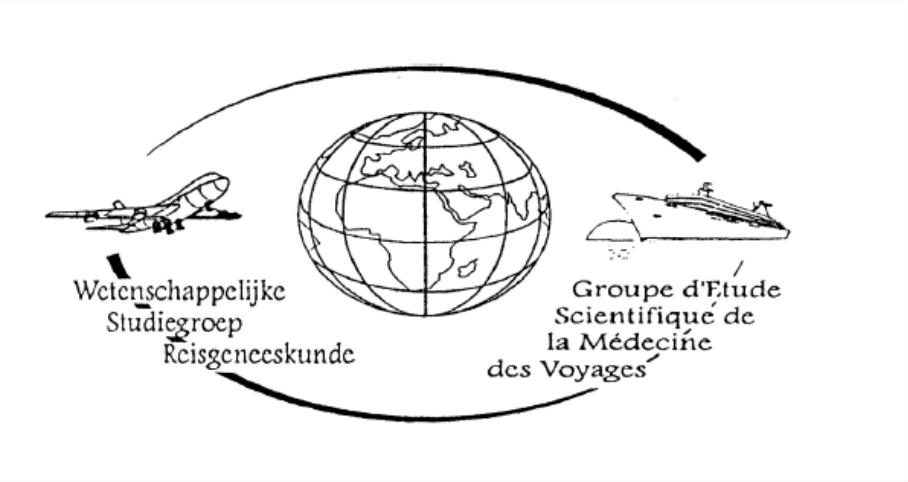
Traveller’s Thrombosis

Dr. Peter Verhamme
Vascular Medicine and Haemostasis
UZ Leuven



11th National Seminar on Travel Medicine
Thursday 19th November 2015

TRAVEL MEDICINE SEMINAR: 20 YEARS LATER

23RD

Annual meeting

LAMOT
Belgium

BSTH

Belgian Society on Thrombosis and Haemostasis

Case 1: To thromboprophylaxe or not

Women, aged 49, BMI 29, Combined Oral Contraceptives.
Family history of provoked VTE.

Travelling to the far east.

1. Life style advice
2. Stockings
3. Low dose Aspirin
4. Prophylactic dose of LMWH
5. Prophylactic dose of NOAC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Case 2: Anticoagulation during travel

Women, aged 34, antiphospholipid syndrome with history of PE.

Well-managed warfarin since 6 years.

Travelling to Nepal for 6 weeks (adventurous).

1. Stop Warfarin
2. Continue Warfarin, test INR before and after.
3. Continue Warfarin, test INR before and after and look for local hospital
4. Continue Warfarin, search for POC device
5. Switch to LMWH during travel
6. Switch to NOAC during travel


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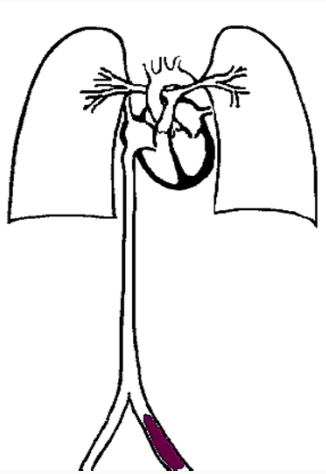
Traveller’s Thrombosis

- Venous thromboembolism is a frequent disease (Incidence 2 - 3 / 1000)

- VTE kills more Europeans each year than:
  - breast cancer
  - prostate cancer
  - HIV/AIDS
  - …and road traffic accidents all together[1]



F. Roosendael

[1]Cohen AT *et al.* VITAE EFIM abstract 2005
[2]Hirsh J, Hoak J *Circulation* 1996;93:2212–45

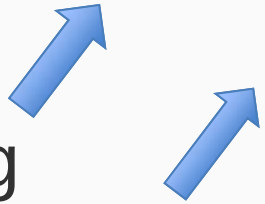
Is the incidence of VTE increasing?

- Awareness for the disease

WORLD THROMBOSIS DAY
OCTOBER 13

Is the incidence of VTE increasing?

- Awareness for the disease
- Diagnostic algorithms & imaging



Is the incidence of VTE increasing?

- Awareness for the disease
- Diagnostic algorithms & imaging
- Prevalence of Risk factors
  - Ageing
  - Surgery / Trauma
  - Cancer and co-morbidities
  - Obesity
  - Hormonal therapy

WORLD THROMBOSIS DAY
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Is the incidence of VTE increasing?

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- Diagnostic algorithms & imaging
- Prevalence of Risk factors
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  - Cancer and co-morbidities
  - Obesity
  - Hormonal therapy

  - **Travelling?**

Travelling as a risk factor?

A ‘voluntary’ trial travelling to ISTH 1989 in Tokyo:

I*-Fibrinogen before departure…

Thrombosis upon arrival?

Travelling as a risk factor?

- Prolonged sitting in a cramped position (economy class syndrome)
- Hypoxia
- Dehyratation
- Alcohol + sleeping pill

+ Individual risk factors

How frequent?

