

# ANTISTOLLING/STOLLINGSCASCADE IN ACUTE SITUATIES

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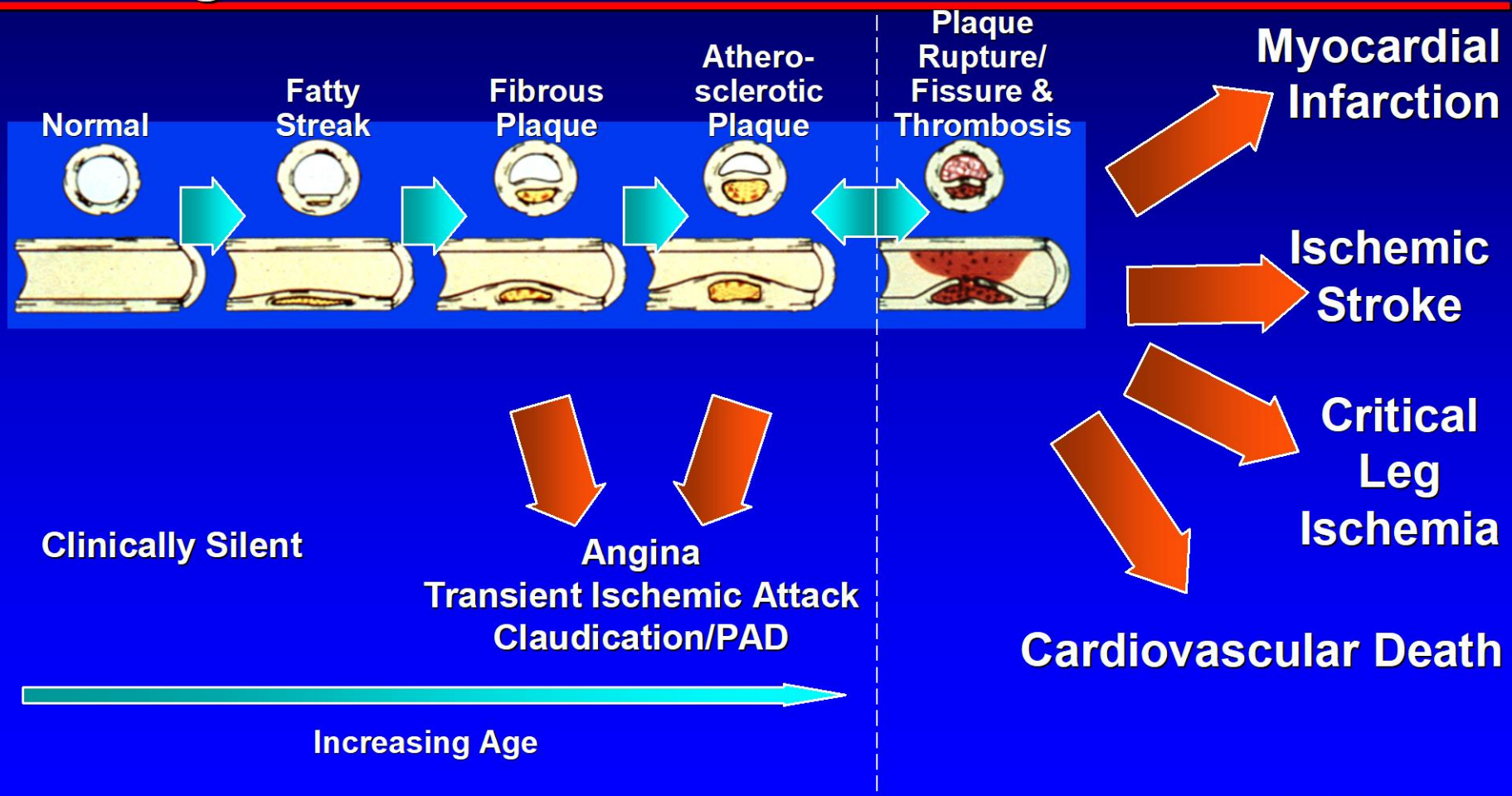
Freek W.A. Verheugt

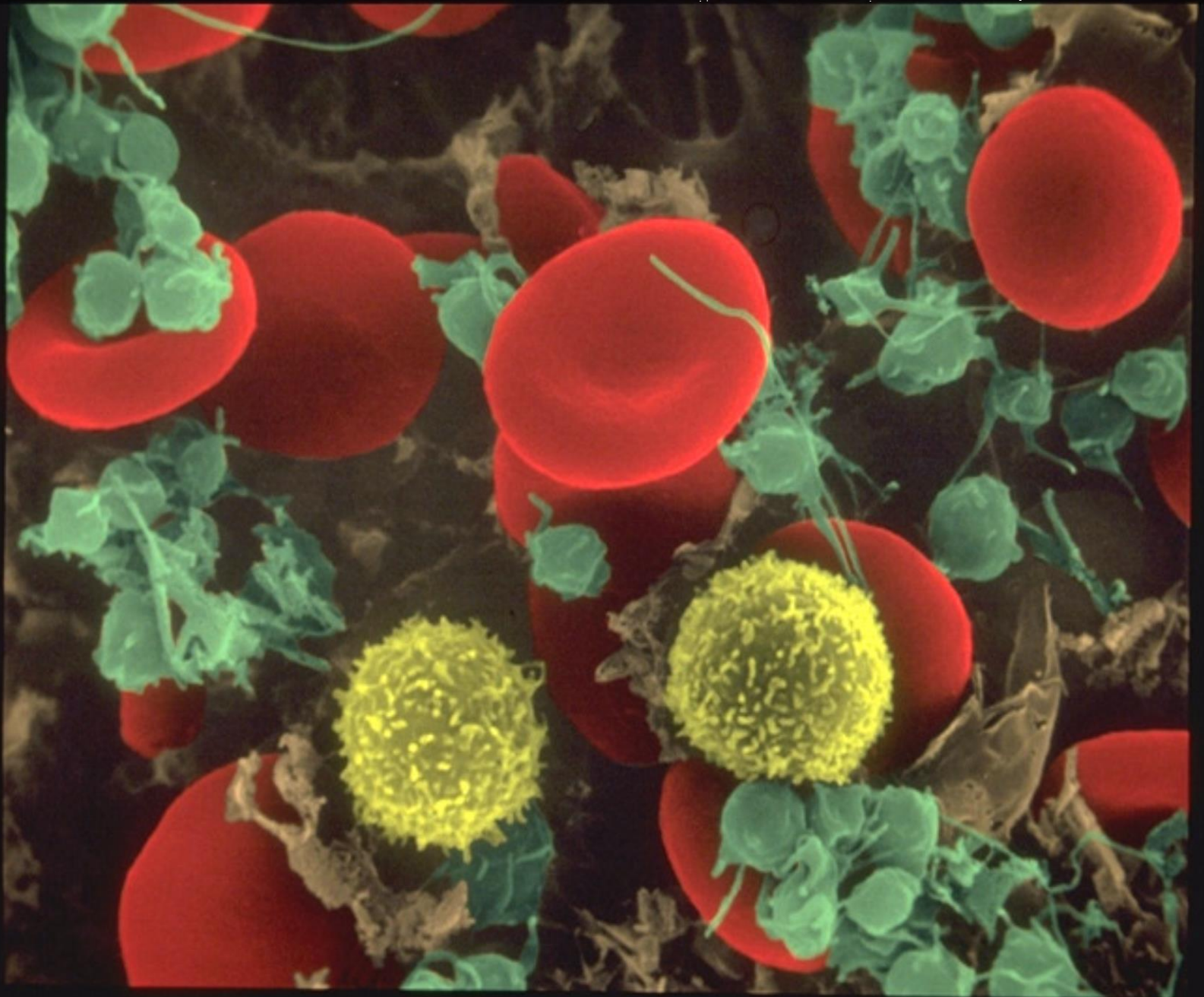
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Amsterdam

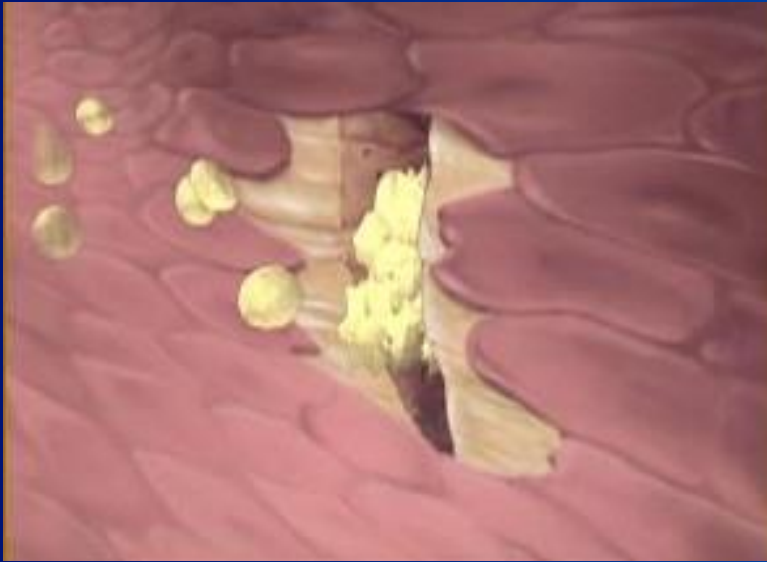
# Atherogenesis and Atherothrombosis: A Progressive Process



