
# Triple therapy after PCI

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Acute Cardiovascular Care Association ACCA
A Registered Branch of the ESC

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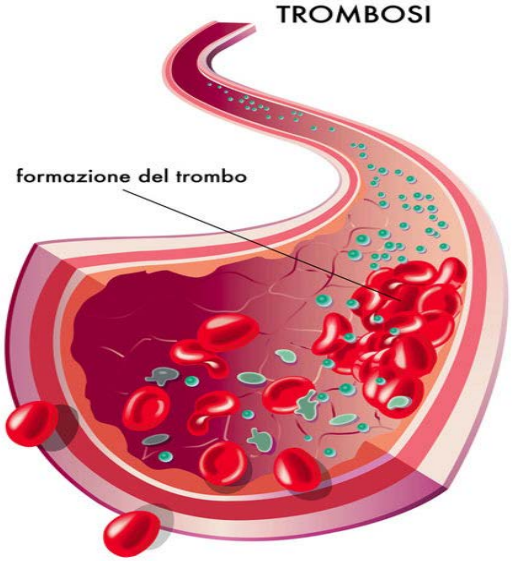
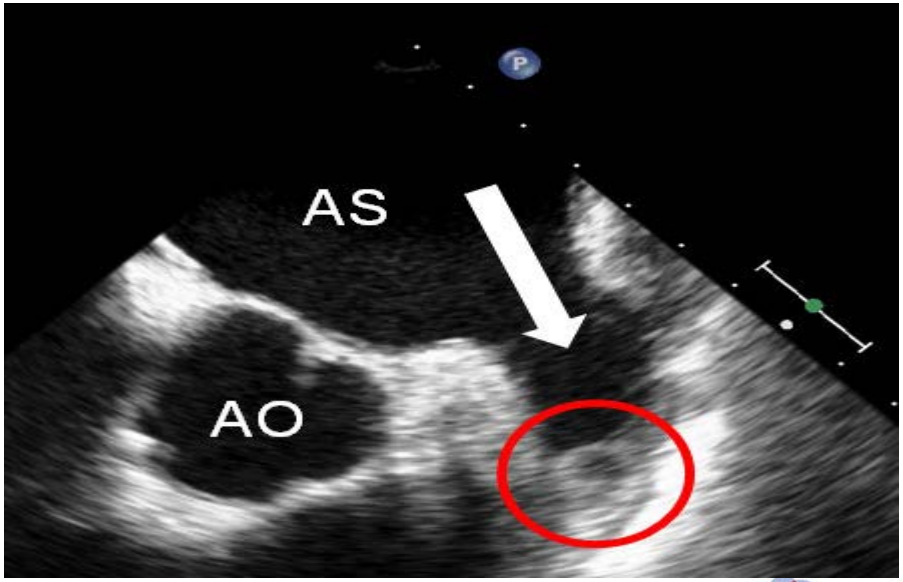
# Disclosure

- **Speaker fee: Aspen, Astra Zeneca, BMS, Boehringer, Eli Lilly, DaichiiSankio, Bayer, Pfizer, Sanofi**
- **Advisory board member: Astra Zeneca, Eli Lilly, Daiichi Sankyo, BMS, Pfizer, Sanofi**

# Arterial and venous thrombosis



# Epidemiology

Approximately 70-80% of all patients in AF have an indication for continuous OAC

Coronary artery disease co-exists in 34% of patients presenting with AF, with 21% of subjects subsequently requiring PCI or CABG over time

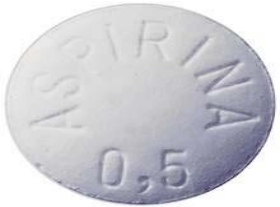
Patients presenting with ACS develop AF in 6-21% of cases

5-7% of pts undergoing PCI have AF or other indications for OAC

With an estimated prevalence of AF in 1-2% of the European population, one to two million anticoagulated patients are candidate for coronary revascularization, often in the form of PCI, usually including stents

# *"Menage a trois"*

- **Prevention of stroke → anticoagulant**
- **Prevention of MI/stent thrombosis → DAPT**
- **Prevention of excess bleeding**

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# What is new since 2010?

- **Stents (**newer generation DES are preferable over BMS)

- **New antiplatelet agents**
  - New generation P2Y12 inhibitors: prasugrel, ticagrelor, cangrelor
  - Thrombin receptor inhibitors: vorapaxar

- **NOACs**
  - NOACs for AF
  - NOACs for post-MI secondary prevention

# Key factors for changes

| Key factors | Suggestion for research |
|---|---|
| New stents | Stent thrombosis, outcome |
| Selection of patients | Risk stratification of pts both for bleeding and for atherothrombotic events |
| Antiplatelet therapy | DAPT duration |
| Triple therapy | New drugs and new associations |
| Can we skip aspirin? | Both in secondary prevention and +OAC/NOAC? |

# How to reduce the probability of a major bleeding complication?

Reducing anticoagulation intensity

Acting on duration of antiplatelet therapy

Type of stent, PCI or CABG,
Vascular access site selection
Prevention of GI bleeding complications

