



Safer stents and strategies: is it time for the de-escalation of dual antiplatelet treatment regimes?

# Aspirin after stenting - Do we still need it?

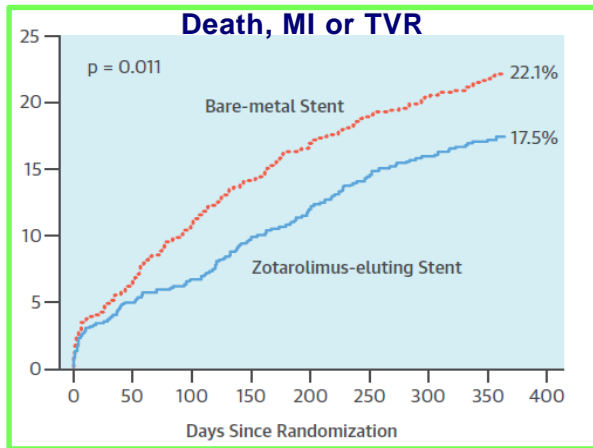
Gilles Montalescot, ACTION Study Group, Paris



STENT

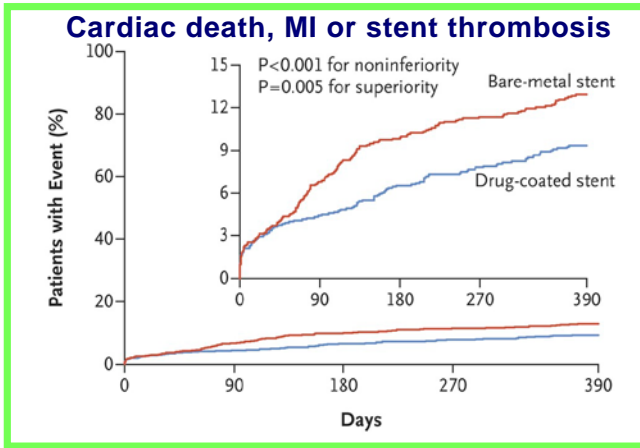
# Duration de-escalation after DES

ZEUS study (n=1606)



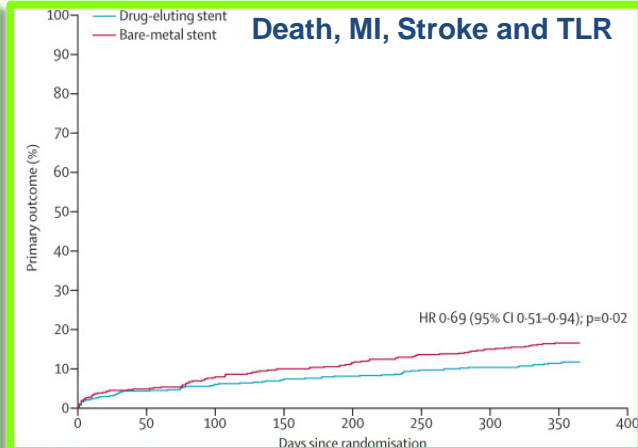
Valgimigli M et al. JACC 2015

LEADERS-FREE study (n=2466)



Urban P et al. NEJM 2015

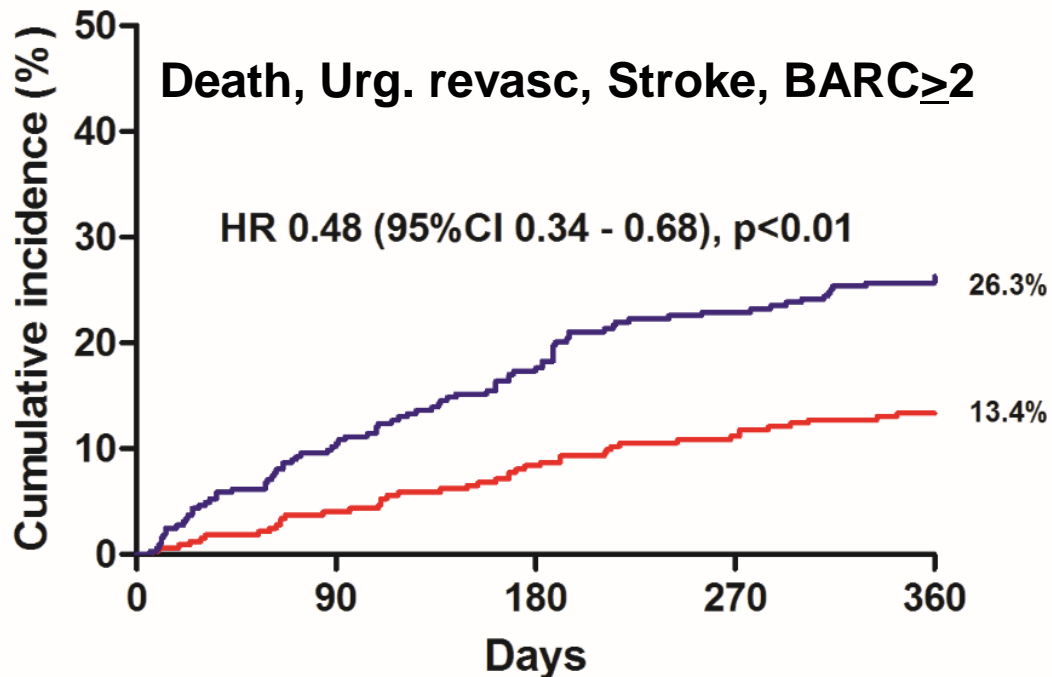
SENIOR study (n=1200)