- DVT after long-haul flight vs. non-travelling:

  2.8% vs. 1%
  Mostly calf DVT (Schwartz 2003)

- PE after long-haul flight
  > 5000 km: 1.5 cases / million travellers
  > 10 000 km: 4.8 cases / million travellers (Lapostolle 2001)

- RR 2-4; AR of symptomatic VTE within 4 weeks after >4h flight: 1 / 4600 flights (Kuipers 2007)

Guidance?

Low risk:

- No additional risk factors

High risk:

- History of VTE
- Recent major surgery
- Immobilisation
- Active Cancer

Guidance?

Medium risk:

- With additional risk factors
  - Preganancy, Post-partum, COC or HRT
  - Age
  - Family history of VTE or thrombophilia
  - Obesity
  - Venous insufficiency / Varicose veins

Guidance?

All:

- Avoid restrictive clothing
- Mobilisation / leg excercises
- Alcohol and sleeping medication?

Moderate risk:

- Compression stockings

High risk:

- Pharmacological prophylaxis

Clark 2006; Schobersberger 2008

Guidance?

Pharmacological prophylaxis

- LMWH in high-prophylactic dose (50 U/kg)
- Prophylactic dose of NOAC?
- “We recommend against the use of LD-ASA”

Clark 2006; Schobersberger 2008

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	Dabigatran	Rivaroxaban	Apixaban
	Pradaxa®	**Xarelto®**	**Eliquis®**
VTE	✓	✓	✓
Acute treatment	LMWH 5-7 days	15 mg BD 3 weeks	10 mg BD 1 weeks
Continued treatment	150 mg BD	20 mg OD	5 mg OD