# DAPT after DES: shorter or longer?

**LEADERS-FREE** and **LEADERS FREE II (NCT02843633)**
very short duration of DAPT, non inferiority as regards to BMS

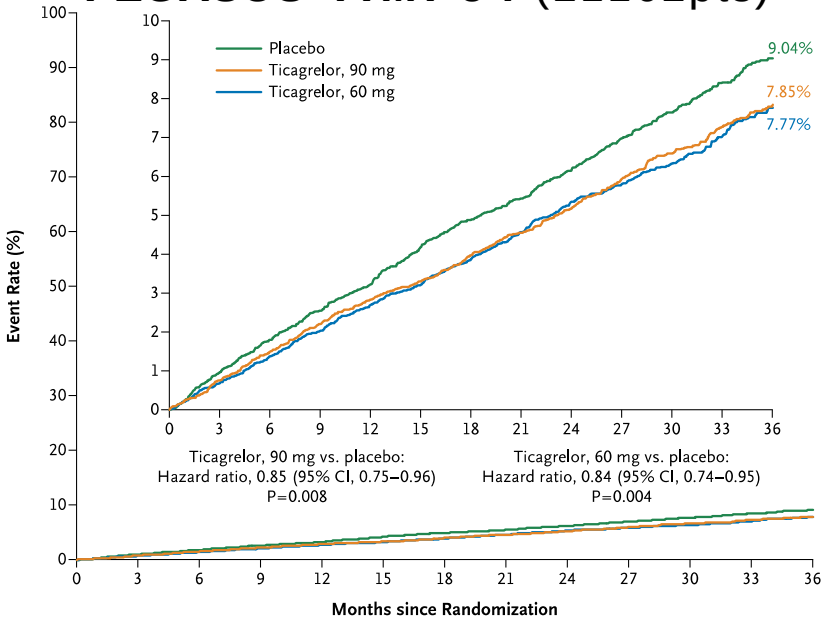
**GLOBAL LEADERS** very short duration of Aspirin treatment

followed by ticagrelor only vs DAPT for one year

NEJM 2015; 373: 2038-47; www.clinicaltrials.gov

# DAPT after DES: shorter or longer?

## PEGASUS-TIMI 54 (21162pts)



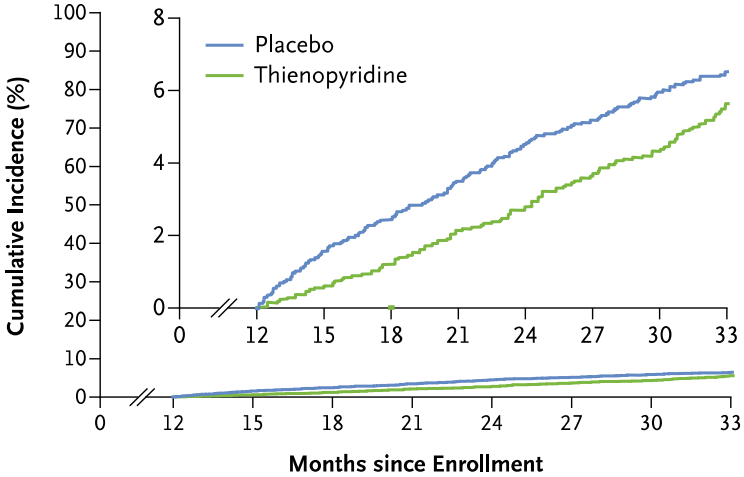

NEJM 2015; 372: 1791-800

## DAPT (9961 pts)

**Major Adverse Cardiovascular and Cerebrovascular Events**

12–30 mo Thienopyridine vs. placebo, 4.3% vs. 5.9%; hazard ratio, 0.71; P<0.001

12–33 mo Thienopyridine vs. placebo, 5.6% vs. 6.5%; hazard ratio, 0.82; P=0.02

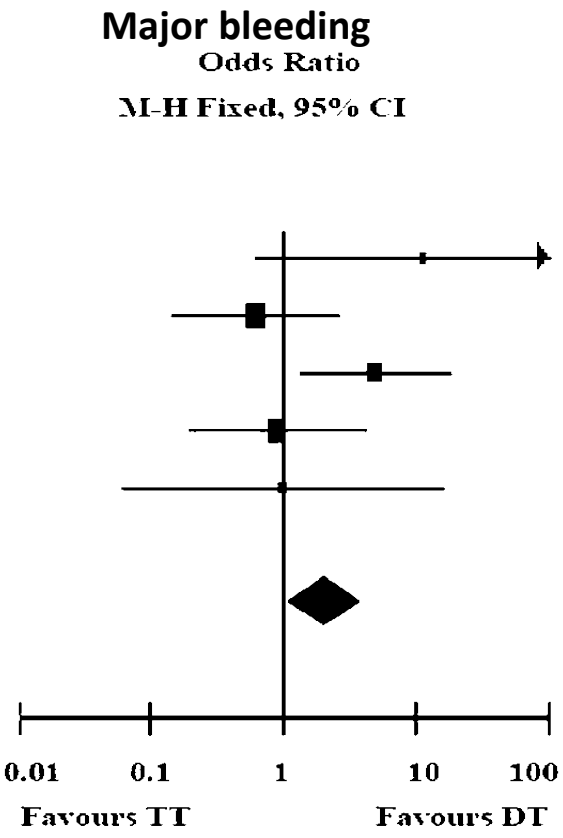



NEJM 2014; 371: 2155-66

| Study | Year | Triple Therapy | | Dual Therapy | |
|---|---|---|---|---|---|
| | | Events | Total | Events | Total |
| Khuram[11] | 2006 | 5 | 107 | 0 | 107 |
| Karjalainen[10] | 2007 | 6 | 106 | 3 | 34 |
| DeEugenio[30] | 2007 | 13 | 86 | 3 | 88 |
| Sarafoff[31] | 2008 | 4 | 306 | 3 | 209 |
| Rossini[15] | 2008 | 1 | 102 | 1 | 102 |
| **Total (95% CI)** | | | **707** | | **540** |
| **Total events** | | **29** | | **10** | |