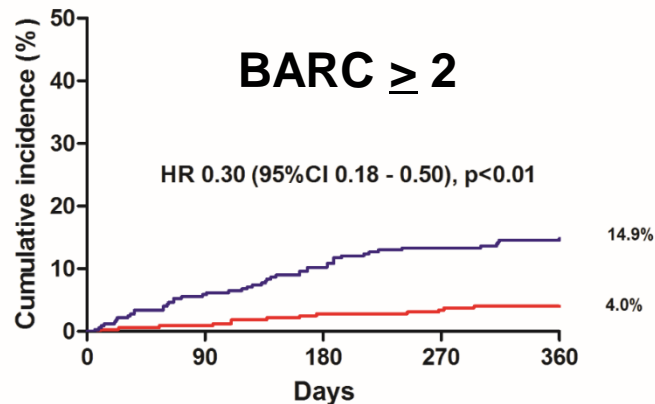
Varenne O et al. Lancet 2017

ACS

# P2Y12 de-escalation after ACS



— Switched DAPT  
— Unchanged DAPT



# Aspirin de-escalation with OAC

**OAC**

**WOEST  
PIONEER  
REDUAL**

Patients with an indication for oral anticoagulation undergoing PCI

Patients with an indication for oral anticoagulation undergoing PCI

Concerns about ischaemic risk prevailing

Concerns about bleeding risk prevailing

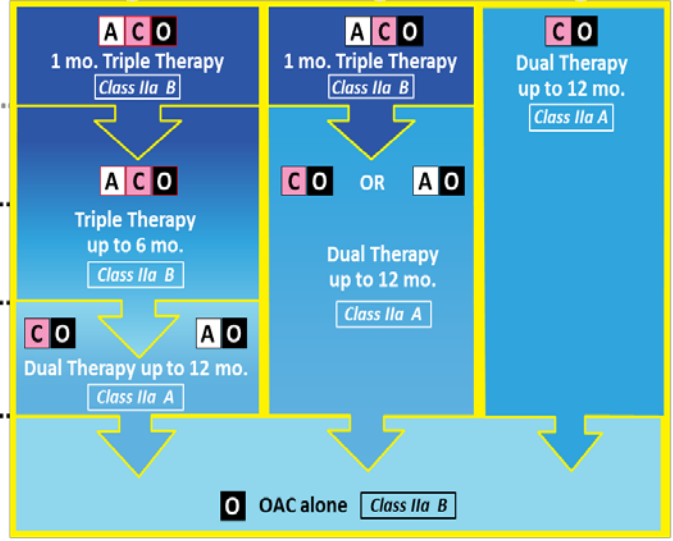
Standard of care

High coronary risk

Stent thrombosis  
Recurrent ACS  
Multiple stenting  
Diabetes

Time from treatment initiation

1 mo.  
3 mo.  
6 mo.  
12 mo.  
Beyond 12 mo.



A = Aspirin  
C = Clopidogrel  
O = Oral anticoagulation

Time from treatment initiation

1 mo.  
3 mo.  
6 mo.  
12 mo.  
Beyond 12 mo.



European Heart Journal  
Journal of the European Society of Cardiology

*The Times They Are A Changin'*  
N. Hammoudi, G. Montalescot

2017

2018

**REMOVING/REPLACING ASA in non-PCI patients**

# Head-to-head comparisons with ASA

Study	n	population	Drug	Efficacy	Safety
CAPRIE	19,185	Prior MI, prior stroke, or PAD	<b>clopidogrel</b>	↓	→
TASS	3,069	Prior stroke or TIA	<b>ticlopidine</b>	↓	→
PERFORM	9,562	Prior stroke or TIA	<b>terutroban</b>	→	→
SOCRATES	13,199	Prior stroke or TIA	<b>ticagrelor</b>	→	→
GEMINI ACS 1	3,037	ACS	<b>rivaroxaban</b>	→	→
COMPASS	27,395	Prior MI or PAD	<b>rivaroxaban</b>	→	↑