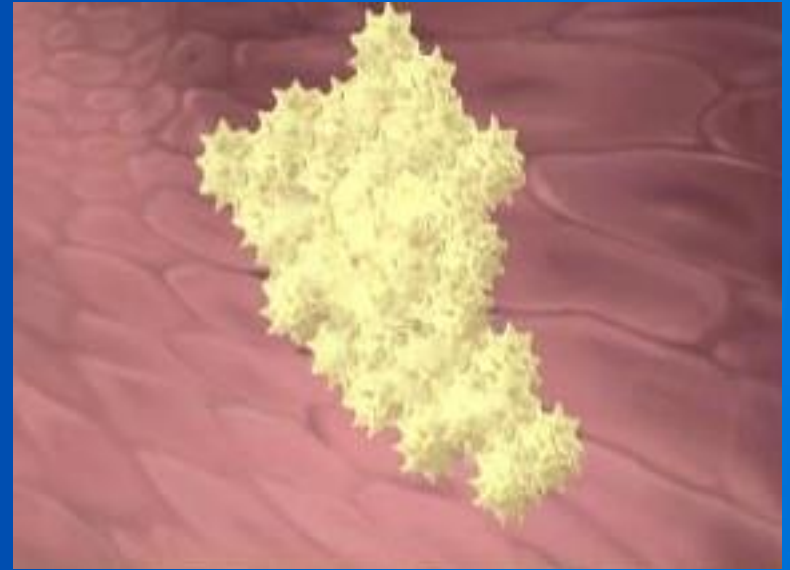


# Bloedplaatjes (Trombocyten)

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*Adhesie*



*Aggregatie*

**Platelet adhesion and aggregation on denuded intima  
(x 3,570)**

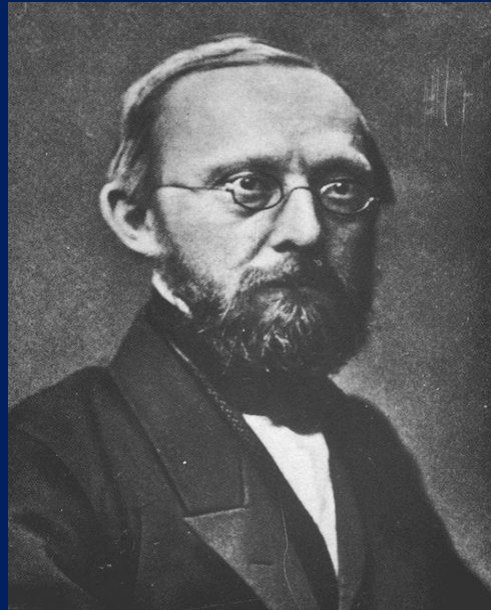


Reproduced from Davies M.J., W.B. Saunders Co., 1992

# Virchow's Triade van Trombogenese

Verandering van bloedsamenstelling

Verandering van bloedstroomsnelheid



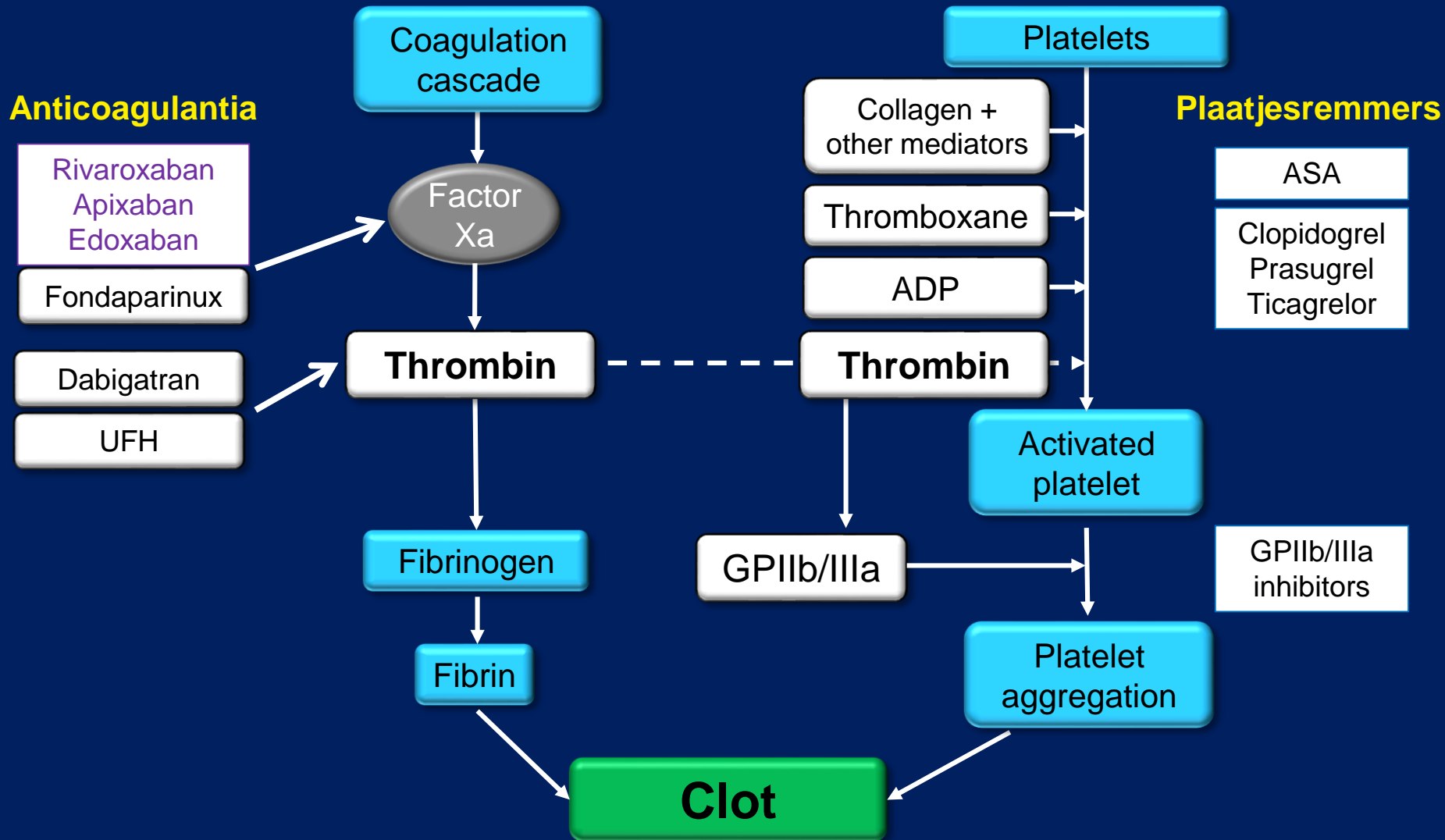
Rudolf Virchow (1821-1902) – Charité, Berlijn