**Heterogeneity: Chi² = 7.31, df = 4 (*P* = 0.12); I² = 45%**

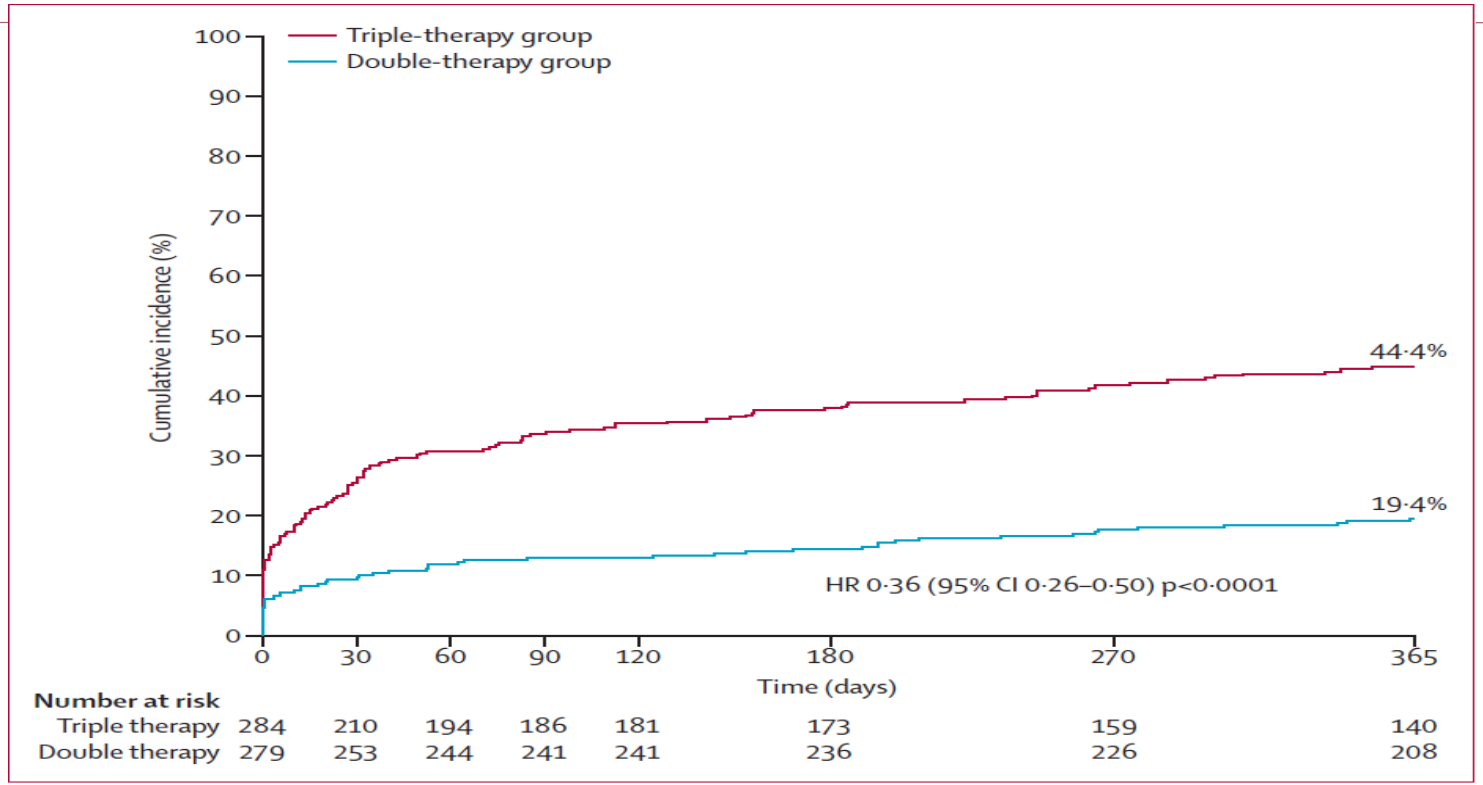
**Test for overall effect: Z = 2.09 (*P* = 0.04)**