# **REMOVING ASA in PCI patients**

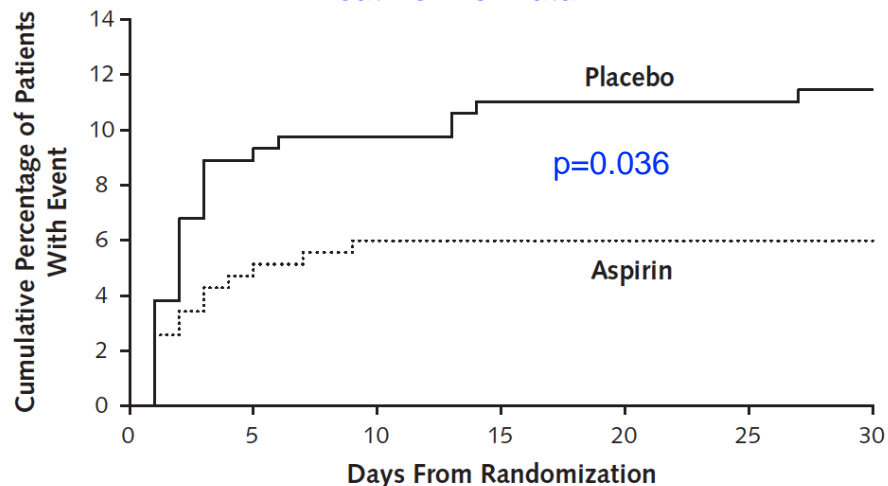
# Removing ASA in patients with previous PCI undergoing noncardiac surgery



Patients with prior PCI (90% stent)
 

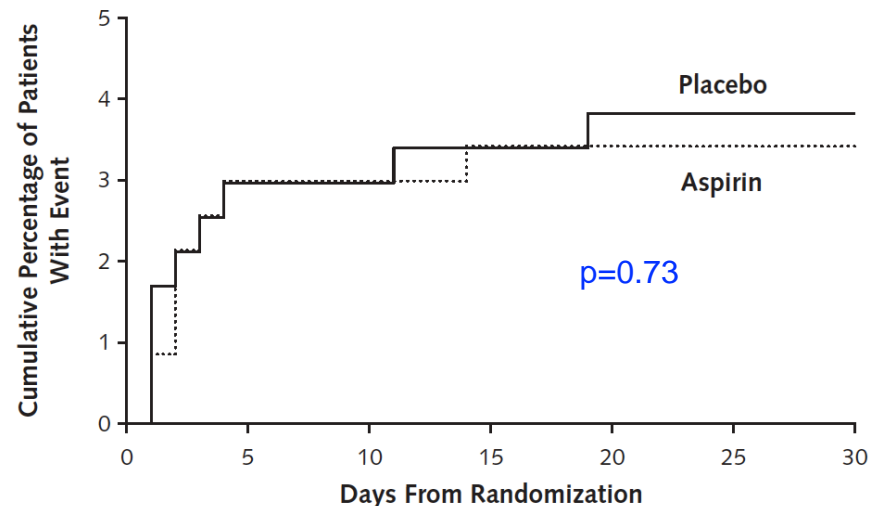
- n=234 aspirin therapy
- n=236 placebo

## Death or non fatal MI



Patients at risk, <i>n</i>							
Placebo	236	215	212	209	209	209	208
Aspirin	234	223	221	221	221	221	221

