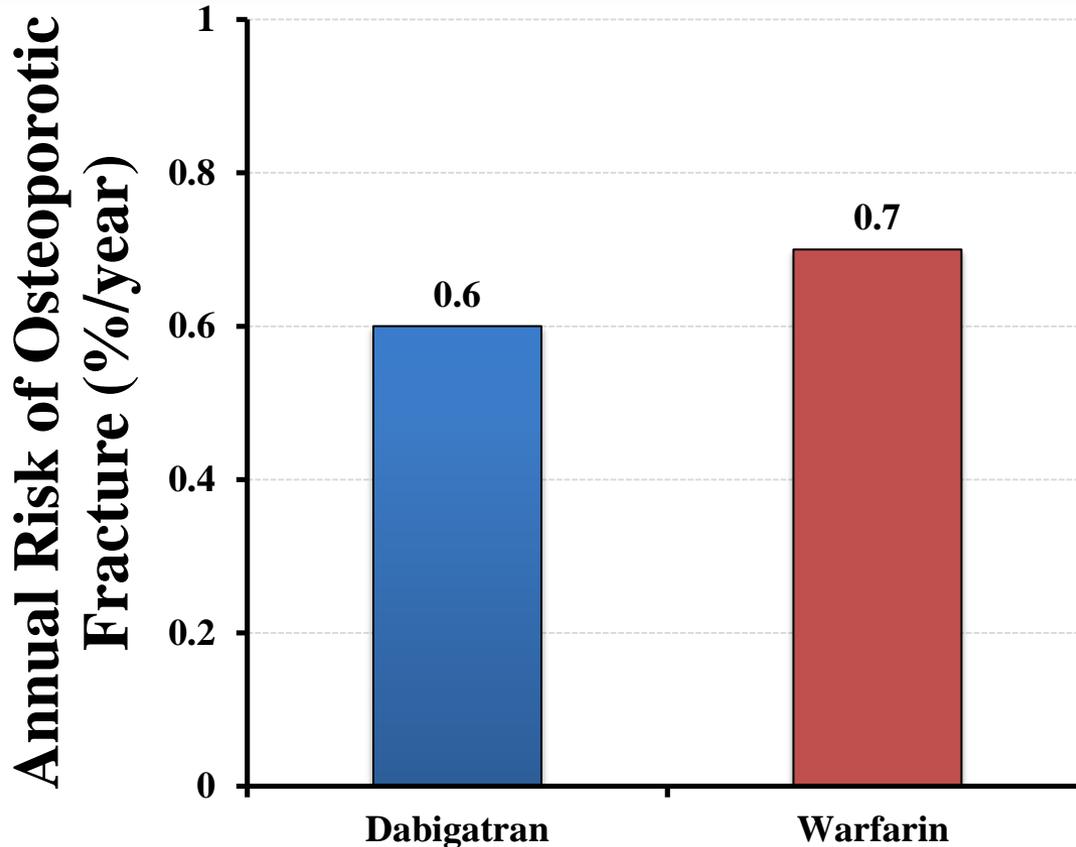
# Greater Protection in Patients with a History of Falls and/or Fractures



- For patients with history of falls/fracture, the incidences of osteoporotic fracture for dabigatran was 1.6%/year compared those on warfarin with 3.6%/year (55% relative risk reduction).



# Greater Protection in Patients without a History of Falls and/or Fractures



- For patients without history of falls/fracture, the incidences of osteoporotic fracture for dabigatran was 0.6%/year compared those on warfarin with 0.7%/year.



# Conclusion and Clinical Implications

- Fracture is a significant cause of morbidity and mortality among the elderly (1/3 patients with hip fracture die within the 1<sup>st</sup> year).
- Dabigatran is associated with lower risk of osteoporotic fracture particularly patients with history of falls/fracture.
- For patients at high risk for osteoporotic fracture (history of fracture or falls), dabigatran may provide additional benefit and advantage over warfarin.



# Strengths and Limitations

- **Strengths:**
  - To our knowledge, this is the first study that compares the risk of osteoporotic fracture with dabigatran vs warfarin
  - Large sample size (over 8,000 patients)
  - Primarily Hong Kong data



# Q & A Session



Thank you