Verandering in de vaatwand

*Virchow R. Zur pathologischen Physiologie des Blutes. Virch Arch 1847;1:546*



# Het stollingsapparaat





# **ANTITROMBOTICA (“ANTISTOLLING”):**

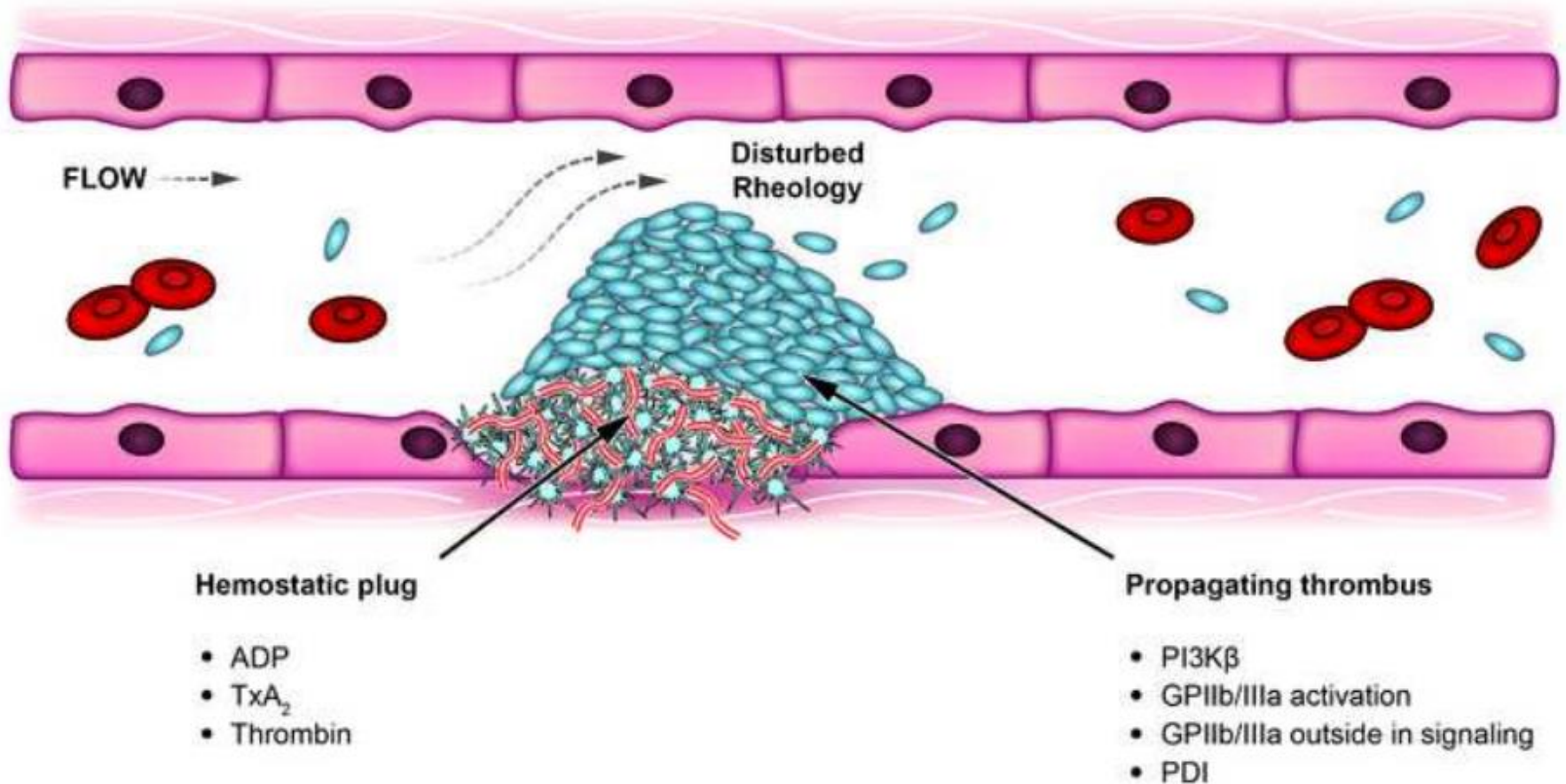
- 1. ANTIPLAATJESTHERAPIE**
- 2. ANTICOAGULANTIA (VOORHEEN “ANTISTOLLING”)**

# ANTITROMBOTICA (“ANTISTOLLING”):

1. ANTIPLAATJESTHERAPIE

2. ANTICOAGULANTIA (VOORHEEN “ANTISTOLLING”)

# Arterial Injury vs Thrombosis

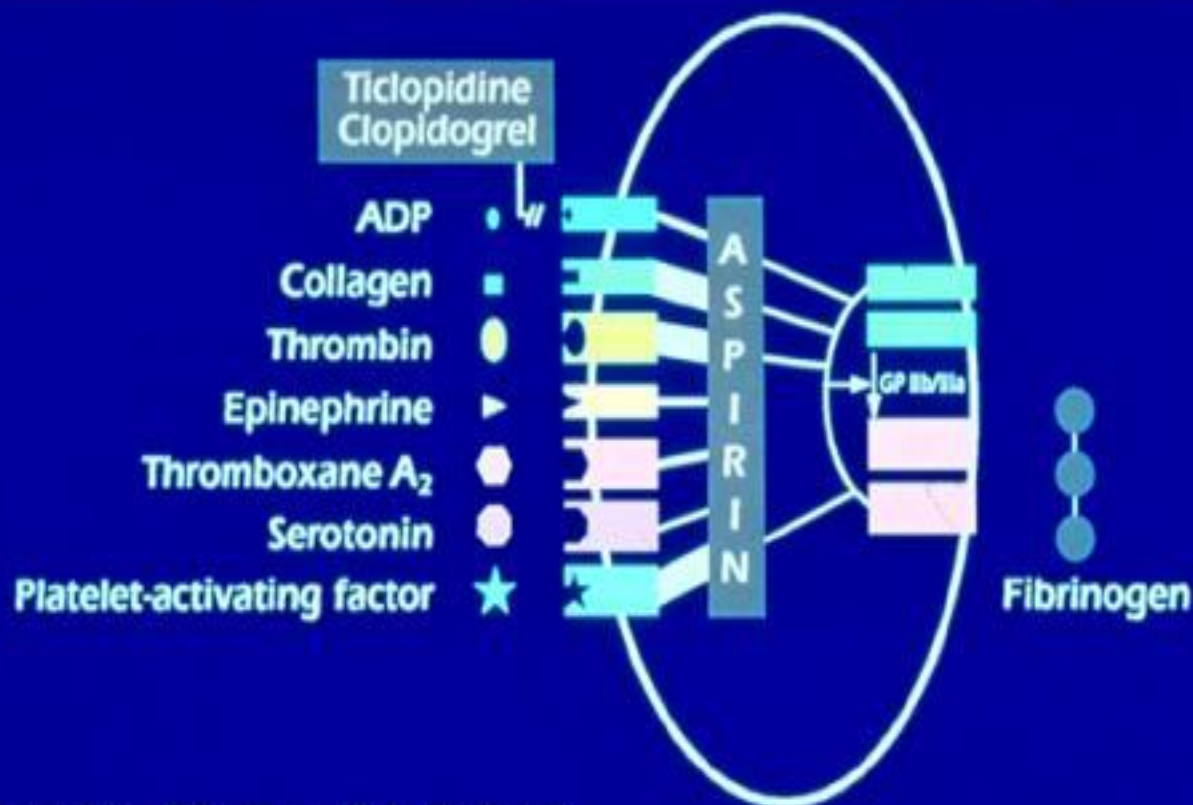


# SIR JOHN VANE



**NOBELPRIJS GENEESKUNDE EN FYSIOLOGIE 1982**

# Effects of Aspirin

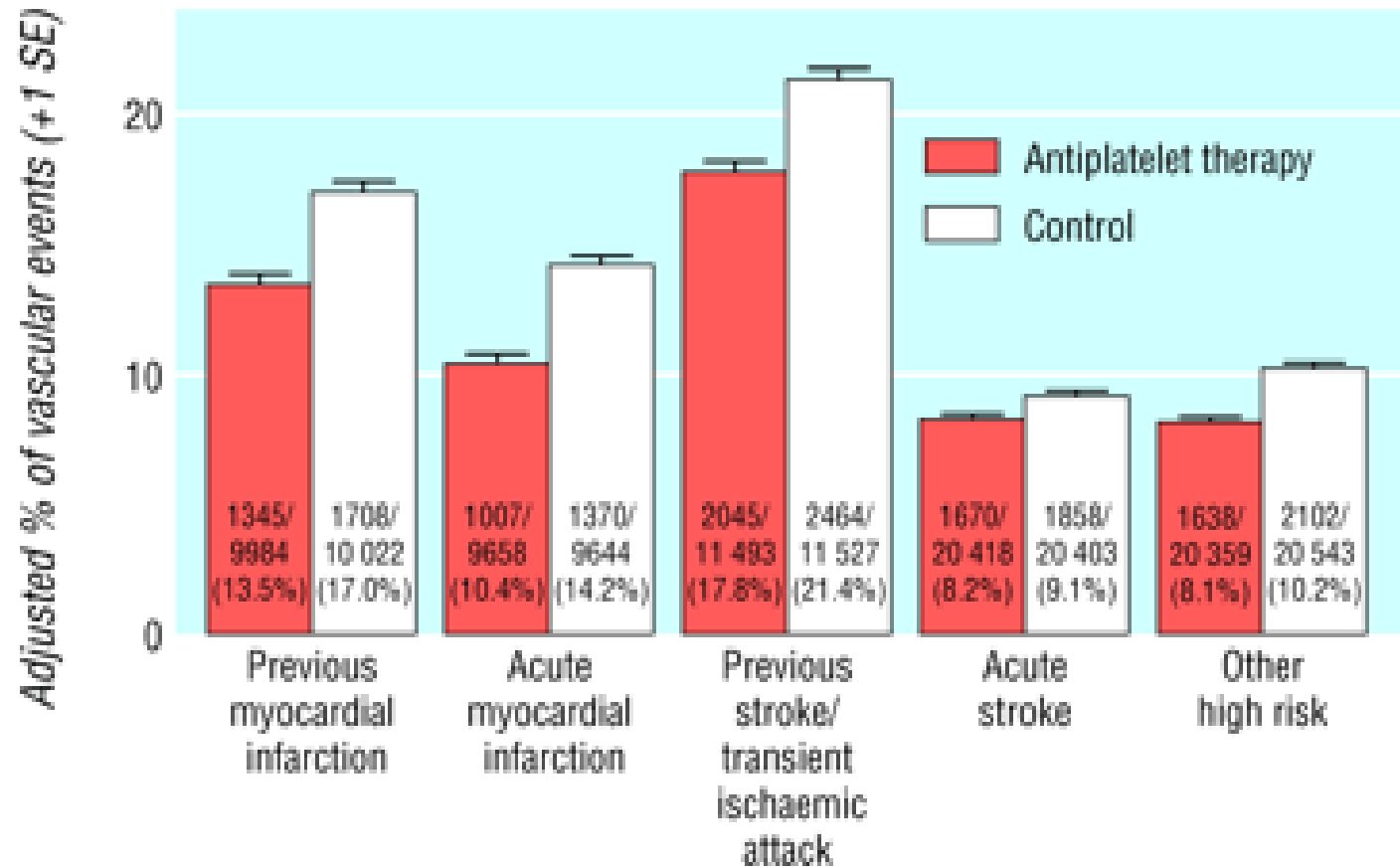


ADP = adenosine diphosphate; GP = glycoprotein

Thickness of line indicates strength of activator

Adapted from Ohman EM et al. Early clinical experience with Integrelin, an inhibitor of the platelet glycoprotein IIb/IIIa integrin receptor. *Eur Heart J* 1995;16[suppl L]:50-55.