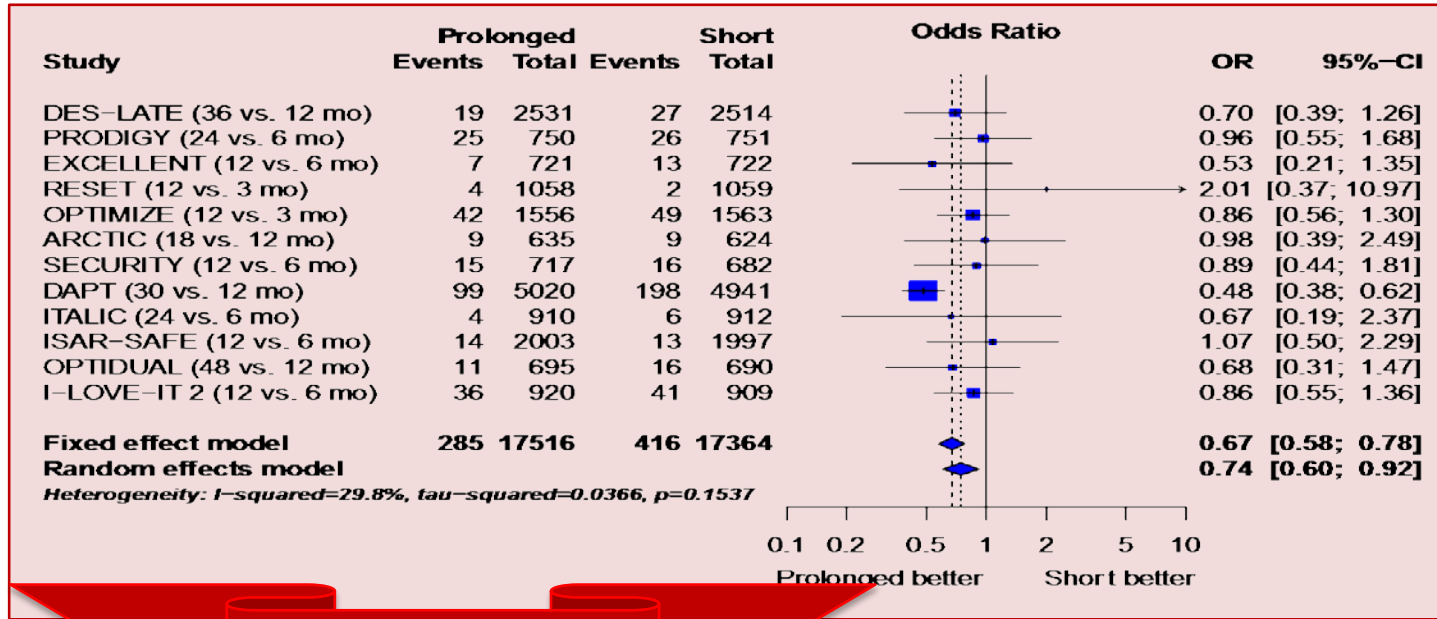
## Major Bleeding



Patients at risk, <i>n</i>							
Placebo	236	228	225	224	223	223	223
Aspirin	234	228	227	226	226	226	226