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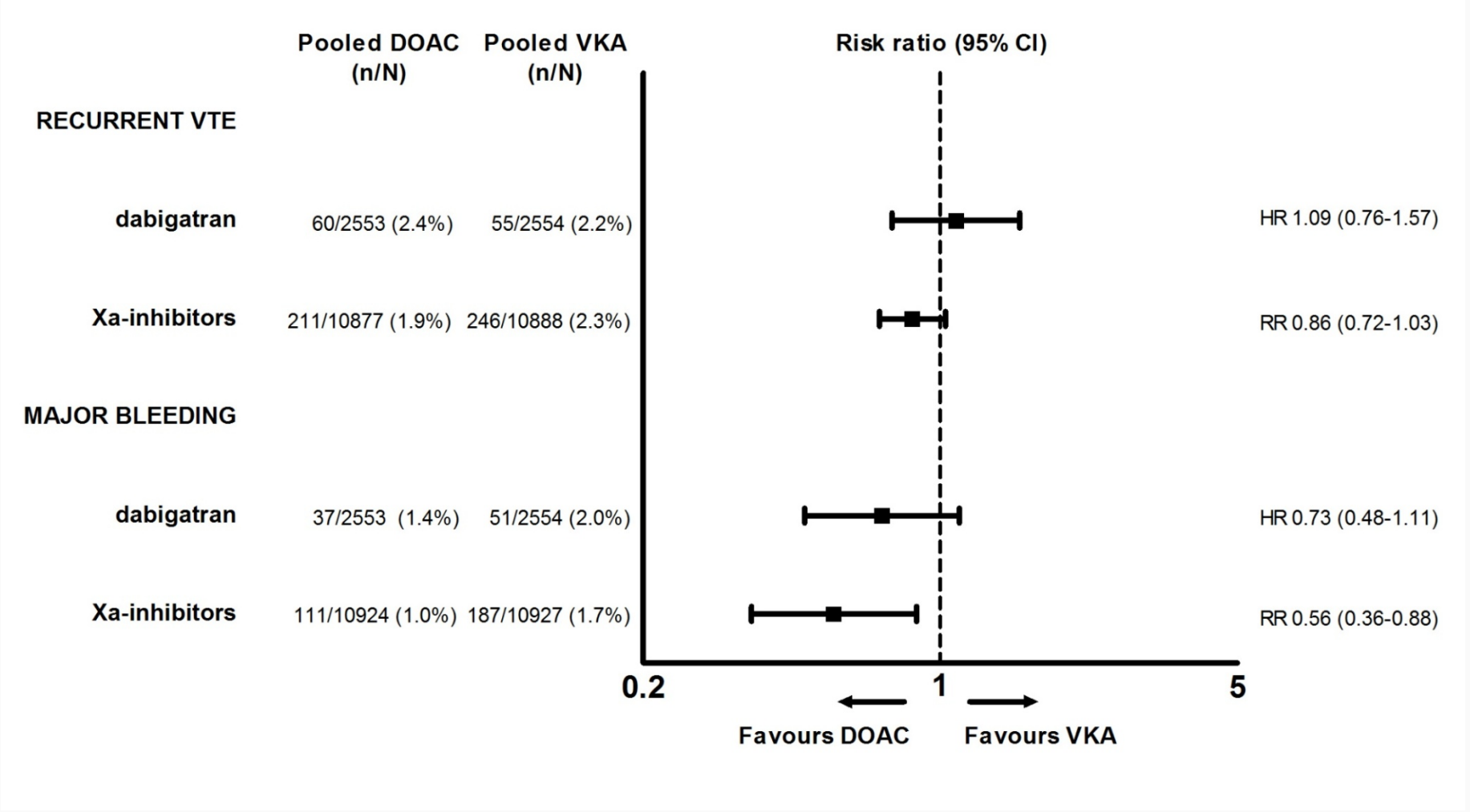
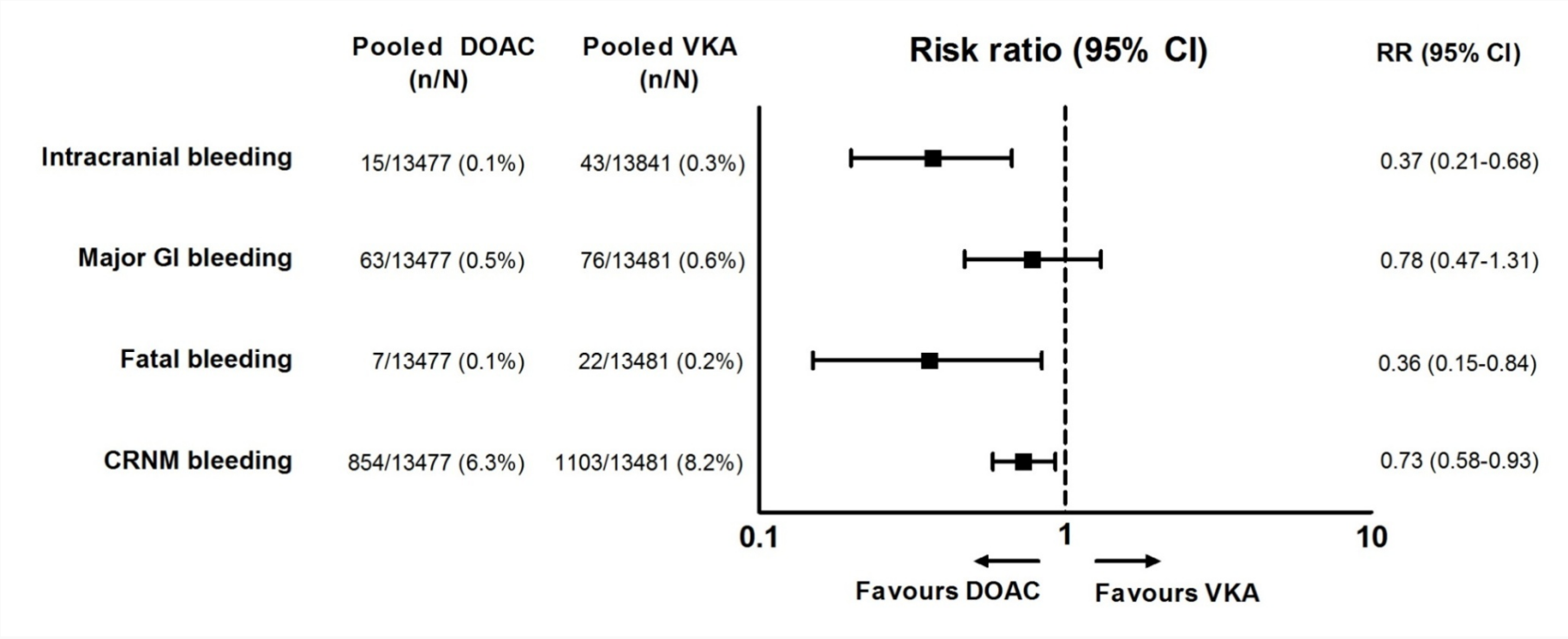
Continued treatment	150 mg BD 110 mg BD (>85 years)	20 mg OD 15 mg OD high bleeding risk	5 mg OD
Primary Prevention (Ortho)	220 mg OD	10 mg OD	2.5 mg BD

Efficacy/safety for Xa and IIa in the treatment of VTE



Van Es et al. Blood 2014;124:1968-75.

Bleeding components in VTE



Van Es et al. Blood 2014;124:1968-75.