Benefit per 1000 patients (SE):	36 (5)	38 (5)	36 (6)	9 (3)	22 (3)
Mean months of treatment:	27	1	29	0.7	22
P value:	<0.0001	<0.0001	<0.0001	0.0009	<0.0001



*APT meta-analysis. BMJ 2002;324:71-86*



Culture

## Health: Drug of the century

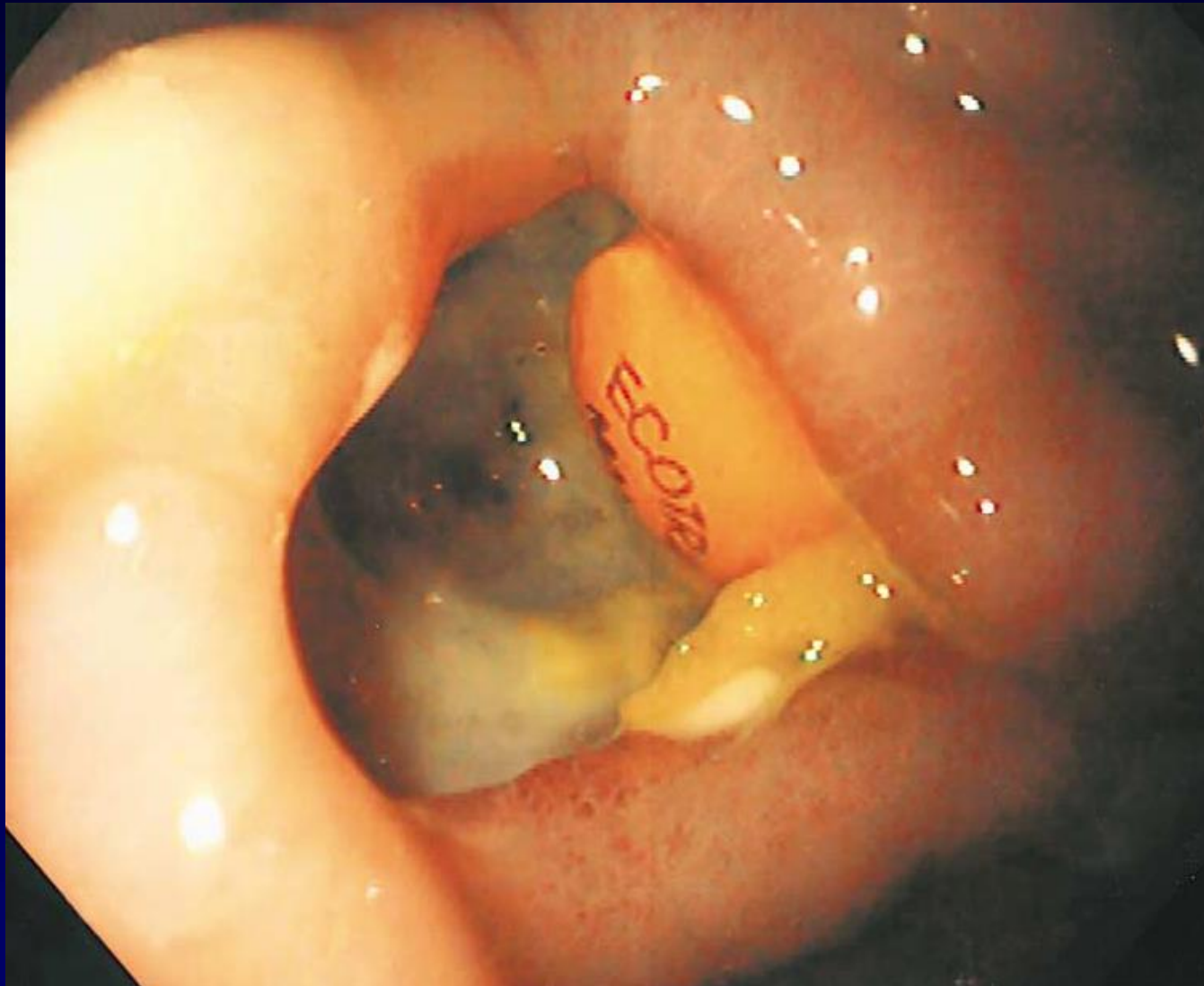
In an age of super-pills, the best medicine of all is also one of the oldest.

Jeremy Laurance | [@jeremylaurance](#) | Tuesday 2 March 1999 |

Most people have a potent anti-cancer agent in the medicine cabinet at home, though few know it. They keep a heart drug at the back of the sock drawer, a fertility promoter buried in their handbag and a cognitive enhancer standing next to the salt pot in the kitchen.

The drug is aspirin, a chemical entity for which new uses are still coming to light 100 years after it was discovered. We know, of course, that it reduces aches and pains, and eases fevers in diseases such as flu. It is now also a standard treatment for heart attacks - take one immediately after calling 999. Tens of thousands of lives