# What have we learnt from clopidogrel removal (keeping ASA) after PCI?



**0.74 (95% CI  
0.60-0.92)**

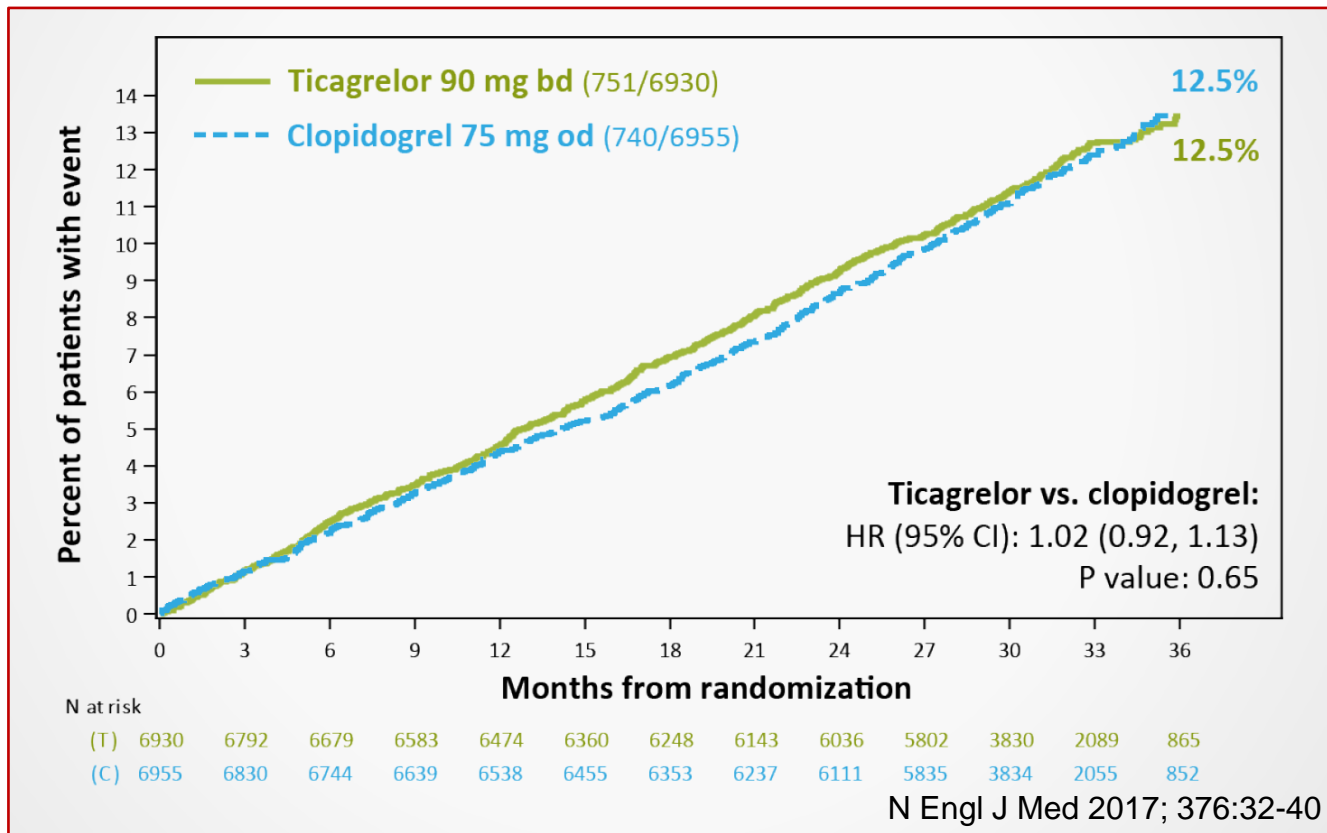
## Absolute changes

↗ 1-2% of MACE

↘ 1% of MB

Neutral on death

# Can we do better with ticagrelor/prasugrel when ASA is removed?



**REMOVING ASA AFTER PCI ?**

# Why de-escalate?

ASA (75-100mg) +  
P2Y12 antagonist  
for 3-12 months

Ongoing or recent major bleeding

Prior Hx of ICH

Prior Hx of any major bleeding

HBR (PRECISE-DAPT<sub>≥25</sub>)

Elderly

Scheduled surgery

Profession at risk of bleeding

Socio-economic

## Not in all PCI patients!

# How de-escalate?

ASA (75-100mg) + ticagrelor (90 bid) *or*  
prasugrel (10mg od) for 12 months

Reduce dose of  
ticagrelor *or*  
prasugrel

**PEGASUS**  
**PRASFIT**

Reduce duration  
of DAPT

**PRODIGY**  
**RESET**  
**EXCELLENT**  
  
*MASTERDAPT*  
*COBRA-REDUCE*

Switch ticagrelor  
*or* prasugrel to  
clopidogrel

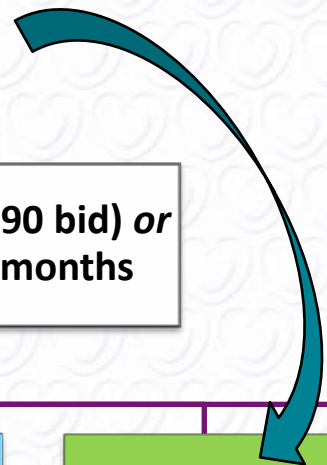