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Full Length Article

Abnormal uterine bleeding in VTE patients treated with rivaroxaban compared to vitamin K antagonists

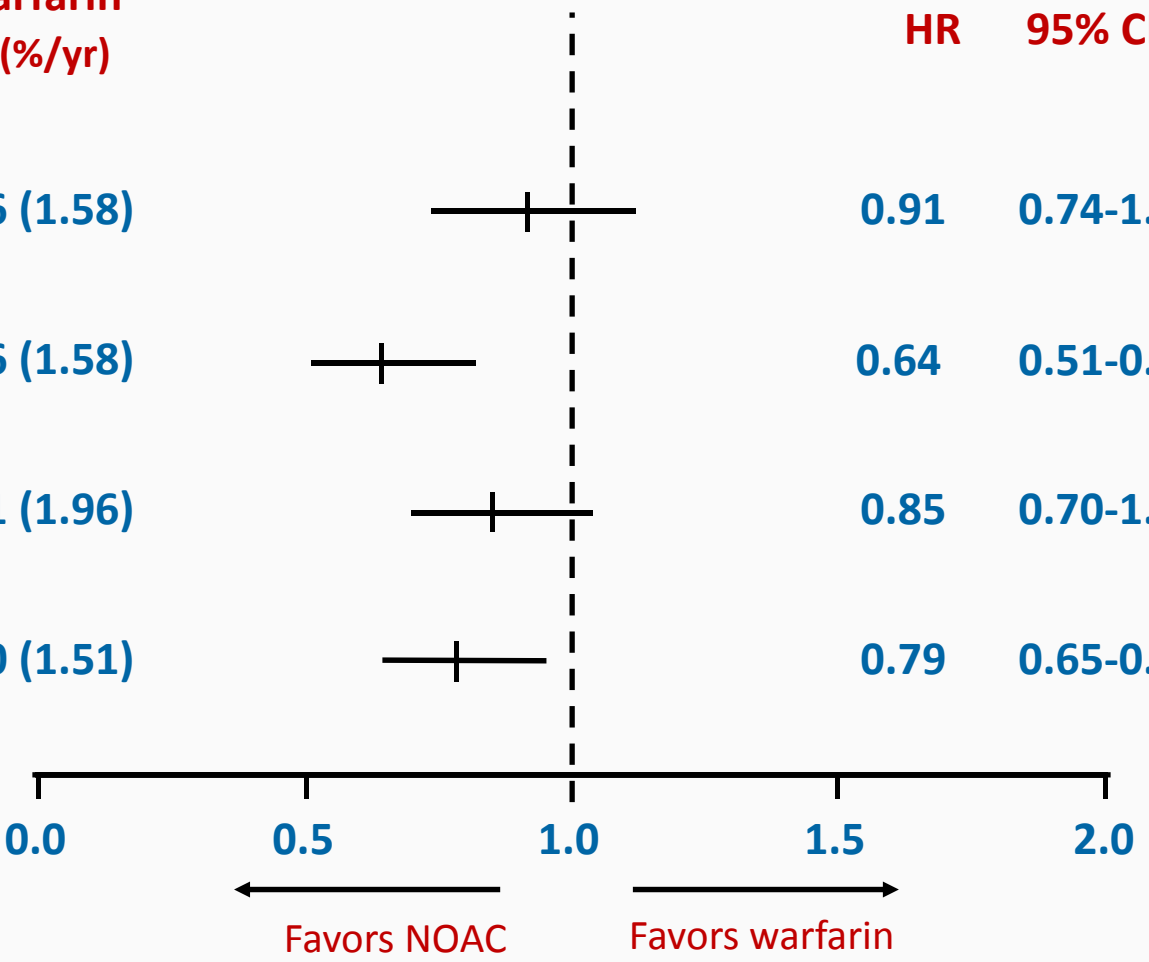
Nico De Crem [a], Kathelijne Peerlinck [b], Thomas Vanassche [b], Kristine Vanheule [b], Barbara Debaveye [b], Saskia Middeldorp [c], Peter Verhamme [b], Marijke Peetermans [a,*]

[a] University Hospital Leuven, Department of Internal Medicine, Herestraat 49, Leuven, Belgium
[b] University Hospital Leuven, Department of Cardiovascular Medicine, Herestraat 49, Leuven, Belgium
[c] Academic Medical Center Amsterdam, Department of Vascular Medicine, Meibergdreef 9, Amsterdam, The Netherlands

	Dabigatran	Rivaroxaban	Apixaban
	Pradaxa®	**Xarelto®**	**Eliquis®**
Afib	✓	✓	✓
Standard	150 mg BD	20 mg OD	5 mg BD
High risk patient • Age • Renal impairment • Body weight • Bleeding risk • Drug-drug interactions • Platelet inhibitors	110 mg BD	15 mg OD	2.5 mg OD