# ASPIRIN TABLET IN GASTRIC ULCER



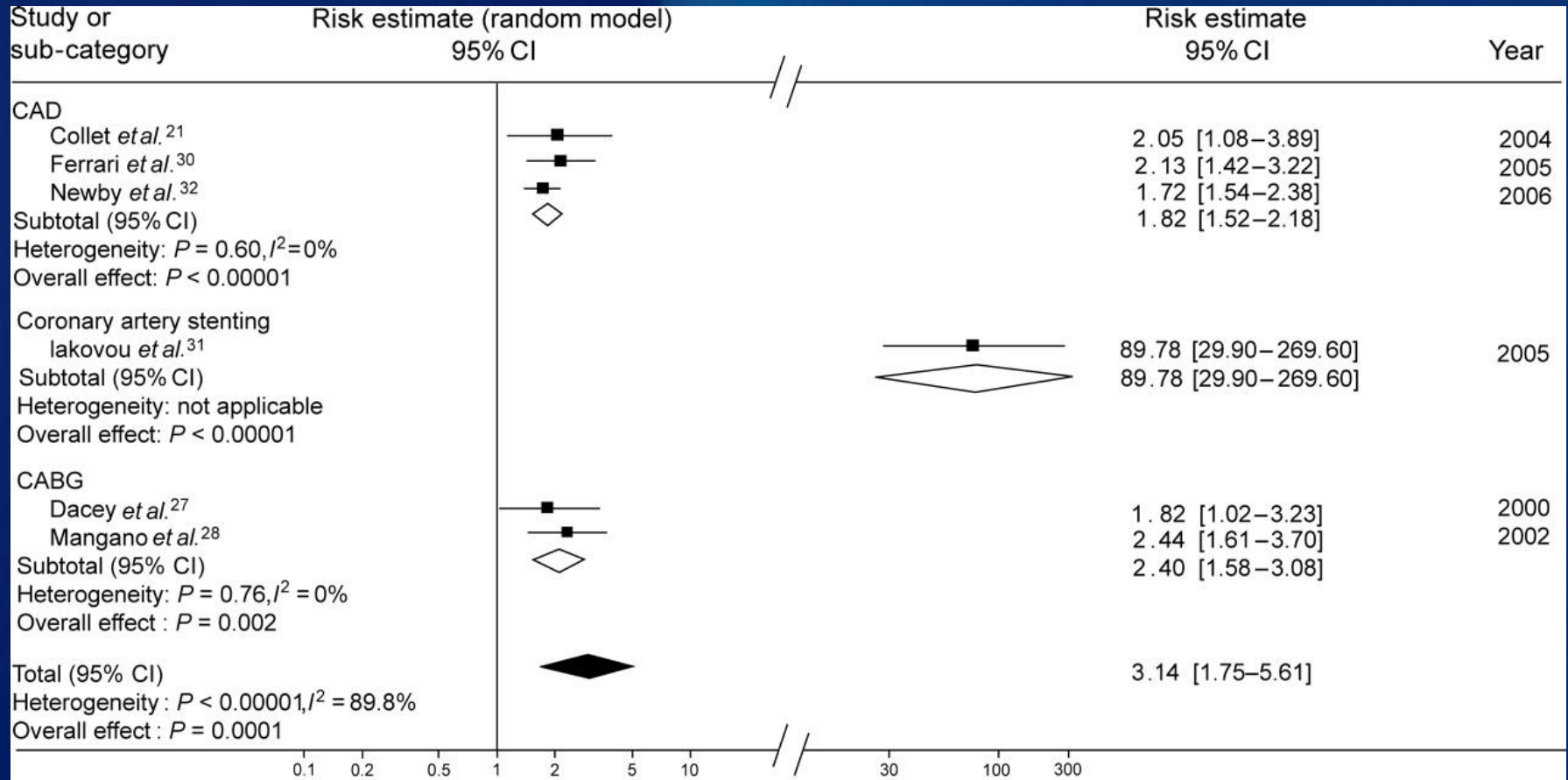
Levy DJ. *N Engl J Med* 2000;343:863

Onze Lieve Vrouwe Gasthuis, Amsterdam



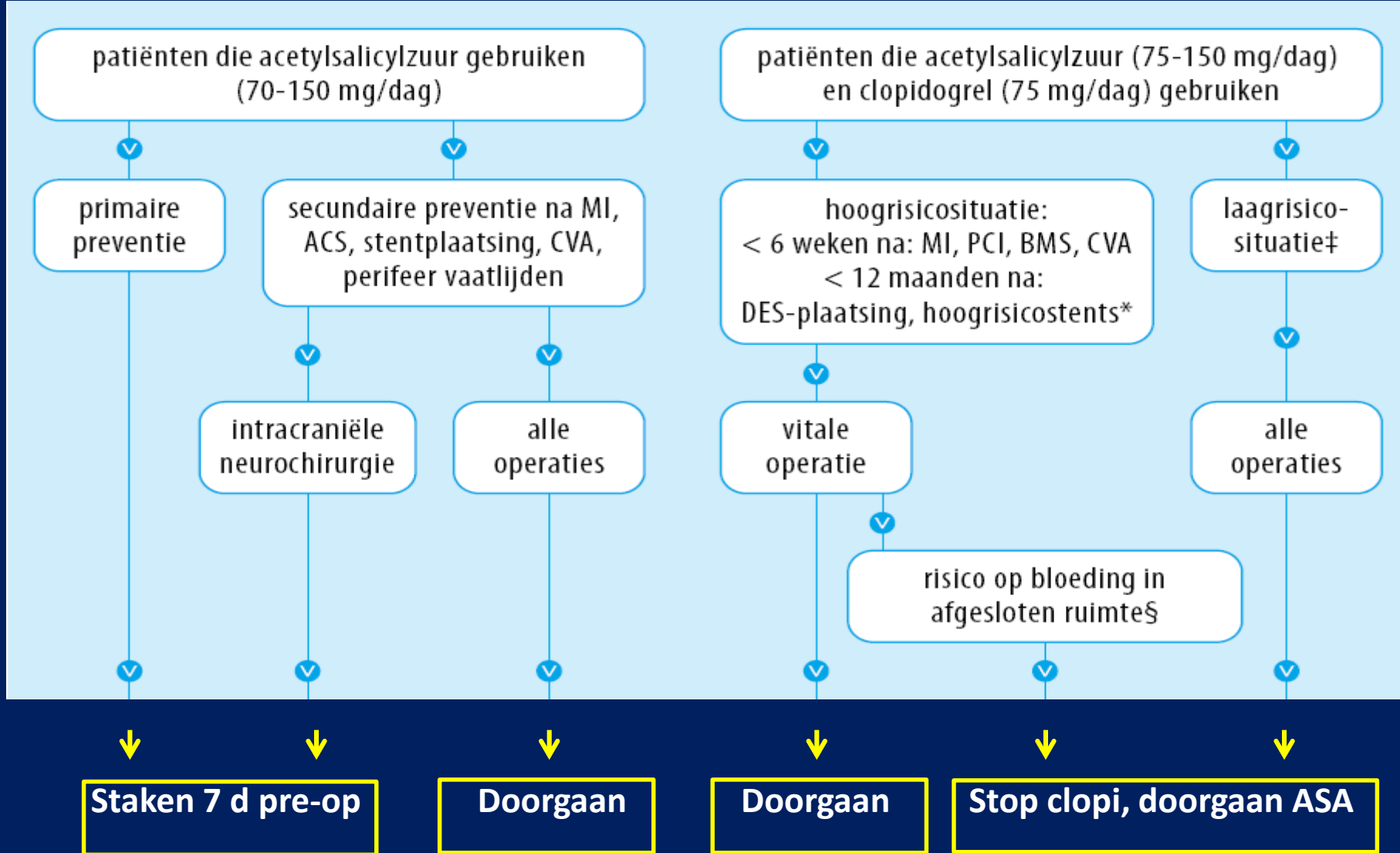
# Hazards of Stopping Antiplatelet therapy