Zhao HJ et al. CHEST 2011; 139(2): 260-270

# The WOEST trial: results




Lancet 2013; 381: 1107-15



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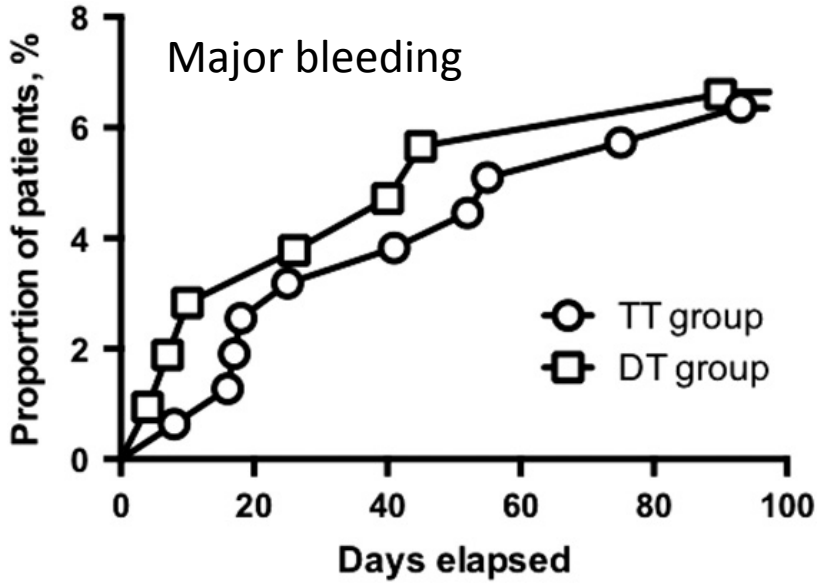
# TRIPLE Therapy: OAC + novel antiplatelet agents




| | | | | |
|---|---|---|---|---|
| Triple-P vs. triple-C | 30 (39.0) | 61 (24.4) | 2.37 (1.36–4.15) | 0.003 |

JACC Cardiovasc Int 2015; 8: 1880

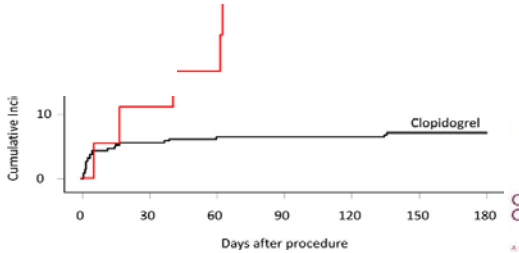
**TICAGRELOR**

107 pts on ticagrelor and 159 controls, enrolled in 2013.

TT = warfarin, clopidogrel, ASA

DT = warfarin and ticagrelor

Thromb Res 2015; 135: 26

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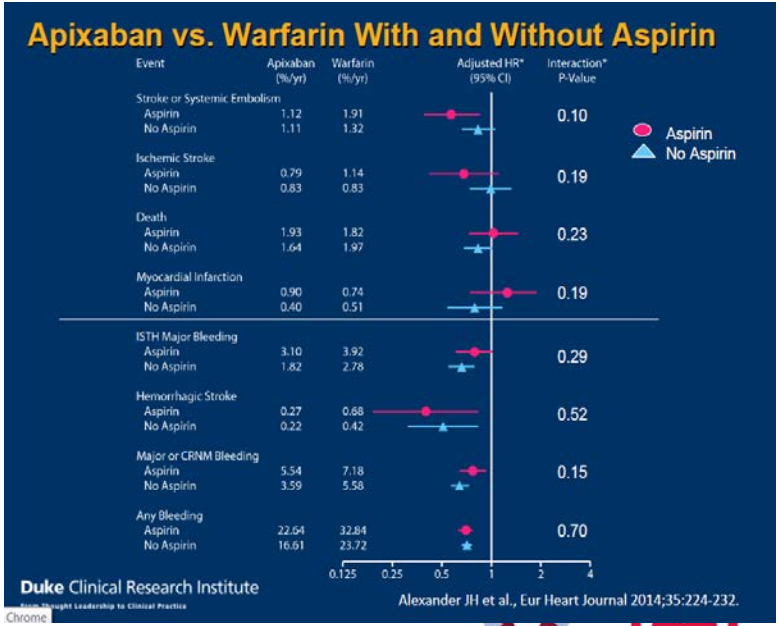
# TRIPLE Therapy: NOAC + antiplatelet agents

## RELY trial

| | Dabigatran 110 mg BID | Dabigatran 150 mg BID | Warfarin |
|---|---|---|---|
| Aspirin & clopidogrel | | | |
| Annual rate, % | 4.72 | 4.66 | 5.21 |
| RR (95% CI) vs warfarin | 0.77 (0.50–1.21) | 0.81 (0.52–1.26) | |
| No Aspirin & clopidogrel | | | |
| Annual rate, % | 2.77 | 3.24 | 3.48 |
| RR (95% CI) vs warfarin | 0.81 (0.61–0.94) | 0.95 (0.82–1.10) | |
| P value for interaction | 0.8727 | 0.5167 | |

## ARISTOTLE trial



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# Large-scale outcome studies evaluating combination of NOACs/VKAs and antiplatelets drugs in AF/CAD pts