Afib: Prevention of Stroke

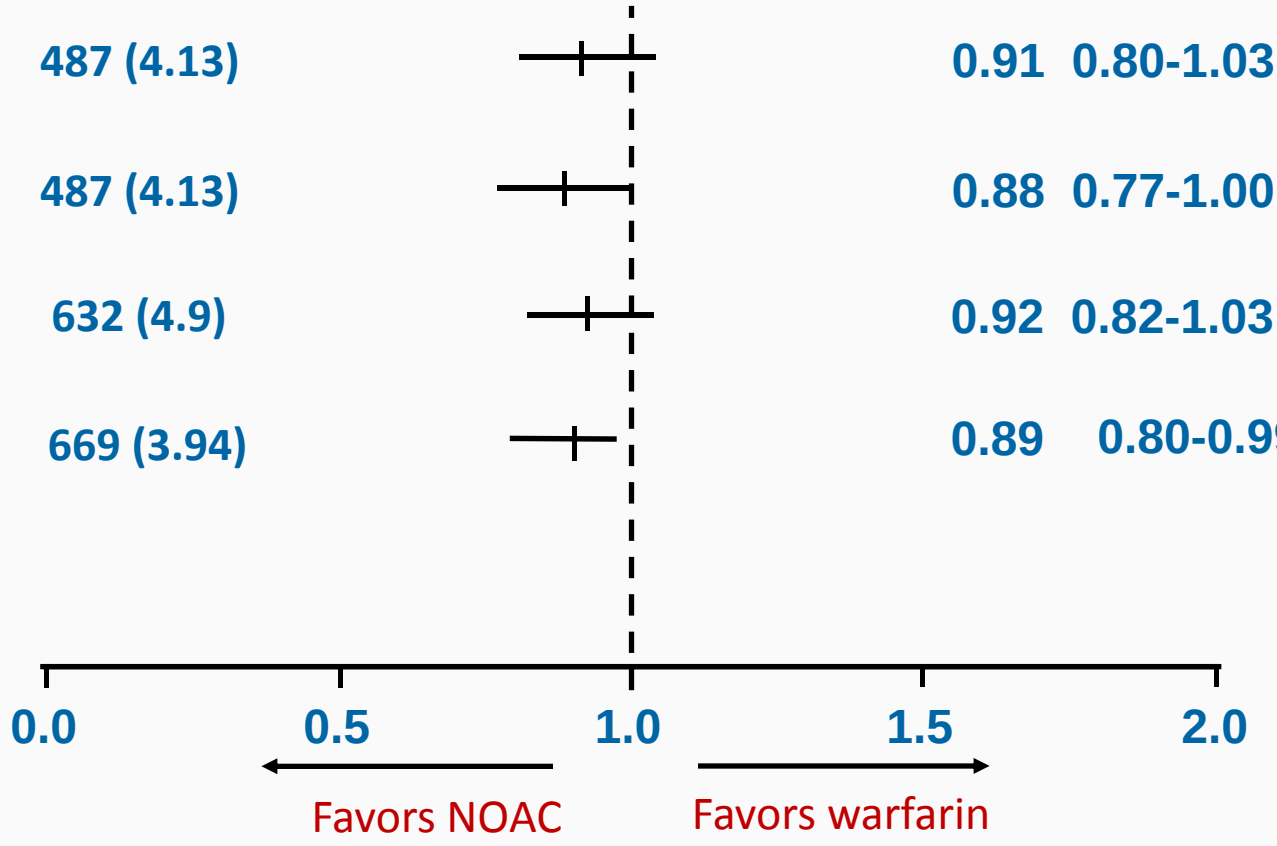
	NOAC	Warfarin	HR	95% CI
	No. of events (%/yr)			
Dabi 110	171 (1.44)	186 (1.58)	0.91	0.74-1.12
Dabi 150	122 (1.01)	186 (1.58)	0.64	0.51-0.81
Riva	184 (1.65)	221 (1.96)	0.85	0.70-1.03
Apixaban	199 (1.19)	250 (1.51)	0.79	0.65-0.95



1. Connolly et al. NEJM 2009; 361: 1139-51. 2. Connolly et al. NEJM 2010; 363: 1875-6.
3. Patel et al. NEJM 2011; 365: 883-91. 4. Granger et al. NEJM 2011; 365: 981-92.

Mortality

	NOAC	Warfarin	HR	95% CI
	No. of events (%/yr)			
Dabi 110	446 (3.75)	487 (4.13)	0.91	0.80-1.03
Dabi 150	438 (3.64)	487 (4.13)	0.88	0.77-1.00
Rivaroxaban	582 (4.5)	632 (4.9)	0.92	0.82-1.03
Apixaban	603 (3.52)	669 (3.94)	0.89	0.80-0.99