## Aspirin Discontinuation in 50,279 CAD Patients



Decreased thrombotic risk      Increased thrombotic risk

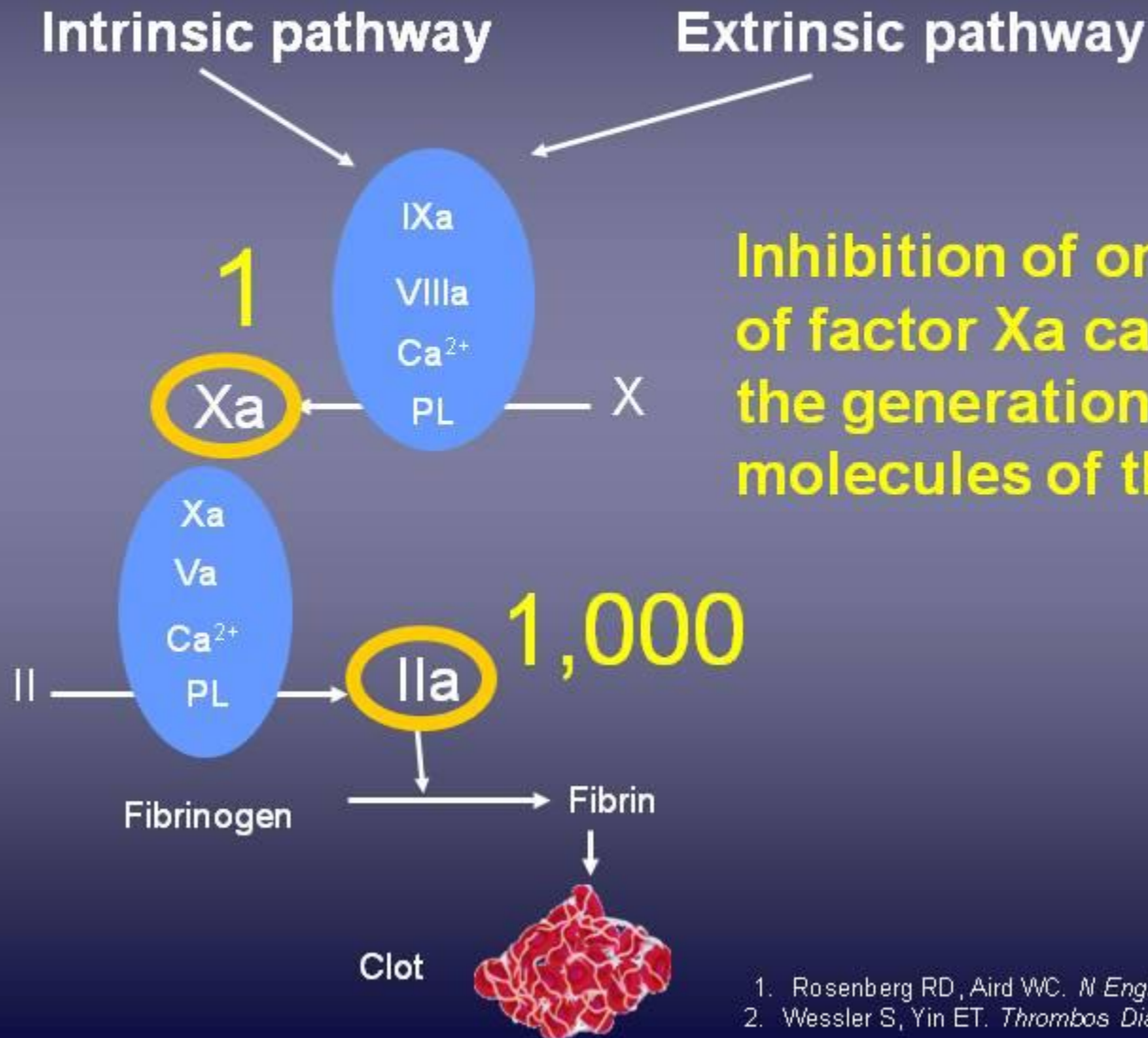
# Peri-procedurele Antiplaatjetherapie



# ANTITROMBOTICA (“ANTISTOLLING”):

1. ANTIPLAATJESTHERAPIE
2. ANTICOAGULANTIA (VOORHEEN “ANTISTOLLING”)

# Factor Xa: At the core of the coagulation cascade<sup>1</sup>

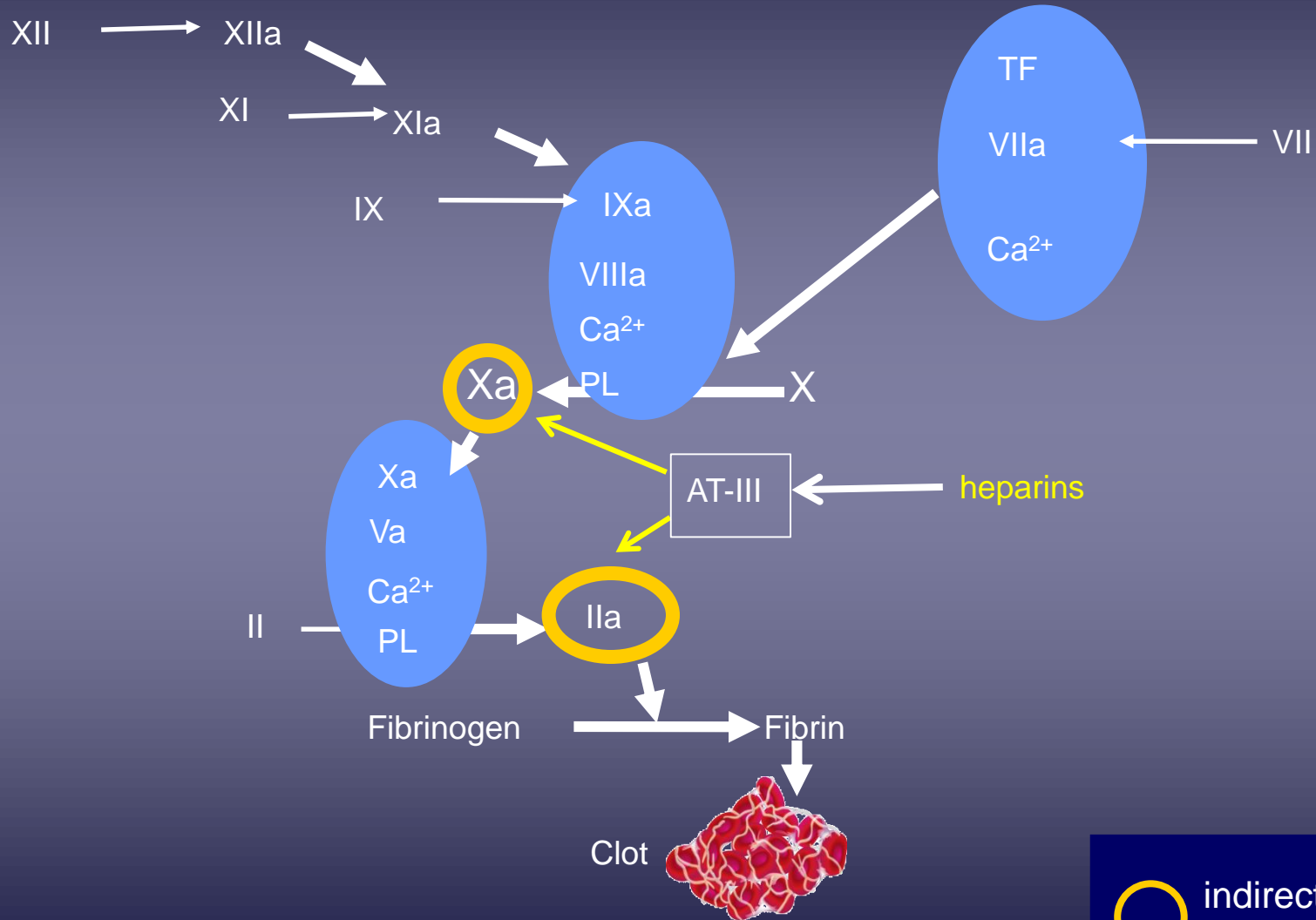



**Inhibition of one molecule of factor Xa can inhibit the generation of 1,000 molecules of thrombin<sup>2</sup>**

1. Rosenberg RD, Aird WC. *N Engl J Med.* 1999;340:1555-1564  
2. Wessler S, Yin ET. *Thrombos Diath Haemorrh.* 1974;32:71-78