## Completed

**PIONEER AF PCI study (**NEJM 2016; 375: 2423**)**

**RE-DUAL PCI (**NEJM 2017; 377(16): 1513 **)**

## Ongoing

**AUGUSTUS trial (**NCT02415400**)**

## Announced

**EVOLVE-AF – PCI**

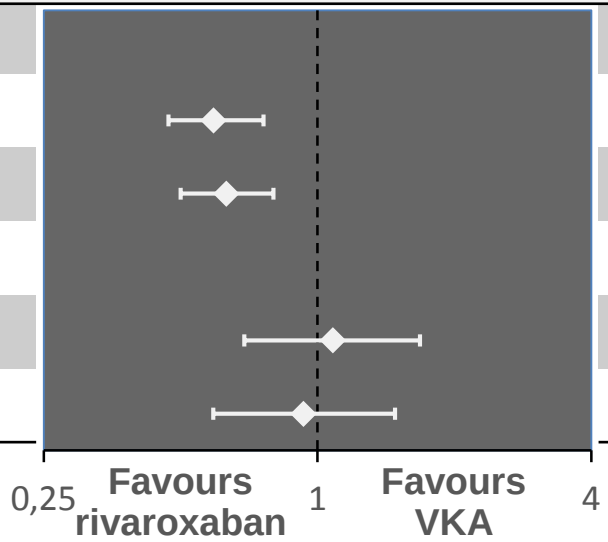
**AAA**

# Completed / Ongoing RCTs

| Study | Anticoagulant | Antiplatelet agent | Duration of DAPT/single drug | Strategy |
|---|---|---|---|---|
| PIONEER-AF PCI | Rivaroxaban | Ticagrelor or prasugrel | 1-6-12 months + low dose ASA | WOEST vs ATLAS ACS |
| RE-DUAL PCI | Dabigatran | Ticagrelor or prasugrel | 1-6-12 months | WOEST |
| AUGUSTUS | Apixaban | Ticagrelor or prasugrel | 1-6 months | WOEST vs TT |

# PIONEER-AF: Improved Safety and Comparable Efficacy vs VKA Plus DAPT

| Endpoints | HR | 95% CI | HR (95% CI) | Interaction *p*-value |
|---|---|---|---|---|
| **Clinically significant bleeding** | | | | |
| Rivaroxaban 15 mg OD plus single antiplatelet vs VKA plus DAPT | 0.59 | 0.47–0.76 | | **<0.001** |
| Rivaroxaban 2.5 mg BID plus DAPT vs VKA plus DAPT | 0.63 | 0.50–0.80 | | **<0.001** |
| **Major adverse CV events** | | | | |
| Rivaroxaban 15 mg OD plus single antiplatelet vs VKA plus DAPT | 1.08 | 0.69–1.68 | | 0.75 |
| Rivaroxaban 2.5 mg BID plus DAPT vs VKA plus DAPT | 0.93 | 0.59–1.48 | | 0.77 |