Meta-analyse 54.000 ptn
HR 0,89 (0,83-0,96)
Dentali et al. Circ 2013

1. Connolly et al. NEJM 2009; 361: 1139-51. 2. Connolly et al. NEJM 2010; 363: 1875-6.
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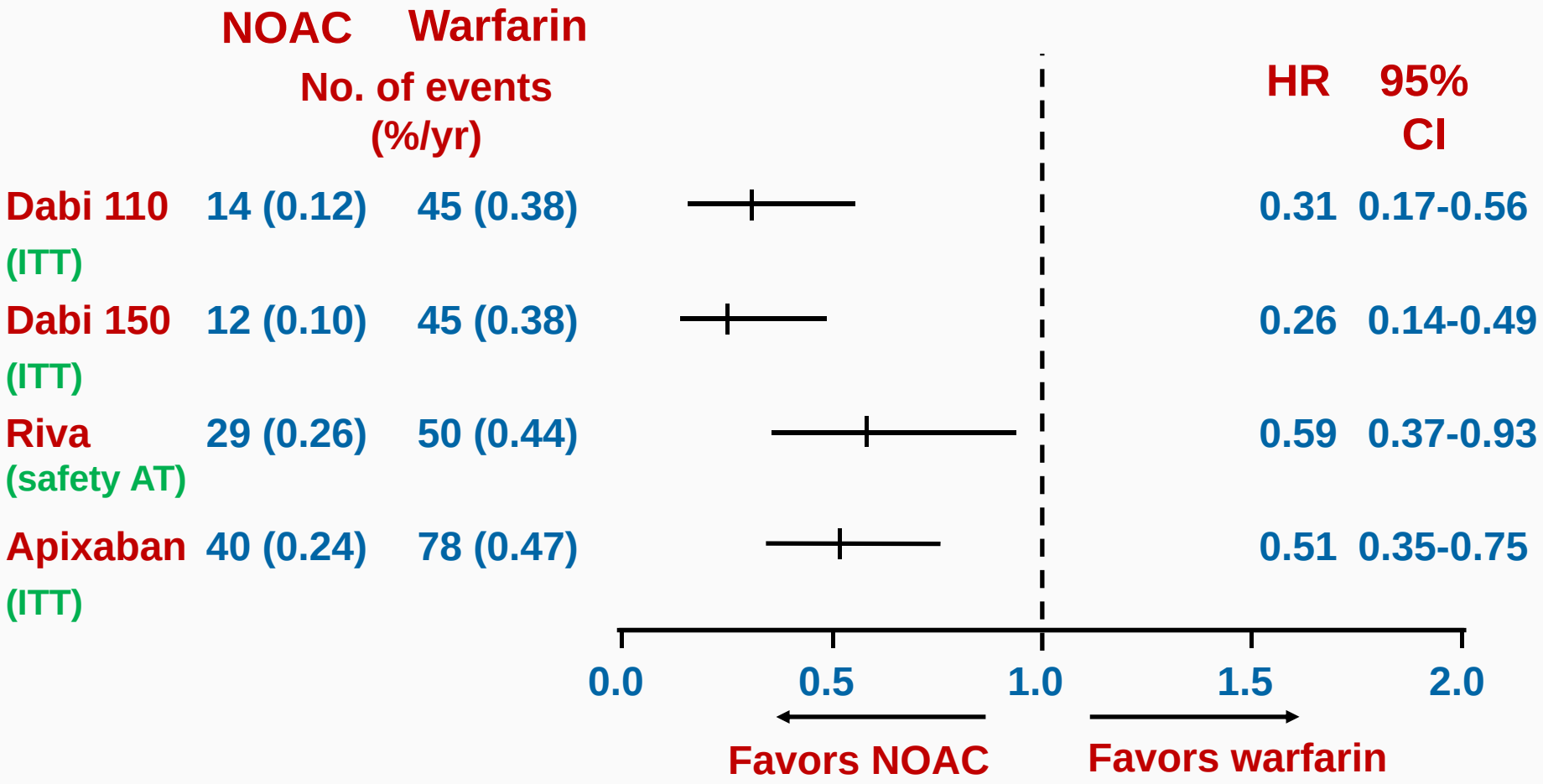
Hemorrhagic stroke



ITT: Intention to Treat – AT: as treated.