**TOPIC**

**Stop ASA early**

**WOEST**  
**PIONEER**  
**REDUAL**  
  
*GLOBAL-LEADERS*  
*TWILIGHT*

Platelet function  
testing

**ANTARCTIC**  
**TROPICAL-ACS**



# Global-leaders

All

1 mth

Ticagrelor

2 yrs

Death/MI

All-comers PCI population (ACS and Stable CAD patients)  
(N = 16,000)

Bivalirudin\* - supported  
BioMatrix Flex™ stent implantation

1 : 1 Randomization, Open-Label Design

Experimental Treatment Strategy



Reference Treatment Strategy



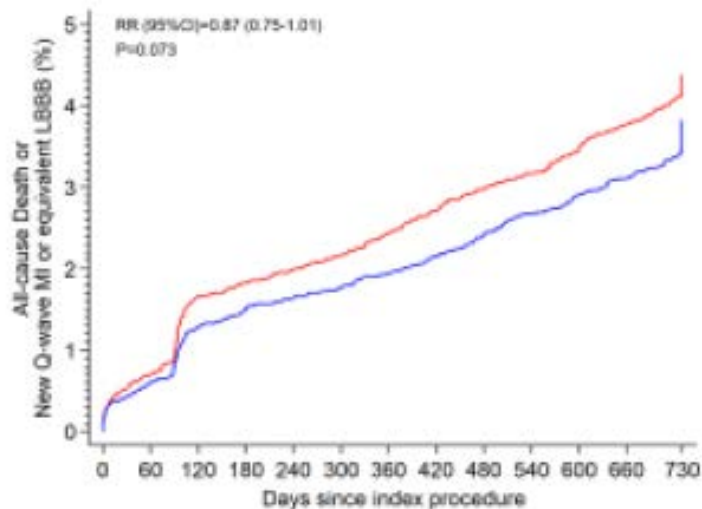
Primary endpoint (Effectiveness):  
Experimental treatment strategy superior to reference treatment strategy on cumulative 2 year composite of all cause mortality and new Q-wave MI

Scientific Grants to ECRI: Biosensors, AstraZeneca and The Medicines Company

\* Inoculation system

# Global-Leaders

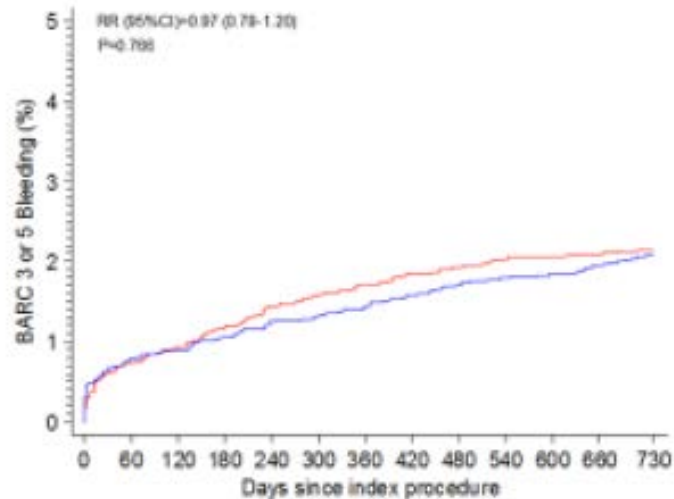
Death or MI



Number at risk

Reference	7988	7930	7854	7841	7827	7813	7792	7768	7747	7729	7706	7680	7610
Experimental	7980	7827	7673	7656	7643	7633	7619	7602	7780	7759	7739	7722	7626