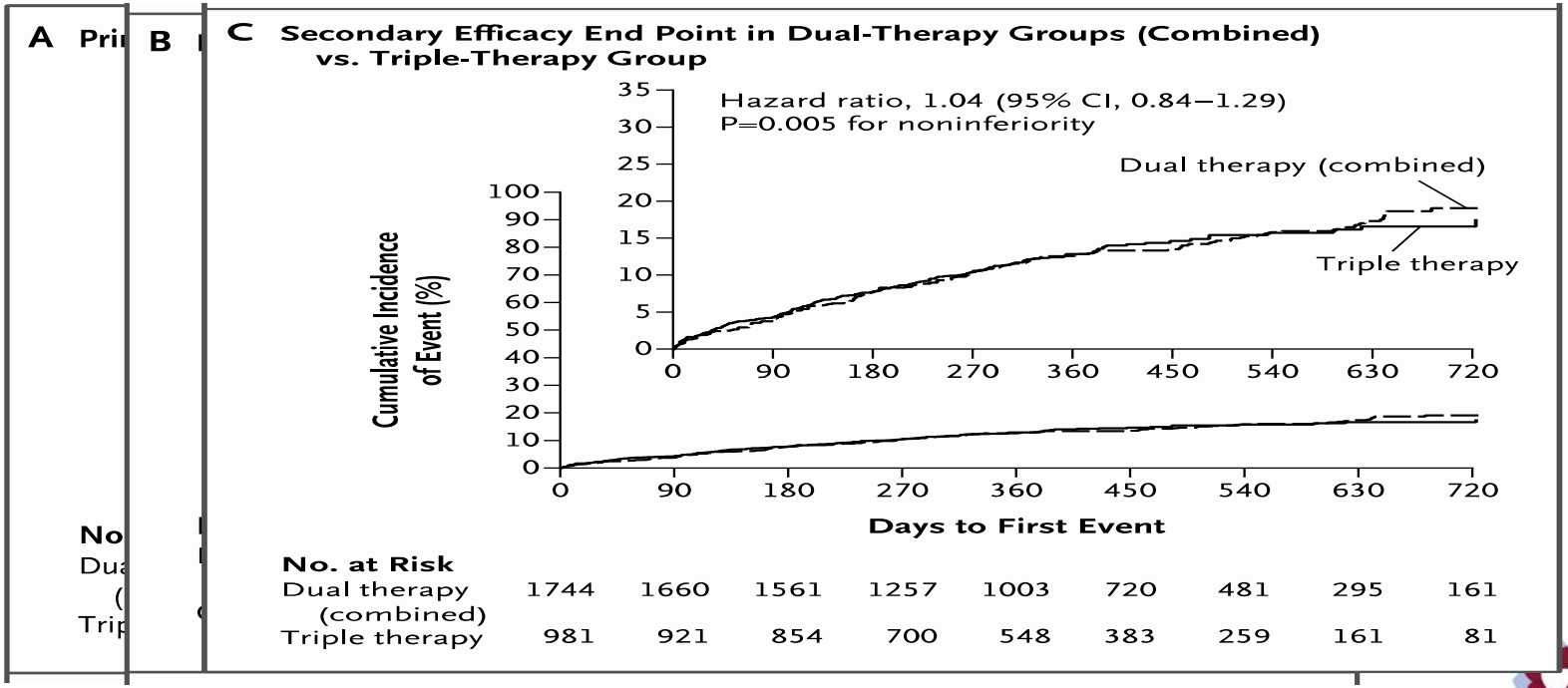



Both rivaroxaban strategies were associated with a significant reduction in incidence of the primary safety endpoint with comparable incidence of major adverse CV events vs the VKA plus DAPT strategy (trial not powered for efficacy)