1. Connolly et al. NEJM 2009; 361: 1139-51. 2. Connolly et al. NEJM 2010; 363: 1875-6.
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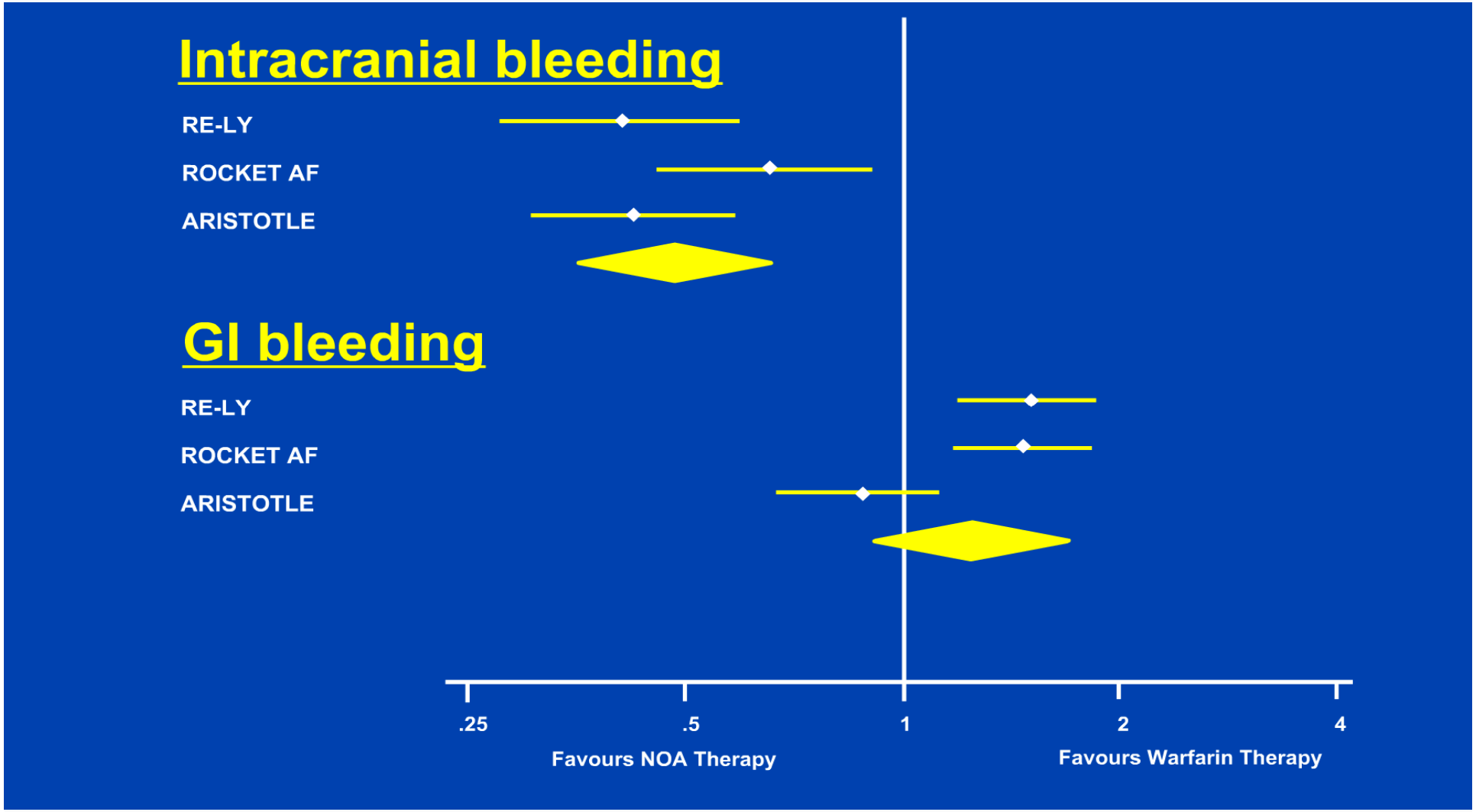
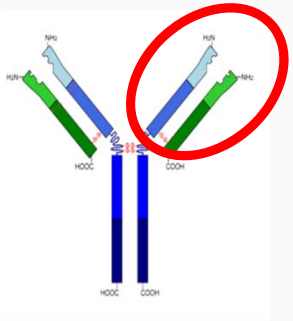
Intracranial vs Gastro-intestinal bleeding