BLEEDING



Number at risk

Reference	7988	7847	7795	7761	7722	7698	7664	7630	7606	7563	7564	7538	7465
Experimental	7980	7798	7755	7726	7692	7678	7655	7617	7587	7562	7526	7501	7386

# TWILIGHT

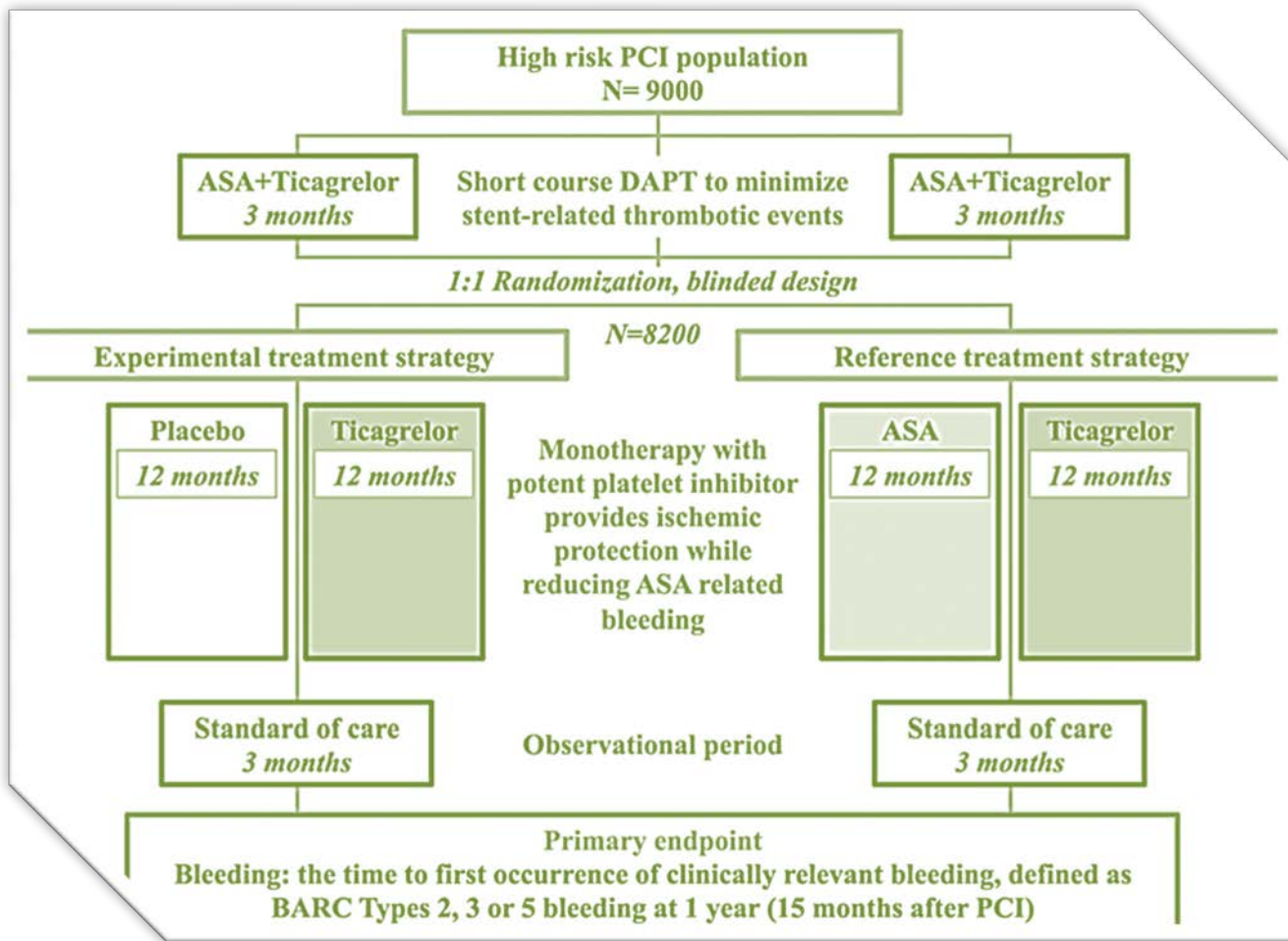
Elective

3 mths

Ticagrelor

1 year

Bleeding

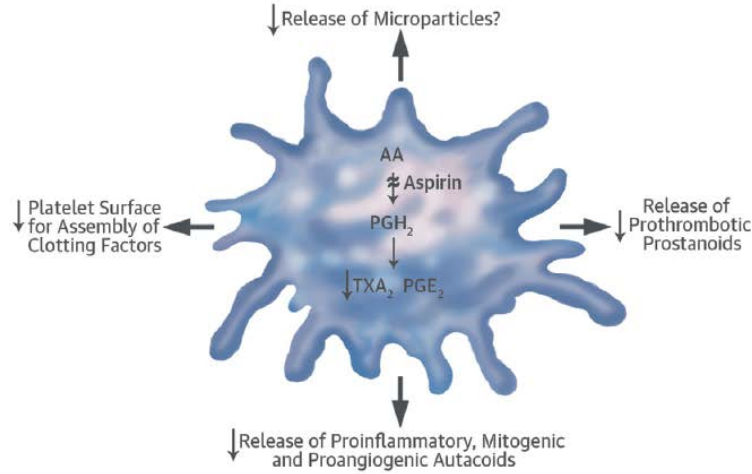




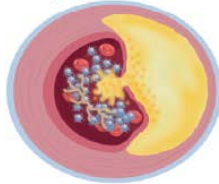
# Removing ASA after PCI

Study	n	Drug left	Efficacy	Safety
GLOBAL-LEADERS	16,000	ticagrelor	→	→
TWILIGHT	9,000	ticagrelor	?	?
TICO	3,056	ticagrelor	?	?
SMART-CHOICE	3,000	clopidogrel	?	?
STOPDAPT-2	3,045	clopidogrel	?	?