Gibson CM et al, *New Engl J Med* 2016; doi: 10.1056/NEJMoa1611594

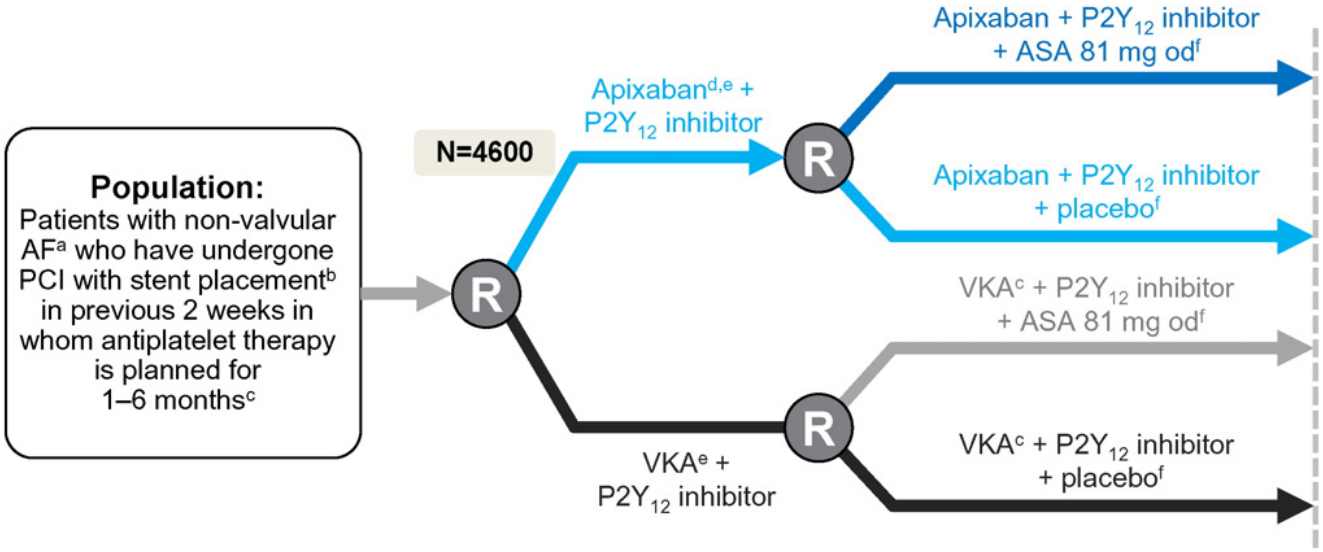
# RE-DUAL PCI: dabigatran + DAPT




NEJM 2017 **DOI: 10.1056/NEJMoa1708454**

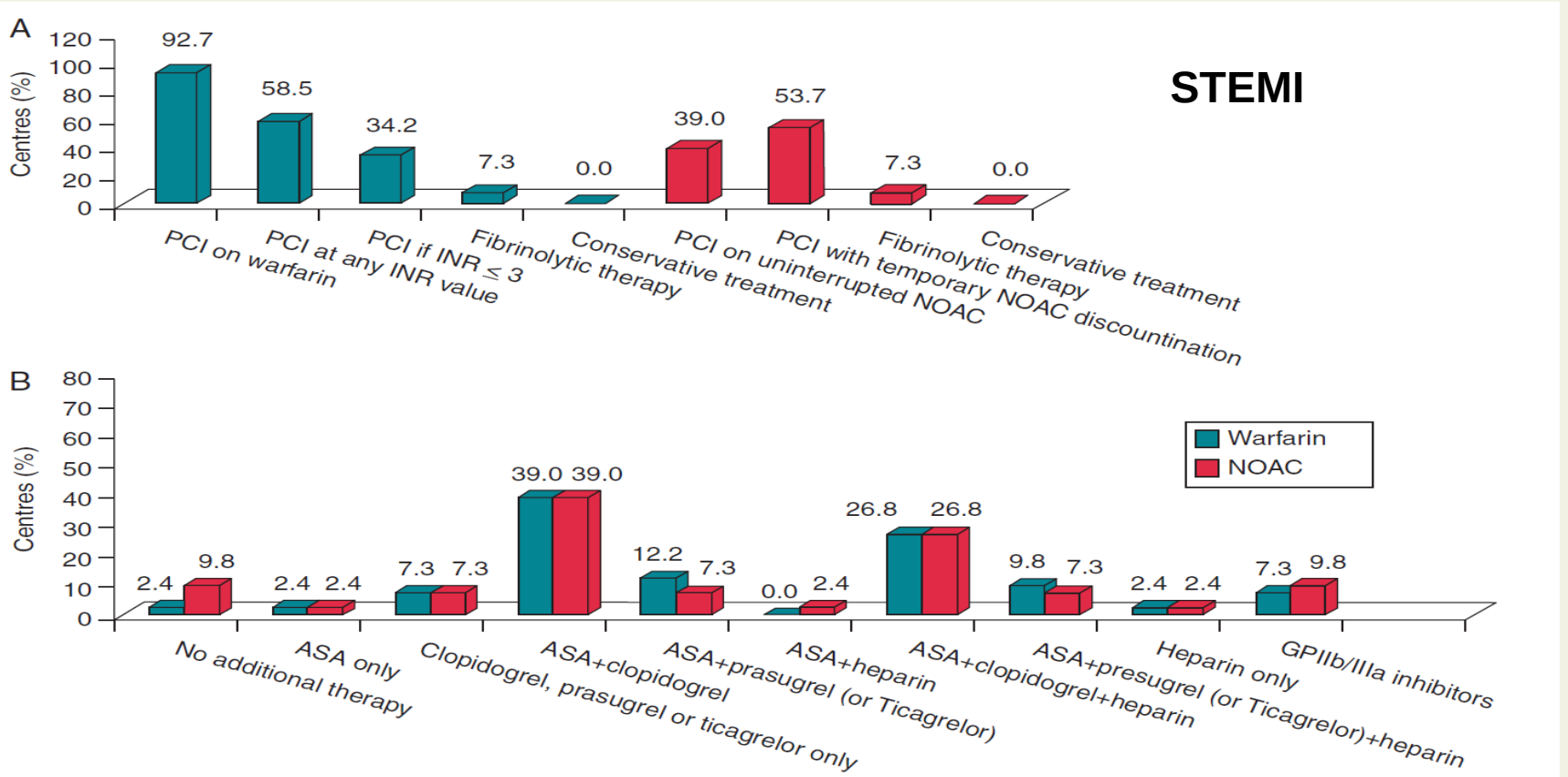
# AUGUSTUS Study design

**Objective:** Safety of apixaban versus VKA and ASA versus ASA placebo in patients with non-valvular AF undergoing PCI



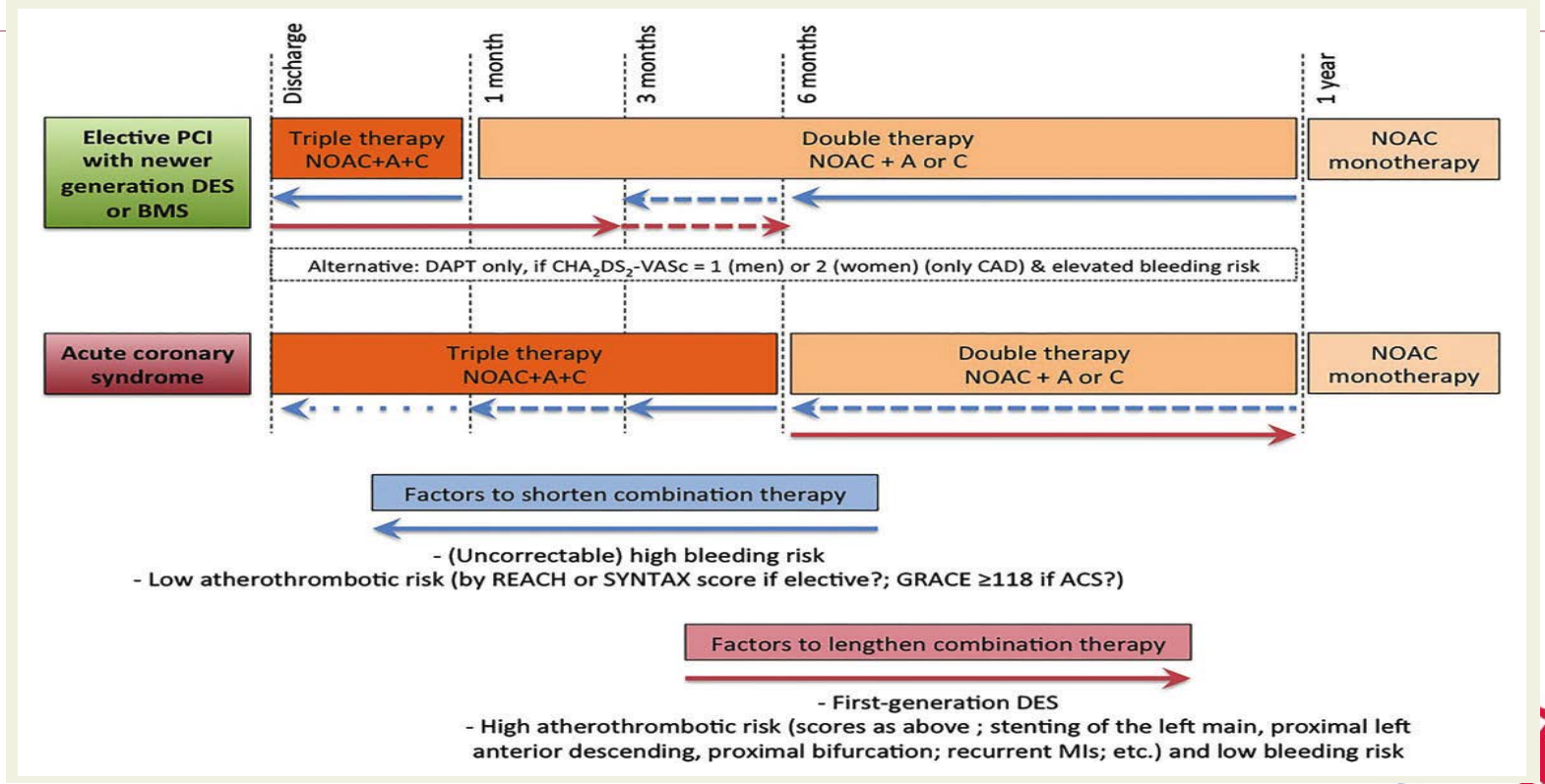

Vascular Pharmacology 2016; 81: 1

# Pazienti in terapia con AO e SCA: la survey della European Heart Rhythm Association (EHRA)




Potpara TS et al. Europace 2014; 16: 293

# Long-term antiplatelet therapy and NOACs: possible scenarios



# ESC Focus update on DAPT 2017

# In Conclusion

- There still are some unmet needs concerning the association of anticoagulation and antiplatelet therapy:
  - a better identification of the bleeding risk of the patient
  - a well defined duration of antiplatelet therapy
  - the optimal dose of novel drugs when they are administered in association