# Intrinsic pathway

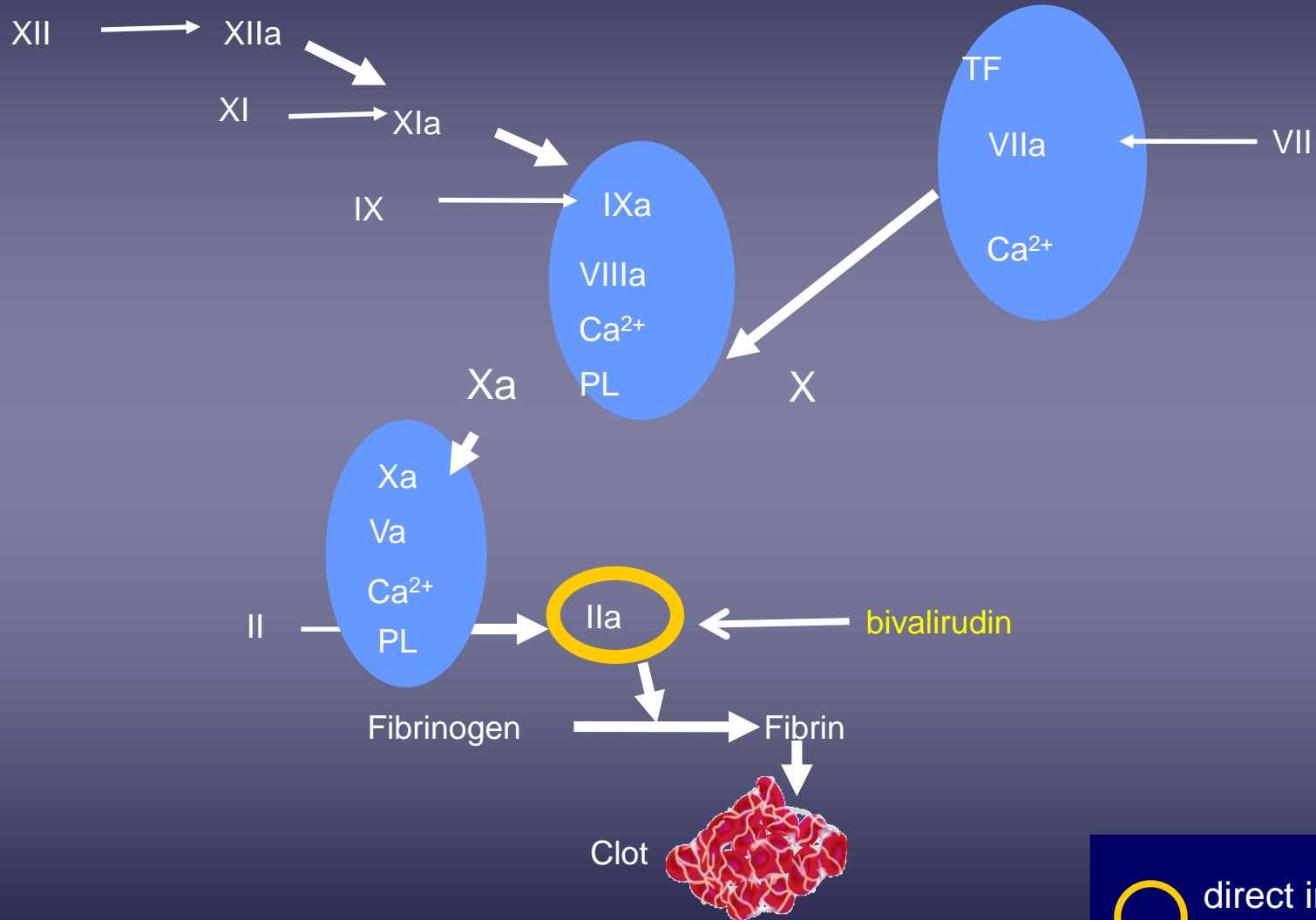
# Extrinsic pathway




 indirect inhibition by heparins

# Intrinsic pathway

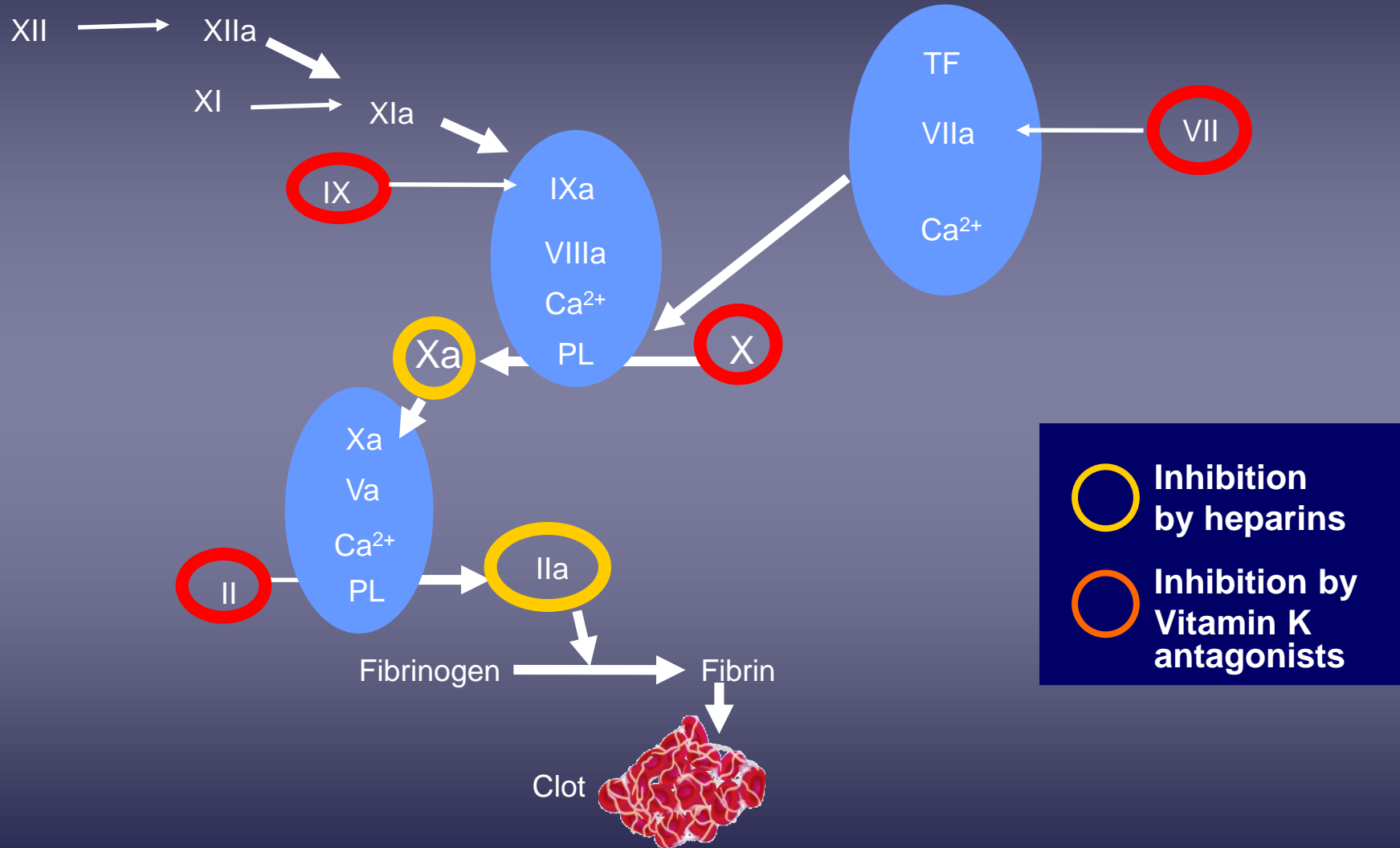
# Extrinsic pathway



 direct inhibition by bivalirudin

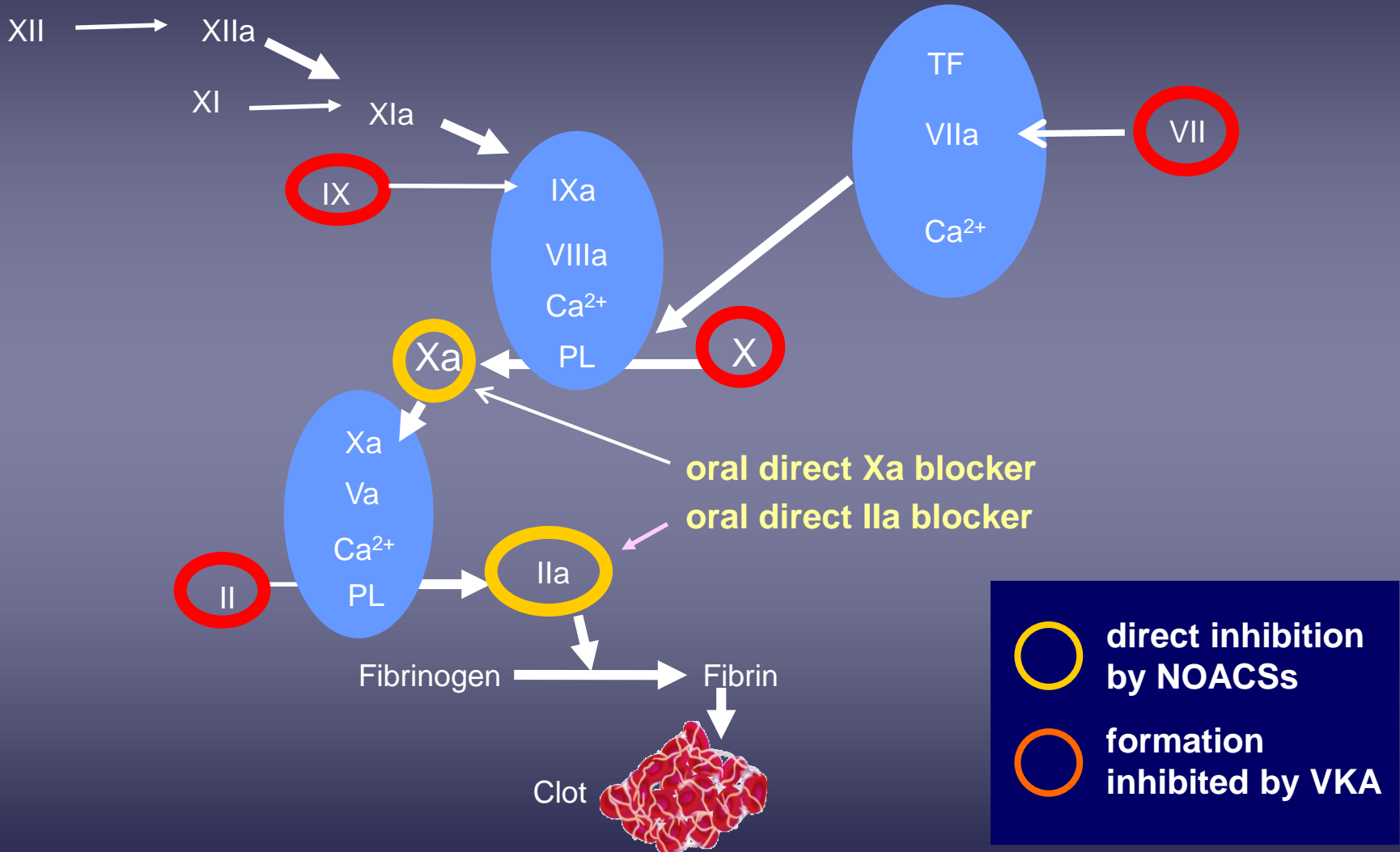
# Intrinsic pathway

# Extrinsic pathway



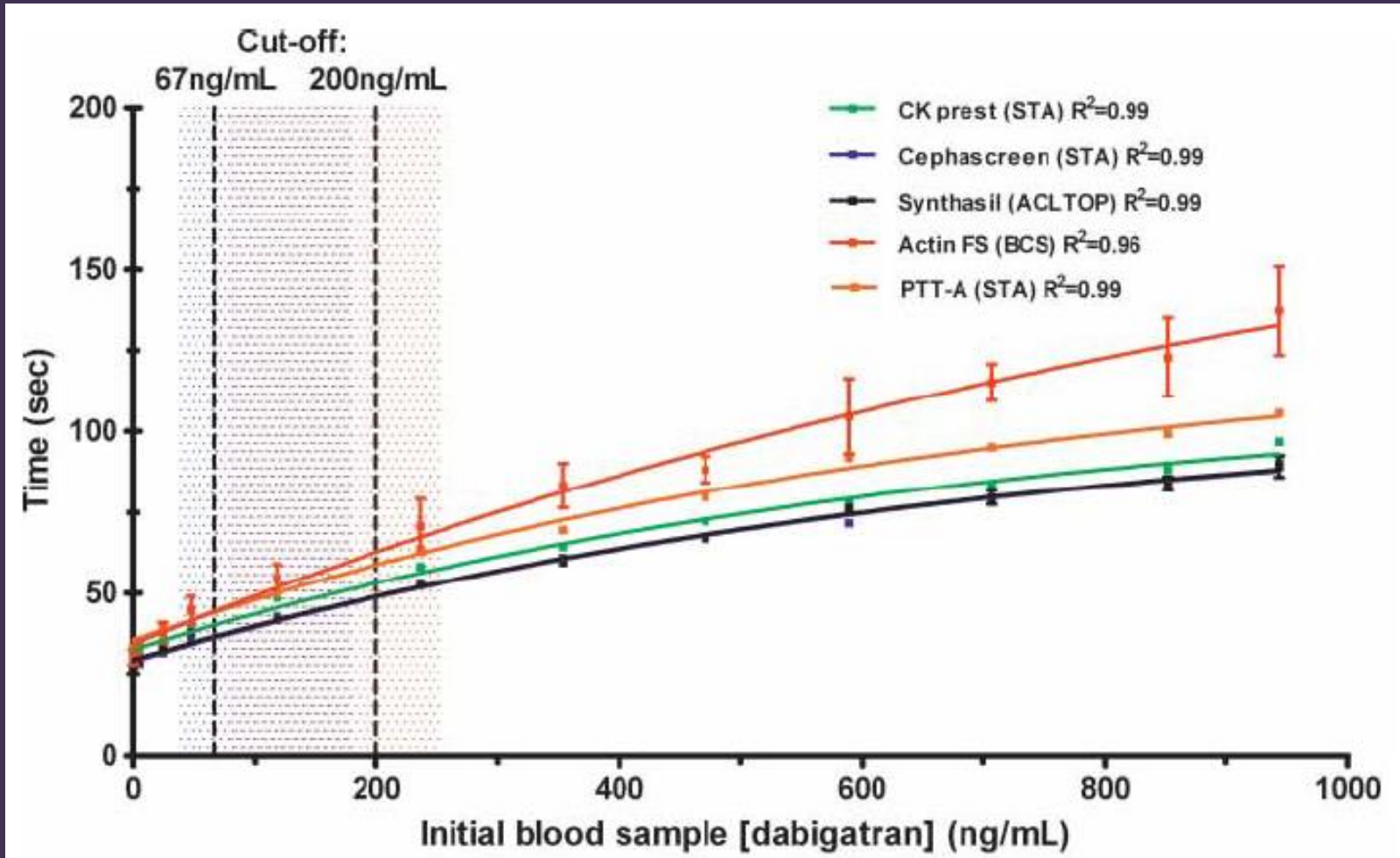
## Intrinsic pathway

## Extrinsic pathway

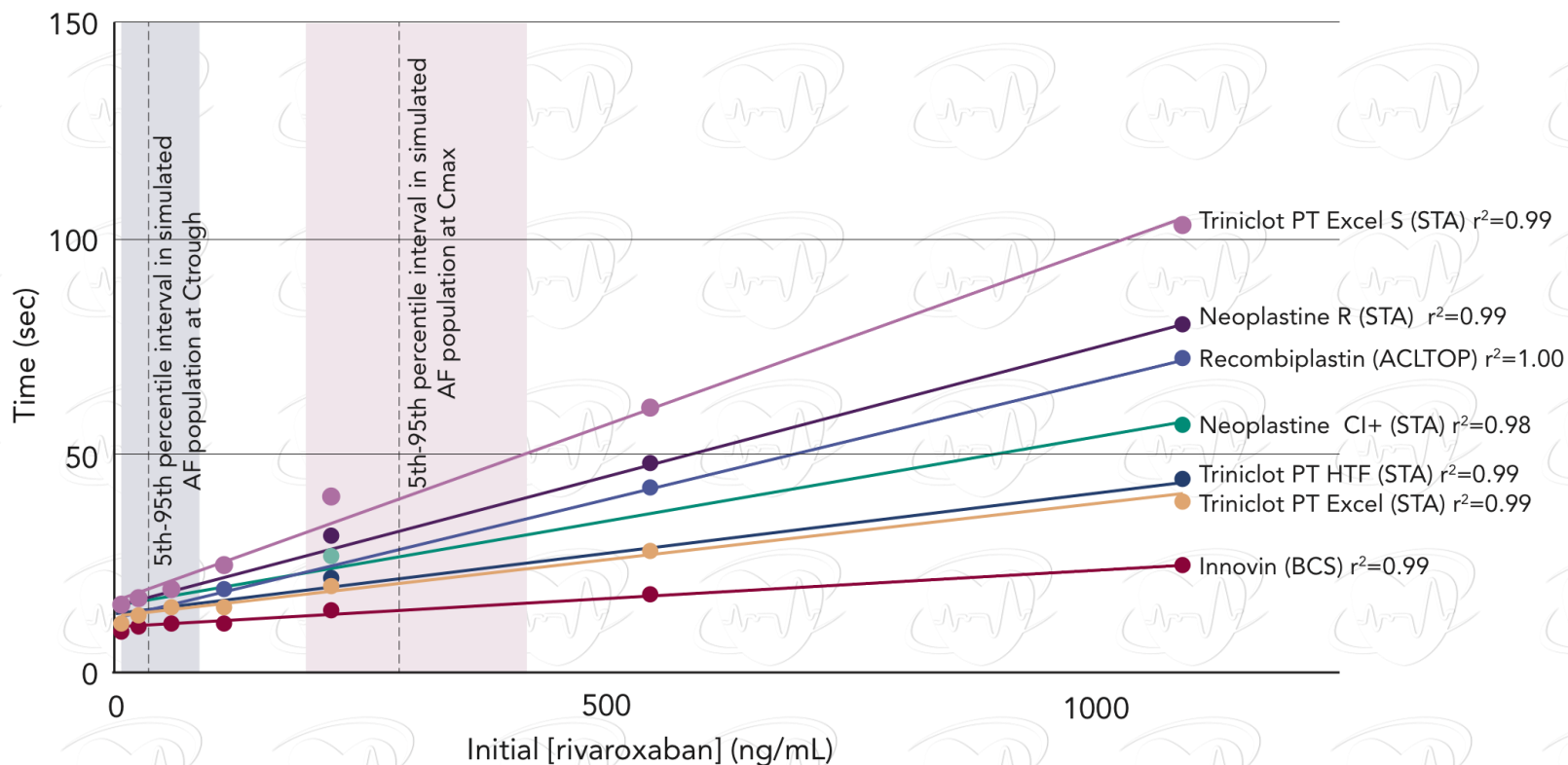




# How should dabigatran be monitored? aPTT



# Relation between PT and FXa inhibitor (rivaroxaban) plasma levels

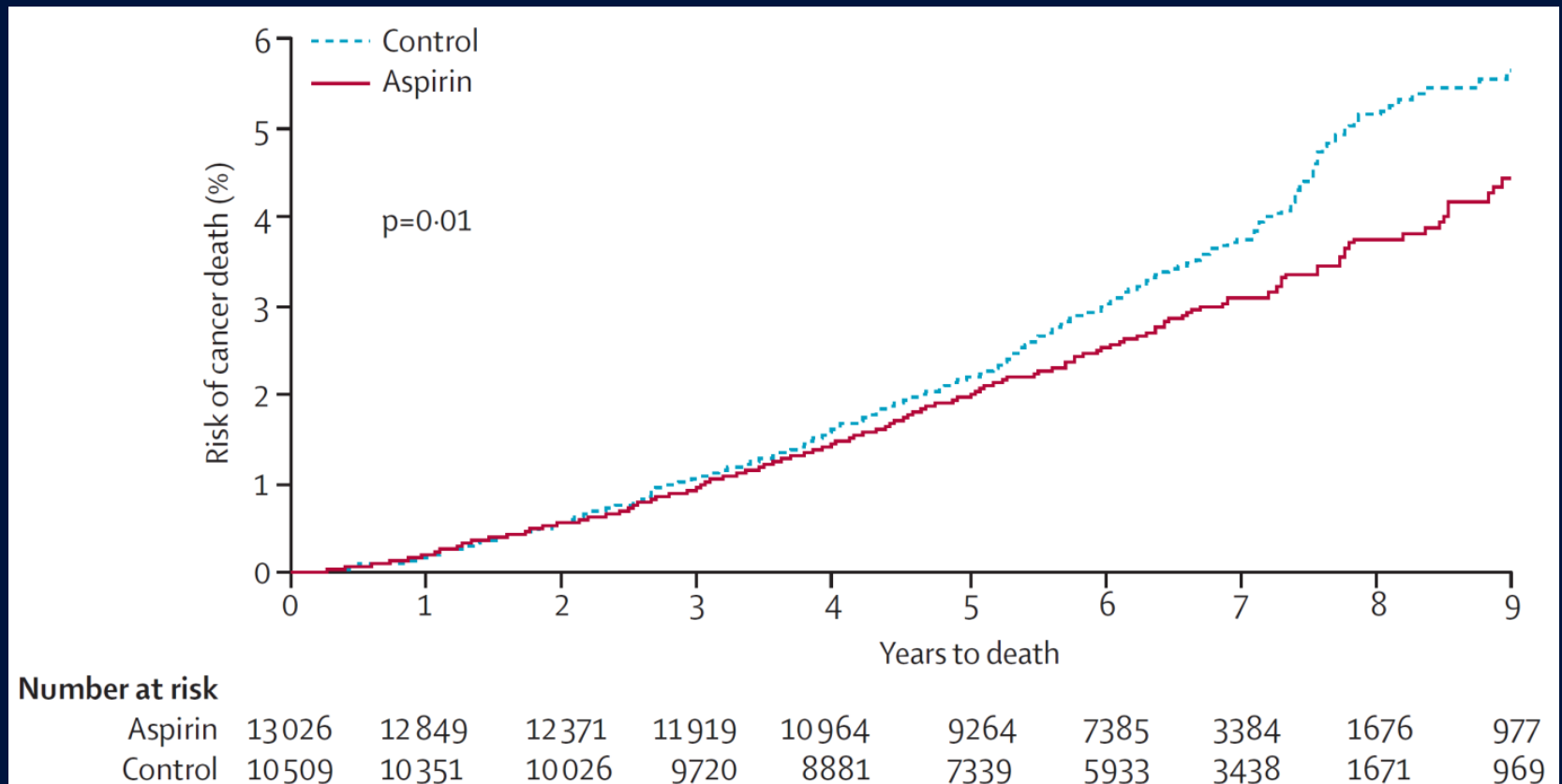


Douxflis et al Thromb Res. 2012;130:956-66

[www.escardio.org/EHRA](http://www.escardio.org/EHRA)

# Cancer Chemoprevention by Aspirin

Effect of daily aspirin on long-term risk of death due to cancer:  
analysis of individual patient data from randomised trials



*Rothwell PM. Lancet 2011;377:31-41*

# ANTISTOLLING/STOLLINGSCASCADE IN ACUTE SITUATIES

## Conclusies

- 1.** Trombose in de coronair- en hersenvaten is een potentieel dodelijke ziekte en kan effectief bestreden worden met plaatjesremmers en anticoagulantia
- 2.** Een simpele en spotgoedkope strategie om dit te bewerkstelligen is één kinderaspirine per dag
- 3.** Heparine is nog altijd het ongeslagen parenterale anticoagulans
- 4.** Een intrigerende nieuwe bevinding is het voorkómen van colorectaal carcinoom met aspirine, maar meer onderzoek is nodig