# The other benefits of aspirin

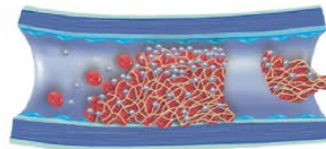


## Coronary Atherothrombosis



Evidence from >50 RCTs and meta-analyses

## Venous Thromboembolism



Evidence from several RCTs and meta-analyses

## Colorectal Cancer

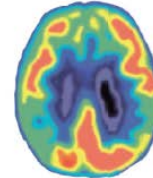


Evidence from observational studies and meta-analyses

Evidence from post-hoc long-term follow-up of RCTs and meta-analyses

Currently being tested prospectively in primary prevention and adjuvant RCTs

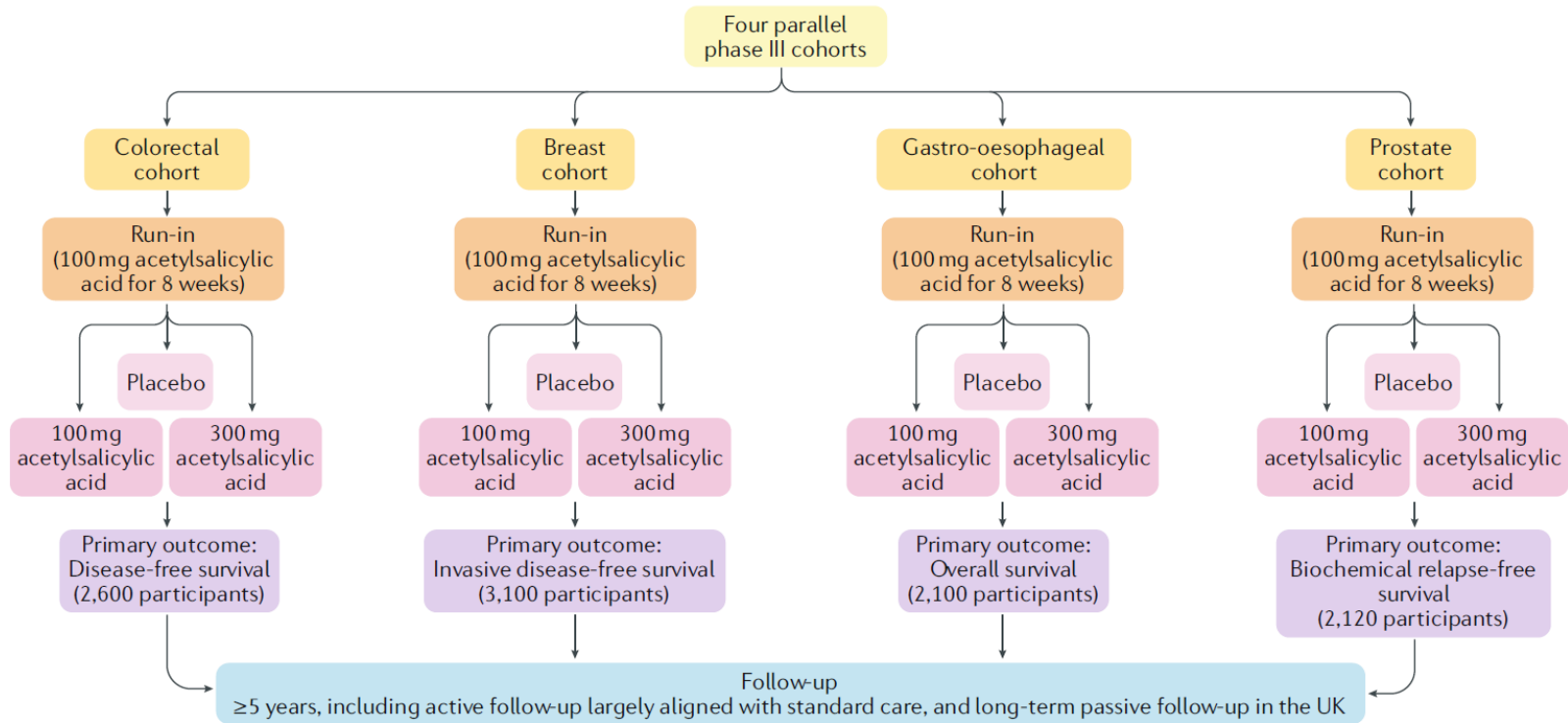
## Cognitive Impairment



Limited evidence from observational studies

Currently being tested in the ASPREE primary prevention trial

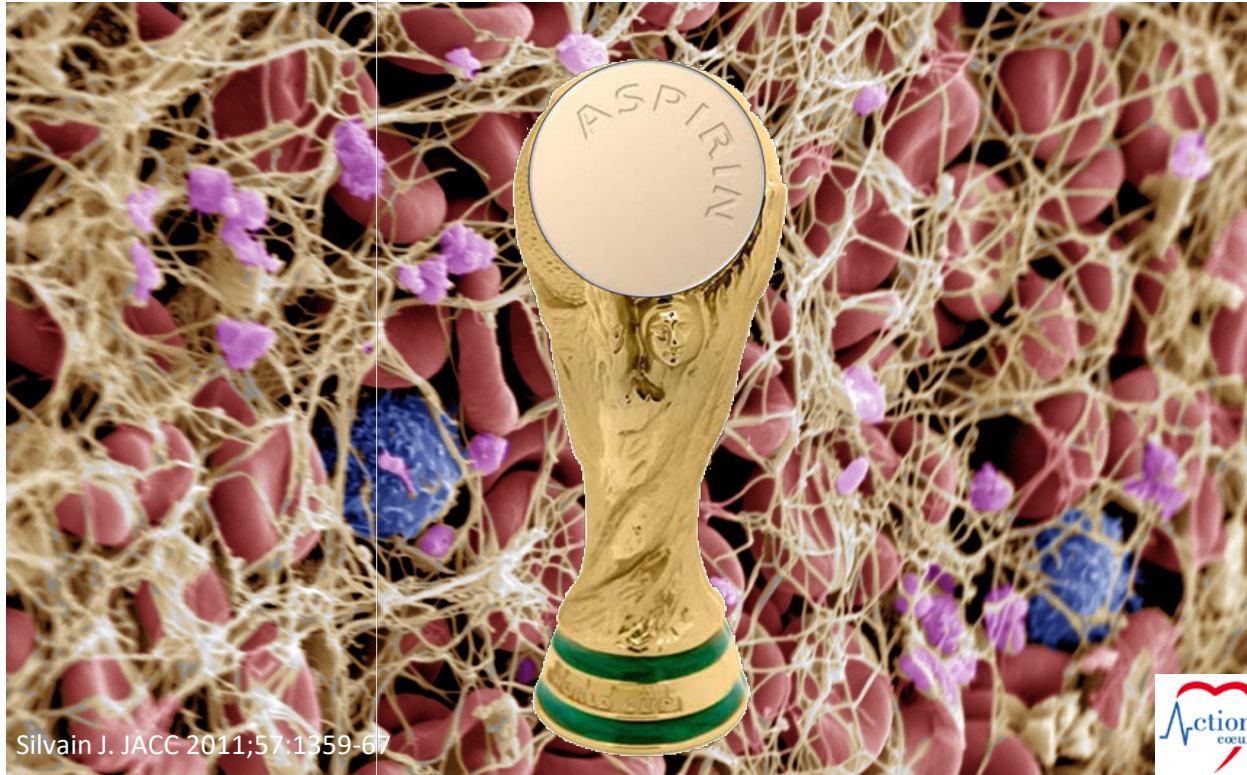
# ADD-Aspirin trial



## Aspirin after stenting - Do we still need it?

- Yes, in the first month, for routine PCI
- Yes, in the first 6 months in ACS *or* high ischemic risk patients,
- No, beyond 1-3 months in high bleeding risk patients
- Otherwise, randomize in the ongoing studies!

# Thank you!



Silvain J. JACC 2011;57:1359-67



Slides available at [www.action-coeur.org](http://www.action-coeur.org)