- Both registries and RCTs will probably give us some answers in the future years and will contribute to a better understanding of the pathophysiology of ACS and cardio-embolic disorders

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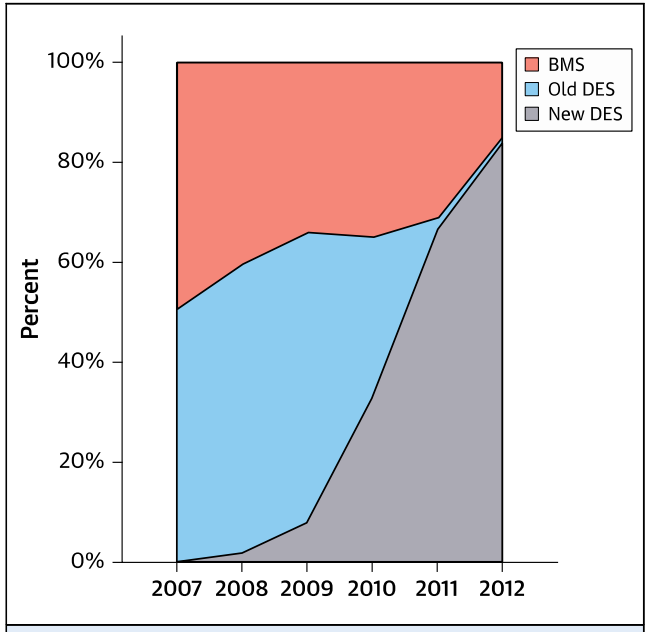
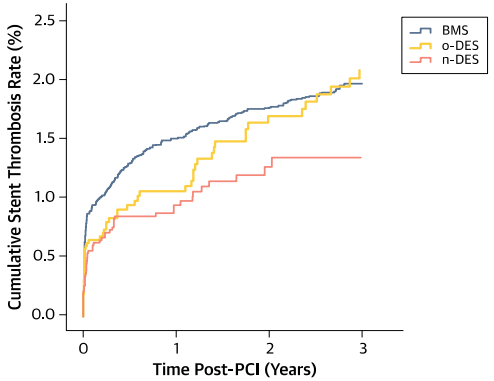
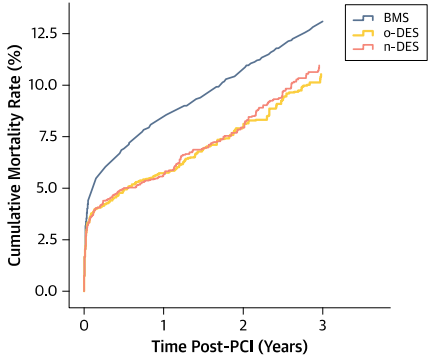
# New-generation DES, ST and mortality




**SCAAR Registry 2007 - 2013**

**TABLE 1** Baseline Characteristics (N = 34,147)

| Variable | n-DES* (n = 4,811) | o-DES† (n = 4,271) | BMS (n = 25,065) |
|---|---|---|---|
| Women | 1,295 (26.9) | 1,119 (26.2) | 7,183 (28.7) |
| Body mass index, kg/m$^2$ | 27.1 ± 4.5 | 27.08 ± 4.3 | 26.7 ± 5.2 |
| Age, yrs | 65.8 ± 10.9 | 66.1 ± 11.2 | 67.3 ± 12.1 |
| Hypertension | 2,181 (45.3) | 1,968 (46.1) | 9,994 (39.9) |
| Diabetes mellitus | 862 (18.0) | 879 (20.6) | 2,979 (11.5) |

*"The current **ESC 2017 STEMI** guidelines have been updated in light of the results of this registry and other RCTs"*

JAmCollCardiol2014;64:16–24

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