Miller, Am J Cardiol 2012

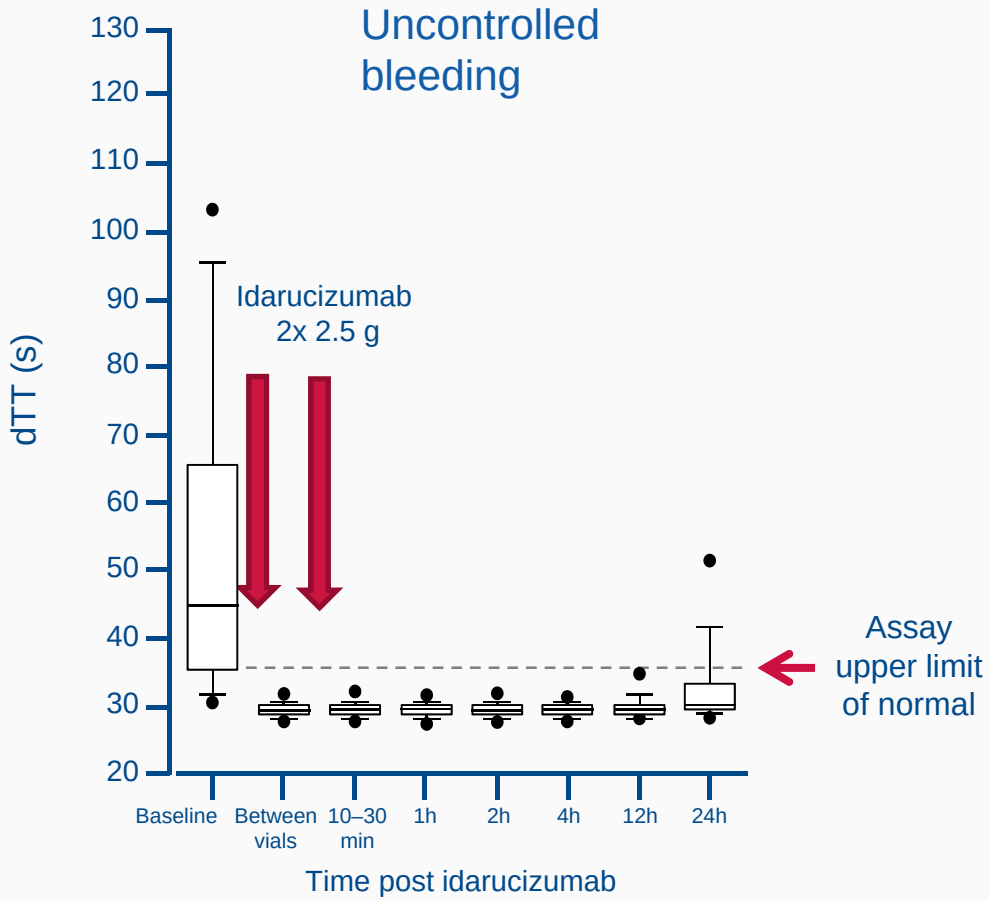
Reversal agents – in development

- Idarucizumab



- Andexanet alfa (AnXa, PRT064445)

Reversal of anticoagulation in patients with bleeding or urgent procedures



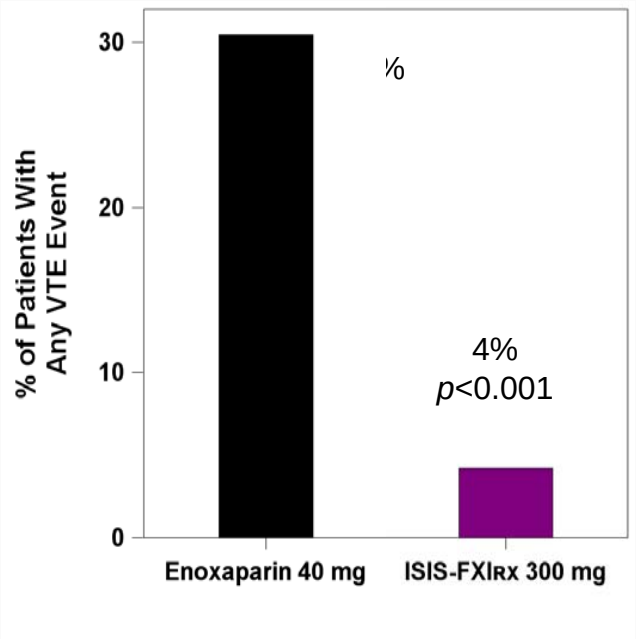
ORIGINAL ARTICLE

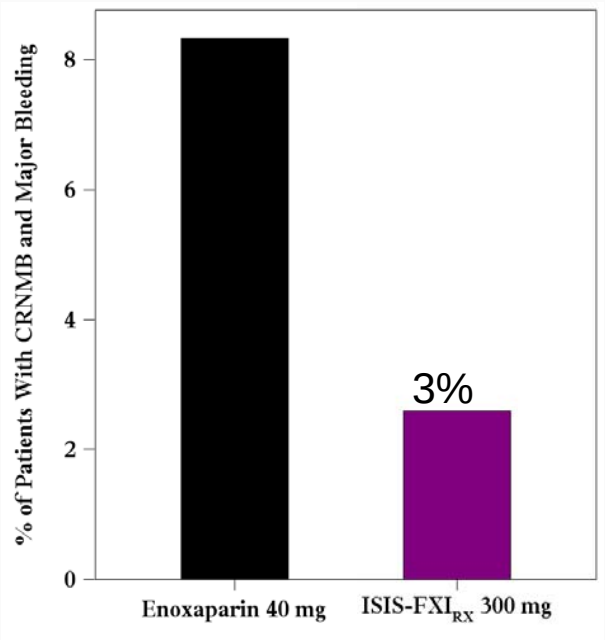
Idarucizumab for Dabigatran Reversal

Charles V. Pollack, Jr., M.D., Paul A. Reilly, Ph.D., John Eikelboom, M.B., B.S., Stephan Glund, Ph.D., Peter Verhamme, M.D., Richard A. Bernstein, M.D., Ph.D., Robert Dubiel, Pharm.D., Menno V. Huisman, M.D., Ph.D., Elaine M. Hylek, M.D., Pieter W. Kamphuisen, M.D., Ph.D., Jörg Kreuzer, M.D., Jerrold H. Levy, M.D., Frank W. Sellke, M.D., Joachim Stangier, Ph.D., Thorsten Steiner, M.D., M.M.E., Bushi Wang, Ph.D., Chak-Wah Kam, M.D., and Jeffrey I. Weitz, M.D.

NEJM 2015

What's next in Thrombosis Research?





ORIGINAL ARTICLE

Factor XI Antisense Oligonucleotide for Prevention of Venous Thrombosis

Harry R. Büller, M.D., Claudette Bethune, Ph.D., Sanjay Bhanot, M.D., Ph.D., David Gailani, M.D., Brett P. Monia, Ph.D., Gary E. Raskob, Ph.D., Annelise Segers, M.D., Peter Verhamme, M.D., and Jeffrey I. Weitz, M.D., for the FXI-ASO TKA Investigators*

NEJM, 2015

Case 2: Anticoagulation during travel

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